

NATIONAL QUALITY FORUM

Measure Evaluation 4.1 January 2010

This form contains the measure information submitted by stewards. Blank fields indicate no information was provided. Attachments also may have been submitted and are provided to reviewers. The sub-criteria and most of the footnotes from the evaluation criteria are provided in Word comments and will appear if your cursor is over the highlighted area (or in the margin if your Word program is set to show revisions in balloons). Hyperlinks to the evaluation criteria and ratings are provided in each section.

TAP/Workgroup (if utilized): Complete all **yellow highlighted** areas of the form. Evaluate the extent to which each sub-criterion is met. Based on your evaluation, summarize the strengths and weaknesses in each section.

Note: If there is no TAP or workgroup, the SC also evaluates the sub-criteria (**yellow highlighted areas**).

Steering Committee: Complete all **pink** highlighted areas of the form. Review the workgroup/TAP assessment of the sub-criterion, noting any areas of disagreement; then evaluate the extent to which each major criterion is met; and finally, indicate your recommendation for the endorsement. Provide the rationale for your ratings.

Evaluation ratings of the extent to which the criteria are met

C = Completely (unquestionably demonstrated to meet the criterion)

P = Partially (demonstrated to partially meet the criterion)

M = Minimally (addressed BUT demonstrated to only minimally meet the criterion)

N = Not at all (NOT addressed; OR incorrectly addressed; OR demonstrated to NOT meet the criterion)

NA = Not applicable (only an option for a few sub-criteria as indicated)

(for NQF staff use) **NQF Review #:** ACP-029-10 **NQF Project:** Ambulatory Care - Additional Outpatient Measures 2010

MEASURE DESCRIPTIVE INFORMATION

De.1 Measure Title: Patient(s) treated with an antibiotic for acute sinusitis that received a first line antibiotic.

De.2 Brief description of measure: This measure identifies patients with acute sinusitis treated with an antibiotic who received a first line antibiotic.

1.1-2 Type of Measure: process

De.3 If included in a composite or paired with another measure, please identify composite or paired measure
Does not apply

De.4 National Priority Partners Priority Area: Overuse

De.5 IOM Quality Domain: effectiveness

De.6 Consumer Care Need: Getting Better

CONDITIONS FOR CONSIDERATION BY NQF

Four conditions must be met before proposed measures may be considered and evaluated for suitability as voluntary consensus standards:

A. The measure is in the public domain or an intellectual property (measure steward agreement) is signed. *Public domain only applies to governmental organizations. All non-government organizations must sign a measure steward agreement even if measures are made publicly and freely available.*

A.1 Do you attest that the measure steward holds intellectual property rights to the measure and the right to use aspects of the measure owned by another entity (e.g., risk model, code set)? Yes

A.2 Indicate if Proprietary Measure (as defined in measure steward agreement): proprietary measure

A.3 Measure Steward Agreement: agreement signed and submitted

A.4 Measure Steward Agreement attached: Measure steward addendum_Ingenix 012510.doc

**NQF
Staff**

A
Y ☐
N ☐

B. The measure owner/steward verifies there is an identified responsible entity and process to maintain and update the measure on a schedule that is commensurate with the rate of clinical innovation, but at least every 3 years. <i>Yes, information provided in contact section</i>	B Y ☐ N ☐
C. The intended use of the measure includes <u>both</u> public reporting <u>and</u> quality improvement. ► Purpose: <i>public reporting, quality improvement Accreditation, Payment Incentive, Accountability</i>	C Y ☐ N ☐
D. The requested measure submission information is complete. Generally, measures should be fully developed and tested so that all the evaluation criteria have been addressed and information needed to evaluate the measure is provided. Measures that have not been tested are only potentially eligible for a time-limited endorsement and in that case, measure owners must verify that testing will be completed within 12 months of endorsement. D.1 Testing: <i>Yes, fully developed and tested</i> D.2 Have NQF-endorsed measures been reviewed to identify if there are similar or related measures? <i>Yes</i>	D Y ☐ N ☐
(for NQF staff use) Have all conditions for consideration been met? Staff Notes to Steward (<i>if submission returned</i>):	Met Y ☐ N ☐
Staff Notes to Reviewers (<i>issues or questions regarding any criteria</i>):	
Staff Reviewer Name(s):	

TAP/Workgroup Reviewer Name:	
Steering Committee Reviewer Name:	
1. IMPORTANCE TO MEASURE AND REPORT	
Extent to which the specific measure focus is important to making significant gains in health care quality (safety, timeliness, effectiveness, efficiency, equity, patient-centeredness) and improving health outcomes for a specific high impact aspect of healthcare where there is variation in or overall poor performance. <i>Measures must be judged to be important to measure and report in order to be evaluated against the remaining criteria.</i> (evaluation criteria) 1a. High Impact	Eval Rating
(for NQF staff use) Specific NPP goal:	
1a.1 Demonstrated High Impact Aspect of Healthcare: <i>affects large numbers, patient/societal consequences of poor quality</i> 1a.2 1a.3 Summary of Evidence of High Impact: <i>Sinusitis affects 1 in 7 adults in the United States; 31 million individuals are diagnosed with sinusitis each year(1). The direct annual healthcare cost of sinusitis is \$5.8 billion. Most of this cost is from ambulatory and emergency department services (2). Indirect costs of sinusitis include 73 million days of restricted activity per year (2). More than 1 in 5 antibiotics prescribed in adults are for sinusitis, making it the fifth most common diagnosis for which an antibiotic is prescribed (3). Despite the high prevalence and economic impact of sinusitis, there is considerable practice variations across and within the multiple disciplines involved in managing the condition (4,5).</i> 1a.4 Citations for Evidence of High Impact: <i>1. Lethbridge-Cejku M, Rose D, Vickerie J. Summary health statistics for U.S. adults: National Health Interview Survey, 2004. National Center for Health Statistics. Vital Health Stat 2006;10(228):19-22. 2. Anand VK. Epidemiology and economic impact of rhinosinusitis. Ann Otol Rhinol Laryngol 2004;193(Suppl):3-5. 3. Sinus and Allergy Health Partnership (SAHP). Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. Otolaryngol Head Neck Surg 2004;130(Suppl):1-45. 4. Kaszuba SM, Stewart MG. Medical management and diagnosis of chronic rhinosinusitis: A survey of treatment patterns by United States otolaryngologists. Am J Rhinol 2006;20:186-90.</i>	1a C ☐ P ☐ M ☐ N ☐

Comment [KP1]: 1a. The measure focus addresses:
 • a specific national health goal/priority identified by NQF's National Priorities Partners; OR
 • a demonstrated high impact aspect of healthcare (e.g., affects large numbers, leading cause of morbidity/mortality, high resource use (current and/or future), severity of illness, and patient/societal consequences of poor quality).

5. Winstead W. Rhinosinusitis. Prim Care 2003;30:137-54.

1b. Opportunity for Improvement

1b.1 Benefits (improvements in quality) envisioned by use of this measure: This measure will facilitate recommended first line antibiotic treatment of acute sinusitis when an antibiotic is prescribed. This will improve treatment efficiency while reducing use of less effective, likely more expensive alternative agents. In addition, it could reduce the prevalence of antibiotic resistance organisms.

1b.2 Summary of data demonstrating performance gap (variation or overall poor performance) across providers:

Using a geographically diverse 15 million member benchmark database (this database represents predominately a commercial population less than 65 year of age) the compliance rate was 61.3 percent, indicating a clear gap in care and opportunity for care improvement.

1b.3 Citations for data on performance gap:

Ingenix EBM Connect benchmark results, September 2009

1b.4 Summary of Data on disparities by population group:

None

1b.5 Citations for data on Disparities:

1b
C ☐
P ☐
M ☐
N ☐

1c. Outcome or Evidence to Support Measure Focus

1c.1 Relationship to Outcomes (For non-outcome measures, briefly describe the relationship to desired outcome. For outcomes, describe why it is relevant to the target population): When antibiotics are prescribed to treat acute sinusitis, a first line antibiotic should be used. This measure will identify patients who did not receive a recommended first line antibiotic for treatment of acute sinusitis. This will improve treatment efficiency while reducing use of less effective, likely more expensive alternative agents. In addition, more targeted antibiotic use will reduce the prevalence of antibiotic resistance organisms.

1c.2-3. Type of Evidence: evidence based guideline, systematic synthesis of research

1c.4 Summary of Evidence (as described in the criteria; for outcomes, summarize any evidence that healthcare services/care processes influence the outcome):

Most cases of acute sinusitis diagnosed in ambulatory care are caused by viral pathogens; symptoms resolve without antibiotic treatment in most cases (1-3). Antibiotics should be reserved for those patients that have failed conservative therapy, present with signs and symptoms of a more severe illness, or have complications of acute sinusitis (3).

Recent guidelines from the Sinus and Allergy Health Partnership separate patients into two categories: those with mild symptoms who have not received an antibiotic within the past 4-6 weeks and those with mild disease who have received antibiotics in the last 4-6 weeks or have moderate disease regardless of recent antibiotic exposure (2). When antibiotic therapy is initiated, any one of the following antibiotics is recommended for these two categories: amoxicillin, amoxicillin/clavulanate, cefpodoxime proxetil, cefuroxime axetil, cefdinir, ceftriaxone. In addition, a respiratory fluoroquinolone (e.g., levofloxacin) can be used in adults (2,4). In patients allergic to penicillin, a respiratory fluoroquinolone or trimethoprim-sulfamethoxazole (TMP/SMX) is an acceptable alternative (1-4).

Macrolides are not recommended for first line therapy (2,4). There is an increasing prevalence of macrolide resistance to bacteria that often cause sinusitis. Although it is tempting to consider macrolides for patients with β -lactam allergies, bacteriologic failure rates of 20% to 25% are possible, and more effective agents are typically available (2,4).

1c.5 Rating of strength/quality of evidence (also provide narrative description of the rating and by

1c
C ☐
P ☐
M ☐
N ☐

Comment [KP2]: 1b. Demonstration of quality problems and opportunity for improvement, i.e., data demonstrating considerable variation, or overall poor performance, in the quality of care across providers and/or population groups (disparities in care).

Comment [k3]: 1 Examples of data on opportunity for improvement include, but are not limited to: prior studies, epidemiologic data, measure data from pilot testing or implementation. If data are not available, the measure focus is systematically assessed (e.g., expert panel rating) and judged to be a quality problem.

Comment [k4]: 1c. The measure focus is:
•an outcome (e.g., morbidity, mortality, function, health-related quality of life) that is relevant to, or associated with, a national health goal/priority, the condition, population, and/or care being addressed;
OR

•if an intermediate outcome, process, structure, etc., there is evidence that supports the specific measure focus as follows:
◦Intermediate outcome - evidence that the measured intermediate outcome (e.g., blood pressure, HbA1c) leads to improved health/avoidance of harm or cost/benefit.
◦Process - evidence that the measured clinical or administrative process leads to improved health/avoidance of harm and if the measure focus is on one step in a multi-step care process, it measures the step that has the greatest effect on improving the specified desired outcome(s).
◦Structure - evidence that the measured structure supports the consistent delivery of effective processes or access that lead to improved health/avoidance of harm or cost/benefit.
◦Patient experience - evidence that an association exists between the measure ... [1]

Comment [k5]: 4 Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multi-step process, the step with the greatest effect on the desired outcome should be selected as the focus of measurement. For example, although assessment of immunization status and recommending immunization are necessary steps, they are not sufficient to achieve the desired impact on health status - patients must be vaccinated to achieve ... [2]

Comment [k6]: 3 The strength of the body of evidence for the specific measure focus should be systematically assessed and rated (e.g., USPSTF grading system
<http://www.ahrq.gov/clinic/uspstf07/methods/benefit.htm>). If the USPSTF grading system was not used, the grading system is explained including how it relates to the USPSTF grades or why it does not. However, evidence is not limited to quantitative studies and the best type of evidence depends upon the question being studied (e.g., randomized controlled trials appropriate for studying drug efficacy are not well suited for complex system ... [3])

Rating: C=Completely; P=Partially; M=Minimally; N=Not at all; NA=Not applicable

whom):

expert panel consensus recommendation from two guidelines

1c.6 Method for rating evidence: This is an expert panel consensus recommendation.

1c.7 Summary of Controversy/Contradictory Evidence: Claims data will not reliably identify patients who are allergic to penicillin related antibiotics. In patients allergic to penicillin, a respiratory fluoroquinolone or trimethoprim-sulfamethoxazole (TMP/SMX) is an acceptable alternative (1-5). For this reason, trimethoprim-sulfamethoxazole (TMP/SMX) is included in this measure as an acceptable "first line" antibiotic.

Macrolides are not recommended for first line therapy (2,4). There is due to the increasing prevalence of macrolide resistance to bacteria that often cause sinusitis. This issue was discussed with sinusitis infectious disease experts who were identified by the Infectious Diseases Society of America (IDSA). There was consensus that macrolides should not be used in the management of acute sinusitis.

1c.8 Citations for Evidence (other than guidelines): 1. Brook I, Gooch WM, Jenkins SG, et al. Medical Management of Acute Bacterial Sinusitis: Recommendations of a Clinical Advisory Committee on Pediatric and Adult Sinusitis. Ann Otol Rhinol Laryngol 2000;109:1-20.
2. see reference in 1c.10
3. see reference in 1c.10
4. Poole, MD, Portugal LG. Treatment of rhinosinusitis in the outpatient setting. AJM 2005;188(7A):45S-50S.

1c.9 Quote the Specific guideline recommendation (including guideline number and/or page number):
2. Sinus and Allergy Health Partnership, page 36

Recommendations for initial therapy for adult patients with mild disease and who have not received antibiotics in the previous 4 to 6 weeks include the following choices: amoxicillin/ clavulanate (1.75 to 4 g/250 mg per day), amoxicillin (1.5 to 4 g/day), cefpodoxime proxetil, cefuroxime axetil, or cefdinir. Recommendations for initial therapy for adults with mild disease who have received antibiotics in the previous 4 to 6 weeks or adults with moderate disease include the following choices: respiratory fluoroquinolone (gatifloxacin, levofloxacin, moxifloxacin) or high-dose amoxicillin/clavulanate (4 g/250 mg per day).

Recommendations for initial therapy for children with mild disease and who have not received antibiotics in the previous 4 to 6 weeks include the following: high-dose amoxicillin/ clavulanate (90 mg/6.4 mg per kg per day), high-dose amoxicillin (90 mg/kg per day), cefpodoxime proxetil, cefuroxime axetil, or cefdinir.

3. ICSI guidelines, page 46:

Amoxicillin is the initial drug of choice. Antibiotics such as amoxicillin/clavulanate, cephalosporins and the newer macrolides have theoretic advantages when β -lactamase producing organisms are present. However, numerous studies have shown no efficacy advantage with these extended spectrum antibiotics compared to amoxicillin even when β -lactamase producing organisms are present. As these drugs typically are five to seven times more expensive than amoxicillin, their use cannot be justified as first-line therapy for acute sinusitis. In patients who are allergic to penicillin, trimethoprim-sulphamethoxazole should be the alternative. Generally quinolone antibiotics should not be used since they are relatively inactive against pneumococci.

1c.10 Clinical Practice Guideline Citation: 2. Sinus and Allergy Health Partnership (SAHP). Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. Otolaryngol Head Neck Surg 2004;130(Suppl):1-45.
3. Institute for Clinical Systems Improvement (ICSI). Health Care Guideline: Diagnosis and Treatment of Respiratory Illness in Children and Adults (Released January 2008). Accessed October 26, 2009. URL: <http://www.icsi.org>.

1c.11 National Guideline Clearinghouse or other URL: <http://www.icsi.org>.

1c.12 Rating of strength of recommendation (also provide narrative description of the rating and by whom):
expert panel consensus recommendation from two guidelines

1c.13 Method for rating strength of recommendation (If different from USPSTF system, also describe rating and how it relates to USPSTF):
This is a consensus statement recommendation from two major guidelines. This would be equivalent to the USPSTF grade A/B classification.

1c.14 Rationale for using this guideline over others:

The Sinus and Allergy Health Partnership, a conjoint group initially sponsored by the American Academy of Otolaryngology Head and Neck Surgery, the American Academy of Otolaryngic Allergy and the American Rhinologic Society, in consultation with representatives of the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and individuals from the fields of infectious disease, pediatric infectious disease, microbiology, and pharmacy have developed these guidelines as an educational tool for healthcare providers involved in managing patients with acute bacterial rhinosinusitis (ABRS). The guidelines, which were initially published in 2000, have been widely accepted. Since this most recent guideline was published in 2004, it does not account new emerging resistance data that has been seen with the macrolides.

ICSI is an independent, non-profit organization that helps its members provide evidence-based health care services to people in Minnesota and surrounding states. ICSI is comprised of 53 medical groups representing 9,000 physicians. Its demonstrated collaborative and innovative processes enable ICSI to unite diverse stakeholders in the health care system to deliver patient-centered and value-driven care. This is the most recent guideline that addresses first line antibiotic use in the management of this condition.

TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria for Importance to Measure and Report?

1

Steering Committee: Was the threshold criterion, Importance to Measure and Report, met? Rationale:

1

Y ☐N ☐

2. SCIENTIFIC ACCEPTABILITY OF MEASURE PROPERTIES

Extent to which the measure, as specified, produces consistent (reliable) and credible (valid) results about the quality of care when implemented. (evaluation criteria)

Eval
Rating

2a. MEASURE SPECIFICATIONS

S.1 Do you have a web page where current detailed measure specifications can be obtained?
S.2 If yes, provide web page URL:

2a. Precisely Specified

2a.1 Numerator Statement (Brief, text description of the numerator - what is being measured about the target population, e.g. target condition, event, or outcome):

Patients who are treated with an antibiotic for acute sinusitis that received a first line antibiotic

2a.2 Numerator Time Window (The time period in which cases are eligible for inclusion in the numerator):

Ten days prior to the initiating acute sinusitis encounter through 21 days after the initiating acute sinusitis encounter

2a.3 Numerator Details (All information required to collect/calculate the numerator, including all codes, logic, and definitions):

Patients who filled a prescription for any antibiotic (code set RX-184) during the following time period: ten days prior to the initiating acute sinusitis encounter through 21 days after the initiating acute sinusitis encounter, and whose FIRST antibiotic prescription during this time window was one of the following:

2a-specs
C ☐
P ☐
M ☐
N ☐

Comment [k7]: USPSTF grading system <http://www.ahrq.gov/clinic/uspstf/grades.htm>: **A** - The USPSTF recommends the service. There is high certainty that the net benefit is substantial. **B** - The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial. **C** - The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is at least moderate certainty that the net benefit is small. Offer or provide this service only if other considerations support the offering or providing the service in an individual patient. **D** - The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits. **I** - The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Comment [KP8]: 2a. The measure is well defined and precisely specified so that it can be implemented consistently within and across organizations and allow for comparability. The required data elements are of high quality as defined by NQF's Health Information Technology Expert Panel (HITEP).

Rating: C=Completely; P=Partially; M=Minimally; N=Not at all; NA=Not applicable

Amoxicillin (code set RX-185)
 Amoxicillin/clavulanate (code set RX-186)
 Cefpodoxime proxetil (code set RX-187)
 Cefuroxime axetil (code set RX-188)
 Cefdinir (code set RX-189)
 Gatifloxacin (code set RX-190)
 Levofloxacin (code set RX-191)
 Moxifloxacin (code set RX-192)
 Ceftriaxone (code set RX-193)
 Trimethoprim-sulfamethoxazole (code set RX-194)

cd. set	RX cd. set	descr. ndc
RX-184	Any Antibiotic	00002032702
RX-184	Any Antibiotic	00002032750
RX-184	Any Antibiotic	00002032902
RX-184	Any Antibiotic	00002032903
RX-184	Any Antibiotic	00002034602
RX-184	Any Antibiotic	00002034603
RX-184	Any Antibiotic	00002034624
RX-184	Any Antibiotic	00002050101
RX-184	Any Antibiotic	00002050301
RX-184	Any Antibiotic	00002050324
RX-184	Any Antibiotic	00002050901
RX-184	Any Antibiotic	00002050924
RX-184	Any Antibiotic	00002144401
RX-184	Any Antibiotic	00002144410
RX-184	Any Antibiotic	00002144425
RX-184	Any Antibiotic	00002145401
RX-184	Any Antibiotic	00002149601
RX-184	Any Antibiotic	00002149701
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RX-184	Any Antibiotic	00002149925
RX-184	Any Antibiotic	00002168101
RX-184	Any Antibiotic	00002204602
RX-184	Any Antibiotic	00002205402
RX-184	Any Antibiotic	00002207502
RX-184	Any Antibiotic	00002230733
RX-184	Any Antibiotic	00002230748
RX-184	Any Antibiotic	00002230768
RX-184	Any Antibiotic	00002230789
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RX-184	Any Antibiotic	00002231648
RX-184	Any Antibiotic	00002231668
RX-184	Any Antibiotic	00002231689
RX-184	Any Antibiotic	00002234305
RX-184	Any Antibiotic	00002237237
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RX-184	Any Antibiotic	00002306115
RX-184	Any Antibiotic	00002306133
RX-184	Any Antibiotic	00002306202
RX-184	Any Antibiotic	00002306215
RX-184	Any Antibiotic	00002306233
RX-184	Any Antibiotic	00002312542
RX-184	Any Antibiotic	00002312642
RX-184	Any Antibiotic	00002317002

RX-184	Any Antibiotic	00002317030
RX-184	Any Antibiotic	00002317102
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RX-184	Any Antibiotic	00002505868
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RX-184	Any Antibiotic	00002513287
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RX-184	Any Antibiotic	00002513587
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RX-184	Any Antibiotic	00002513648
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RX-186	Amoxicillin/clavulanate	63304050920
RX-186	Amoxicillin/clavulanate	63304071320
RX-186	Amoxicillin/clavulanate	63304075320
RX-186	Amoxicillin/clavulanate	63304075420
RX-186	Amoxicillin/clavulanate	63304076801
RX-186	Amoxicillin/clavulanate	63304076802
RX-186	Amoxicillin/clavulanate	63304076807

RX-186	Amoxicillin/clavulanate	63304097701
RX-186	Amoxicillin/clavulanate	63304097703
RX-186	Amoxicillin/clavulanate	63304097704
RX-186	Amoxicillin/clavulanate	63304097901
RX-186	Amoxicillin/clavulanate	63304097903
RX-186	Amoxicillin/clavulanate	63304097904
RX-186	Amoxicillin/clavulanate	63629124801
RX-186	Amoxicillin/clavulanate	63629124802
RX-186	Amoxicillin/clavulanate	63629124803
RX-186	Amoxicillin/clavulanate	63874010301
RX-186	Amoxicillin/clavulanate	63874010321
RX-186	Amoxicillin/clavulanate	63874010330
RX-186	Amoxicillin/clavulanate	63874011501
RX-186	Amoxicillin/clavulanate	63874011508
RX-186	Amoxicillin/clavulanate	63874011510
RX-186	Amoxicillin/clavulanate	63874011512
RX-186	Amoxicillin/clavulanate	63874011514
RX-186	Amoxicillin/clavulanate	63874011515
RX-186	Amoxicillin/clavulanate	63874011520
RX-186	Amoxicillin/clavulanate	63874011521
RX-186	Amoxicillin/clavulanate	63874011530
RX-186	Amoxicillin/clavulanate	63874011612
RX-186	Amoxicillin/clavulanate	63874011615
RX-186	Amoxicillin/clavulanate	63874011620
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RX-186	Amoxicillin/clavulanate	63874011630
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RX-186	Amoxicillin/clavulanate	63874011712
RX-186	Amoxicillin/clavulanate	63874011714
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RX-186	Amoxicillin/clavulanate	63874011720
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RX-186	Amoxicillin/clavulanate	63874014710
RX-186	Amoxicillin/clavulanate	63874014715
RX-186	Amoxicillin/clavulanate	63874014775
RX-186	Amoxicillin/clavulanate	63874014810
RX-186	Amoxicillin/clavulanate	63874014815
RX-186	Amoxicillin/clavulanate	63874014875
RX-186	Amoxicillin/clavulanate	63874122602
RX-186	Amoxicillin/clavulanate	66116015214
RX-186	Amoxicillin/clavulanate	66116024030
RX-186	Amoxicillin/clavulanate	66116067820
RX-186	Amoxicillin/clavulanate	66116067930
RX-186	Amoxicillin/clavulanate	66116068015
RX-186	Amoxicillin/clavulanate	66116068130
RX-186	Amoxicillin/clavulanate	66116068220
RX-186	Amoxicillin/clavulanate	66267044415
RX-186	Amoxicillin/clavulanate	66267071203
RX-186	Amoxicillin/clavulanate	66267071210
RX-186	Amoxicillin/clavulanate	66267085703
RX-186	Amoxicillin/clavulanate	66267085704
RX-186	Amoxicillin/clavulanate	66267085903
RX-186	Amoxicillin/clavulanate	66267085904
RX-186	Amoxicillin/clavulanate	66267099120
RX-186	Amoxicillin/clavulanate	66267099220
RX-186	Amoxicillin/clavulanate	66267100101
RX-186	Amoxicillin/clavulanate	66267100201
RX-186	Amoxicillin/clavulanate	66336007421

RX-186	Amoxicillin/clavulanate	66685100100
RX-186	Amoxicillin/clavulanate	66685100101
RX-186	Amoxicillin/clavulanate	66685100200
RX-186	Amoxicillin/clavulanate	66685100202
RX-186	Amoxicillin/clavulanate	66685101100
RX-186	Amoxicillin/clavulanate	66685101101
RX-186	Amoxicillin/clavulanate	66685101102
RX-186	Amoxicillin/clavulanate	66685101200
RX-186	Amoxicillin/clavulanate	66685101201
RX-186	Amoxicillin/clavulanate	66685101202
RX-186	Amoxicillin/clavulanate	68030126103
RX-186	Amoxicillin/clavulanate	68030126104
RX-186	Amoxicillin/clavulanate	68030604201
RX-186	Amoxicillin/clavulanate	68030605002
RX-186	Amoxicillin/clavulanate	68071006330
RX-186	Amoxicillin/clavulanate	68084023501
RX-186	Amoxicillin/clavulanate	68084023511
RX-186	Amoxicillin/clavulanate	68084023601
RX-186	Amoxicillin/clavulanate	68084023611
RX-186	Amoxicillin/clavulanate	68115038620
RX-186	Amoxicillin/clavulanate	68115046320
RX-186	Amoxicillin/clavulanate	68115048840
RX-186	Amoxicillin/clavulanate	68115099020
RX-186	Amoxicillin/clavulanate	68115099120
RX-186	Amoxicillin/clavulanate	68118038620
RX-186	Amoxicillin/clavulanate	68387058015
RX-186	Amoxicillin/clavulanate	68387058530

cd.	set RX code set descrp.	ndc
RX-187	Cefpodoxime proxetil	00009353101
RX-187	Cefpodoxime proxetil	00009353102
RX-187	Cefpodoxime proxetil	00009353103
RX-187	Cefpodoxime proxetil	00009361501
RX-187	Cefpodoxime proxetil	00009361502
RX-187	Cefpodoxime proxetil	00009361503
RX-187	Cefpodoxime proxetil	00009361701
RX-187	Cefpodoxime proxetil	00009361702
RX-187	Cefpodoxime proxetil	00009361703
RX-187	Cefpodoxime proxetil	00009361801
RX-187	Cefpodoxime proxetil	00009361802
RX-187	Cefpodoxime proxetil	00009361803
RX-187	Cefpodoxime proxetil	00247033920
RX-187	Cefpodoxime proxetil	00403069114
RX-187	Cefpodoxime proxetil	00403453714
RX-187	Cefpodoxime proxetil	00781543820
RX-187	Cefpodoxime proxetil	00781543901
RX-187	Cefpodoxime proxetil	00781543920
RX-187	Cefpodoxime proxetil	00781616846
RX-187	Cefpodoxime proxetil	00781616852
RX-187	Cefpodoxime proxetil	00781616946
RX-187	Cefpodoxime proxetil	00781616952
RX-187	Cefpodoxime proxetil	12280010520
RX-187	Cefpodoxime proxetil	16714021101
RX-187	Cefpodoxime proxetil	16714021201
RX-187	Cefpodoxime proxetil	33358006820
RX-187	Cefpodoxime proxetil	52959062710
RX-187	Cefpodoxime proxetil	52959062720
RX-187	Cefpodoxime proxetil	52959065820

RX-187 Cefpodoxime proxetil	52959079610
RX-187 Cefpodoxime proxetil	54569377400
RX-187 Cefpodoxime proxetil	54569377500
RX-187 Cefpodoxime proxetil	54569405800
RX-187 Cefpodoxime proxetil	54569405801
RX-187 Cefpodoxime proxetil	54569478300
RX-187 Cefpodoxime proxetil	55045221001
RX-187 Cefpodoxime proxetil	55175010100
RX-187 Cefpodoxime proxetil	55175010101
RX-187 Cefpodoxime proxetil	55175010102
RX-187 Cefpodoxime proxetil	55175010201
RX-187 Cefpodoxime proxetil	55175010301
RX-187 Cefpodoxime proxetil	55289039002
RX-187 Cefpodoxime proxetil	55289039010
RX-187 Cefpodoxime proxetil	55289039020
RX-187 Cefpodoxime proxetil	55289039028
RX-187 Cefpodoxime proxetil	55289039079
RX-187 Cefpodoxime proxetil	60346098114
RX-187 Cefpodoxime proxetil	63304052001
RX-187 Cefpodoxime proxetil	63304052020
RX-187 Cefpodoxime proxetil	63304052101
RX-187 Cefpodoxime proxetil	63304052120
RX-187 Cefpodoxime proxetil	63304096503
RX-187 Cefpodoxime proxetil	63304096504
RX-187 Cefpodoxime proxetil	63304096603
RX-187 Cefpodoxime proxetil	63304096604
RX-187 Cefpodoxime proxetil	65862009520
RX-187 Cefpodoxime proxetil	65862009620
RX-187 Cefpodoxime proxetil	65862014001
RX-187 Cefpodoxime proxetil	65862014050
RX-187 Cefpodoxime proxetil	65862014101
RX-187 Cefpodoxime proxetil	65862014150

cd. set RX code set descrp.	ndc
RX-188 Cefuroxime axetil	00002535725
RX-188 Cefuroxime axetil	00002535801
RX-188 Cefuroxime axetil	00002535810
RX-188 Cefuroxime axetil	00002535901
RX-188 Cefuroxime axetil	00002535910
RX-188 Cefuroxime axetil	00002536001
RX-188 Cefuroxime axetil	00002536010
RX-188 Cefuroxime axetil	00002536101
RX-188 Cefuroxime axetil	00002536115
RX-188 Cefuroxime axetil	00002536116
RX-188 Cefuroxime axetil	00002536225
RX-188 Cefuroxime axetil	00002536310
RX-188 Cefuroxime axetil	00002727101
RX-188 Cefuroxime axetil	00002727125
RX-188 Cefuroxime axetil	00002727201
RX-188 Cefuroxime axetil	00002727210
RX-188 Cefuroxime axetil	00002727301
RX-188 Cefuroxime axetil	00002727310
RX-188 Cefuroxime axetil	00002727401
RX-188 Cefuroxime axetil	00002727410
RX-188 Cefuroxime axetil	00002727501
RX-188 Cefuroxime axetil	00002727516
RX-188 Cefuroxime axetil	00002727601
RX-188 Cefuroxime axetil	00002727624

RX-188	Cefuroxime axetil	00002727701
RX-188	Cefuroxime axetil	00002727724
RX-188	Cefuroxime axetil	00002727801
RX-188	Cefuroxime axetil	00002727825
RX-188	Cefuroxime axetil	00002727901
RX-188	Cefuroxime axetil	00002727910
RX-188	Cefuroxime axetil	00002899425
RX-188	Cefuroxime axetil	00002899510
RX-188	Cefuroxime axetil	00002899519
RX-188	Cefuroxime axetil	00002950001
RX-188	Cefuroxime axetil	00093107334
RX-188	Cefuroxime axetil	00143997603
RX-188	Cefuroxime axetil	00143997691
RX-188	Cefuroxime axetil	00143997722
RX-188	Cefuroxime axetil	00143997790
RX-188	Cefuroxime axetil	00143997922
RX-188	Cefuroxime axetil	00143997990
RX-188	Cefuroxime axetil	00173035210
RX-188	Cefuroxime axetil	00173035230
RX-188	Cefuroxime axetil	00173035231
RX-188	Cefuroxime axetil	00173035332
RX-188	Cefuroxime axetil	00173035410
RX-188	Cefuroxime axetil	00173035434
RX-188	Cefuroxime axetil	00173035435
RX-188	Cefuroxime axetil	00173035632
RX-188	Cefuroxime axetil	00173038700
RX-188	Cefuroxime axetil	00173038701
RX-188	Cefuroxime axetil	00173038706
RX-188	Cefuroxime axetil	00173038742
RX-188	Cefuroxime axetil	00173039400
RX-188	Cefuroxime axetil	00173039401
RX-188	Cefuroxime axetil	00173039442
RX-188	Cefuroxime axetil	00173039500
RX-188	Cefuroxime axetil	00173039501
RX-188	Cefuroxime axetil	00173039502
RX-188	Cefuroxime axetil	00173040000
RX-188	Cefuroxime axetil	00173040600
RX-188	Cefuroxime axetil	00173040601
RX-188	Cefuroxime axetil	00173040604
RX-188	Cefuroxime axetil	00173042400
RX-188	Cefuroxime axetil	00173042500
RX-188	Cefuroxime axetil	00173043600
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RX-188	Cefuroxime axetil	00173055400
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RX-188	Cefuroxime axetil	00182269015
RX-188	Cefuroxime axetil	00182269026
RX-188	Cefuroxime axetil	00209113022
RX-188	Cefuroxime axetil	00209113142
RX-188	Cefuroxime axetil	00209113222
RX-188	Cefuroxime axetil	00209113342
RX-188	Cefuroxime axetil	00209113452
RX-188	Cefuroxime axetil	00247026202

RX-188 Cefuroxime axetil	00247026204
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RX-188 Cefuroxime axetil	00247026210
RX-188 Cefuroxime axetil	00247026214
RX-188 Cefuroxime axetil	00247026216
RX-188 Cefuroxime axetil	00247026220
RX-188 Cefuroxime axetil	00247094120
RX-188 Cefuroxime axetil	00247116401
RX-188 Cefuroxime axetil	00247116405
RX-188 Cefuroxime axetil	00264311211
RX-188 Cefuroxime axetil	00264311411
RX-188 Cefuroxime axetil	00338204341
RX-188 Cefuroxime axetil	00338204348
RX-188 Cefuroxime axetil	00364288134
RX-188 Cefuroxime axetil	00364288593
RX-188 Cefuroxime axetil	00403244314
RX-188 Cefuroxime axetil	00403244320
RX-188 Cefuroxime axetil	00403464518
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RX-188 Cefuroxime axetil	00409080201
RX-188 Cefuroxime axetil	00409080301
RX-188 Cefuroxime axetil	00440724503
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RX-188 Cefuroxime axetil	00781392446
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RX-188 Cefuroxime axetil	00781920680
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RX-188 Cefuroxime axetil	00781920746
RX-188 Cefuroxime axetil	00781920795
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RX-188 Cefuroxime axetil	00904595861
RX-188 Cefuroxime axetil	10019062001
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RX-188 Cefuroxime axetil	10019062103
RX-188 Cefuroxime axetil	10019062120
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RX-188 Cefuroxime axetil	10515012501
RX-188 Cefuroxime axetil	10515012502
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RX-188 Cefuroxime axetil	16714023202
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RX-188 Cefuroxime axetil	49999078520
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RX-188 Cefuroxime axetil	54868498700
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RX-188 Cefuroxime axetil	54868502201

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RX-188 Cefuroxime axetil	55045154605
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RX-188 Cefuroxime axetil	55175176300
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RX-188 Cefuroxime axetil	55175176304
RX-188 Cefuroxime axetil	55175176400
RX-188 Cefuroxime axetil	55175176401
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RX-188 Cefuroxime axetil	55175526502
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RX-188 Cefuroxime axetil	55887024420
RX-188 Cefuroxime axetil	55887024430
RX-188 Cefuroxime axetil	55887065220
RX-188 Cefuroxime axetil	55887065230
RX-188 Cefuroxime axetil	57362066509
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RX-188 Cefuroxime axetil	58016011415
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RX-188 Cefuroxime axetil	58016011530
RX-188 Cefuroxime axetil	58016011560
RX-188 Cefuroxime axetil	58864069020
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RX-188 Cefuroxime axetil	59762108301
RX-188 Cefuroxime axetil	59762108302
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RX-188 Cefuroxime axetil	59772655002
RX-188 Cefuroxime axetil	59772655101
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RX-188 Cefuroxime axetil	59772656901
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RX-188 Cefuroxime axetil	60346036925
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RX-188 Cefuroxime axetil	60505120103
RX-188 Cefuroxime axetil	60505120200

RX-188 Cefuroxime axetil	60505120203
RX-188 Cefuroxime axetil	60505268102
RX-188 Cefuroxime axetil	60505268106
RX-188 Cefuroxime axetil	60505268202
RX-188 Cefuroxime axetil	60505268206
RX-188 Cefuroxime axetil	61703033311
RX-188 Cefuroxime axetil	61703033433
RX-188 Cefuroxime axetil	63304075120
RX-188 Cefuroxime axetil	63304075160
RX-188 Cefuroxime axetil	63304075220
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RX-188 Cefuroxime axetil	63304094810
RX-188 Cefuroxime axetil	63304096304
RX-188 Cefuroxime axetil	63304096403
RX-188 Cefuroxime axetil	63304096404
RX-188 Cefuroxime axetil	63323030110
RX-188 Cefuroxime axetil	63323031220
RX-188 Cefuroxime axetil	63323031361
RX-188 Cefuroxime axetil	63323035210
RX-188 Cefuroxime axetil	63323035320
RX-188 Cefuroxime axetil	63323035461
RX-188 Cefuroxime axetil	64679092101
RX-188 Cefuroxime axetil	64679092102
RX-188 Cefuroxime axetil	64679092201
RX-188 Cefuroxime axetil	64679092202
RX-188 Cefuroxime axetil	65862003420
RX-188 Cefuroxime axetil	65862003460
RX-188 Cefuroxime axetil	65862003520
RX-188 Cefuroxime axetil	65862003560
RX-188 Cefuroxime axetil	65939038700
RX-188 Cefuroxime axetil	65939038701
RX-188 Cefuroxime axetil	65939038742
RX-188 Cefuroxime axetil	65939039400
RX-188 Cefuroxime axetil	65939039401
RX-188 Cefuroxime axetil	65939039442
RX-188 Cefuroxime axetil	65939039501
RX-188 Cefuroxime axetil	65939040600
RX-188 Cefuroxime axetil	65939055400
RX-188 Cefuroxime axetil	65939055500
RX-188 Cefuroxime axetil	66288207501
RX-188 Cefuroxime axetil	66288222501
RX-188 Cefuroxime axetil	66336036920
RX-188 Cefuroxime axetil	66814060120
RX-188 Cefuroxime axetil	66814060160
RX-188 Cefuroxime axetil	66814060220
RX-188 Cefuroxime axetil	66814060260
RX-188 Cefuroxime axetil	66860003003
RX-188 Cefuroxime axetil	66860003103
RX-188 Cefuroxime axetil	66860003202
RX-188 Cefuroxime axetil	66860073003
RX-188 Cefuroxime axetil	66860073103
RX-188 Cefuroxime axetil	66860073202
RX-188 Cefuroxime axetil	67253078002
RX-188 Cefuroxime axetil	67253078102
RX-188 Cefuroxime axetil	68084021801
RX-188 Cefuroxime axetil	68084021811

RX-188	Cefuroxime axetil	68084021901
RX-188	Cefuroxime axetil	68084021911
RX-188	Cefuroxime axetil	68180030220
RX-188	Cefuroxime axetil	68180030260
RX-188	Cefuroxime axetil	68180030320
RX-188	Cefuroxime axetil	68180030360
RX-188	Cefuroxime axetil	68722035210
RX-188	Cefuroxime axetil	68722035320

cd. set RX code set descrp. ndc

RX-189	Cefdinir	00071006720
RX-189	Cefdinir	00071200616
RX-189	Cefdinir	00071200618
RX-189	Cefdinir	00074376910
RX-189	Cefdinir	00074376930
RX-189	Cefdinir	00074376960
RX-189	Cefdinir	00074377113
RX-189	Cefdinir	00074377160
RX-189	Cefdinir	00074615113
RX-189	Cefdinir	00074615160
RX-189	Cefdinir	00093316006
RX-189	Cefdinir	00093413664
RX-189	Cefdinir	00093413673
RX-189	Cefdinir	00093413764
RX-189	Cefdinir	00093413773
RX-189	Cefdinir	00781217660
RX-189	Cefdinir	00781217664
RX-189	Cefdinir	00781217669
RX-189	Cefdinir	00781607746
RX-189	Cefdinir	00781607761
RX-189	Cefdinir	00781607846
RX-189	Cefdinir	00781607861
RX-189	Cefdinir	35356003820
RX-189	Cefdinir	35356011960
RX-189	Cefdinir	35356019000
RX-189	Cefdinir	52959013420
RX-189	Cefdinir	54569487700
RX-189	Cefdinir	54569521400
RX-189	Cefdinir	54569521401
RX-189	Cefdinir	54569521500
RX-189	Cefdinir	54569564900
RX-189	Cefdinir	54569565000
RX-189	Cefdinir	54868073700
RX-189	Cefdinir	54868073701
RX-189	Cefdinir	54868436600
RX-189	Cefdinir	54868436601
RX-189	Cefdinir	54868468200
RX-189	Cefdinir	54868468201
RX-189	Cefdinir	54868576700
RX-189	Cefdinir	54868576701
RX-189	Cefdinir	54868576800
RX-189	Cefdinir	54868576801
RX-189	Cefdinir	54868576900
RX-189	Cefdinir	54868576901
RX-189	Cefdinir	55289008120
RX-189	Cefdinir	55289083120
RX-189	Cefdinir	55887018760
RX-189	Cefdinir	59762218001

RX-189	Cefdinir	65862017760
RX-189	Cefdinir	65862021801
RX-189	Cefdinir	65862021860
RX-189	Cefdinir	65862021901
RX-189	Cefdinir	65862021960
RX-189	Cefdinir	66336010406
RX-189	Cefdinir	66336010420
RX-189	Cefdinir	67253000760
RX-189	Cefdinir	67253000841
RX-189	Cefdinir	67253000846
RX-189	Cefdinir	67253000941
RX-189	Cefdinir	67253000946
RX-189	Cefdinir	68180071160
RX-189	Cefdinir	68180072210
RX-189	Cefdinir	68180072220
RX-189	Cefdinir	68180072310
RX-189	Cefdinir	68180072320
RX-189	Cefdinir	68820006306
RX-189	Cefdinir	68820006309
RX-189	Cefdinir	68820006319
RX-189	Cefdinir	68820006417
RX-189	Cefdinir	68820006437
RX-189	Cefdinir	68820006517
RX-189	Cefdinir	68820006537

cd. set RX code set descrp. ndc

RX-190	Gatifloxacin	00015111750
RX-190	Gatifloxacin	00015111780
RX-190	Gatifloxacin	00015117719
RX-190	Gatifloxacin	00015117721
RX-190	Gatifloxacin	00015117760
RX-190	Gatifloxacin	00015117780
RX-190	Gatifloxacin	00015117880
RX-190	Gatifloxacin	00015117980
RX-190	Gatifloxacin	00015118078
RX-190	Gatifloxacin	00015118079
RX-190	Gatifloxacin	00015118080
RX-190	Gatifloxacin	00015118178
RX-190	Gatifloxacin	00015118179
RX-190	Gatifloxacin	00015118180
RX-190	Gatifloxacin	49999036601
RX-190	Gatifloxacin	49999036610
RX-190	Gatifloxacin	54569492100
RX-190	Gatifloxacin	54569492101
RX-190	Gatifloxacin	54569492102
RX-190	Gatifloxacin	54569492103
RX-190	Gatifloxacin	54569519900
RX-190	Gatifloxacin	54868433000
RX-190	Gatifloxacin	54868433001
RX-190	Gatifloxacin	54868433002
RX-190	Gatifloxacin	54868448300
RX-190	Gatifloxacin	55045344905
RX-190	Gatifloxacin	55289070910
RX-190	Gatifloxacin	55289070915
RX-190	Gatifloxacin	55887037503
RX-190	Gatifloxacin	55887037506
RX-190	Gatifloxacin	55887037520
RX-190	Gatifloxacin	55887037530

RX-190	Gatifloxacin	58864074210
RX-190	Gatifloxacin	58864079010
RX-190	Gatifloxacin	58864081110
RX-190	Gatifloxacin	66116027507
RX-190	Gatifloxacin	66116027510

cd. set RX code set descrp. ndc

RX-191	Levofloxacin	00045006555
RX-191	Levofloxacin	00045006601
RX-191	Levofloxacin	00045006701
RX-191	Levofloxacin	00045006801
RX-191	Levofloxacin	00045006951
RX-191	Levofloxacin	00045006955
RX-191	Levofloxacin	00045151501
RX-191	Levofloxacin	00045152010
RX-191	Levofloxacin	00045152050
RX-191	Levofloxacin	00045152510
RX-191	Levofloxacin	00045152550
RX-191	Levofloxacin	00045153005
RX-191	Levofloxacin	00045153010
RX-191	Levofloxacin	00045153020
RX-191	Levofloxacin	00045153050
RX-191	Levofloxacin	00440772405
RX-191	Levofloxacin	00440772407
RX-191	Levofloxacin	00440772503
RX-191	Levofloxacin	00440772507
RX-191	Levofloxacin	00440772510
RX-191	Levofloxacin	00440772514
RX-191	Levofloxacin	00440772602
RX-191	Levofloxacin	00440772603
RX-191	Levofloxacin	00440772607
RX-191	Levofloxacin	00440772610
RX-191	Levofloxacin	00440772614
RX-191	Levofloxacin	12280003150
RX-191	Levofloxacin	13411011203
RX-191	Levofloxacin	13411015403
RX-191	Levofloxacin	16590055914
RX-191	Levofloxacin	16590055920
RX-191	Levofloxacin	16590055930
RX-191	Levofloxacin	16590057805
RX-191	Levofloxacin	18837020014
RX-191	Levofloxacin	21695046407
RX-191	Levofloxacin	21695051907
RX-191	Levofloxacin	23490703202
RX-191	Levofloxacin	23490926000
RX-191	Levofloxacin	23490926001
RX-191	Levofloxacin	23490926003
RX-191	Levofloxacin	23490926005
RX-191	Levofloxacin	33358020200
RX-191	Levofloxacin	33358020210
RX-191	Levofloxacin	33358020230
RX-191	Levofloxacin	33358020260
RX-191	Levofloxacin	43063011303
RX-191	Levofloxacin	49999041710
RX-191	Levofloxacin	49999041802
RX-191	Levofloxacin	49999041807
RX-191	Levofloxacin	49999041810
RX-191	Levofloxacin	49999041830

RX-191	Levofloxacin	49999041850
RX-191	Levofloxacin	50458016420
RX-191	Levofloxacin	50458016530
RX-191	Levofloxacin	50458017001
RX-191	Levofloxacin	50458092010
RX-191	Levofloxacin	50458092050
RX-191	Levofloxacin	50458092510
RX-191	Levofloxacin	50458092550
RX-191	Levofloxacin	50458093010
RX-191	Levofloxacin	50458093020
RX-191	Levofloxacin	52959049201
RX-191	Levofloxacin	52959049202
RX-191	Levofloxacin	52959049204
RX-191	Levofloxacin	52959049206
RX-191	Levofloxacin	52959049207
RX-191	Levofloxacin	52959049210
RX-191	Levofloxacin	52959049212
RX-191	Levofloxacin	52959049214
RX-191	Levofloxacin	52959049230
RX-191	Levofloxacin	52959069003
RX-191	Levofloxacin	52959069005
RX-191	Levofloxacin	52959069007
RX-191	Levofloxacin	52959069014
RX-191	Levofloxacin	52959069030
RX-191	Levofloxacin	52959078207
RX-191	Levofloxacin	52959078220
RX-191	Levofloxacin	54569448900
RX-191	Levofloxacin	54569448901
RX-191	Levofloxacin	54569448902
RX-191	Levofloxacin	54569448903
RX-191	Levofloxacin	54569448904
RX-191	Levofloxacin	54569448905
RX-191	Levofloxacin	54569467700
RX-191	Levofloxacin	54569491500
RX-191	Levofloxacin	54569491501
RX-191	Levofloxacin	54569491502
RX-191	Levofloxacin	54569555701
RX-191	Levofloxacin	54868392300
RX-191	Levofloxacin	54868392301
RX-191	Levofloxacin	54868392302
RX-191	Levofloxacin	54868392303
RX-191	Levofloxacin	54868392304
RX-191	Levofloxacin	54868392305
RX-191	Levofloxacin	54868417500
RX-191	Levofloxacin	54868417501
RX-191	Levofloxacin	54868417502
RX-191	Levofloxacin	54868417503
RX-191	Levofloxacin	54868417504
RX-191	Levofloxacin	54868417505
RX-191	Levofloxacin	54868497100
RX-191	Levofloxacin	54868497101
RX-191	Levofloxacin	55045259701
RX-191	Levofloxacin	55045259702
RX-191	Levofloxacin	55045259703
RX-191	Levofloxacin	55045259705
RX-191	Levofloxacin	55045259706
RX-191	Levofloxacin	55045259708
RX-191	Levofloxacin	55175190001

RX-191	Levofloxacin	55289039405
RX-191	Levofloxacin	55289039407
RX-191	Levofloxacin	55289071107
RX-191	Levofloxacin	55289071110
RX-191	Levofloxacin	55289071114
RX-191	Levofloxacin	55289084103
RX-191	Levofloxacin	55289084110
RX-191	Levofloxacin	57866658401
RX-191	Levofloxacin	57866658402
RX-191	Levofloxacin	57866658403
RX-191	Levofloxacin	57866658501
RX-191	Levofloxacin	57866658502
RX-191	Levofloxacin	57866658503
RX-191	Levofloxacin	58016057300
RX-191	Levofloxacin	58016057307
RX-191	Levofloxacin	58016057310
RX-191	Levofloxacin	58016057320
RX-191	Levofloxacin	58016057330
RX-191	Levofloxacin	58016057360
RX-191	Levofloxacin	58016057390
RX-191	Levofloxacin	58016092400
RX-191	Levofloxacin	58016092430
RX-191	Levofloxacin	58016092460
RX-191	Levofloxacin	58016092490
RX-191	Levofloxacin	58016097500
RX-191	Levofloxacin	58016097530
RX-191	Levofloxacin	58016097560
RX-191	Levofloxacin	58016097590
RX-191	Levofloxacin	58864003410
RX-191	Levofloxacin	58864003414
RX-191	Levofloxacin	62682103903
RX-191	Levofloxacin	66105047705
RX-191	Levofloxacin	66105047805
RX-191	Levofloxacin	66116020007
RX-191	Levofloxacin	66116020107
RX-191	Levofloxacin	66116020114
RX-191	Levofloxacin	66267036307
RX-191	Levofloxacin	66267036310
RX-191	Levofloxacin	66336038607
RX-191	Levofloxacin	66336038610
RX-191	Levofloxacin	66336083005
RX-191	Levofloxacin	68030658401
RX-191	Levofloxacin	68030658402
RX-191	Levofloxacin	68030658403
RX-191	Levofloxacin	68030658501
RX-191	Levofloxacin	68030658502
RX-191	Levofloxacin	68030658503
RX-191	Levofloxacin	68115019610
RX-191	Levofloxacin	68115019710

cd. set RX code set descrp. ndc

RX-192	Moxifloxacin	00026858141
RX-192	Moxifloxacin	00026858169
RX-192	Moxifloxacin	00026858188
RX-192	Moxifloxacin	00026858231
RX-192	Moxifloxacin	00085173301
RX-192	Moxifloxacin	00085173302
RX-192	Moxifloxacin	00085173303

RX-192	Moxifloxacin	00085173305
RX-192	Moxifloxacin	00085173701
RX-192	Moxifloxacin	00490008500
RX-192	Moxifloxacin	00490008530
RX-192	Moxifloxacin	00490008560
RX-192	Moxifloxacin	00490008590
RX-192	Moxifloxacin	13411010803
RX-192	Moxifloxacin	49999045505
RX-192	Moxifloxacin	49999045510
RX-192	Moxifloxacin	49999045530
RX-192	Moxifloxacin	52959000405
RX-192	Moxifloxacin	54569492200
RX-192	Moxifloxacin	54569492201
RX-192	Moxifloxacin	54569514900
RX-192	Moxifloxacin	54868436700
RX-192	Moxifloxacin	54868436701
RX-192	Moxifloxacin	54868436702
RX-192	Moxifloxacin	54868436703
RX-192	Moxifloxacin	54868436704
RX-192	Moxifloxacin	55045284304
RX-192	Moxifloxacin	55045284305
RX-192	Moxifloxacin	55289007710
RX-192	Moxifloxacin	58864062105
RX-192	Moxifloxacin	58864062110
RX-192	Moxifloxacin	58864062130
RX-192	Moxifloxacin	58864088307
RX-192	Moxifloxacin	68115092505

cd. set RX code set descrp. ndc

RX-193	Ceftriaxone	00004196201
RX-193	Ceftriaxone	00004196202
RX-193	Ceftriaxone	00004196301
RX-193	Ceftriaxone	00004196302
RX-193	Ceftriaxone	00004196401
RX-193	Ceftriaxone	00004196402
RX-193	Ceftriaxone	00004196403
RX-193	Ceftriaxone	00004196404
RX-193	Ceftriaxone	00004196405
RX-193	Ceftriaxone	00004196439
RX-193	Ceftriaxone	00004196501
RX-193	Ceftriaxone	00004196502
RX-193	Ceftriaxone	00004196503
RX-193	Ceftriaxone	00004196505
RX-193	Ceftriaxone	00004197101
RX-193	Ceftriaxone	00004199578
RX-193	Ceftriaxone	00004199678
RX-193	Ceftriaxone	00004200278
RX-193	Ceftriaxone	00004200378
RX-193	Ceftriaxone	00004201392
RX-193	Ceftriaxone	00004201492
RX-193	Ceftriaxone	00069448003
RX-193	Ceftriaxone	00069448010
RX-193	Ceftriaxone	00069448103
RX-193	Ceftriaxone	00069448110
RX-193	Ceftriaxone	00069448203
RX-193	Ceftriaxone	00069448210
RX-193	Ceftriaxone	00069448303
RX-193	Ceftriaxone	00069448310

RX-193	Ceftriaxone	00143976801
RX-193	Ceftriaxone	00143985625
RX-193	Ceftriaxone	00143985725
RX-193	Ceftriaxone	00143985825
RX-193	Ceftriaxone	00143985925
RX-193	Ceftriaxone	00247033101
RX-193	Ceftriaxone	00247033110
RX-193	Ceftriaxone	00264315311
RX-193	Ceftriaxone	00264315511
RX-193	Ceftriaxone	00338500241
RX-193	Ceftriaxone	00338500341
RX-193	Ceftriaxone	00403185118
RX-193	Ceftriaxone	00403185318
RX-193	Ceftriaxone	00403185518
RX-193	Ceftriaxone	00403418118
RX-193	Ceftriaxone	00403419318
RX-193	Ceftriaxone	00409733201
RX-193	Ceftriaxone	00409733261
RX-193	Ceftriaxone	00409733304
RX-193	Ceftriaxone	00409733349
RX-193	Ceftriaxone	00409733410
RX-193	Ceftriaxone	00409733503
RX-193	Ceftriaxone	00409733561
RX-193	Ceftriaxone	00409733604
RX-193	Ceftriaxone	00409733649
RX-193	Ceftriaxone	00409733701
RX-193	Ceftriaxone	00409733801
RX-193	Ceftriaxone	00517871110
RX-193	Ceftriaxone	00517872210
RX-193	Ceftriaxone	00517872510
RX-193	Ceftriaxone	00517875010
RX-193	Ceftriaxone	00703031503
RX-193	Ceftriaxone	00703032503
RX-193	Ceftriaxone	00703033501
RX-193	Ceftriaxone	00703033504
RX-193	Ceftriaxone	00703034603
RX-193	Ceftriaxone	00703035901
RX-193	Ceftriaxone	00781320685
RX-193	Ceftriaxone	00781320695
RX-193	Ceftriaxone	00781320785
RX-193	Ceftriaxone	00781320795
RX-193	Ceftriaxone	00781320885
RX-193	Ceftriaxone	00781320895
RX-193	Ceftriaxone	00781320990
RX-193	Ceftriaxone	00781320995
RX-193	Ceftriaxone	00781321046
RX-193	Ceftriaxone	00781932695
RX-193	Ceftriaxone	00781932795
RX-193	Ceftriaxone	00781932885
RX-193	Ceftriaxone	00781932895
RX-193	Ceftriaxone	00781932990
RX-193	Ceftriaxone	00781932995
RX-193	Ceftriaxone	00781933046
RX-193	Ceftriaxone	10019009801
RX-193	Ceftriaxone	10019009871
RX-193	Ceftriaxone	10019068501
RX-193	Ceftriaxone	10019068571
RX-193	Ceftriaxone	10019068602

RX-193	Ceftriaxone	10019068671
RX-193	Ceftriaxone	10019068703
RX-193	Ceftriaxone	10019068771
RX-193	Ceftriaxone	10019068804
RX-193	Ceftriaxone	10019068827
RX-193	Ceftriaxone	10019068905
RX-193	Ceftriaxone	10019068911
RX-193	Ceftriaxone	12280007310
RX-193	Ceftriaxone	21695020210
RX-193	Ceftriaxone	21695035210
RX-193	Ceftriaxone	25021010410
RX-193	Ceftriaxone	25021010510
RX-193	Ceftriaxone	25021010610
RX-193	Ceftriaxone	25021010720
RX-193	Ceftriaxone	25021010899
RX-193	Ceftriaxone	35356026701
RX-193	Ceftriaxone	43063000210
RX-193	Ceftriaxone	49999058601
RX-193	Ceftriaxone	49999058610
RX-193	Ceftriaxone	54569137700
RX-193	Ceftriaxone	54569138600
RX-193	Ceftriaxone	54569180201
RX-193	Ceftriaxone	54569320700
RX-193	Ceftriaxone	54569347700
RX-193	Ceftriaxone	54569347800
RX-193	Ceftriaxone	54569347900
RX-193	Ceftriaxone	54569441500
RX-193	Ceftriaxone	54569572000
RX-193	Ceftriaxone	54569572100
RX-193	Ceftriaxone	54569572200
RX-193	Ceftriaxone	54569572300
RX-193	Ceftriaxone	54569572400
RX-193	Ceftriaxone	54569572500
RX-193	Ceftriaxone	54868093400
RX-193	Ceftriaxone	54868093401
RX-193	Ceftriaxone	54868248800
RX-193	Ceftriaxone	54868248801
RX-193	Ceftriaxone	54868322100
RX-193	Ceftriaxone	54868322101
RX-193	Ceftriaxone	54868553300
RX-193	Ceftriaxone	54868558900
RX-193	Ceftriaxone	55045350301
RX-193	Ceftriaxone	55045351101
RX-193	Ceftriaxone	55045351102
RX-193	Ceftriaxone	55045351601
RX-193	Ceftriaxone	55081106300
RX-193	Ceftriaxone	55081106400
RX-193	Ceftriaxone	55390030910
RX-193	Ceftriaxone	55390031010
RX-193	Ceftriaxone	55390031110
RX-193	Ceftriaxone	55390031210
RX-193	Ceftriaxone	55390031601
RX-193	Ceftriaxone	57866979701
RX-193	Ceftriaxone	58016478601
RX-193	Ceftriaxone	58016479001
RX-193	Ceftriaxone	58016483401
RX-193	Ceftriaxone	58016487301
RX-193	Ceftriaxone	58016943801

RX-193	Ceftriaxone	58016945301	
RX-193	Ceftriaxone	58016955101	
RX-193	Ceftriaxone	60505067905	
RX-193	Ceftriaxone	60505067908	
RX-193	Ceftriaxone	60505067909	
RX-193	Ceftriaxone	60505075000	
RX-193	Ceftriaxone	60505075004	
RX-193	Ceftriaxone	60505075100	
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RX-194	Trimethoprim-Sulfamethoxazole	58864047220
RX-194	Trimethoprim-Sulfamethoxazole	58864047806
RX-194	Trimethoprim-Sulfamethoxazole	58864047810
RX-194	Trimethoprim-Sulfamethoxazole	58864047814
RX-194	Trimethoprim-Sulfamethoxazole	58864047820
RX-194	Trimethoprim-Sulfamethoxazole	58864047830
RX-194	Trimethoprim-Sulfamethoxazole	59772013901
RX-194	Trimethoprim-Sulfamethoxazole	59772013902
RX-194	Trimethoprim-Sulfamethoxazole	59772017001
RX-194	Trimethoprim-Sulfamethoxazole	59772017010

RX-194	Trimethoprim-Sulfamethoxazole	59772017401
RX-194	Trimethoprim-Sulfamethoxazole	59772017402
RX-194	Trimethoprim-Sulfamethoxazole	59911586001
RX-194	Trimethoprim-Sulfamethoxazole	60346006734
RX-194	Trimethoprim-Sulfamethoxazole	60346006755
RX-194	Trimethoprim-Sulfamethoxazole	60346006771
RX-194	Trimethoprim-Sulfamethoxazole	60346008702
RX-194	Trimethoprim-Sulfamethoxazole	60346008703
RX-194	Trimethoprim-Sulfamethoxazole	60346008706
RX-194	Trimethoprim-Sulfamethoxazole	60346008708
RX-194	Trimethoprim-Sulfamethoxazole	60346008710
RX-194	Trimethoprim-Sulfamethoxazole	60346008714
RX-194	Trimethoprim-Sulfamethoxazole	60346008720
RX-194	Trimethoprim-Sulfamethoxazole	60346008725
RX-194	Trimethoprim-Sulfamethoxazole	60346008728
RX-194	Trimethoprim-Sulfamethoxazole	60346008730
RX-194	Trimethoprim-Sulfamethoxazole	60346008740
RX-194	Trimethoprim-Sulfamethoxazole	60346008744
RX-194	Trimethoprim-Sulfamethoxazole	60346008760
RX-194	Trimethoprim-Sulfamethoxazole	60346009704
RX-194	Trimethoprim-Sulfamethoxazole	60346009734
RX-194	Trimethoprim-Sulfamethoxazole	60346009755
RX-194	Trimethoprim-Sulfamethoxazole	60346009769
RX-194	Trimethoprim-Sulfamethoxazole	60346009771
RX-194	Trimethoprim-Sulfamethoxazole	60346009788
RX-194	Trimethoprim-Sulfamethoxazole	60346009789
RX-194	Trimethoprim-Sulfamethoxazole	60346055920
RX-194	Trimethoprim-Sulfamethoxazole	60346055928
RX-194	Trimethoprim-Sulfamethoxazole	60346055940
RX-194	Trimethoprim-Sulfamethoxazole	60364008714
RX-194	Trimethoprim-Sulfamethoxazole	60429017014
RX-194	Trimethoprim-Sulfamethoxazole	60429017020
RX-194	Trimethoprim-Sulfamethoxazole	60760006920
RX-194	Trimethoprim-Sulfamethoxazole	61392078230
RX-194	Trimethoprim-Sulfamethoxazole	61392078231
RX-194	Trimethoprim-Sulfamethoxazole	61392078232
RX-194	Trimethoprim-Sulfamethoxazole	61392078239
RX-194	Trimethoprim-Sulfamethoxazole	61392078245
RX-194	Trimethoprim-Sulfamethoxazole	61392078251
RX-194	Trimethoprim-Sulfamethoxazole	61392078254
RX-194	Trimethoprim-Sulfamethoxazole	61392078260
RX-194	Trimethoprim-Sulfamethoxazole	61392078290
RX-194	Trimethoprim-Sulfamethoxazole	61392078291
RX-194	Trimethoprim-Sulfamethoxazole	61392078330
RX-194	Trimethoprim-Sulfamethoxazole	61392078331
RX-194	Trimethoprim-Sulfamethoxazole	61392078332
RX-194	Trimethoprim-Sulfamethoxazole	61392078339
RX-194	Trimethoprim-Sulfamethoxazole	61392078345
RX-194	Trimethoprim-Sulfamethoxazole	61392078351
RX-194	Trimethoprim-Sulfamethoxazole	61392078354
RX-194	Trimethoprim-Sulfamethoxazole	61392078360
RX-194	Trimethoprim-Sulfamethoxazole	61392078390
RX-194	Trimethoprim-Sulfamethoxazole	61392078391
RX-194	Trimethoprim-Sulfamethoxazole	61570005011
RX-194	Trimethoprim-Sulfamethoxazole	61570005016
RX-194	Trimethoprim-Sulfamethoxazole	61570005116
RX-194	Trimethoprim-Sulfamethoxazole	61570005201
RX-194	Trimethoprim-Sulfamethoxazole	61570005301

RX-194	Trimethoprim-Sulfamethoxazole	61570005305
RX-194	Trimethoprim-Sulfamethoxazole	61570005320
RX-194	Trimethoprim-Sulfamethoxazole	61570005352
RX-194	Trimethoprim-Sulfamethoxazole	61570005410
RX-194	Trimethoprim-Sulfamethoxazole	61570005510
RX-194	Trimethoprim-Sulfamethoxazole	61570005610
RX-194	Trimethoprim-Sulfamethoxazole	61579005305
RX-194	Trimethoprim-Sulfamethoxazole	61808032005
RX-194	Trimethoprim-Sulfamethoxazole	62584085601
RX-194	Trimethoprim-Sulfamethoxazole	62584085701
RX-194	Trimethoprim-Sulfamethoxazole	62584085733
RX-194	Trimethoprim-Sulfamethoxazole	63629149001
RX-194	Trimethoprim-Sulfamethoxazole	63629149002
RX-194	Trimethoprim-Sulfamethoxazole	63629149003
RX-194	Trimethoprim-Sulfamethoxazole	63629149004
RX-194	Trimethoprim-Sulfamethoxazole	63629176501
RX-194	Trimethoprim-Sulfamethoxazole	63629176502
RX-194	Trimethoprim-Sulfamethoxazole	63629176503
RX-194	Trimethoprim-Sulfamethoxazole	63629176504
RX-194	Trimethoprim-Sulfamethoxazole	63629176505
RX-194	Trimethoprim-Sulfamethoxazole	63629176506
RX-194	Trimethoprim-Sulfamethoxazole	63629176507
RX-194	Trimethoprim-Sulfamethoxazole	63739022801
RX-194	Trimethoprim-Sulfamethoxazole	63739022802
RX-194	Trimethoprim-Sulfamethoxazole	63739022803
RX-194	Trimethoprim-Sulfamethoxazole	63739022810
RX-194	Trimethoprim-Sulfamethoxazole	63874011801
RX-194	Trimethoprim-Sulfamethoxazole	63874011803
RX-194	Trimethoprim-Sulfamethoxazole	63874011806
RX-194	Trimethoprim-Sulfamethoxazole	63874011807
RX-194	Trimethoprim-Sulfamethoxazole	63874011810
RX-194	Trimethoprim-Sulfamethoxazole	63874011812
RX-194	Trimethoprim-Sulfamethoxazole	63874011814
RX-194	Trimethoprim-Sulfamethoxazole	63874011815
RX-194	Trimethoprim-Sulfamethoxazole	63874011818
RX-194	Trimethoprim-Sulfamethoxazole	63874011820
RX-194	Trimethoprim-Sulfamethoxazole	63874011821
RX-194	Trimethoprim-Sulfamethoxazole	63874011824
RX-194	Trimethoprim-Sulfamethoxazole	63874011828
RX-194	Trimethoprim-Sulfamethoxazole	63874011830
RX-194	Trimethoprim-Sulfamethoxazole	63874011840
RX-194	Trimethoprim-Sulfamethoxazole	63874011850
RX-194	Trimethoprim-Sulfamethoxazole	63874011860
RX-194	Trimethoprim-Sulfamethoxazole	63874015010
RX-194	Trimethoprim-Sulfamethoxazole	63874015020
RX-194	Trimethoprim-Sulfamethoxazole	64248000410
RX-194	Trimethoprim-Sulfamethoxazole	64248011710
RX-194	Trimethoprim-Sulfamethoxazole	65162020201
RX-194	Trimethoprim-Sulfamethoxazole	65162020202
RX-194	Trimethoprim-Sulfamethoxazole	65162020208
RX-194	Trimethoprim-Sulfamethoxazole	65162020214
RX-194	Trimethoprim-Sulfamethoxazole	65162027110
RX-194	Trimethoprim-Sulfamethoxazole	65162027150
RX-194	Trimethoprim-Sulfamethoxazole	65162027210
RX-194	Trimethoprim-Sulfamethoxazole	65162027250
RX-194	Trimethoprim-Sulfamethoxazole	65162031301
RX-194	Trimethoprim-Sulfamethoxazole	65162031302
RX-194	Trimethoprim-Sulfamethoxazole	65162031308

RX-194 Trimethoprim-Sulfamethoxazole	65162031314
RX-194 Trimethoprim-Sulfamethoxazole	66116022110
RX-194 Trimethoprim-Sulfamethoxazole	66116022114
RX-194 Trimethoprim-Sulfamethoxazole	66116022120
RX-194 Trimethoprim-Sulfamethoxazole	66116022128
RX-194 Trimethoprim-Sulfamethoxazole	66116060314
RX-194 Trimethoprim-Sulfamethoxazole	66116063620
RX-194 Trimethoprim-Sulfamethoxazole	66116063710
RX-194 Trimethoprim-Sulfamethoxazole	66267019606
RX-194 Trimethoprim-Sulfamethoxazole	66267019610
RX-194 Trimethoprim-Sulfamethoxazole	66267019614
RX-194 Trimethoprim-Sulfamethoxazole	66267019620
RX-194 Trimethoprim-Sulfamethoxazole	66267019628
RX-194 Trimethoprim-Sulfamethoxazole	66267019660
RX-194 Trimethoprim-Sulfamethoxazole	66267093900
RX-194 Trimethoprim-Sulfamethoxazole	66336008706
RX-194 Trimethoprim-Sulfamethoxazole	66336008710
RX-194 Trimethoprim-Sulfamethoxazole	66336008714
RX-194 Trimethoprim-Sulfamethoxazole	66336008720
RX-194 Trimethoprim-Sulfamethoxazole	66336008740
RX-194 Trimethoprim-Sulfamethoxazole	66336008760
RX-194 Trimethoprim-Sulfamethoxazole	66689001850
RX-194 Trimethoprim-Sulfamethoxazole	67046071530
RX-194 Trimethoprim-Sulfamethoxazole	68030010901
RX-194 Trimethoprim-Sulfamethoxazole	68030010902
RX-194 Trimethoprim-Sulfamethoxazole	68030469302
RX-194 Trimethoprim-Sulfamethoxazole	68030469304
RX-194 Trimethoprim-Sulfamethoxazole	68084023001
RX-194 Trimethoprim-Sulfamethoxazole	68084023011
RX-194 Trimethoprim-Sulfamethoxazole	68115032200
RX-194 Trimethoprim-Sulfamethoxazole	68115032206
RX-194 Trimethoprim-Sulfamethoxazole	68115032214
RX-194 Trimethoprim-Sulfamethoxazole	68115032220
RX-194 Trimethoprim-Sulfamethoxazole	68115032228
RX-194 Trimethoprim-Sulfamethoxazole	68115032240
RX-194 Trimethoprim-Sulfamethoxazole	68258102301
RX-194 Trimethoprim-Sulfamethoxazole	68258901601
RX-194 Trimethoprim-Sulfamethoxazole	68387038520
RX-194 Trimethoprim-Sulfamethoxazole	68387038530
RX-194 Trimethoprim-Sulfamethoxazole	68387038560

2a.4 Denominator Statement (Brief, text description of the denominator - target population being measured):

Patients who are 3 years of age or older at the end of the report period who are diagnosed with sinusitis and who are treated with an antibiotic

2a.5 Target population gender: Female, Male

2a.6 Target population age range: Patients 3 years of age or older at the end of the report period

2a.7 Denominator Time Window (The time period in which cases are eligible for inclusion in the denominator):

The following time period will be used to find eligible sinusitis events: 60 days after the start of the 12-month report period through 21 days prior to the end of the 12-month report period. The following time period will be used to ascertain whether the patient is taking an antibiotic: ten days prior to the initiating acute sinusitis encounter through 21 days after the initiating acute sinusitis encounter

2a.8 Denominator Details (All information required to collect/calculate the denominator - the target population being measured - including all codes, logic, and definitions):

Criteria for inclusion in the denominator are as follows:

1. All males or females that are 3 years of age or older at the end of the report period
2. Build an event with a claim during the following window of time: 60 days after the start of the 12-month report period through 21 days prior to the end of the 12-month report period, where the diagnosis is acute sinusitis (code set DX0167) and the procedure on the claim is one of the following:

Ambulatory visit (code set PR0111, RV0111)

Facility Event – emergency room

The sinusitis event will encompass the following period of time: 60 days prior to the initiating sinusitis encounter through 21 days after that encounter. EBM Connect® allows multiple sinusitis events within the time period defined in the “denominator time window” section if denominator requirements are met for all events.

3. The patient must be continuously enrolled in both medical and pharmacy benefits throughout the acute sinusitis event. The event is defined as 60 days prior to the initiating sinusitis encounter through 21 days after that encounter. The standard EBM Connect® enrollment break logic allows unlimited breaks in coverage of no more than 45 days and no breaks greater than 45 days.

Code Set	Code Set Description	DX Code	Diagnosis Code Description
DX0167	Acute sinusitis 461	ACUTE SINUSITIS	
DX0167	Acute sinusitis 461.0	ACUTE MAXILLARY SINUSITIS	
DX0167	Acute sinusitis 461.1	ACUTE FRONTAL SINUSITIS	
DX0167	Acute sinusitis 461.2	ACUTE ETHMOIDAL SINUSITIS	
DX0167	Acute sinusitis 461.3	ACUTE SPHENOIDAL SINUSITIS	
DX0167	Acute sinusitis 461.8	OTHER ACUTE SINUSITIS	
DX0167	Acute sinusitis 461.9	ACUTE SINUSITIS, UNSPECIFIED	

Code Set	Code Set Description	Procedure Code
PR0111	Ambulatory visit codes 99201	
PR0111	Ambulatory visit codes 99202	
PR0111	Ambulatory visit codes 99203	
PR0111	Ambulatory visit codes 99204	
PR0111	Ambulatory visit codes 99205	
PR0111	Ambulatory visit codes 99211	
PR0111	Ambulatory visit codes 99212	
PR0111	Ambulatory visit codes 99213	
PR0111	Ambulatory visit codes 99214	
PR0111	Ambulatory visit codes 99215	
PR0111	Ambulatory visit codes 99241	
PR0111	Ambulatory visit codes 99242	
PR0111	Ambulatory visit codes 99243	
PR0111	Ambulatory visit codes 99244	
PR0111	Ambulatory visit codes 99245	
PR0111	Ambulatory visit codes 99271	
PR0111	Ambulatory visit codes 99272	
PR0111	Ambulatory visit codes 99273	
PR0111	Ambulatory visit codes 99274	
PR0111	Ambulatory visit codes 99275	
PR0111	Ambulatory visit codes 99341	
PR0111	Ambulatory visit codes 99342	
PR0111	Ambulatory visit codes 99343	
PR0111	Ambulatory visit codes 99344	
PR0111	Ambulatory visit codes 99345	
PR0111	Ambulatory visit codes 99347	
PR0111	Ambulatory visit codes 99348	
PR0111	Ambulatory visit codes 99349	
PR0111	Ambulatory visit codes 99350	
PR0111	Ambulatory visit codes 99381	
PR0111	Ambulatory visit codes 99382	
PR0111	Ambulatory visit codes 99383	

PR0111 Ambulatory visit codes99384
 PR0111 Ambulatory visit codes99385
 PR0111 Ambulatory visit codes99386
 PR0111 Ambulatory visit codes99387
 PR0111 Ambulatory visit codes99391
 PR0111 Ambulatory visit codes99392
 PR0111 Ambulatory visit codes99393
 PR0111 Ambulatory visit codes99394
 PR0111 Ambulatory visit codes99395
 PR0111 Ambulatory visit codes99396
 PR0111 Ambulatory visit codes99397
 PR0111 Ambulatory visit codes99401
 PR0111 Ambulatory visit codes99402
 PR0111 Ambulatory visit codes99403
 PR0111 Ambulatory visit codes99404
 PR0111 Ambulatory visit codes99411
 PR0111 Ambulatory visit codes99412
 PR0111 Ambulatory visit codes99420
 PR0111 Ambulatory visit codes99429

Code Set	Code Set Description	Revenue Code
RV0111	Ambulatory visit codes	0983

2a.9 Denominator Exclusions (Brief text description of exclusions from the target population): 1. Exclude acute sinusitis events without a preceding disease-free window
 2. Exclude acute sinusitis events with hospitalizations or outpatient surgeries during the event
 3. Exclude patients with recent organ transplant
 4. Exclude additional complex patients who have histories of immunodeficiencies, cystic fibrosis, leukemia, chronic sinusitis, malignant neoplasm of ear/nose/throat, or congenital & acquired anomalies of ear/nose/throat
 5. Exclude patients who had concomitant infections during the sinusitis event
 6. Exclude patients who had recent antibiotic use
 7. Exclude patients who did not fill a prescription for an antibiotic during the acute sinusitis event

2a.10 Denominator Exclusion Details (All information required to collect exclusions to the denominator, including all codes, logic, and definitions):

1. Exclude the event if, during the following time period: 60 days prior to the initiating sinusitis encounter through the day prior to the initiating sinusitis encounter, there is a claim with a diagnosis of acute sinusitis (code set DX0167) and the procedure on the claim is also one of the following:
 - Professional Encounter code set (PR0107 or RV0107)
 - Professional Supervision code set (PR0108)
 - Facility Event – Confinement/Admission (i.e., hospital admission)
 - Facility Event – Emergency Room
 - Facility Event – Outpatient Surgery
2. Exclude the event if either of the following occurred (for any diagnosis) during the acute sinusitis event (defined as 60 days prior to the initiating sinusitis encounter through 21 days after that encounter): facility event – outpatient surgery or facility event – confinement/admission (i.e., hospitalization)
3. Exclude the patient if, during the following window of time: 12-month report period, there is a claim where the diagnosis is organ transplant (code set DX0111) and the procedure on the claim is one of the following:
 - Professional Encounter code set (PR0107 or RV0107)
 - Professional Supervision code set (PR0108)
 - Facility Event – Confinement/Admission (i.e., hospital admission)
 - Facility Event – Emergency Room
 - Facility Event – Outpatient Surgery
4. Exclude patients that had any of the following diagnoses at any time within the available data:
 - Immunodeficiencies (code set 130800000)
 - Cystic fibrosis (code set 165200000)

Comment [k9]: 11 Risk factors that influence outcomes should not be specified as exclusions.
 12 Patient preference is not a clinical exception to eligibility and can be influenced by provider interventions.

Leukemia (code set 207200000)
 Chronic sinusitis (code set 403500000)
 Malignant neoplasm of ear/nose/throat (code set 404300000)
 Congenital & acquired anomalies of ear/nose/throat (code set 404700000)

5. Exclude patients who, during the following time period: 21 days prior to the initiating encounter through 21 days after the initiating encounter, had a claim where the diagnosis is acute pharyngitis, tonsillitis, and adenoiditis (code set DX0166), bronchitis and bronchiectasis (code set DX 0169), other ENT infections (code set DX0177), otitis media (code set DX0178), or pneumonia (code set DX0180) where the procedure on the claim was one of the following:

- Professional Encounter code set (PR0107 or RV0107)
- Professional Supervision code set (PR0108)
- Facility Event – Confinement/Admission (i.e., hospital admission)
- Facility Event – Emergency Room
- Facility Event – Outpatient Surgery

6. Exclude patients who, during the following time period: 60 days prior to the initiating encounter through 11 days prior to the initiating encounter, filled a prescription for any antibiotic (code set RX-184)

7. Exclude patients who, did NOT fill a prescription for any antibiotic (code set RX-184) during the acute sinusitis event (10 days prior to the initiating acute sinusitis encounter through 21 days after the initiating acute sinusitis encounter)

Cd. Set	Code Set Description	DX Code	Diagnosis Code Description
DX0111	Organ transplant status 414.06	COR	ATHEROSLERO COR ART TRANSPLNTD HEART
DX0111	Organ transplant status 414.07	COR	ATHEROSLERO BYPS GRFT TRANSPLNTD HRT
DX0111	Organ transplant status V42	ORGAN OR TISSUE	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.0	KIDNEY	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.1	HEART	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.2	HEART VALVE	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.3	SKIN	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.4	BONE	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.5	CORNEA	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.6	LUNG	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.7	LIVER	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.8	OTH SPEC ORGAN/	TISSUE REPLACED TRANSPLNT
DX0111	Organ transplant status V42.81	BONE MARROW	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.82	PERIPHERL STEM CELLS	REPLCD BY TRANSPLNT
DX0111	Organ transplant status V42.83	PANCREAS	REPLACED BY TRANSPLANT
DX0111	Organ transplant status V42.84	ORGAN OR TISS REPLCD	TRNSPLNT INTESTINES
DX0111	Organ transplant status V42.89	OTH ORGAN OR TISSUE	REPLACED BY TRNSPLNT
DX0111	Organ transplant status V42.9	UNSPEC ORG OR TISS	RPLCD TRNSPLNT

Cd. St	Code Set Description	DX Cd	DX Code Description
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 034	STREP	SORE THROAT/SCAR FVR
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 034.0	STREPTOCOCCAL	SORE THROAT
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 460	ACUTE	NASOPHARYNGITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 462	ACUTE	PHARYNGITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 463	ACUTE	TONSILLITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464	ACU	LARYNGITIS& TRACHEITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.0	ACUTE	LARYNGITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.00	ACU	LYRNG W/O MENT OBSTRCT
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.01	ACU	LYRNGTIS W OBSTRUCTION
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.1	ACUTE	TRACHEITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.10	ACU	TRCHTIS W/O MENT OBSTR
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.11	ACU	TRCHTIS W OBSTRUCTION
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.2	ACUTE	LARYNGOTRACHEITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.20	AC	LRNGTRCHTS W/O MNT OBST
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.21	AC	LRNGOTRCHTIS W OBSTRUCT
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.3	ACUTE	EPIGLOTTITIS
DX0166	Acute pharyngitis/ tonsillitis/adenoiditis 464.30	AC	EPGLOTTIS W/O MENT OBSTR

DX0166 Acut pharyngitis/ tonsillitis/adenoiditis 464.31AC EPIGLTIS W OBSTRUCTION
 DX0166 Acut pharyngitis/ tonsillitis/adenoiditis 464.4 CROUP
 DX0166 Acut pharyngitis/ tonsillitis/adenoiditis 464.5 SUPRAGLOTTITIS UNSPECIFIED
 DX0166 Acut pharyngitis/ tonsillitis/adenoiditis 464.50UNSP SPRGLTTS W/O MNT OBST
 DX0166 Acut pharyngitis/ tonsillitis/adenoiditis 464.51UNSPEC SPRGLTTS W OBSTRUCT
 DX0166 Acut pharyngitis/ tonsillitis/adenoiditis 465.0 ACUTE LARYNGOPHARYNGITIS

Code Set	Code Set Description	Diagnosis Code	Diagnosis Code Description
DX0167	Acute sinusitis 461		ACUTE SINUSITIS
DX0167	Acute sinusitis 461.0		ACUTE MAXILLARY SINUSITIS
DX0167	Acute sinusitis 461.1		ACUTE FRONTAL SINUSITIS
DX0167	Acute sinusitis 461.2		ACUTE ETHMOIDAL SINUSITIS
DX0167	Acute sinusitis 461.3		ACUTE SPHENOIDAL SINUSITIS
DX0167	Acute sinusitis 461.8		OTHER ACUTE SINUSITIS
DX0167	Acute sinusitis 461.9		ACUTE SINUSITIS, UNSPECIFIED

Cd. Set	Code Set Description	DX Code	Diagnosis Code Description
DX0169	Bronchitis/bronchiectasis 466		ACUTE BRONCHITIS & BRONCHIOLITIS
DX0169	Bronchitis/bronchiectasis 466.0		ACUTE BRONCHITIS
DX0169	Bronchitis/bronchiectasis 466.1		ACUTE BRONCHIOLITIS
DX0169	Bronchitis/bronchiectasis 466.11		ACUTE BRONCHIOLITIS DUE TO RSV
DX0169	Bronchitis/bronchiectasis 466.19		ACU BRONCHIOLITIS D/T INFECTS ORGNMS
DX0169	Bronchitis/bronchiectasis 490		BRONCHITIS NOT SPEC AS ACUTE OR CHRON
DX0169	Bronchitis/bronchiectasis 491		CHRONIC BRONCHITIS
DX0169	Bronchitis/bronchiectasis 491.0		SIMPLE CHRONIC BRONCHITIS
DX0169	Bronchitis/bronchiectasis 491.1		MUCOPURULENT CHRONIC BRONCHITIS
DX0169	Bronchitis/bronchiectasis 491.2		OBSTRUCTIVE CHRONIC BRONCHITIS
DX0169	Bronchitis/bronchiectasis 491.20		OBSTRCTV CHRON BRONCHITIS W/O EXACERBT
DX0169	Bronchitis/bronchiectasis 491.21		OBSTRCTV CHRON BRONCHITIS W EXACERBATN
DX0169	Bronchitis/bronchiectasis 491.22		OBST CHRONIC BRONCHITIS W/ACUTE BRONCH
DX0169	Bronchitis/bronchiectasis 491.8		OTHER CHRONIC BRONCHITIS
DX0169	Bronchitis/bronchiectasis 491.9		UNSPECIFIED CHRONIC BRONCHITIS
DX0169	Bronchitis/bronchiectasis 494		BRONCHIECTASIS
DX0169	Bronchitis/bronchiectasis 494.0		BRONCHIECTASIS W/O ACUTE EXACERBATION
DX0169	Bronchitis/bronchiectasis 494.1		BRONCHIECTASIS WITH ACUTE EXACERBATION

Cd. Set	Code Set Description	Dx Code	Diagnosis Code Description
DX0177	Other ENT infections	053.71	OTITIS EXTERNA DUE TO HERPES ZOSTER
DX0177	Other ENT infections	054.2	HERPETIC GINGIVOSTOMATITIS
DX0177	Other ENT infections	054.73	HERPES SIMPLEX OTITIS EXTERNA
DX0177	Other ENT infections	055	MEASLES
DX0177	Other ENT infections	055.2	POSTMEASLES OTITIS MEDIA
DX0177	Other ENT infections	055.8	UNSPECIFIED MEASLES COMPLICATION
DX0177	Other ENT infections	056	RUBELLA
DX0177	Other ENT infections	056.8	UNSPECIFIED RUBELLA COMPLICATIONS
DX0177	Other ENT infections	077.2	PHARYNGOCONJUNCTIVAL FEVER
DX0177	Other ENT infections	101	VINCENTS ANGINA
DX0177	Other ENT infections	112.0	CANDIDIASIS OF MOUTH
DX0177	Other ENT infections	112.82	CANDIDAL OTITIS EXTERNA
DX0177	Other ENT infections	380.0	PERICHONDritis AND CHONDritis OF PINNA
DX0177	Other ENT infections	380.00	UNSPECIFIED PERICHONDritis OF PINNA
DX0177	Other ENT infections	380.01	ACUTE PERICHONDritis OF PINNA
DX0177	Other ENT infections	380.02	CHRONIC PERICHONDritis OF PINNA
DX0177	Other ENT infections	380.03	CHONDritis OF PINNA
DX0177	Other ENT infections	380.1	INFECTIVE OTITIS EXTERNA
DX0177	Other ENT infections	380.10	UNSPECIFIED INFECTIVE OTITIS EXTERNA
DX0177	Other ENT infections	380.11	ACUTE INFECTION OF PINNA
DX0177	Other ENT infections	380.12	ACUTE SWIMMERS EAR

DX0177 Other ENT infections	380.13	OTHER ACUTE INFECTIONS OF EXTERNAL EAR
DX0177 Other ENT infections	380.14	MALIGNANT OTITIS EXTERNA
DX0177 Other ENT infections	380.15	CHRONIC MYCOTIC OTITIS EXTERNA
DX0177 Other ENT infections	380.16	OTHER CHRONIC INFECTIVE OTITIS EXTERNA
DX0177 Other ENT infections	380.2	OTHER OTITIS EXTERNA
DX0177 Other ENT infections	380.21	CHOLESTEATOMA OF EXTERNAL EAR
DX0177 Other ENT infections	380.22	OTHER ACUTE OTITIS EXTERNA
DX0177 Other ENT infections	380.23	OTHER CHRONIC OTITIS EXTERNA
DX0177 Other ENT infections	383	MASTOIDITIS AND RELATED CONDITIONS
DX0177 Other ENT infections	383.0	ACUTE MASTOIDITIS
DX0177 Other ENT infections	383.00	ACUTE MASTOIDITIS WITHOUT COMPLICATIONS
DX0177 Other ENT infections	383.01	SUBPERIOSTEAL ABSCESS OF MASTOID
DX0177 Other ENT infections	383.02	ACUTE MASTOIDITIS WITH OTH COMPLICATIONS
DX0177 Other ENT infections	383.1	CHRONIC MASTOIDITIS
DX0177 Other ENT infections	383.2	PETROSITIS
DX0177 Other ENT infections	383.20	UNSPECIFIED PETROSITIS
DX0177 Other ENT infections	383.21	ACUTE PETROSITIS
DX0177 Other ENT infections	383.22	CHRONIC PETROSITIS
DX0177 Other ENT infections	383.3	COMPLICATIONS FOLLOWING MASTOIDECTOMY
DX0177 Other ENT infections	383.30	UNSPEC POSTMASTOIDECTOMY COMPLICATION
DX0177 Other ENT infections	383.31	MUCOSAL CYST OF POSTMASTOIDECTOMY CAVITY
DX0177 Other ENT infections	383.32	RECRNT CHOLESTEATOMA PSTMASTOIDECT CAVT
DX0177 Other ENT infections	383.33	GRANULATIONS OF POSTMASTOIDECTOMY CAVITY
DX0177 Other ENT infections	383.8	OTHER DISORDERS OF MASTOID
DX0177 Other ENT infections	383.81	POSTAURICULAR FISTULA
DX0177 Other ENT infections	383.89	OTHER DISORDER OF MASTOID
DX0177 Other ENT infections	383.9	UNSPECIFIED MASTOIDITIS
DX0177 Other ENT infections	385.3	CHOLESTEATOMA OF MIDDLE EAR AND MASTOID
DX0177 Other ENT infections	385.30	UNSPECIFIED CHOLESTEATOMA
DX0177 Other ENT infections	385.31	CHOLESTEATOMA OF ATTIC
DX0177 Other ENT infections	385.32	CHOLESTEATOMA OF MIDDLE EAR
DX0177 Other ENT infections	385.33	CHOLESTEATOMA OF MIDDLE EAR AND MASTOID
DX0177 Other ENT infections	385.35	DIFFUSE CHOLESTEATOSIS OF MDL EAR& MASTD
DX0177 Other ENT infections	386.33	SUPPURATIVE LABYRINTHITIS
DX0177 Other ENT infections	386.35	VIRAL LABYRINTHITIS
DX0177 Other ENT infections	388.6	OTORRHEA
DX0177 Other ENT infections	388.60	UNSPECIFIED OTORRHEA
DX0177 Other ENT infections	388.69	OTHER OTORRHEA
DX0177 Other ENT infections	478	OTH DISEASES OF UPPER RESPIRATORY TRACT
DX0177 Other ENT infections	478.8	UPP RESP TRACT HYPERSNS REACT SITE UNSPC
DX0177 Other ENT infections	478.9	OTH&UNSPC DISEASES UPP RESPIRATORY TRACT
DX0177 Other ENT infections	526.5	ALVEOLITIS OF JAW
DX0177 Other ENT infections	527	DISEASES OF THE SALIVARY GLANDS
DX0177 Other ENT infections	527.2	SIALOADENITIS
DX0177 Other ENT infections	527.3	ABSCESS OF SALIVARY GLAND
DX0177 Other ENT infections	527.4	FISTULA OF SALIVARY GLAND
DX0177 Other ENT infections	527.5	SIALOLITHIASIS
DX0177 Other ENT infections	527.6	MUCOCELE OF SALIVARY GLAND
DX0177 Other ENT infections	527.7	DISTURBANCE OF SALIVARY SECRETION
DX0177 Other ENT infections	527.8	OTHER SPEC DISEASES OF SALIVARY GLANDS
DX0177 Other ENT infections	527.9	UNSPEC DISEASE OF THE SALIVARY GLANDS
DX0177 Other ENT infections	528.5	DISEASES OF LIPS
DX0177 Other ENT infections	528.7	OTH DISTURB ORAL EPITHELM INCLUD TONGUE
DX0177 Other ENT infections	528.71	MINML KERATINIZED RESIDUAL RIDGE MUCOSA
DX0177 Other ENT infections	528.72	EXCSSV KERATINIZED RESIDUAL RIDGE MUCOSA
DX0177 Other ENT infections	528.79	OTH DISTRB ORAL EPITHELIUM INCLUD TONGUE
DX0177 Other ENT infections	683	ACUTE LYMPHADENITIS

Cd. Set Cd. Set Descrp	Dx Code	Diagnosis Code Description
DX0178 Otitis media	381	NONSUPPURATIVE OTITIS MEDIA&EUSTACHIAN TUBE D/O
DX0178 Otitis media	381.0	ACUTE NONSUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	381.00	UNSPECIFIED ACUTE NONSUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	381.01	ACUTE SEROUS OTITIS MEDIA
DX0178 Otitis media	381.02	ACUTE MUCOID OTITIS MEDIA
DX0178 Otitis media	381.03	ACUTE SANGUINOUS OTITIS MEDIA
DX0178 Otitis media	381.04	ACUTE ALLERGIC SEROUS OTITIS MEDIA
DX0178 Otitis media	381.05	ACUTE ALLERGIC MUCOID OTITIS MEDIA
DX0178 Otitis media	381.06	ACUTE ALLERGIC SANGUINOUS OTITIS MEDIA
DX0178 Otitis media	381.1	CHRONIC SEROUS OTITIS MEDIA
DX0178 Otitis media	381.10	SIMPLE/UNSPECIFIED CHRONIC SEROUS OTITIS MEDIA
DX0178 Otitis media	381.19	OTHER CHRONIC SEROUS OTITIS MEDIA
DX0178 Otitis media	381.2	CHRONIC MUCOID OTITIS MEDIA
DX0178 Otitis media	381.20	SIMPLE/UNSPECIFIED CHRONIC MUCOID OTITIS MEDIA
DX0178 Otitis media	381.29	OTHER CHRONIC MUCOID OTITIS MEDIA
DX0178 Otitis media	381.3	OTHER&UNSPEC CHRONIC NONSUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	381.4	NONSUPPRATV OTITIS MEDIA NOT SPEC AS ACUT/CHRON
DX0178 Otitis media	381.5	EUSTACHIAN SALPINGITIS
DX0178 Otitis media	381.50	UNSPECIFIED EUSTACHIAN SALPINGITIS
DX0178 Otitis media	381.51	ACUTE EUSTACHIAN SALPINGITIS
DX0178 Otitis media	381.52	CHRONIC EUSTACHIAN SALPINGITIS
DX0178 Otitis media	381.6	OBSTRUCTION OF EUSTACHIAN TUBE
DX0178 Otitis media	381.60	UNSPECIFIED OBSTRUCTION OF EUSTACHIAN TUBE
DX0178 Otitis media	381.61	OSSEOUS OBSTRUCTION OF EUSTACHIAN TUBE
DX0178 Otitis media	381.62	INTRINSIC CARTNOUS OBSTRUCTION EUSTACHIAN TUBE
DX0178 Otitis media	381.63	EXTRINSIC CARTNOUS OBSTRUCTION EUSTACHIAN TUBE
DX0178 Otitis media	381.7	PATULOUS EUSTACHIAN TUBE
DX0178 Otitis media	381.8	OTHER DISORDERS OF EUSTACHIAN TUBE
DX0178 Otitis media	381.81	DYSFUNCTION OF EUSTACHIAN TUBE
DX0178 Otitis media	381.89	OTHER DISORDERS OF EUSTACHIAN TUBE
DX0178 Otitis media	381.9	UNSPECIFIED EUSTACHIAN TUBE DISORDER
DX0178 Otitis media	382	SUPPURATIVE AND UNSPECIFIED OTITIS MEDIA
DX0178 Otitis media	382.0	ACUTE SUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	382.00	ACUT SUPPRATV OTITIS MEDIA W/O SPONT RUP EARDRUM
DX0178 Otitis media	382.01	ACUT SUPPRATV OTITIS MEDIA W/SPONT RUP EARDRUM
DX0178 Otitis media	382.02	ACUTE SUPPURATIVE OTITIS MEDIA DZ CLASS ELSW
DX0178 Otitis media	382.1	CHRONIC TUBOTYMPANIC SUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	382.2	CHRONIC ATTICOANTRAL SUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	382.3	UNSPECIFIED CHRONIC SUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	382.4	UNSPECIFIED SUPPURATIVE OTITIS MEDIA
DX0178 Otitis media	382.9	UNSPECIFIED OTITIS MEDIA
DX0178 Otitis media	384.0	ACUTE MYRINGITIS WITHOUT MENTION OF OTITIS MEDIA
DX0178 Otitis media	384.00	UNSPECIFIED ACUTE MYRINGITIS
DX0178 Otitis media	384.01	BULLOUS MYRINGITIS
DX0178 Otitis media	384.09	OTH ACUTE MYRINGITIS W/O MENTION OTITIS MEDIA
DX0178 Otitis media	384.1	CHRONIC MYRINGITIS WITHOUT MENTION OTITIS MEDIA

Cd. Set Cd. Set Descrp	Dx Code	Diagnosis Code Description
DX0180 Pneumonia	006.4	AMEBIC LUNG ABSCESS
DX0180 Pneumonia	039.1	PULMONARY ACTINOMYCOTIC INFECTION
DX0180 Pneumonia	041.2	PNEUMOCOCCUS INFECTION IN CCE & UNS SITE
DX0180 Pneumonia	079.6	RESPIRATORY SYNCYTIAL VIRUS
DX0180 Pneumonia	112.4	CANDIDIASIS OF LUNG
DX0180 Pneumonia	114	COCCIDIOIDOMYCOSIS
DX0180 Pneumonia	114.0	PRIMARY COCCIDIOIDOMYCOSIS
DX0180 Pneumonia	114.4	CHRONIC PULMONARY COCCIDIOIDOMYCOSIS
DX0180 Pneumonia	114.5	UNSPECIFIED PULMONARY COCCIDIOIDOMYCOSIS

DX0180 Pneumonia	114.9	UNSPECIFIED COCCIDIOIDOMYCOSIS
DX0180 Pneumonia	115	HISTOPLASMOSIS
DX0180 Pneumonia	115.0	HISTOPLASMA CAPSULATUM
DX0180 Pneumonia	115.00	HISTOPLASMA CAPSULATUM WITHOUT MENTION MANIFEST
DX0180 Pneumonia	115.05	HISTOPLASMA CAPSULATUM PNEUMONIA
DX0180 Pneumonia	115.09	HISTOPLASMA CAPSULATUM W/MENTION OTH MANIFEST
DX0180 Pneumonia	115.1	HISTOPLASMA DUBOISII
DX0180 Pneumonia	115.10	HISTOPLASMA DUBOISII WITHOUT MENTION MANIFEST
DX0180 Pneumonia	115.13	HISTOPLASMA DUBOISII PERICARDITIS
DX0180 Pneumonia	115.14	HISTOPLASMA DUBOISII ENDOCARDITIS
DX0180 Pneumonia	115.15	HISTOPLASMA DUBOISII PNEUMONIA
DX0180 Pneumonia	115.19	HISTOPLASMA DUBOISII W/MENTION OTH MANIFESTATION
DX0180 Pneumonia	115.9	UNSPECIFIED HISTOPLASMOSIS
DX0180 Pneumonia	115.90	UNSPEC HISTOPLASMOSIS WITHOUT MENTION MANIFEST
DX0180 Pneumonia	115.93	UNSPECIFIED HISTOPLASMOSIS PERICARDITIS
DX0180 Pneumonia	115.94	UNSPECIFIED HISTOPLASMOSIS ENDOCARDITIS
DX0180 Pneumonia	115.95	UNSPECIFIED HISTOPLASMOSIS PNEUMONIA
DX0180 Pneumonia	115.99	UNSPEC HISTOPLASMOSIS W/MENTION OTH MANIFEST
DX0180 Pneumonia	116	BLASTOMYCOTIC INFECTION
DX0180 Pneumonia	116.0	BLASTOMYCOSIS
DX0180 Pneumonia	116.1	PARACOCCIDIOIDOMYCOSIS
DX0180 Pneumonia	116.2	LOBOMYCOSIS
DX0180 Pneumonia	117.3	ASPERGILLOSIS
DX0180 Pneumonia	130.4	PNEUMONITIS DUE TO TOXOPLASMOSIS
DX0180 Pneumonia	136.3	PNEUMOCYSTOSIS
DX0180 Pneumonia	480	VIRAL PNEUMONIA
DX0180 Pneumonia	480.0	PNEUMONIA DUE TO ADENOVIRUS
DX0180 Pneumonia	480.1	PNEUMONIA DUE TO RESPIRATORY SYNCYTIAL VIRUS
DX0180 Pneumonia	480.2	PNEUMONIA DUE TO PARAINFLUENZA VIRUS
DX0180 Pneumonia	480.3	PNEUMONIA DUE TO SARS-ASSOCIATED CORONAVIRUS
DX0180 Pneumonia	480.8	PNEUMONIA DUE TO OTHER VIRUS NEC
DX0180 Pneumonia	480.9	UNSPECIFIED VIRAL PNEUMONIA
DX0180 Pneumonia	481	PNEUMOCOCCAL PNEUMONIA
DX0180 Pneumonia	482	OTHER BACTERIAL PNEUMONIA
DX0180 Pneumonia	482.0	PNEUMONIA DUE TO KLEBSIELLA PNEUMONIAE
DX0180 Pneumonia	482.1	PNEUMONIA DUE TO PSEUDOMONAS
DX0180 Pneumonia	482.2	PNEUMONIA DUE TO HEMOPHILUS INFLUENZAE
DX0180 Pneumonia	482.3	PNEUMONIA DUE TO STREPTOCOCCUS
DX0180 Pneumonia	482.30	PNEUMONIA DUE TO UNSPECIFIED STREPTOCOCCUS
DX0180 Pneumonia	482.31	PNEUMONIA DUE TO STREPTOCOCCUS GROUP A
DX0180 Pneumonia	482.32	PNEUMONIA DUE TO STREPTOCOCCUS GROUP B
DX0180 Pneumonia	482.39	PNEUMONIA DUE TO OTHER STREPTOCOCCUS
DX0180 Pneumonia	482.4	PNEUMONIA DUE TO STAPHYLOCOCCUS
DX0180 Pneumonia	482.40	PNEUMONIA DUE TO STAPHYLOCOCCUS UNSPECIFIED
DX0180 Pneumonia	482.41	METHICILLIN SUSEPTIBLE PNEUMONIA STAPH AUREUS
DX0180 Pneumonia	482.42	METHICILLIN RESISTANT PNEUMONIA D/T STAPH AUREUS
DX0180 Pneumonia	482.49	OTHER STAPHYLOCOCCUS PNEUMONIA
DX0180 Pneumonia	482.8	PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA
DX0180 Pneumonia	482.81	PNEUMONIA DUE TO ANAEROBES
DX0180 Pneumonia	482.82	PNEUMONIA DUE TO ESCHERICHIA COLI
DX0180 Pneumonia	482.83	PNEUMONIA DUE TO OTHER GRAM-NEGATIVE BACTERIA
DX0180 Pneumonia	482.84	LEGIONNAIRES' DISEASE
DX0180 Pneumonia	482.89	PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA
DX0180 Pneumonia	482.9	UNSPECIFIED BACTERIAL PNEUMONIA
DX0180 Pneumonia	483	PNEUMONIA DUE TO OTHER SPECIFIED ORGANISM
DX0180 Pneumonia	483.0	PNEUMONIA DUE TO MYCOPLASMA PNEUMONIAE
DX0180 Pneumonia	483.1	PNEUMONIA DUE TO CHLAMYDIA
DX0180 Pneumonia	483.8	PNEUMONIA DUE TO OTHER SPECIFIED ORGANISM

DX0180 Pneumonia	484	PNEUMONIA INFECTIOUS DISEASES CLASSIFIED ELSW
DX0180 Pneumonia	484.1	PNEUMONIA IN CYTOMEGALIC INCLUSION DISEASE
DX0180 Pneumonia	484.3	PNEUMONIA IN WHOOPING COUGH
DX0180 Pneumonia	484.5	PNEUMONIA IN ANTHRAX
DX0180 Pneumonia	484.6	PNEUMONIA IN ASPERGILLOSIS
DX0180 Pneumonia	484.7	PNEUMONIA IN OTHER SYSTEMIC MYCOSES
DX0180 Pneumonia	484.8	PNEUMONIA OTH INFECTIOUS DISEASES CLASS ELSW
DX0180 Pneumonia	485	BRONCHOPNEUMONIA ORGANISM UNSPECIFIED
DX0180 Pneumonia	486	PNEUMONIA, ORGANISM UNSPECIFIED
DX0180 Pneumonia	487	INFLUENZA
DX0180 Pneumonia	487.0	INFLUENZA WITH PNEUMONIA
DX0180 Pneumonia	487.1	INFLUENZA WITH OTHER RESPIRATORY MANIFESTATIONS
DX0180 Pneumonia	487.8	INFLUENZA WITH OTHER MANIFESTATIONS
DX0180 Pneumonia	488	FLU D/T CERTN IDENTIFID FLU VIRUSES
DX0180 Pneumonia	510	EMPHYEMA
DX0180 Pneumonia	510.0	EMPHYEMA WITH FISTULA
DX0180 Pneumonia	510.9	EMPHYEMA WITHOUT MENTION OF FISTULA
DX0180 Pneumonia	511.1	PLEURISY W/EFFUS W/BACTERL CAUSE OTH THAN TB
DX0180 Pneumonia	511.8	PLEURISY W/OTH SPEC FORMS EFFUS NO TUBERCULOUS
DX0180 Pneumonia	511.89	OTHER SPEC FORMS OF EFFUSION EXCEPT TUBERCULOUS
DX0180 Pneumonia	513	ABSCESS OF LUNG AND MEDIASTINUM
DX0180 Pneumonia	513.0	ABSCESS OF LUNG
DX0180 Pneumonia	513.1	ABSCESS OF MEDIASTINUM
DX0180 Pneumonia	518.6	ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

code set cd. st. dscrp. DX cd. DX code description

130800000 Immunodeficiencies	279	DISORDERS INVOLVING THE IMMUNE MECHANISM
130800000 Immunodeficiencies	279.0	DEFICIENCY OF HUMORAL IMMUNITY
130800000 Immunodeficiencies	279.00	HYPOGAMMAGLOBULINEMIA UNSPECIFIED
130800000 Immunodeficiencies	279.01	SELECTIVE IGA IMMUNODEFICIENCY
130800000 Immunodeficiencies	279.02	SELECTIVE IGM IMMUNODEFICIENCY
130800000 Immunodeficiencies	279.03	OTH SELECTIVE IMMUNOGLOBULIN DEFICIENCIES
130800000 Immunodeficiencies	279.04	CONGENITAL HYPOGAMMAGLOBULINEMIA
130800000 Immunodeficiencies	279.05	IMMUNODEFICIENCY WITH INCREASED IGM
130800000 Immunodeficiencies	279.06	COMMON VARIABLE IMMUNODEFICIENCY
130800000 Immunodeficiencies	279.09	OTHER DEFICIENCY OF HUMORAL IMMUNITY
130800000 Immunodeficiencies	279.1	DEFICIENCY OF CELL-MEDIATED IMMUNITY
130800000 Immunodeficiencies	279.10	IMMUNODEFIC W PREDMNT T-CELL DEFECT UNSPEC
130800000 Immunodeficiencies	279.11	DIGEORGE'S SYNDROME
130800000 Immunodeficiencies	279.12	WISKOTT-ALDRICH SYNDROME
130800000 Immunodeficiencies	279.13	NEZELOF'S SYNDROME
130800000 Immunodeficiencies	279.19	OTHER DEFICIENCY OF CELL-MEDIATED IMMUNITY
130800000 Immunodeficiencies	279.2	COMBINED IMMUNITY DEFICIENCY
130800000 Immunodeficiencies	279.3	UNSPECIFIED IMMUNITY DEFICIENCY
130800000 Immunodeficiencies	279.4	AUTOIMMUNE DISEASE NOT ELSEWHR CLASSIFIED
130800000 Immunodeficiencies	279.8	OTH SPECIF DISORDERS INVOLVING IMMUNE SYST
130800000 Immunodeficiencies	279.9	UNSPECIFIED DISORDER OF IMMUNE MECHANISM

code set cd. st. dscrp. DX cd. DX code description

165200000 Cystic fibrosis	277.0	CYSTIC FIBROSIS
165200000 Cystic fibrosis	277.00	CYSTIC FIBROSIS WITHOUT MECONIUM ILEUS
165200000 Cystic fibrosis	277.01	CYSTIC FIBROSIS WITH MECONIUM ILEUS
165200000 Cystic fibrosis	277.02	CYSTIC FIBROSIS WITH PULMONARY MANIFESTATIONS
165200000 Cystic fibrosis	277.03	CYSTIC FIBROSIS W GASTROINTEST MANIFESTATIONS
165200000 Cystic fibrosis	277.09	CYSTIC FIBROSIS WITH OTHER MANIFESTATIONS

code set cd st dscrp. DX cd. DX code description

207200000 Leukemia	204	LYMPHOID LEUKEMIA
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207200000 Leukemia	204.0	ACUTE LYMPHOID LEUKEMIA
207200000 Leukemia	204.00	ACUTE LYMPHOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	204.01	ACUTE LYMPHOID LEUKEMIA IN REMISSION
207200000 Leukemia	204.02	ACUTE LYMPHOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	204.1	CHRONIC LYMPHOID LEUKEMIA
207200000 Leukemia	204.10	CHRONIC LYMPHOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	204.11	CHRONIC LYMPHOID LEUKEMIA IN REMISSION
207200000 Leukemia	204.12	CHRONIC LYMPHOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	204.2	SUBACUTE LYMPHOID LEUKEMIA
207200000 Leukemia	204.20	SUBACUTE LYMPHOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	204.21	SUBACUTE LYMPHOID LEUKEMIA IN REMISSION
207200000 Leukemia	204.22	SUBACUTE LYMPHOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	204.8	OTHER LYMPHOID LEUKEMIA
207200000 Leukemia	204.80	OTHER LYMPHOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	204.81	OTHER LYMPHOID LEUKEMIA IN REMISSION
207200000 Leukemia	204.82	OTHER LYMPHOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	204.9	UNSPECIFIED LYMPHOID LEUKEMIA
207200000 Leukemia	204.90	UNSPECIFIED LYMPHOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	204.91	UNSPECIFIED LYMPHOID LEUKEMIA IN REMISSION
207200000 Leukemia	204.92	UNSPECIFIED LYMPHOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	205	MYELOID LEUKEMIA
207200000 Leukemia	205.0	ACUTE MYELOID LEUKEMIA
207200000 Leukemia	205.00	ACUTE MYELOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	205.01	ACUTE MYELOID LEUKEMIA IN REMISSION
207200000 Leukemia	205.02	ACUTE MYELOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	205.1	CHRONIC MYELOID LEUKEMIA
207200000 Leukemia	205.10	CHRONIC MYELOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	205.11	CHRONIC MYELOID LEUKEMIA IN REMISSION
207200000 Leukemia	205.12	CHRONIC MYELOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	205.2	SUBACUTE MYELOID LEUKEMIA
207200000 Leukemia	205.20	SUBACUTE MYELOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	205.21	SUBACUTE MYELOID LEUKEMIA IN REMISSION
207200000 Leukemia	205.22	SUBACUTE MYELOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	205.3	MYELOID SARCOMA
207200000 Leukemia	205.30	MYELOID SARCOMA W/O MENTION OF REMISSION
207200000 Leukemia	205.31	MYELOID SARCOMA IN REMISSION
207200000 Leukemia	205.32	MYELOID SARCOMA, IN RELAPSE
207200000 Leukemia	205.8	OTHER MYELOID LEUKEMIA
207200000 Leukemia	205.80	OTHER MYELOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	205.81	OTHER MYELOID LEUKEMIA IN REMISSION
207200000 Leukemia	205.82	OTHER MYELOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	205.9	UNSPECIFIED MYELOID LEUKEMIA
207200000 Leukemia	205.90	UNSPECIFIED MYELOID LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	205.91	UNSPECIFIED MYELOID LEUKEMIA IN REMISSION
207200000 Leukemia	205.92	UNSPECIFIED MYELOID LEUKEMIA, IN RELAPSE
207200000 Leukemia	206	MONOCYTIC LEUKEMIA
207200000 Leukemia	206.0	ACUTE MONOCYTIC LEUKEMIA
207200000 Leukemia	206.00	ACUTE MONOCYTIC LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	206.01	ACUTE MONOCYTIC LEUKEMIA IN REMISSION
207200000 Leukemia	206.02	ACUTE MONOCYTIC LEUKEMIA, IN RELAPSE
207200000 Leukemia	206.1	CHRONIC MONOCYTIC LEUKEMIA
207200000 Leukemia	206.10	CHRONIC MONOCYTIC LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	206.11	CHRONIC MONOCYTIC LEUKEMIA IN REMISSION
207200000 Leukemia	206.12	CHRONIC MONOCYTIC LEUKEMIA, IN RELAPSE
207200000 Leukemia	206.2	SUBACUTE MONOCYTIC LEUKEMIA
207200000 Leukemia	206.20	SUBACUTE MONOCYTIC LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	206.21	SUBACUTE MONOCYTIC LEUKEMIA IN REMISSION
207200000 Leukemia	206.22	SUBACUTE MONOCYTIC LEUKEMIA, IN RELAPSE

207200000 Leukemia	206.8	OTHER MONOCYTIC LEUKEMIA
207200000 Leukemia	206.80	OTHER MONOCYTIC LEUKEMIA W/O MENTION REMISSION
207200000 Leukemia	206.81	OTHER MONOCYTIC LEUKEMIA IN REMISSION
207200000 Leukemia	206.82	OTHER MONOCYTIC LEUKEMIA, IN RELAPSE
207200000 Leukemia	206.9	UNSPECIFIED MONOCYTIC LEUKEMIA
207200000 Leukemia	206.90	UNSPECIF MONOCYTIC LEUKEMIA W/O MENTION REMISSN
207200000 Leukemia	206.91	UNSPECIFIED MONOCYTIC LEUKEMIA IN REMISSION
207200000 Leukemia	206.92	UNSPECIFIED MONOCYTIC LEUKEMIA, IN RELAPSE
207200000 Leukemia	207	OTHER SPECIFIED LEUKEMIA
207200000 Leukemia	207.0	ACUTE ERYTHREMIA AND ERYTHROLEUKEMIA
207200000 Leukemia	207.00	ACUTE ERYTHREMIA&ERYTHROLEUKEMIA W/O MENT REMSSN
207200000 Leukemia	207.01	ACUTE ERYTHREMIA AND ERYTHROLEUKEMIA IN REMISSN
207200000 Leukemia	207.02	ACUTE ERYTHREMIA AND ERYTHROLEUKEMIA, IN RELAPSE
207200000 Leukemia	207.1	CHRONIC ERYTHREMIA
207200000 Leukemia	207.10	CHRONIC ERYTHREMIA W/O MENTION OF REMISSION
207200000 Leukemia	207.11	CHRONIC ERYTHREMIA IN REMISSION
207200000 Leukemia	207.12	CHRONIC ERYTHREMIA, IN RELAPSE
207200000 Leukemia	207.2	MEGAKARYOCYTIC LEUKEMIA
207200000 Leukemia	207.20	MEGAKARYOCYTIC LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	207.21	MEGAKARYOCYTIC LEUKEMIA IN REMISSION
207200000 Leukemia	207.22	MEGAKARYOCYTIC LEUKEMIA, IN RELAPSE
207200000 Leukemia	207.8	OTHER SPECIFIED LEUKEMIA
207200000 Leukemia	207.80	OTHER SPECIFIED LEUKEMIA W/O MENTION OF REMISSN
207200000 Leukemia	207.81	OTHER SPECIFIED LEUKEMIA IN REMISSION
207200000 Leukemia	207.82	OTHER SPECIFIED LEUKEMIA, IN RELAPSE
207200000 Leukemia	208	LEUKEMIA OF UNSPECIFIED CELL TYPE
207200000 Leukemia	208.0	ACUTE LEUKEMIA OF UNSPECIFIED CELL TYPE
207200000 Leukemia	208.00	AC LEUKEMIA UNSPEC CELL TYPE W/O MENTION REMISSN
207200000 Leukemia	208.01	ACUTE LEUKEMIA OF UNSPECIF CELL TYPE IN REMSSN
207200000 Leukemia	208.02	ACUTE LEUKEMIA OF UNSPECIF CELL TYPE IN RELAPSE
207200000 Leukemia	208.1	CHRONIC LEUKEMIA OF UNSPECIFIED CELL TYPE
207200000 Leukemia	208.10	CHRON LEUKEMIA UNSPEC CELL TYPE W/O MENT REMSSN
207200000 Leukemia	208.11	CHRONIC LEUKEMIA OF UNSPECIF CELL TYPE IN REMSSN
207200000 Leukemia	208.12	CHRON LEUKEMIA OF UNSPECIF CELL TYPE, IN RELAPSE
207200000 Leukemia	208.2	SUBACUTE LEUKEMIA OF UNSPECIFIED CELL TYPE
207200000 Leukemia	208.20	SUBAC LEUKEMIA UNSPEC CELL TYPE W/O MENT REMISSN
207200000 Leukemia	208.21	SUBAC LEUKEMIA UNSPECIF CELL TYPE IN REMISSION
207200000 Leukemia	208.22	SUBAC LEUKEMIA OF UNSPECIF CELL TYPE IN RELAPSE
207200000 Leukemia	208.8	OTHER LEUKEMIA OF UNSPECIFIED CELL TYPE
207200000 Leukemia	208.80	OTH LEUKEMIA UNSPECIF CELL TYPE W/O MENT REMISSN
207200000 Leukemia	208.81	OTH LEUKEMIA OF UNSPECIF CELL TYPE IN REMISSION
207200000 Leukemia	208.82	OTH LEUKEMIA OF UNSPECIF CELL TYPE IN RELAPSE
207200000 Leukemia	208.9	UNSPECIFIED LEUKEMIA
207200000 Leukemia	208.90	UNSPECIFIED LEUKEMIA W/O MENTION OF REMISSION
207200000 Leukemia	208.91	UNSPECIFIED LEUKEMIA IN REMISSION
207200000 Leukemia	208.92	UNSPECIFIED LEUKEMIA, IN RELAPSE

code set	cd.	st.	dscrp.	DX cd.	DX code description
403500000	Chronic	sinusitis		472.0	CHRONIC RHINITIS
403500000	Chronic	sinusitis		473	CHRONIC SINUSITIS
403500000	Chronic	sinusitis		473.0	CHRONIC MAXILLARY SINUSITIS
403500000	Chronic	sinusitis		473.1	CHRONIC FRONTAL SINUSITIS
403500000	Chronic	sinusitis		473.2	CHRONIC ETHMOIDAL SINUSITIS
403500000	Chronic	sinusitis		473.3	CHRONIC SPHENOIDAL SINUSITIS
403500000	Chronic	sinusitis		473.8	OTHER CHRONIC SINUSITIS
403500000	Chronic	sinusitis		473.9	UNSPECIFIED SINUSITIS (CHRONIC)
403500000	Chronic	sinusitis		478.0	HYPERTROPHY OF NASAL TURBINATES

code set	cd.	st.	dscrp.	DX cd.	DX code description
404300000	Malign neopls	ear/nose/throat	141	MALIGNANT	NEOPLASM OF TONGUE
404300000	Malign neopls	ear/nose/throat	141.0		MALIGNANT NEOPLASM BASE TONGUE
404300000	Malign neopls	ear/nose/throat	141.1		MALIG NEPLSM DORSAL SURFC TONGUE
404300000	Malign neopls	ear/nose/throat	141.2		MALIG NEPLSM VENTRAL SRFC TONGUE
404300000	Malign neopls	ear/nose/throat	141.3		MLG NSM ANTER 2/3 TNG PART UNSPC
404300000	Malign neopls	ear/nose/throat	141.4		MALIG NEPLSM JUNCTNL ZONE TONGUE
404300000	Malign neopls	ear/nose/throat	141.5		MALIG NEOPLASM OF LINGUAL TONSIL
404300000	Malign neopls	ear/nose/throat	141.6		MALIG NEOPLASM OF BASE OF TONGUE
404300000	Malign neopls	ear/nose/throat	141.8		MALIG NEOPLASM OTH SITES TONGUE
404300000	Malign neopls	ear/nose/throat	141.9		MALIG NEOPLASM OF TONGUE, UNSPEC
404300000	Malign neopls	ear/nose/throat	142	MALIG	NEPLSM MAJOR SALIVRY GLNDS
404300000	Malign neopls	ear/nose/throat	142.0		MALIG NEOPLASM OF PAROTID GLAND
404300000	Malign neopls	ear/nose/throat	142.1		MALIG NEPLSM SUBMANDIBULAR GLAND
404300000	Malign neopls	ear/nose/throat	142.2		MALIG NEOPLASM SUBLINGUAL GLAND
404300000	Malign neopls	ear/nose/throat	142.8		MLG NPLSM OTH MAJOR SALVRY GLNDS
404300000	Malign neopls	ear/nose/throat	142.9		MALIG NEPLSM SALIVRY GLND UNSPEC
404300000	Malign neopls	ear/nose/throat	143	MALIGNANT	NEOPLASM OF GUM
404300000	Malign neopls	ear/nose/throat	143.0		MALIGNANT NEOPLASM OF UPPER GUM
404300000	Malign neopls	ear/nose/throat	143.1		MALIGNANT NEOPLASM OF LOWER GUM
404300000	Malign neopls	ear/nose/throat	143.8		MALIG NEOPLASM OTHER SITES GUM
404300000	Malign neopls	ear/nose/throat	143.9		MALIG NEOPLASM OF GUM, UNSPECIF
404300000	Malign neopls	ear/nose/throat	144	MALIG	NEOPLASM FLOOR OF MOUTH
404300000	Malign neopls	ear/nose/throat	144.0		MLG NSM ANTER PORTN FLOOR MOUTH
404300000	Malign neopls	ear/nose/throat	144.1		MLG NSM LATRL PORTN FLOOR MOUTH
404300000	Malign neopls	ear/nose/throat	144.8		MLG NEPLSM OTH SITES FLOOR MOUTH
404300000	Malign neopls	ear/nose/throat	144.9		MLG NPSM FLOOR MOUTH PART UNSPEC
404300000	Malign neopls	ear/nose/throat	145	MLG NSM	OTH & UNSPEC PARTS MOUTH
404300000	Malign neopls	ear/nose/throat	145.0		MALIG NEOPLASM OF CHEEK MUCOSA
404300000	Malign neopls	ear/nose/throat	145.1		MALIG NEPLSM VESTIBULE OF MOUTH
404300000	Malign neopls	ear/nose/throat	145.2		MALIG NEOPLASM OF HARD PALATE
404300000	Malign neopls	ear/nose/throat	145.3		MALIG NEOPLASM OF SOFT PALATE
404300000	Malign neopls	ear/nose/throat	145.4		MALIGNANT NEOPLASM OF UVULA
404300000	Malign neopls	ear/nose/throat	145.5		MALIG NEOPLASM PALATE, UNSPECIF
404300000	Malign neopls	ear/nose/throat	145.6		MALIG NEOPLASM RETROMOLAR AREA
404300000	Malign neopls	ear/nose/throat	145.8		MLG NSM OTHER SPECIF PARTS MOUTH
404300000	Malign neopls	ear/nose/throat	145.9		MALIG NEOPLASM OF MOUTH UNSPECIF
404300000	Malign neopls	ear/nose/throat	146	MALIGNANT	NEOPLASM OF OROPHARYNX
404300000	Malign neopls	ear/nose/throat	146.0		MALIGNANT NEOPLASM OF TONSIL
404300000	Malign neopls	ear/nose/throat	146.1		MALIG NEOPLASM TONSILLAR FOSSA
404300000	Malign neopls	ear/nose/throat	146.2		MLG NSM TNSLLR PILLRS (ANT POST)
404300000	Malign neopls	ear/nose/throat	146.3		MLG NEPLSM VALLECULA EPIGLOTTICA
404300000	Malign neopls	ear/nose/throat	146.4		MLG NEPLSM ANTER ASPECT EPGLOTTIS
404300000	Malign neopls	ear/nose/throat	146.5		MLG NSM JUNCTNL REGN OROPHARYNX
404300000	Malign neopls	ear/nose/throat	146.6		MLG NSM LATRL WALL OROPHARYNX
404300000	Malign neopls	ear/nose/throat	146.7		MLG NSM POST WALL OF OROPHARYNX
404300000	Malign neopls	ear/nose/throat	146.8		MLG NSM OTH SPEC SITES OROPHARNX
404300000	Malign neopls	ear/nose/throat	146.9		MLG NSM OROPHARYNX, UNSPEC SITE
404300000	Malign neopls	ear/nose/throat	147	MALIG	NEOPLASM OF NASOPHARYNX
404300000	Malign neopls	ear/nose/throat	147.0		MLG NPLSM SUPER WALL NASOPHARYNX
404300000	Malign neopls	ear/nose/throat	147.1		MLG NPLSM POST WALL NASOPHARYNX
404300000	Malign neopls	ear/nose/throat	147.2		MLG NPLSM LATRL WALL NASOPHARYNX
404300000	Malign neopls	ear/nose/throat	147.3		MLG NPLSM ANTER WALL NASOPHARYNX
404300000	Malign neopls	ear/nose/throat	147.8		MLG NPLSM OTH SPEC SITES NSPHRNX
404300000	Malign neopls	ear/nose/throat	147.9		MLG NPLSM NSPHARYNX UNSPEC SITE
404300000	Malign neopls	ear/nose/throat	148	MALIGNANT	NEOPLASM HYPOPHARYNX
404300000	Malign neopls	ear/nose/throat	148.0		MLG NPSM POSTCRICOID RGN HYPHRNX
404300000	Malign neopls	ear/nose/throat	148.1		MALIG NEOPLASM PYRIFORM SINUS

404300000	Malign neoplsm ear/nose/throat 148.2	MG NM ARYEPGLTC FLD HYPHRL ASPC
404300000	Malign neoplsm ear/nose/throat 148.3	MLG NSM POST HYPOPHARYNGEAL WALL
404300000	Malign neoplsm ear/nose/throat 148.8	MLG NPLSM OTH SPEC SITES HYPHRNX
404300000	Malign neoplsm ear/nose/throat 148.9	MLG NSM HYPOPHARYNX UNSPEC SITE
404300000	Malign neoplsm ear/nose/throat 149 MN	OT&IL-DFN SITES LIP ORL CV&PX
404300000	Malign neoplsm ear/nose/throat 149.0	MALIG NPLSM PHARYNX, UNSPECIFIED
404300000	Malign neoplsm ear/nose/throat 149.1	MALIG NEOPLASM WALDEYER'S RING
404300000	Malign neoplsm ear/nose/throat 149.8	ML NSM OT SITES W/IN LIP/ORL CAV
404300000	Malign neoplsm ear/nose/throat 149.9	MN OT IL-DFN STS W/IN LIP&ORL CV
404300000	Malign neoplsm ear/nose/throat 160 MN	NAS CAV/MDL EAR/ACSS SINUSES
404300000	Malign neoplsm ear/nose/throat 160.0	MLG NPLSM NASAL CAVITIES
404300000	Malign neoplsm ear/nose/throat 160.1	MN AUDT TUB/MD EAR/MSTD AIR CLLS
404300000	Malign neoplsm ear/nose/throat 160.2	MLG NPLSM MAXILLARY SINUS
404300000	Malign neoplsm ear/nose/throat 160.3	MLG NPLSM ETHMOIDAL SINUS
404300000	Malign neoplsm ear/nose/throat 160.4	MLG NPLSM FRONTAL SINUS
404300000	Malign neoplsm ear/nose/throat 160.5	MLG NPLSM SPHENOIDAL SINUS
404300000	Malign neoplsm ear/nose/throat 160.8	MLG NPLSM OTH ACCESSORY SINUSES
404300000	Malign neoplsm ear/nose/throat 160.9	MLG NPLSM ACCESSORY SINUS UNSPEC
404300000	Malign neoplsm ear/nose/throat 161	MALIGNANT NEOPLASM OF LARYNX
404300000	Malign neoplsm ear/nose/throat 161.0	MALIGNANT NEOPLASM OF GLOTTIS
404300000	Malign neoplsm ear/nose/throat 161.1	MALIG NEOPLASM SUPRAGLOTTIS
404300000	Malign neoplsm ear/nose/throat 161.2	MALIG NEOPLASM SUBGLOTTIS
404300000	Malign neoplsm ear/nose/throat 161.3	MALIG NPLSM LARYNGEAL CARTILAGES
404300000	Malign neoplsm ear/nose/throat 161.8	MLG NPLSM OTH SPEC SITES LARYNX
404300000	Malign neoplsm ear/nose/throat 161.9	MALIG NPLSM LARYNX, UNSPECIFIED
404300000	Malign neoplsm ear/nose/throat 176.2	KAPOSI'S SARCOMA PALATE
404300000	Malign neoplsm ear/nose/throat 195.0	MALIG NEOPLSM HEAD, FACE, & NECK
404300000	Malign neoplsm ear/nose/throat 230.0	CARC IN SITU LIP/ORAL CAV/PHARNX
404300000	Malign neoplsm ear/nose/throat 231.0	CARCINOMA IN SITU OF LARYNX

code set	cd.	st.	dscrp.	DX cd	DX code description
404700000	Congenital&acquired	ENT anomalies 470	DEVIATED NASAL SEPTUM		
404700000	Congenital&acquired	ENT anomalies 478.74	STENOSIS OF LARYNX		
404700000	Congenital&acquired	ENT anomalies 524.0	MAJOR ANOMALIES OF JAW SIZE		
404700000	Congenital&acquired	ENT anomalies 524.00	MAJ ANML JAW SIZE UNSPEC ANML		
404700000	Congenital&acquired	ENT anomalies 524.01	MAJ ANML JAW SZ MXLLRY HYPRPS		
404700000	Congenital&acquired	ENT anomalies 524.02	MAJ ANML JAW SZ MNDBLR HYPRPS		
404700000	Congenital&acquired	ENT anomalies 524.03	MAJ ANML JAW SZ MXLLRY HYPOPS		
404700000	Congenital&acquired	ENT anomalies 524.04	MAJ ANML JAW SZ MNDBLR HYPOPS		
404700000	Congenital&acquired	ENT anomalies 524.05	MAJ ANML JAW SZ MACROGENIA		
404700000	Congenital&acquired	ENT anomalies 524.06	MAJ ANML JAW SZ MICROGENIA		
404700000	Congenital&acquired	ENT anomalies 524.07	EXCESSIVE TUBEROSITY OF JAW		
404700000	Congenital&acquired	ENT anomalies 524.09	MAJ ANML JAW SZ OT SPEC ANMLY		
404700000	Congenital&acquired	ENT anomalies 524.1	ANMLS RLTNSHP JAW CRANL BASE		
404700000	Congenital&acquired	ENT anomalies 524.10	ANMLS R/S JAW CRN BS UNSP ANM		
404700000	Congenital&acquired	ENT anomalies 524.11	ANMLS R/S JAW CRN B MXLR ASYM		
404700000	Congenital&acquired	ENT anomalies 524.12	ANMLS R/S JAW CB OT JAW ASYM		
404700000	Congenital&acquired	ENT anomalies 524.19	ANMLS R/S JW CRN B OT SPC ASM		
404700000	Congenital&acquired	ENT anomalies 524.2	ANMLS DENT ARCH RELATIONSHIP		
404700000	Congenital&acquired	ENT anomalies 524.20	UNSPEC ANML DENT ARCH RLTNSHP		
404700000	Congenital&acquired	ENT anomalies 524.21	ANGLE'S CLASS I		
404700000	Congenital&acquired	ENT anomalies 524.22	ANGLE'S CLASS III		
404700000	Congenital&acquired	ENT anomalies 524.23	ANGLE'S CLASS III		
404700000	Congenital&acquired	ENT anomalies 524.24	OPEN ANTER OCCLSL RELATIONSHIP		
404700000	Congenital&acquired	ENT anomalies 524.25	OPEN POSTR OCCLSL RELATIONSHIP		
404700000	Congenital&acquired	ENT anomalies 524.26	EXCESSIVE HORIZONTAL OVERLAP		
404700000	Congenital&acquired	ENT anomalies 524.27	REVERSE ARTICULATIONS		
404700000	Congenital&acquired	ENT anomalies 524.28	ANOMALIES INTERARCH DISTANCE		

404700000 Congenital&acquired ENT anomalies 524.29 OTH ANMLS DENT ARCH RELATNSHP
 404700000 Congenital&acquired ENT anomalies 738.0 ACQUIRED DEFORMITY OF NOSE
 404700000 Congenital&acquired ENT anomalies 738.11 OT ACQ DEFRM HD ZYGMT HYPRPLS
 404700000 Congenital&acquired ENT anomalies 738.12 OT ACQ DEFRM HD ZYGMT HYPOPLS
 404700000 Congenital&acquired ENT anomalies 738.7 CAULIFLOWER EAR
 404700000 Congenital&acquired ENT anomalies 744 CONGEN ANML EAR/FACE/NECK
 404700000 Congenital&acquired ENT anomalies 744.0 CONG ANM EAR CSNG HEAR IMPAIR
 404700000 Congenital&acquired ENT anomalies 744.00 UNSPC CONG ANML EAR W HR IMPR
 404700000 Congenital&acquired ENT anomalies 744.01 CONGEN ABSENCE EXTERNAL EAR
 404700000 Congenital&acquired ENT anomalies 744.02 OT CNGN ANML EXTN EAR W HR IM
 404700000 Congenital&acquired ENT anomalies 744.03 CONGN ANML MDL EAR EXPT OSCLS
 404700000 Congenital&acquired ENT anomalies 744.04 CONGN ANOMALIES EAR OSSICLES
 404700000 Congenital&acquired ENT anomalies 744.05 CONGN ANOMALIES OF INNER EAR
 404700000 Congenital&acquired ENT anomalies 744.09 OT CNGN ANML EAR CASNG HR IMP
 404700000 Congenital&acquired ENT anomalies 744.1 ACCESSORY AURICLE
 404700000 Congenital&acquired ENT anomalies 744.2 OTH SPEC CONGEN ANOMALIES EAR
 404700000 Congenital&acquired ENT anomalies 744.21 ABSENCE EAR LOBE CONGENITAL
 404700000 Congenital&acquired ENT anomalies 744.22 MACROTIA
 404700000 Congenital&acquired ENT anomalies 744.23 MICROTIA
 404700000 Congenital&acquired ENT anomalies 744.24 SPEC CONGEN ANML EUSTACH TUBE
 404700000 Congenital&acquired ENT anomalies 744.29 OTH CONGEN ANOMAL OF EAR
 404700000 Congenital&acquired ENT anomalies 744.3 UNSPEC CONGENIT ANOMALY EAR
 404700000 Congenital&acquired ENT anomalies 744.4 BRNC CL CYS/FISTL; PREAUR SNS
 404700000 Congenital&acquired ENT anomalies 744.41 BRANCHL CLFT SINUS OR FISTULA
 404700000 Congenital&acquired ENT anomalies 744.42 BRANCHIAL CLEFT CYST
 404700000 Congenital&acquired ENT anomalies 744.43 CERVICAL AURICLE
 404700000 Congenital&acquired ENT anomalies 744.46 PREAURICULAR SINUS OR FISTULA
 404700000 Congenital&acquired ENT anomalies 744.47 PREAURICULAR CYST
 404700000 Congenital&acquired ENT anomalies 744.49 OT BR CL CYS/FSTL; PREARC SNS
 404700000 Congenital&acquired ENT anomalies 744.5 WEBBING OF NECK
 404700000 Congenital&acquired ENT anomalies 744.8 OTH SPEC CONGN ANML FACE&NECK
 404700000 Congenital&acquired ENT anomalies 744.81 MACROCHELIA
 404700000 Congenital&acquired ENT anomalies 744.82 MICROCHELIA
 404700000 Congenital&acquired ENT anomalies 744.83 MACROSTOMIA
 404700000 Congenital&acquired ENT anomalies 744.84 MICROSTOMIA
 404700000 Congenital&acquired ENT anomalies 744.89 OTH SPEC CONGEN ANML FACE&NCK
 404700000 Congenital&acquired ENT anomalies 744.9 UNSPEC CONGEN ANML FACE&NECK
 404700000 Congenital&acquired ENT anomalies 748.0 CHOANAL ATRESIA
 404700000 Congenital&acquired ENT anomalies 748.1 OTH CONGEN ANOMALIES OF NOSE
 404700000 Congenital&acquired ENT anomalies 748.2 WEB OF LARYNX
 404700000 Congenital&acquired ENT anomalies 748.3 OTH CONGN ANML LRX/TRCH/BRNC
 404700000 Congenital&acquired ENT anomalies 749 CLEFT PALATE AND CLEFT LIP
 404700000 Congenital&acquired ENT anomalies 749.0 CLEFT PALATE
 404700000 Congenital&acquired ENT anomalies 749.00 CLEFT PALATE UNSPECIFIED
 404700000 Congenital&acquired ENT anomalies 749.01 CLEFT PALATE UNLATRL COMPLETE
 404700000 Congenital&acquired ENT anomalies 749.02 CLEFT PALATE UNLATRL INCOMPLT
 404700000 Congenital&acquired ENT anomalies 749.03 CLEFT PALATE BILATRL COMPLETE
 404700000 Congenital&acquired ENT anomalies 749.04 CLEFT PALATE BILATRL INCOMPLT
 404700000 Congenital&acquired ENT anomalies 749.1 CLEFT LIP
 404700000 Congenital&acquired ENT anomalies 749.10 CLEFT LIP UNSPECIFIED
 404700000 Congenital&acquired ENT anomalies 749.11 CLEFT LIP UNILATERAL COMPLETE
 404700000 Congenital&acquired ENT anomalies 749.12 CLEFT LIP UNILATRL INCOMPLETE
 404700000 Congenital&acquired ENT anomalies 749.13 CLEFT LIP BILATERAL COMPLETE
 404700000 Congenital&acquired ENT anomalies 749.14 CLEFT LIP BILATRL INCOMPLETE
 404700000 Congenital&acquired ENT anomalies 749.2 CLEFT PALATE WITH CLEFT LIP
 404700000 Congenital&acquired ENT anomalies 749.20 CLEFT PALATE W CLFT LIP UNSPC
 404700000 Congenital&acquired ENT anomalies 749.21 CLF PLT W CLF LP UNLAT COMPLT
 404700000 Congenital&acquired ENT anomalies 749.22 CLF PLT W CLF LP UNLAT INCMPL

404700000 Congenital&acquired ENT anomalies 749.23 CLF PLT W CLF LIP BILAT CMPLT
 404700000 Congenital&acquired ENT anomalies 749.24 CLF PLT W CLF LIP BIL INCMPLT
 404700000 Congenital&acquired ENT anomalies 749.25 OTH COMBOS CLF PLT W CLF LIP
 404700000 Congenital&acquired ENT anomalies 750.0 TONGUE TIE
 404700000 Congenital&acquired ENT anomalies 750.1 OTHER CONGEN ANOMAL OF TONGUE
 404700000 Congenital&acquired ENT anomalies 750.10 CONGEN ANOMALY TONGUE UNSPEC
 404700000 Congenital&acquired ENT anomalies 750.11 AGLOSSIA
 404700000 Congenital&acquired ENT anomalies 750.12 CONGENITAL ADHESIONS TONGUE
 404700000 Congenital&acquired ENT anomalies 750.13 CONGENITAL FISSURE OF TONGUE
 404700000 Congenital&acquired ENT anomalies 750.15 MACROGLOSSIA
 404700000 Congenital&acquired ENT anomalies 750.16 MICROGLOSSIA
 404700000 Congenital&acquired ENT anomalies 750.19 OTHER CONGENITAL ANML TONGUE
 404700000 Congenital&acquired ENT anomalies 750.2 OT SPEC CONGN ANML MTH/PHRYNX
 404700000 Congenital&acquired ENT anomalies 750.21 CONGEN ABSENCE OF SALIVR GLND
 404700000 Congenital&acquired ENT anomalies 750.22 ACCESSORY SALIVARY GLAND
 404700000 Congenital&acquired ENT anomalies 750.23 CONGEN ATRESIA SALIVARY DUCT
 404700000 Congenital&acquired ENT anomalies 750.24 CONGEN FISTULA SALIVARY GLAND
 404700000 Congenital&acquired ENT anomalies 750.25 CONGENITAL FISTULA OF LIP
 404700000 Congenital&acquired ENT anomalies 750.26 OTH SPECIF CONGEN ANML MOUTH
 404700000 Congenital&acquired ENT anomalies 750.27 CONGEN DIVERTICULUM PHARYNX
 404700000 Congenital&acquired ENT anomalies 750.29 OTH SPECIFIED ANOMAL PHARYNX
 404700000 Congenital&acquired ENT anomalies 754.0 CNGN MUSCSKL DFRM SKL/FCE/JAW

Code Set	Code Set Description	Procedure Code
PR0107	Professional encounter	99201
PR0107	Professional encounter	99202
PR0107	Professional encounter	99203
PR0107	Professional encounter	99204
PR0107	Professional encounter	99205
PR0107	Professional encounter	99211
PR0107	Professional encounter	99212
PR0107	Professional encounter	99213
PR0107	Professional encounter	99214
PR0107	Professional encounter	99215
PR0107	Professional encounter	99217
PR0107	Professional encounter	99218
PR0107	Professional encounter	99219
PR0107	Professional encounter	99220
PR0107	Professional encounter	99221
PR0107	Professional encounter	99222
PR0107	Professional encounter	99223
PR0107	Professional encounter	99231
PR0107	Professional encounter	99232
PR0107	Professional encounter	99233
PR0107	Professional encounter	99234
PR0107	Professional encounter	99235
PR0107	Professional encounter	99236
PR0107	Professional encounter	99238
PR0107	Professional encounter	99239
PR0107	Professional encounter	99241
PR0107	Professional encounter	99242
PR0107	Professional encounter	99243
PR0107	Professional encounter	99244
PR0107	Professional encounter	99245
PR0107	Professional encounter	99251
PR0107	Professional encounter	99252
PR0107	Professional encounter	99253
PR0107	Professional encounter	99254

PR0107	Professional encounter	99255
PR0107	Professional encounter	99261
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PR0107	Professional encounter	S0273

Code Set	Code Set Description	Procedure Code
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PR0108	Professional supervision	99444
PR0108	Professional supervision	G0179
PR0108	Professional supervision	G0180
PR0108	Professional supervision	G0181
PR0108	Professional supervision	G0182

Code Set	Code Set Description	Revenue Code
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RV0107	Professional encounter	0981
RV0107	Professional encounter	0983

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RX-184	Any Antibiotic	68115002921
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RX-184	Any Antibiotic	68115002940
RX-184	Any Antibiotic	68115002942
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RX-184	Any Antibiotic	68115003014
RX-184	Any Antibiotic	68115003228
RX-184	Any Antibiotic	68115003321
RX-184	Any Antibiotic	68115003328
RX-184	Any Antibiotic	68115004714
RX-184	Any Antibiotic	68115004720
RX-184	Any Antibiotic	68115004814
RX-184	Any Antibiotic	68115006530
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RX-184	Any Antibiotic	68115007209
RX-184	Any Antibiotic	68115007212
RX-184	Any Antibiotic	68115007215
RX-184	Any Antibiotic	68115007220
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RX-184	Any Antibiotic	68115007306
RX-184	Any Antibiotic	68115007309
RX-184	Any Antibiotic	68115007310
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RX-184	Any Antibiotic	68115007314
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RX-184	Any Antibiotic	68115007330
RX-184	Any Antibiotic	68115007340
RX-184	Any Antibiotic	68115007348
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RX-184	Any Antibiotic	68115008620
RX-184	Any Antibiotic	68115008621
RX-184	Any Antibiotic	68115008628
RX-184	Any Antibiotic	68115008636
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RX-184	Any Antibiotic	68115010520
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RX-184	Any Antibiotic	68115012520
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RX-184	Any Antibiotic	68115012560
RX-184	Any Antibiotic	68115012597
RX-184	Any Antibiotic	68115012599
RX-184	Any Antibiotic	68115012606
RX-184	Any Antibiotic	68115012621
RX-184	Any Antibiotic	68115012628
RX-184	Any Antibiotic	68115012630
RX-184	Any Antibiotic	68115012640
RX-184	Any Antibiotic	68115012656
RX-184	Any Antibiotic	68115013106
RX-184	Any Antibiotic	68115013115
RX-184	Any Antibiotic	68115013121
RX-184	Any Antibiotic	68115013130
RX-184	Any Antibiotic	68115013140
RX-184	Any Antibiotic	68115013220
RX-184	Any Antibiotic	68115013228
RX-184	Any Antibiotic	68115013420
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RX-184	Any Antibiotic	68115013506
RX-184	Any Antibiotic	68115013520
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RX-184	Any Antibiotic	68115013540
RX-184	Any Antibiotic	68115013628
RX-184	Any Antibiotic	68115013640
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RX-184	Any Antibiotic	68115026912
RX-184	Any Antibiotic	68115026920
RX-184	Any Antibiotic	68115026921
RX-184	Any Antibiotic	68115026928
RX-184	Any Antibiotic	68115026930
RX-184	Any Antibiotic	68115026940
RX-184	Any Antibiotic	68115032200
RX-184	Any Antibiotic	68115032206
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RX-184	Any Antibiotic	68115032220
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RX-184	Any Antibiotic	68115032240
RX-184	Any Antibiotic	68115032528
RX-184	Any Antibiotic	68115032540
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RX-184	Any Antibiotic	68115032660
RX-184	Any Antibiotic	68115036404
RX-184	Any Antibiotic	68115036450
RX-184	Any Antibiotic	68115038620
RX-184	Any Antibiotic	68115042109
RX-184	Any Antibiotic	68115044522
RX-184	Any Antibiotic	68115044601
RX-184	Any Antibiotic	68115044606
RX-184	Any Antibiotic	68115044608
RX-184	Any Antibiotic	68115044610
RX-184	Any Antibiotic	68115044614
RX-184	Any Antibiotic	68115044620
RX-184	Any Antibiotic	68115044630
RX-184	Any Antibiotic	68115046320
RX-184	Any Antibiotic	68115048840
RX-184	Any Antibiotic	68115054150
RX-184	Any Antibiotic	68115058220
RX-184	Any Antibiotic	68115087206
RX-184	Any Antibiotic	68115090400
RX-184	Any Antibiotic	68115090450
RX-184	Any Antibiotic	68115090480
RX-184	Any Antibiotic	68115092505
RX-184	Any Antibiotic	68115093106
RX-184	Any Antibiotic	68115099020
RX-184	Any Antibiotic	68115099120
RX-184	Any Antibiotic	68115099350
RX-184	Any Antibiotic	68115099400
RX-184	Any Antibiotic	68118038620
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RX-184	Any Antibiotic	68180012102
RX-184	Any Antibiotic	68180012201
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RX-184	Any Antibiotic	68180012302
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RX-184	Any Antibiotic	68258904101
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RX-184	Any Antibiotic	68258905901
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RX-184	Any Antibiotic	68330001525
RX-184	Any Antibiotic	68387011730
RX-184	Any Antibiotic	68387019020
RX-184	Any Antibiotic	68387019021
RX-184	Any Antibiotic	68387019030
RX-184	Any Antibiotic	68387019040
RX-184	Any Antibiotic	68387019120
RX-184	Any Antibiotic	68387038020
RX-184	Any Antibiotic	68387038120
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RX-184	Any Antibiotic	68387038530
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RX-184	Any Antibiotic	68774030235
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RX-184	Any Antibiotic	68820001610
RX-184	Any Antibiotic	68820001708
RX-184	Any Antibiotic	68820001815
RX-184	Any Antibiotic	68820001816

RX-184	Any Antibiotic	68820001817
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RX-184	Any Antibiotic	99207049010
RX-184	Any Antibiotic	99207049110
RX-184	Any Antibiotic	99207049111
RX-184	Any Antibiotic	99207049211
RX-184	Any Antibiotic	99207049250
RX-184	Any Antibiotic	99207049705
RX-184	Any Antibiotic	99207049710
RX-184	Any Antibiotic	99207049711
RX-184	Any Antibiotic	99207049805
RX-184	Any Antibiotic	99207049811
RX-184	Any Antibiotic	99207049850
RX-184	Any Antibiotic	99207049905
RX-184	Any Antibiotic	99207049910
RX-184	Any Antibiotic	99207049911

2a.11 Stratification Details/Variables (*All information required to stratify the measure including the stratification variables, all codes, logic, and definitions*):
Does not apply

2a.12-13 Risk Adjustment Type: no risk adjustment necessary

2a.14 Risk Adjustment Methodology/Variables (*List risk adjustment variables and describe conceptual models, statistical models, or other aspects of model or method*):

2a.15-17 Detailed risk model available Web page URL or attachment:

2a.18-19 Type of Score: rate/proportion

2a.20 Interpretation of Score: better quality = higher score

2a.21 Calculation Algorithm (*Describe the calculation of the measure as a flowchart or series of steps*):

1. Exclude members who meet denominator exclusion criteria
2. Assign a YES or NO result to remaining members based on numerator response
3. Rate = YES/[YES+NO]

2a.22 Describe the method for discriminating performance (e.g., significance testing): Over 410,000 patients met the denominator from a geographically diverse 15 million member benchmark database. More than 8,000 patients did not meet numerator compliance, indicating a significant population with a gap in care (i.e., patients that received an antibiotic who did not receive a recommended first line antibiotic). The subsequent compliance rate was 61.3 percent. 2a.23 Sampling (Survey) Methodology <i>If measure is based on a sample (or survey), provide instructions for obtaining the sample, conducting the survey and guidance on minimum sample size (response rate):</i> A 15 million patient population sample was chosen to analyze the potential patient safety gap in care. The sample was derived from more than 60 million patients based on criteria including national geographic representation, commercial health coverage and patient age less than 65. 2a.24 Data Source <i>(Check the source(s) for which the measure is specified and tested)</i> pharmacy data, Electronic administrative data/claims 2a.25 Data source/data collection instrument <i>(Identify the specific data source/data collection instrument, e.g. name of database, clinical registry, collection instrument, etc.):</i> Our data source is a proprietary Ingenix provider database that includes more than 60 million patients, over multiple years. It includes data from multiple payors. This measure specifically uses the following data from this database: member demographics, ICD-9 codes, revenue codes, CPT codes, place of service codes, and pharmacy lab data. 2a.26-28 Data source/data collection instrument reference web page URL or attachment: 2a.29-31 Data dictionary/code table web page URL or attachment: Attachment Input Guide_NQF-634012375912643236.doc 2a.32-35 Level of Measurement/Analysis <i>(Check the level(s) for which the measure is specified and tested)</i> Clinicians: Individual, Clinicians: Group, Facility/Agency, Integrated delivery system, Health Plan, Multi-site/corporate chain, Program: Disease management, Program: QIO, Can be measured at all levels 2a.36-37 Care Settings <i>(Check the setting(s) for which the measure is specified and tested)</i> Ambulatory Care: Clinic, Ambulatory Care: Emergency Dept, Ambulatory Care: Hospital Outpatient, nursing home (NH) /Skilled Nursing Facility (SNF), Rehabilitation Facility 2a.38-41 Clinical Services <i>(Healthcare services being measured, check all that apply)</i> Clinicians: PA/NP/Advanced Practice Nurse, Clinicians: Physicians (MD/DO)	
TESTING/ANALYSIS	
2b. Reliability testing 2b.1 Data/sample <i>(description of data/sample and size):</i> Reliability is tested by using multiple databases. There are three primary databases that we use: 1) a customer acceptance (CAT) database that includes approximately 4000 members who satisfy the condition confirmation criteria; 2) a one million member face validity testing (FVT) database that is geographically diverse; and 3) a 15 million member benchmark database that is geographically diverse. All databases represent predominately a commercial population less than 65 year of age. 2b.2 Analytic Method <i>(type of reliability & rationale, method for testing):</i> Quality assurance of each measure is accomplished through the testing using multiple methods and databases. Types of testing, data samples and volume vary to ensure the integrity of the measure. Rigorous development, analysis and testing processes are deployed for creating measure specifications. Software testing ensures the software is working as designed. Reliability and validity testing of measures is based on differing data samples and volume of members. National benchmarks are created on a large volume set of data representing members throughout the United States. All quality checks for all measure results must have consistent results and meet expected outcomes based on industry knowledge and experience.	2b C ☐ P ☐ M ☐ N ☐

Comment [KP10]: 2b. Reliability testing demonstrates the measure results are repeatable, producing the same results a high proportion of the time when assessed in the same population in the same time period.

Comment [k11]: 8 Examples of reliability testing include, but are not limited to: inter-rater/abstractor or intra-rater/abstractor studies; internal consistency for multi-item scales; test-retest for survey items. Reliability testing may address the data items or final measure score.

Customer Acceptance Testing (CAT) is an important quality process. CAT ensures that the clinical measures are functioning as intended and that they generate accurate results for typical billing patterns. Using actual claims data a team of business analysts, nurses, and health services researchers conducts a detailed analysis of the output. For each clinical condition in the product (e.g., Diabetes Mellitus, Coronary Artery Disease, etc.) there is a set of CAT data with at least 4000 members who satisfy the condition confirmation criteria. This data is extracted from a large (50+ million member) multi-payer benchmark database and contains inpatient, outpatient, pharmacy, and laboratory data. The testing team analyzes claims from individual members and compares the creation of denominators (target population), numerators, and exclusions from this manual review process to output results from the quality measure.

Regression testing is the part of CAT that verifies the reliability of the product across software releases. For a new release the testing team confirms that every unchanged measure produces the same results as in previous releases, accounting for systematic changes to the software (e.g., code updates, logic changes, etc). Regression testing is conducted at multiple points throughout the software development cycle.

2b.3 Testing Results (*reliability statistics, assessment of adequacy in the context of norms for the test conducted*):

Given the size of our benchmark database, it is the most reliable source for compliance results. Over 4,000 members from the benchmark database met the denominator definition for this measure. The overall compliance rate was 61.3 percent.

2c. Validity testing

2c.1 Data/sample (*description of data/sample and size*): Our data sample for face validity testing includes a geographically diverse one million member database. Our data sample for benchmark testing includes a geographically diverse 15 million member database. Both databases represent predominately a commercial population less than 65 year of age.

2c.2 Analytic Method (*type of validity & rationale, method for testing*):

Face Validity Testing (FVT) is the final testing step in the software release cycle. One million members are randomly selected from the large multi-payer benchmark database and their claims data is processed through the software. The Medical Director reviews the results to verify that:

1. Prevalence rates for a condition are comparable to nationally published rates
2. Compliance rates for a measure are comparable to the rates reported in the published literature or by other national sources (e.g. HEDIS). If no comparable sources are available, the rates are judged based on what is clinically reasonable.

In addition, all results are reviewed for face validity by members of an external physician clinical consultant panel.

A similar review of benchmark test results occurs in conjunction with a software release. With benchmark testing, 15 million members are randomly selected from the large multi-payer benchmark database and their claims data is processed through the software.

Our claims-based measures have been validated using a chart review comparison process. This validation project is summarized below:

Goal: evaluate the reliability of claims-based measure results using chart review as the gold standard

Methods:

The charts of 100 members from two clinics in one city were reviewed. Results from our claims-based measures were compared to information present in the chart. During this process, 726 measures were evaluated.

Results:

The overall error rate was less than 5%. The error rate varied depending on the type of claim required for numerator compliance and is summarized as follows:

o The error rate was highest with medications, with an 11 percent error rate (2/18). From chart review, it was difficult to tell if this represented a real error, a medication sample was provided, or the prescription was never filled).

Comment [KP12]: 2c. Validity testing demonstrates that the measure reflects the quality of care provided, adequately distinguishing good and poor quality. If face validity is the only validity addressed, it is systematically assessed.

Comment [k13]: 9 Examples of validity testing include, but are not limited to: determining if measure scores adequately distinguish between providers known to have good or poor quality assessed by another valid method; correlation of measure scores with another valid indicator of quality for the specific topic; ability of measure scores to predict scores on some other related valid measure; content validity for multi-item scales/tests. Face validity is a subjective assessment by experts of whether the measure reflects the quality of care (e.g., whether the proportion of patients with BP < 140/90 is a marker of quality). If face validity is the only validity addressed, it is systematically assessed (e.g., ratings by relevant stakeholders) and the measure is judged to represent quality care for the specific topic and that the measure focus is the most important aspect of quality for the specific topic.

2c
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o The error rate was 4 percent (14/318) for measures that required labs for numerator compliance. It was noted that a claims-based measure approach sometimes identified labs that were missing in chart review.

o The error rate for office visit and specialty appointments was 2 percent (8/390). Of note, administrative claims was more likely than chart review to identify relevant office and specialty visits, particularly for appointments that occurred outside the clinic or network.

o Errors were found related to coding in claims data, not due to the claims-based measures or methodology. These errors were not quantified.

2c.3 Testing Results (statistical results, assessment of adequacy in the context of norms for the test conducted):

Summarized in 2b3

2d. Exclusions Justified

2d.1 Summary of Evidence supporting exclusion(s):

Prior antibiotic use is a major risk factor associated with the development of infection with antimicrobial-resistant strains. Because recent antimicrobial exposure increases the risk of carriage of and infection due to resistant organisms, antimicrobial therapy should be based upon the patient's history of recent antibiotic use (1). These guidelines do not address the management of patients with chronic sinusitis or patients with underlying immunodeficiency states or structural abnormalities.

These guideline recommendations, along with consultant panel consensus, were used to develop the exclusion criteria for this measure. Exclusions include the following:

1. Patients are excluded if there is evidence of recurrent episodes of infections (i.e., a 60 day clear window prior to the initiating sinusitis encounter is required) or chronic sinusitis;
2. Patients are excluded if there is an underlying immunodeficiency or structural abnormalities (e.g., congenital and acquired anomalies);
3. Patients are excluded if there was a hospitalization or outpatient surgery associated with the sinusitis event;
4. Patients are excluded if there are relevant head, neck, or respiratory infections that might indicate a complicated case of sinusitis or concurrent infection that might alter antibiotic selection.

Finally, patients are excluded if they received "any antibiotic" within the time period 60 to 11 days prior to the initiating sinusitis event. This would identify patients with previous antibiotic exposure who may be unresponsive to previous treatment or be at increased risk for resistant organisms.

2d.2 Citations for Evidence:

1. Sinus and Allergy Health Partnership (SAHP). Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. Otolaryngol Head Neck Surg 2004;130(Suppl):1-45.

2d.3 Data/sample (description of data/sample and size): This measure applies exclusion criteria using two different methods. The first method applies exclusion criteria at the level of building the sinusitis event. The second method applies exclusion criteria after the sinusitis event has been defined.

Our customer acceptance (CAT) database, that includes approximately 4000 members who satisfy the condition confirmation criteria, was used to evaluate the impact of exclusion criteria applied when building the sinusitis event.

Our 15 million member benchmark database was used to evaluate the impact of exclusion criteria applied after the sinusitis event was built.

2d.4 Analytic Method (type analysis & rationale):

A frequency analysis is used to assess the impact of exclusion criteria. These results are then reviewed for face validity by our external consultant panel.

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NA ☐

Comment [KP14]: 2d. Clinically necessary measure exclusions are identified and must be:

- supported by evidence of sufficient frequency of occurrence so that results are distorted without the exclusion;

AND

- a clinically appropriate exception (e.g., contraindication) to eligibility for the measure focus;

AND

- precisely defined and specified:

–if there is substantial variability in exclusions across providers, the measure is specified so that exclusions are computable and the effect on the measure is transparent (i.e., impact clearly delineated, such as number of cases excluded, exclusion rates by type of exclusion);

if patient preference (e.g., informed decision-making) is a basis for exclusion, there must be evidence that it strongly impacts performance on the measure and the measure must be specified so that the information about patient preference and the effect on the measure is transparent (e.g., numerator category computed separately, denominator exclusion category computed separately).

Comment [k15]: 10 Examples of evidence that an exclusion distorts measure results include, but are not limited to: frequency of occurrence, sensitivity analyses with and without the exclusion, and variability of exclusions across providers.

2d.5 Testing Results (e.g., frequency, variability, sensitivity analyses): Our CAT database was used to evaluate the impact of exclusion criteria applied when building the sinusitis event. Results were as follows: 1. Two percent were excluded due to recurrent episodes of infections (i.e., a 60 day clear window prior to the initiating sinusitis encounter is required) or chronic sinusitis; 2. Two percent were excluded due to underlying immunodeficiency; 3. Less than one percent were excluded due to hospitalization or outpatient surgery associated with the sinusitis event. Our 15 million member benchmark database was used to evaluate the impact of exclusion criteria applied after the sinusitis event was built. Fifty percent were excluded due to relevant head, neck, or respiratory infections that might indicate a complicated case of sinusitis or concurrent infection that would require systemic antibiotic therapy OR because they received "any antibiotic" within the time period 60-11 days prior to the initiating sinusitis event.		Comment [KP16]: 2e. For outcome measures and other measures (e.g., resource use) when indicated: •an evidence-based risk-adjustment strategy (e.g., risk models, risk stratification) is specified and is based on patient clinical factors that influence the measured outcome (but not disparities in care) and are present at start of care; Error! Bookmark not defined. OR rationale/data support no risk adjustment.
2e. Risk Adjustment for Outcomes/ Resource Use Measures 2e.1 Data/sample (description of data/sample and size): This measure does not include risk adjustment. 2e.2 Analytic Method (type of risk adjustment, analysis, & rationale): 2e.3 Testing Results (risk model performance metrics): 2e.4 If outcome or resource use measure is not risk adjusted, provide rationale:	2e C ☐ P ☐ M ☐ N ☐ NA ☐	Comment [k17]: 13 Risk models should not obscure disparities in care for populations by including factors that are associated with differences/inequalities in care such as race, socioeconomic status, gender (e.g., poorer treatment outcomes of African American men with prostate cancer, inequalities in treatment for CVD risk factors between men and women). It is preferable to stratify measures by race and socioeconomic status rather than adjusting out differences.
2f. Identification of Meaningful Differences in Performance 2f.1 Data/sample from Testing or Current Use (description of data/sample and size): Our benchmark data sample includes a geographically diverse 15 million member benchmark database. The database represents predominately a commercial population less than 65 year of age. 2f.2 Methods to identify statistically significant and practically/meaningfully differences in performance (type of analysis & rationale): During benchmark testing, 15 million members are randomly selected from the large multi-payer benchmark database and their claims data is processed through the software. The Medical Director reviews the results to verify that: 1. Prevalence rates for a condition are comparable to nationally published rates 2. Compliance rates for a measure are comparable to the rates reported in the published literature or by other national sources (e.g. HEDIS). If no comparable sources are available, the rates are judged based on what is clinically reasonable. In addition, all results are systematically reviewed for face validity by members of an external physician clinical consultant panel. 2f.3 Provide Measure Scores from Testing or Current Use (description of scores, e.g., distribution by quartile, mean, median, SD, etc.; identification of statistically significant and meaningfully differences in performance): Summarized in 2b3	2f C ☐ P ☐ M ☐ N ☐	Comment [KP18]: 2f. Data analysis demonstrates that methods for scoring and analysis of the specified measure allow for identification of statistically significant and practically/clinically meaningful differences in performance. Comment [k19]: 14 With large enough sample sizes, small differences that are statistically significant may or may not be practically or clinically meaningful. The substantive question may be, for example, whether a statistically significant difference of one percentage point in the percentage of patients who received smoking cessation counseling (e.g., 74% v. 75%) is clinically meaningful; or whether a statistically significant difference of \$25 in cost for an episode of care (e.g., \$5,000 v. \$5,025) is practically meaningful. Measures with overall poor performance may not demonstrate much variability across providers.
2g. Comparability of Multiple Data Sources/Methods 2g.1 Data/sample (description of data/sample and size): 2g.2 Analytic Method (type of analysis & rationale):	2g C ☐ P ☐ M ☐ N ☐ NA ☐	Comment [KP20]: 2g. If multiple data sources/methods are allowed, there is demonstration they produce comparable results.

2g.3 Testing Results (e.g., correlation statistics, comparison of rankings):	
2h. Disparities in Care	2h
2h.1 If measure is stratified, provide stratified results (scores by stratified categories/cohorts):	C ☐
2h.2 If disparities have been reported/identified, but measure is not specified to detect disparities, provide follow-up plans:	P ☐
	M ☐
	N ☐
	NA ☐
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria for Scientific Acceptability of Measure Properties?	2
Steering Committee: Overall, to what extent was the criterion, Scientific Acceptability of Measure Properties, met?	2
Rationale:	C ☐
	P ☐
	M ☐
	N ☐
3. USABILITY	
Extent to which intended audiences (e.g., consumers, purchasers, providers, policy makers) can understand the results of the measure and are likely to find them useful for decision making. (evaluation criteria)	Eval Rating
3a. Meaningful, Understandable, and Useful Information	
3a.1 Current Use: in use	
3a.2 Use in a public reporting initiative (disclosure of performance results to the public at large) (If used in a public reporting initiative, provide name of initiative(s), locations, Web page URL(s). <u>If not publicly reported</u> , state the plans to achieve public reporting within 3 years): Health plans, physicians (individuals and groups), care management, and other vendors/customers are using this measure on a national level. However, we do not know if this specific measure is being used as part of a public reporting initiative.	
3a.3 If used in other programs/initiatives (If used in quality improvement or other programs/initiatives, name of initiative(s), locations, Web page URL(s). <u>If not used for QI</u> , state the plans to achieve use for QI within 3 years): Health plans, physicians (individuals and groups), care management, and other vendors/customers use many of our measures on a national level for quality improvement, disease management, and physician sharing programs. Customers are able to select their measures depending on their business needs. As such, we do not know which specific measures are used by our customers.	
Testing of Interpretability (Testing that demonstrates the results are understood by the potential users for public reporting and quality improvement)	
3a.4 Data/sample (description of data/sample and size): Results are summarized and reported by users/customers depending on their business need - we do not have access to this information. Because of us my multiple users/customers, there is no single data sample, methodology, or public reporting format.	
3a.5 Methods (e.g., focus group, survey, QI project):	3a
	C ☐
	P ☐
	M ☐
	N ☐
3a.6 Results (qualitative and/or quantitative results and conclusions):	
3b/3c. Relation to other NQF-endorsed measures	
3b.1 NQF # and Title of similar or related measures:	
(for NQF staff use) Notes on similar/related endorsed or submitted measures:	

Comment [KP21]: 2h. If disparities in care have been identified, measure specifications, scoring, and analysis allow for identification of disparities through stratification of results (e.g., by race, ethnicity, socioeconomic status, gender); OR rationale/data justifies why stratification is not necessary or not feasible.

Comment [KP22]: 3a. Demonstration that information produced by the measure is meaningful, understandable, and useful to the intended audience(s) for both public reporting (e.g., focus group, cognitive testing) and informing quality improvement (e.g., quality improvement initiatives). An important outcome that may not have an identified improvement strategy still can be useful for informing quality improvement by identifying the need for and stimulating new approaches to improvement.

3b. Harmonization If this measure is related to measure(s) already endorsed by NQF (e.g., same topic, but different target population/setting/data source or different topic but same target population): 3b.2 Are the measure specifications harmonized? If not, why?	3b C ☐ P ☐ M ☐ N ☐ NA ☐
3c. Distinctive or Additive Value 3c.1 Describe the distinctive, improved, or additive value this measure provides to existing NQF-endorsed measures: 5.1 Competing Measures If this measure is similar to measure(s) already endorsed by NQF (i.e., on the same topic and the same target population), describe why it is a more valid or efficient way to measure quality:	3c C ☐ P ☐ M ☐ N ☐
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria for Usability?	3
Steering Committee: Overall, to what extent was the criterion, Usability, met? Rationale:	3 C ☐ P ☐ M ☐ N ☐
4. FEASIBILITY	
Extent to which the required data are readily available, retrievable without undue burden, and can be implemented for performance measurement. (evaluation criteria)	Eval Rating
4a. Data Generated as a Byproduct of Care Processes 4a.1-2 How are the data elements that are needed to compute measure scores generated? coding/abstraction performed by someone other than person obtaining original information,	4a C ☐ P ☐ M ☐ N ☐
4b. Electronic Sources 4b.1 Are all the data elements available electronically? (elements that are needed to compute measure scores are in defined, computer-readable fields, e.g., electronic health record, electronic claims) Yes 4b.2 If not, specify the near-term path to achieve electronic capture by most providers.	4b C ☐ P ☐ M ☐ N ☐
4c. Exclusions 4c.1 Do the specified exclusions require additional data sources beyond what is required for the numerator and denominator specifications? No 4c.2 If yes, provide justification.	4c C ☐ P ☐ M ☐ N ☐ NA ☐
4d. Susceptibility to Inaccuracies, Errors, or Unintended Consequences 4d.1 Identify susceptibility to inaccuracies, errors, or unintended consequences of the measure and describe how these potential problems could be audited. If audited, provide results. As mentioned earlier, a claims-based measure will not identify with absolute confidence patients who cannot take a penicillin related antibiotic due to an allergy or medication intolerance. For this reason, this measure allows recommended alternatives for PCN allergic patients to meet numerator compliance.	4d C ☐ P ☐ M ☐ N ☐

Comment [KP23]: 3b. The measure specifications are harmonized with other measures, and are applicable to multiple levels and settings.

Comment [k24]: 16 Measure harmonization refers to the standardization of specifications for similar measures on the same topic (e.g., *influenza immunization* of patients in hospitals or nursing homes), or related measures for the same target population (e.g., eye exam and HbA1c for *patients with diabetes*), or definitions applicable to many measures (e.g., age designation for children) so that they are uniform or compatible, unless differences are dictated by the evidence. The dimensions of harmonization can include numerator, denominator, exclusions, and data source and collection instructions. The extent of harmonization depends on the relationship of the measures, the evidence for the specific measure focus, and differences in data sources.

Comment [KP25]: 3c. Review of existing endorsed measures and measure sets demonstrates that the measure provides a distinctive or additive value to existing NQF-endorsed measures (e.g., provides a more complete picture of quality for a particular condition or aspect of healthcare).

Comment [k26]: 5. Demonstration that the measure is superior to competing measures – new submissions and/or endorsed measures (e.g., is a more valid or efficient way to measure).

Comment [KP27]: 4a. For clinical measures, required data elements are routinely generated concurrent with and as a byproduct of care processes during care delivery. (e.g., BP recorded in the electronic record, not abstracted from the record later by other personnel; patient self-assessment tools, e.g., depression scale; lab values, meds, etc.)

Comment [KP28]: 4b. The required data elements are available in electronic sources. If the required data are not in existing electronic sources, a credible, near-term path to electronic collection by most providers is specified and clinical data elements are specified for transition to the electronic health record.

Comment [KP29]: 4c. Exclusions should not require additional data sources beyond what is required for scoring the measure (e.g., numerator and denominator) unless justified as supporting measure validity.

Comment [KP30]: 4d. Susceptibility to inaccuracies, errors, or unintended consequences and the ability to audit the data items to detect such problems are identified.

4e. Data Collection Strategy/Implementation 4e.1 Describe what you have learned/modified as a result of testing and/or operational use of the measure regarding data collection, availability of data/missing data, timing/frequency of data collection, patient confidentiality, time/cost of data collection, other feasibility/ implementation issues: Since gatifloxacin has been removed from the market, this medication will be removed from this measure during our 2011 release. Also, based upon feedback from sinusitis experts associated with IDSA who reviewed this measure, we will remove moxifloxacin due to risk of hepatotoxicity associated with this medication. Finally, we will shorten the post window timeframe (i.e., the time period after the initiating acute sinusitis event) from 21 to 10 days. This will result in a shorter period of time where we are looking for a prescribed antibiotic. This is more consistent with current practice patterns. 4e.2 Costs to implement the measure (costs of data collection, fees associated with proprietary measures): We do not have access to this information. This would vary based on the customer/vendor, patient population, and programs/interventions associated with measure use. 4e.3 Evidence for costs: 4e.4 Business case documentation:	4e C ☐ P ☐ M ☐ N ☐
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria for Feasibility?	4
Steering Committee: Overall, to what extent was the criterion, Feasibility, met? Rationale:	4 C ☐ P ☐ M ☐ N ☐
RECOMMENDATION	
(for NQF staff use) Check if measure is untested and only eligible for time-limited endorsement.	Time-limited ☐
Steering Committee: Do you recommend for endorsement? Comments:	Y ☐ N ☐ A ☐
CONTACT INFORMATION	
Co.1 Measure Steward (Intellectual Property Owner) Co.1 Organization Ingenix 12125 Technology Drive Eden Prairie Minnesota 55344 Co.2 Point of Contact Kay Schwebke, Medical Director kay.schwebke@ingenix.com 952-833-7154	
Measure Developer If different from Measure Steward Co.3 Organization Ingenix 12125 Technology Drive Eden Prairie Minnesota 55344 Co.4 Point of Contact Kay Schwebke, Medical Director kay.schwebke@ingenix.com 952-833-7154	
Co.5 Submitter If different from Measure Steward POC Kay Schwebke, Medical Director kay.schwebke@ingenix.com 952-833-7154- Ingenix	
Co.6 Additional organizations that sponsored/participated in measure development The definition of "first line antibiotics" used in this measure was reviewed by sinusitis infectious disease experts	

Comment [KP31]: 4e. Demonstration that the data collection strategy (e.g., source, timing, frequency, sampling, patient confidentiality, etc.) can be implemented (e.g., already in operational use, or testing demonstrates that it is ready to put into operational use).

who were identified by the Infectious Diseases Society of America (IDSA). This was felt necessary given the evolving recommendations of antibiotic use based on emerging antibiotic resistance data.

In addition, this measure has been reviewed and supported by the American Academy of Family Physicians.

ADDITIONAL INFORMATION

Workgroup/Expert Panel involved in measure development

Ad.1 Provide a list of sponsoring organizations and workgroup/panel members' names and organizations.

Describe the members' role in measure development.

We have an external consultant panel that participates in the original literature search process, measure development, code set review, testing review, and maintenance processes. Panel members include the following:

NAME & Title Employer/Position

Alexander, Beth Pharm D, BCPS Assistant Professor, Augsburg College
 Ayenew, Woubeshet, MD Hennepin Faculty Associates; Hennepin County Medical Center
 Becker, Keith, MD Fairview Medical Center
 Betcher, Susan, MD Allina Medical Clinic
 Bruer, Paul, MD Comprehensive Ophthalmology, LLC
 Capecchi, Joseph, MD Allina Medical Clinic
 Giesler, Janell, MD Allina Medical Clinic
 Grabowski, Carol, MD Allina Medical Clinic
 Hansen, Calvin, MD Iowa Health Physicians
 Hargrove, Jody, MD Arthritis and Rheumatology Consultants
 Hermann, Richard, MD Tufts - New England Medical Center
 Jemming, Brian, Pharm D CentraCare Health System
 Kohen, Jeffrey, MD Veterans Affairs Medical Center
 McCarthy, Teresa, MD University of Minnesota, Department of Family Medicine & Community Health
 McEvoy, Charlene, MD, MPH HealthPartners & HealthPartners Research Foundation; Assistant Professor of Medicine, University of Minnesota
 McGee, Deanna, Pharm D, BCPS Retail Pharmacy
 Ogle, Kathleen, MD Hennepin Faculty Associates; Hennepin County Medical Center: Assistant Professor of Medicine, University of Minnesota Medical School
 Peter, Kathleen, MD Park Nicollet Medical Center
 Pieper-Bigelow, Christina, MD Allina Medical Clinic
 Redmon, Bruce, MD University of Minnesota Physicians
 Scharpf, Steven, MD Mountain Valleys Health Centers
 Weitz, Carol, MD Independent

Ad.2 If adapted, provide name of original measure:

Ad.3-5 If adapted, provide original specifications URL or attachment

Measure Developer/Steward Updates and Ongoing Maintenance

Ad.6 Year the measure was first released: 2007

Ad.7 Month and Year of most recent revision: 2009-10

Ad.8 What is your frequency for review/update of this measure? every three years at minimum

Ad.9 When is the next scheduled review/update for this measure? 2012-10

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Ad.11 -13 Additional Information web page URL or attachment: [Attachment SAHP 2004.pdf](#)

Date of Submission (MM/DD/YY): [02/17/2010](#)

1c. The measure focus is:

- an outcome (e.g., morbidity, mortality, function, health-related quality of life) that is relevant to, or associated with, a national health goal/priority, the condition, population, and/or care being addressed;

OR

- if an intermediate outcome, process, structure, etc., there is **evidence** that supports the specific measure focus as follows:
 - Intermediate outcome – evidence that the measured intermediate outcome (e.g., blood pressure, HbA1c) leads to improved health/avoidance of harm or cost/benefit.
 - Process – evidence that the measured clinical or administrative process leads to improved health/avoidance of harm and
if the measure focus is on one step in a multi-step care process, it measures the step that has the greatest effect on improving the specified desired outcome(s).
 - Structure – evidence that the measured structure supports the consistent delivery of effective processes or access that lead to improved health/avoidance of harm or cost/benefit.
 - Patient experience – evidence that an association exists between the measure of patient experience of health care and the outcomes, values and preferences of individuals/ the public.
 - Access – evidence that an association exists between access to a health service and the outcomes of, or experience with, care.
 - Efficiency – demonstration of an association between the measured resource use and level of performance with respect to one or more of the other five IOM aims of quality.

4 Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multi-step process, the step with the greatest effect on the desired outcome should be selected as the focus of measurement. For example, although assessment of immunization status and recommending immunization are necessary steps, they are not sufficient to achieve the desired impact on health status – patients must be vaccinated to achieve immunity. This does not preclude consideration of measures of preventive screening interventions where there is a strong link with desired outcomes (e.g., mammography) or measures for multiple care processes that affect a single outcome.

3 The strength of the body of evidence for the specific measure focus should be systematically assessed and rated (e.g., USPSTF grading system <http://www.ahrq.gov/clinic/uspstf07/methods/benefit.htm>). If the USPSTF grading system was not used, the grading system is explained including how it relates to the USPSTF grades or why it does not. However, evidence is not limited to quantitative studies and the best type of evidence depends upon the question being studied (e.g., randomized controlled trials appropriate for studying drug efficacy are not well suited for complex system changes). When qualitative studies are used, appropriate qualitative research criteria are used to judge the strength of the evidence.

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Input Guide

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What Input Files to Prepare

The following list specifies what input files you prepare for processing:

- The claims data file (required)
- The member data file (required)
- The member term data file (required)

Field Type Definitions and Input File Requirements

This chapter lists the field requirements for your input files. One of the attributes listed among the requirements is defined as "Type". There are four field types used to describe a field's value, and they are defined below.

Field Type	Definition
AlphaNum	A value made of letters and/or numbers. If a value of this type is made of numbers only, it will not be a value that can be operated on mathematically. For example, it would be inappropriate to subtract one procedure code from another procedure code even though both values may contain only numbers.
Num	A value made of numbers only, and which can logically be operated on mathematically. Age is an example of this type. One particular field, while not used in mathematical calculations, is defined in the EBM Connect software as such that it accepts only numeric values. (To enter a non-numeric value would cause EBM Connect processing to stop.) Therefore, this field is defined as Num. It is the Case ID field in the optional disease registry input file.
Date	A value which can be interpreted as a date value. Values should always use four-digit years but the format may vary otherwise.
DecNum	A value made of numbers and a decimal point. These values can also logically be operated on mathematically.

Claims Input File

The claims file contains detailed information on services that were billed or performed or otherwise rendered. The claims file includes:

- Medical claims, including medical services, facility services and clinic services
- Pharmacy claims, including billed prescriptions and drugs
- Lab claims, including lab test and results information

Field Name	Type	Length	Required or Optional
Family ID	AlphaNum	1-30	Always required for all claims
Patient ID	AlphaNum	0-2	Optional
Amount Paid	DecNum	1-11	Required for all claims
Amount Allowed	DecNum	0-11	Required for all claims
Procedure Code	AlphaNum	5	Required if there is no revenue code, NDC, or LOINC® code
Procedure Code Modifier	AlphaNum	2	Required for medical claims
Revenue Code	AlphaNum	0 or 4	Optional (applies to medical claims when used)
First Diagnosis Code	AlphaNum	5 or 6	Required for medical claims
Second Diagnosis Code	AlphaNum	0, 5 or 6	Optional (applies to medical claims when used)
Third Diagnosis Code	AlphaNum	0, 5 or 6	Optional (applies to medical claims when used)
Fourth Diagnosis Code	AlphaNum	0, 5 or 6	Optional (applies to medical claims when used)
First Date of Service	Date	8 or 10	Always required for all claims
Last Date of Service	Date	8 or 10	Required for all claims

Paid Date	Date	0, 8 or 10	Optional
Type of Service	AlphaNum	0-10	Optional
Provider ID	AlphaNum	1-20	Required for medical claims
Ordering Provider ID	AlphaNum	0-20	Optional
Provider Type	AlphaNum	1-10	Required for medical claims
Provider Specialty Type	AlphaNum	1-10	Required for medical claims
Provider Key	AlphaNum	1-20	Required for medical claims
NDC	AlphaNum	0 or 11	Required for Rx claims
Day Supply	Num	0-4	Required for Rx claims
Quantity Count	DecNum	0-10	Required for Rx claims
LOINC®	AlphaNum	0 or 7	Required for lab claims
Lab Test Result	AlphaNum	0-18	Required for lab claims
Place of Service	AlphaNum	1-10	Required for medical claims
Unique Record ID	AlphaNum	1-28	Required for all claims
Claim Number	AlphaNum	1-28	Required for all claims
Bill Type Frequency Indicator	Num	0 or 1	Optional
Patient Status	AlphaNum	1-2	Required for facility claims (involving admission or confinement).
Facility Type	AlphaNum	0-2	Optional
Bed Type	AlphaNum	0-1	Optional
First ICD-9 Procedure Code	AlphaNum	0, 4 or 5	Optional, but will impact results (applies to medical claims when used)
Second ICD-9 Procedure Code	AlphaNum	0, 4 or 5	Optional (see above)
Third ICD-9 Procedure Code	AlphaNum	0, 4 or 5	Optional (see above)
Fourth ICD-9 Procedure Code	AlphaNum	0, 4 or 5	Optional (see above)

Field Descriptions

Instructions for each input field are as follows:

Family ID

This field identifies all members of a family and can be any alphanumeric string.

Note: Remember that each Family ID (and Patient ID) listed in your claims input file must have a corresponding record in your member input data file and your member term data file.

Patient ID

This field identifies individual members within a family. If present, this field must be sorted within Family ID, so that all records for an individual are contiguous. If the Family ID uniquely identifies an individual, this field need not be specified (that is, its length in the dictionary will be zero).

Amount Paid

The amount paid for this claim line.

Amount Allowed

The allowed amount for this claim line. This amount typically represents the total amount reimbursed including deductibles, copays, coinsurance, insurer paid, etc.

Procedure Code

The procedure code must be one of:

- A procedure code specified in the Physician's Current Procedure Terminology, 4th Edition (CPT® -4 codes) defined by the American Medical Association, for the years 1997 and later.
- A procedure code specified by the HCFA Common Procedure Coding System, Level II code (HCPCS) defined by the Centers for Medicare and Medicaid Services (CMS) for the years 1999 and later.
- A National Uniform Billing Committee (NUBC) revenue code.

Note: When the NUBC code is entered in the Procedure Code field, it should be padded to the right with blanks because the Procedure Code field always occupies five characters.

- If your organization defines its own procedure codes and/or revenue codes, they must be mapped to standard procedure and revenue codes.

Procedure Code Modifier

Use this field to specify any procedure code modifier that accompanies the procedure code.

Revenue Code

The revenue code, if one was entered for the claim. Supported values in this field are NUBC revenue codes. If your organization defines its own revenue codes, they must be mapped to standard revenue codes.

The revenue code is an optional field, allowing you to define your input records so that you can place an NUBC revenue code and a CPT/HCPCS procedure code on a single record line.

For claim records that do not have a revenue code, leave the revenue code field blank.

First Diagnosis Code Through Fourth Diagnosis Code

Up to four diagnoses may be entered for each claim, but only the first is required.

If your organization defines its own diagnosis codes, they must be mapped to standard ICD-9 diagnosis codes.

First Date of Service and Last Date of Service

The first date and last date represented by the claim line. If you choose to use a date format with separators (such as YYYY/MM/DD or YYYY-MM-DD), the separators are ignored on input, so you can use any character as a separator. Valid formats include: YYYYMMDD, MMDDYYYY, DDMMYYYY, YYYY/MM/DD, MM/DD/YYYY, and DD/MM/YYYY, where the separator can be any character.

Paid Date

This field is optional. This is the date the claim was paid. The format of the paid date must be the same as that used in the First and Last Date of Service.

Type of Service

This is an optional code which represents the type of service (TOS) performed for this claim. If no specific value is available for this field, it should be filled with blanks. If this field is not used (i.e., its length is set to zero in the configuration), non-pharmaceutical claims with no procedure code will be treated as ancillary records.

Provider ID

Provider identification number from the claim. Used to identify who performed the service.

Ordering Provider ID

This is an optional field. This is the identification number of the provider who ordered the service.

Provider Type

This code represents the type of provider who performed the service. Examples of provider types would be chiropractor, nurse practitioner, medical doctor, counselor, pharmacy, hospital or treatment facility.

Provider Specialty Type

This code represents the specialty of the provider who performed the service.

Provider Key

Unique number or code for a physician who has multiple provider IDs or specialties. A single health care provider may have multiple provider IDs in your input claims data, but this person or entity should have only one provider key.

NDC

If this is a pharmaceutical claim, this field should contain the drug's NDC code. For non-pharmaceutical claim records, the NDC field should be filled with blanks.

Day Supply

For pharmacy records, the number of days a filled prescription is expected to last. If you have no pharmacy records, the Days Supply is an optional field.

Quantity Count

Quantity of drug dispensed in metric units:

Each - solid oral dosage forms (tablet, capsule), powder filled (dry) vials, packets, patches, units of use packages, suppositories, bars.

Milliliter - (cc) liquid oral dosage forms, liquid filled vials, ampules, reconstituted oral products.

Grams - ointments, bulk powders (not IV).

If you have no pharmacy records, the Quantity Count is an optional field.

LOINC®

Logical Observation Identifiers Names and Codes (LOINC®). The LOINC Code is a universal identifier for a lab test for a particular analyte. The LOINC User's Guide and database can be found at www.regenstrief.org.

Enter a LOINC code if the record is a lab record. For non-lab records, leave the LOINC field blank.

If you have no lab records in your claims input, the LOINC code is optional.

Notes:

- (1) When using lab results data that has not been mapped to a LOINC code, map the comparable vendor-specific test number provided by the laboratory vendor(s) to one of these default codes.
- (2) This is a retired code which may be present on historical data, or which some laboratories may be continuing to use. Input record data with this code is included in the definition of this test.

Lab Test Result

If the record is a lab record, use this field to enter the result value of lab test. For non-lab records, this field should be blank.

If you have no lab records in your claims input, the Lab Test Result is optional.

Place of Service

Place of service (POS). You must map your internal POS codes to Centers for Medicare and Medicaid Services (CMS) standard POS codes.

Unique Record ID

This required field contains a unique identifier representing the service line from the claim. For medical services, this ID typically represents the service row from the CMS 1500 or CMS 1450/UB92 claim form.

Claim Number

A unique identifier used to link service lines for a specific claim submitted for a member. If a claim has multiple service lines, each service will have a unique record ID and the same claim number to represent the claim.

Bill Type Frequency Indicator

This optional field is used to indicate the disposition of confinements.

Patient Status

This field is required for facility claims. The contents will be the patient status indicator field from the NUBC UB-92 form. This field can denote whether the member died during a confinement.

Facility Type

This field is optional. Space for it is provided to allow for additional post grouping analysis. The contents will typically be the UB-92 facility type data value. This would allow records to be easily selected for diagnosis related grouping (DRG) based on the facility type.

Bed Type

If a value is present, this field acts as an additional discriminator in determining whether a Facility record extends an existing confinement or starts a new confinement.

First ICD-9 Procedure Code Through Fourth ICD-9 Procedure Code

If your claims have ICD-9 procedure codes, include them in your claims input file.

If a decimal point will appear in this field in your claim records, the length should be given as 5. If the decimal separator is not used, the length is 4. If these fields are unused, the length is zero.

Member Input File

The member data file contains the most current information about the member.

Field Descriptions

Field	Type	Length	Required or Optional
Family ID	AlphaNum	1-30	Required
Patient ID	AlphaNum	0-2	Optional
Patient Gender	AlphaNum	1	Required
Date of Birth	Date	8 or 10	Required
Member Beginning Eligibility Date	Date	0, 8 or 10	Optional
Member Ending Eligibility Date	Date	0, 8 or 10	Optional

Instructions for each input field are as follows:

Family ID

This field identifies all members of a family and can be any alphanumeric string. The records in the member file must be sorted first on the Family ID (together with Patient ID, if available) so that all records for an individual are contiguous.

Patient ID

This field identifies individual members within a family. If present, this field must be sorted within Family ID, so that all records for an individual are contiguous. If the Family ID uniquely identifies an individual, this field need not be specified (that is, its length in the dictionary will be zero).

Patient Gender and Date of Birth

The member's gender (F or M) and date of birth. If you choose to use a date format with separators (such as YYYY/MM/DD or YYYY-MM-DD), the separators are ignored on input, so you can use any character as a separator. Valid date formats include: YYYYMMDD, MMDDYYYY, DDMMYYYY, YYYY/MM/DD, MM/DD/YYYY, and DD/MM/YYYY, where the separator can be any character.

Member Beginning Eligibility Date and Ending Eligibility Date

The first date on which the member became covered under the plan and the last date of the member's coverage. If you choose to use a date format with separators (such as YYYY/MM/DD or YYYY-MM-DD), the separators are ignored on input, so you can use any character as a separator. Valid formats include: YYYYMMDD, MMDDYYYY, DDMMYYYY, YYYY/MM/DD, MM/DD/YYYY, and DD/MM/YYYY, where the separator can be any character.

Member Term Input File

The member term data file contains member coverage and term activity information. Plan coverage begin and end dates are required in order to correctly calculate the other fields in the member term file. There may be more than one record per individual member.

Field Descriptions

Field	Type	Length	Required or Optional
Family ID	AlphaNum	1-30	Required
Patient ID	AlphaNum	0-2	Optional
Member Beginning Eligibility Date	Date	8 or 10	Required
Member Ending Eligibility Date	Date	8 or 10	Required
Primary Care Provider	AlphaNum	20	Required
Provider Specialty Type	AlphaNum	1-10	Required
Medical Flag	AlphaNum	1	Required
Pharmacy Flag	AlphaNum	1	Required

Instructions for each input field are as follows:

Family ID

This field identifies all members of a family and can be any alphanumeric string. The records in the member term file must be sorted first on the Family ID (together with Patient ID, if available) so that all records for an individual are contiguous.

Patient ID

This field identifies individual members within a family.

Member Beginning Eligibility Date and Member Ending Eligibility Date

The first date on which the member became covered under the plan and the last date of the member's coverage. If you choose to use a date format with separators (such as YYYY/MM/DD or YYYY-MM-DD), the separators are ignored on input, so you can use any character as a separator. Valid formats include: YYYYMMDD, MMDDYYYY, DDMMYYYY, YYYY/MM/DD, MM/DD/YYYY, and DD/MM/YYYY, where the separator can be any character.

Primary Care Provider

The provider key for the member's primary care physician. A single health care physician may have multiple provider IDs in your input claims data, but this person should have only one provider key.

Provider Specialty Type

This code represents the specialty of the primary care physician.

Medical Flag

Identifies whether the member has medical coverage (Y or N).

Pharmacy Flag

Identifies whether the member has pharmacy coverage (Y or N).

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Antimicrobial treatment guidelines for acute bacterial rhinosinusitis

Executive Summary

SINUS AND ALLERGY HEALTH PARTNERSHIP*

Treatment guidelines developed by the Sinus and Allergy Health Partnership for acute bacterial rhinosinusitis (ABRS) were originally published in 2000. These guidelines were designed to: (1) educate clinicians and patients (or patients' families) about the differences between viral and bacterial rhinosinusitis; (2) reduce the use of antibiotics for nonbacterial nasal/sinus disease; (3) provide recommendations for the diagnosis and optimal treatment of ABRS; (4) promote the use of appropriate antibiotic therapy when bacterial infection is likely; and (5) describe the current understanding of pharmacokinetic and pharmacodynamics and how they relate to the effectiveness of antimicrobial therapy. The original guidelines are updated here to include the most recent information on manage-

ment principles, antimicrobial susceptibility patterns, and therapeutic options.

Burden of Disease

An estimated 20 million cases of ABRS occur annually in the United States. According to National Ambulatory Medical Care Survey (NAMCS) data, sinusitis is the fifth most common diagnosis for which an antibiotic is prescribed. Sinusitis accounted for 9% and 21% of all pediatric and adult antibiotic prescriptions, respectively, written in 2002. The primary diagnosis of sinusitis results in expenditures of approximately \$3.5 billion per year in the United States.

Definition and Diagnosis of ABRS

ABRS is most often preceded by a viral upper respiratory tract infection (URI). Allergy, trauma, dental infection, or other factors that lead to inflammation of the nose and paranasal sinuses may also predispose individuals to developing ABRS.

Patients with a "common cold" (viral URI) usually report some combination of the following symptoms: sneezing, rhinorrhea, nasal congestion, hyposmia/anosmia, facial pressure, postnasal drip, sore throat, cough, ear fullness, fever, and myalgia. A change in the color or the characteristic of the nasal discharge is not a specific sign of a bacterial infection. Bacterial superinfection may occur at any time during the course of a viral URI. The risk that bacterial superinfection has occurred is greater if the illness is still present after 10 days.

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*The Sinus and Allergy Health Partnership is a not-for-profit organization created through the joint efforts of the American Academy of Otolaryngic Allergy, the American Academy of Otolaryngology-Head and Neck Surgery, and the American Rhinologic Society. Development of this paper was funded by the Sinus and Allergy Health Partnership. Some antibiotics discussed in this document currently are not approved by the US Food and Drug Administration for the treatment of maxillary sinusitis in adults or children, while the value of others approved when antimicrobial resistance rates were very low is now very limited.

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Because there may be cases that fall out of the “norm” of this typical progression, practicing clinicians need to rely on their clinical judgment when using these guidelines. In general, however, a diagnosis of ABRS may be made in adults or children with symptoms of a viral URI that have not improved after 10 days or worsen after 5 to 7 days. There may be some or all of the following signs and symptoms: nasal drainage, nasal congestion, facial pressure/pain (especially when unilateral and focused in the region of a particular sinus), postnasal drainage, hyposmia/anosmia, fever, cough, fatigue, maxillary dental pain, and ear pressure/fullness.

Physical examination provides limited information in the diagnosis of ABRS.

While sometimes helpful, plain film radiographs, computed tomography (CT), and magnetic resonance imaging scans are not necessary for cases of ABRS.

Microbiology of ABRS

The most common bacterial species isolated from the maxillary sinuses of patients with ABRS are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, the latter being more common in children. Other streptococcal species, anaerobic bacteria and *Staphylococcus aureus* cause a small percentage of cases.

Bacterial Resistance in ABRS

The increasing prevalence of penicillin nonsusceptibility and resistance to other drug classes among *S pneumoniae* has been a problem in the United States, with 15% being penicillin-intermediate and 25% being penicillin-resistant in recent studies. Resistance to macrolides and trimethoprim/sulfamethoxazole (TMP/SMX) is also common in *S pneumoniae*. The prevalence of β -lactamase-producing isolates of *H influenzae* is approximately 30%, while essentially all *M catarrhalis* isolates produce β -lactamases. Resistance of *H influenzae* to TMP/SMX is also common.

Antimicrobial Treatment Guidelines for ABRS

These guidelines apply to both adults and children. When selecting antibiotic therapy for ABRS,

the clinician should consider the severity of the disease, the rate of progression of the disease, and recent antibiotic exposure. The guidelines now divide patients with ABRS into two general categories: (1) those with mild symptoms who have not received antibiotics within the past 4 to 6 weeks, and (2) those with mild disease who have received antibiotics within the past 4 to 6 weeks or those with moderate disease regardless of recent antibiotic exposure. The difference in severity of disease does not imply infection with a resistant pathogen. Rather, this terminology indicates the relative degree of acceptance of possible treatment failure and the likelihood of spontaneous resolution of symptoms—patients with more severe symptoms are less likely to resolve their disease spontaneously. The primary goal of antibiotic therapy is to eradicate bacteria from the site of infection, which, in turn, helps (1) return the sinuses back to health; (2) decrease the duration of symptoms to allow patients to resume daily activities more quickly; (3) prevent severe complications such as meningitis and brain abscess; and (4) decrease the development of chronic disease. Severe or life-threatening infections with or without complications are rare, and are not addressed in these guidelines.

Prior antibiotic use is a major risk factor associated with the development of infection with antimicrobial-resistant strains. Because recent antimicrobial exposure increases the risk of carriage of and infection due to resistant organisms, antimicrobial therapy should be based upon the patient's history of recent antibiotic use. The panel's guidelines, therefore, stratify patients according to antibiotic exposure in the previous 4 to 6 weeks.

Lack of response to therapy at ≥ 72 hours is an arbitrary time established to define treatment failures. Clinicians should monitor the response to antibiotic therapy, which may include instructing the patient to call the office or clinic if symptoms persist or worsen over the next few days.

The predicted bacteriologic and clinical efficacy of antibiotics in adults and children has been determined according to mathematical modeling of ABRS developed by Michael Poole, MD, PhD, based on pathogen distribution, resolution rates without treatment, and in vitro microbiologic activity.

Antibiotics can be placed into the following relative rank order of predicted clinical efficacy for adults: 90% to 92% = respiratory fluoroquinolones (gatifloxacin, levofloxacin, moxifloxacin), ceftriaxone, high-dose amoxicillin/clavulanate (4 g/250 mg/day), and amoxicillin/clavulanate (1.75 g/250 mg/day); 83% to 88% = high-dose amoxicillin (4 g/day), amoxicillin (1.5 g/day), cefpodoxime proxetil, cefixime (based on *H influenzae* and *M catarrhalis* coverage), cefuroxime axetil, cefdinir, and TMP/SMX; 77% to 81% = doxycycline, clindamycin (based on gram-positive coverage only), azithromycin, clarithromycin and erythromycin, and telithromycin; 65% to 66% = cefaclor and loracarbef. The predicted spontaneous resolution rate in patients with a clinical diagnosis of ABRS is 62%.

Antibiotics can be placed into the following relative rank order of predicted clinical efficacy in children with ABRS: 91% to 92% = ceftriaxone, high-dose amoxicillin/clavulanate (90 mg/6.4 mg per kg per day) and amoxicillin/clavulanate (45 mg/6.4 mg per kg per day); 82% to 87% = high-dose amoxicillin (90 mg/kg per day), amoxicillin (45 mg/kg per day), cefpodoxime proxetil, cefixime (based on *H influenzae* and *M catarrhalis* coverage only), cefuroxime axetil, cefdinir, and TMP/SMX; and 78% to 80% = clindamycin (based on gram-positive coverage only), cefprozil, azithromycin, clarithromycin, and erythromycin; 67% to 68% = cefaclor and loracarbef. The predicted spontaneous resolution rate in untreated children with a presumed diagnosis of ABRS is 63%.

Recommendations for initial therapy for adult patients with mild disease (who have not received antibiotics in the previous 4 to 6 weeks) include the following choices: amoxicillin/clavulanate (1.75 to 4 g/250 mg per day), amoxicillin (1.5 to 4 g/day), cefpodoxime proxetil, cefuroxime axetil, or cefdinir. While TMP/SMX, doxycycline, azithromycin, clarithromycin, erythromycin, or telithromycin may be considered for patients with β -lactam allergies, bacteriologic failure rates of 20% to 25% are possible. Failure to respond to antimicrobial therapy after 72 hours should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 4). When a change in antibiotic therapy is made,

the clinician should consider the limitations in coverage of the initial agent.

Recommendations for initial therapy for adults with mild disease who have received antibiotics in the previous 4 to 6 weeks or adults with moderate disease include the following choices: respiratory fluoroquinolone (eg, gatifloxacin, levofloxacin, moxifloxacin) or high-dose amoxicillin/clavulanate (4 g/250 mg per day). The widespread use of respiratory fluoroquinolones for patients with milder disease may promote resistance of a wide spectrum of organisms to this class of agents. Ceftriaxone (parenteral, 1 to 2 g/day for 5 days) or combination therapy with adequate gram-positive and negative coverage may also be considered. Examples of appropriate regimens of combination therapy include high-dose amoxicillin or clindamycin plus cefixime, or high-dose amoxicillin or clindamycin plus rifampin. While the clinical effectiveness of ceftriaxone and these combinations for ABRS is unproven; the panel considers these reasonable therapeutic options based on the spectrum of activity of these agents and on data extrapolated from acute otitis media studies. Rifampin should not be used as monotherapy, casually, or for longer than 10 to 14 days, as resistance quickly develops to this agent. Rifampin is also a well-known inducer of several cytochrome p450 isoenzymes and therefore has a high potential for drug interactions. Failure of a patient to respond to antimicrobial therapy after 72 hours of therapy should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 4). When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent. Patients who have received effective antibiotic therapy and continue to be symptomatic may need further evaluation. A CT scan, fiberoptic endoscopy or sinus aspiration and culture may be necessary.

Recommendations for initial therapy for children with *mild* disease and who have *not* received antibiotics in the previous 4 to 6 weeks include the following: high-dose amoxicillin/clavulanate (90 mg/6.4 mg per kg per day), amoxicillin (90 mg/kg per day), cefpodoxime proxetil, cefuroxime axetil, or cefdinir. TMP/SMX, azithromycin, clarithromycin, or erythromycin is recommended if the

patient has a history of immediate Type I hypersensitivity reaction to β -lactams. These antibiotics have limited effectiveness against the major pathogens of ABRS and bacterial failure of 20% to 25% is possible. The clinician should differentiate an immediate hypersensitivity reaction from other less dangerous side effects. Children with immediate hypersensitivity reactions to β -lactams may need: desensitization, sinus cultures, or other ancillary procedures and studies. Children with other types of reactions and side effects may tolerate one specific β -lactam, but not another. Failure to respond to antimicrobial therapy after 72 hours should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 5). When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent.

The recommended initial therapy for children with *mild* disease who *have* received antibiotics in the previous 4 to 6 weeks or children with *moderate* disease is high-dose amoxicillin/clavulanate (90 mg/6.4 mg per kg per day). Cefpodoxime proxetil, cefuroxime axetil, or cefdinir may be used if there is a penicillin allergy (eg, penicillin rash); in such instances, cefdinir is preferred because of high patient acceptance. TMP/SMX, azithromycin, clarithromycin, or erythromycin is

recommended if the patient is β -lactam allergic, but these do not provide optimal coverage. Clindamycin is appropriate if *S pneumoniae* is identified as a pathogen. Ceftriaxone (parenteral, 50 mg/kg per day for 5 days) or combination therapy with adequate gram-positive and -negative coverage may also be considered. Examples of appropriate regimens of combination therapy include high-dose amoxicillin or clindamycin plus cefixime, or high-dose amoxicillin or clindamycin plus rifampin. The clinical effectiveness of ceftriaxone and these combinations for ABRS is unproven; the panel considers these reasonable therapeutic options based on spectrum of activity and on data extrapolated from acute otitis media studies. Rifampin should not be used as monotherapy, casually, or for longer than 10 to 14 days as resistance quickly develops to this agent. Failure to respond to antimicrobial therapy after 72 hours of therapy should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 5). When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent. Patients who have received effective antibiotic therapy and continue to be symptomatic may need further evaluation. A CT scan, fiberoptic endoscopy or sinus aspiration and culture may be necessary.

INTRODUCTION

The Sinus and Allergy Health Partnership, a conjoint group initially sponsored by the American Academy of Otolaryngology Head and Neck Surgery, the American Academy of Otolaryngic Allergy and the American Rhinologic Society, in consultation with representatives of the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and individuals from the fields of infectious disease, pediatric infectious disease, microbiology, and pharmacy have developed these guidelines as an educational tool for healthcare providers involved in managing patients with acute bacterial rhinosinusitis (ABRS). The guidelines, which were published in 2000,¹ were widely accepted; however, recent data (since the time of publication) and the approval of new antimicrobial agents/classes may impact the utility of those recommendations. As a result, the guidelines are updated here to include the most recent information on management principles, antimicrobial susceptibility patterns, and therapeutic options. Significant updates from the previous version of the guidelines include:

- Diagnostic modalities, including serial sinus aspirate sampling;
- Current antimicrobial susceptibility patterns in the United States;
- Pharmacodynamic principles reflecting area under the concentration-time curve (AUC)/minimal inhibitory concentration (MIC) ratio as the parameter that correlates with efficacy for macrolides/azalides;
- Antimicrobial treatment recommendations that reflect a better understanding of pharmacodynamic/pharmacokinetic (PK/PD) principles;
- Consideration of new/other agents (eg, extended-release [adult] and extra strength [children] amoxicillin/clavulanate, cefdinir, telithromycin); and
- Modification of the Poole model to include predicted bacteriologic outcomes in patients with bacteriologic disease and predicted clinical outcomes for a patient population with a clinical only diagnosis of ABRS

While this revised version includes many updates, much of this document is reprinted from the original recommendations because several key

concepts have not changed since the time of their publication.

There are several issues we attempted to address during the process of writing this document: (1) the diagnosis of bacterial “sinusitis” is made too frequently—patients with viral illnesses of only a few days duration are inappropriately labeled as having bacterial disease and, therefore; (2) patients are prescribed an antibiotic that is not only ineffective against a viral pathogen but also has the risk of leading to; (3) increased resistance among respiratory tract pathogens, particularly *Streptococcus pneumoniae*.

In this document, the reader is taken through a stepwise approach to this complex disease. The burden, pathophysiology, and definition of ABRS are reviewed, along with the attributes and limitations of various diagnostic modalities. Also included in these guidelines is a critical review of antimicrobial treatment options for ABRS. Clinical trials conducted in this era of widespread antimicrobial resistance are just beginning to provide sufficient evidence to use as the basis for recommending treatment options but, in general, they are not sufficiently powered to be of objective use. In lieu of evidence, several factors may be useful to clinicians in selecting therapy for individual patients. These factors include pathogen distribution in ABRS, pharmacokinetic and pharmacodynamic principles, mechanisms of antimicrobial resistance, and data from in vitro surveillance studies. Many of these factors have been incorporated into a mathematical model that can be used to objectively compare various antimicrobial options for ABRS.

Our hope is that these guidelines will continue to be a well-accepted part of national and international efforts coordinated by the CDC and the FDA aimed at educating healthcare providers and patients about judicious antimicrobial use and avoidance of the abuse and overuse of these valuable agents. The misuse of antibiotics should not be a replacement for spending time talking with and examining the patient and teaching that patient and/or family members the differences between viral and bacterial infections. We cannot rely on the pharmaceutical industry to continue to develop new drugs as organisms become resistant; rather, we must decrease unnecessary antimicro-

bial use as a means to reduce the spread of resistance.

We believe further research is necessary in order to (1) develop better methods to diagnose ABRS; (2) further explore the clinical application of the antibiotic recommendations presented in this document; (3) monitor antimicrobial resistance patterns among respiratory tract pathogens—especially for *S pneumoniae* and *Haemophilus influenzae*.

VIRAL Versus Bacterial Rhinosinusitis

Each year in the United States, children and adults experience an average of 3 to 8 and 2 to 3 acute viral respiratory illnesses, respectively.^{2,3} Up to 90% of these patients will actually have computed tomographic (CT) scan evidence of paranasal sinus involvement (ie, viral rhinosinusitis [VRS]).^{2,4} Secondary bacterial infections, also referred to as ABRS, complicate a small number of viral infections and positive bacterial cultures can be obtained in roughly 0.5% to 2% of VRS episodes.^{2,5} Approximately 20 million cases of ABRS would therefore be expected, based on the more than 1 billion viral respiratory illnesses that occur each year. Sinusitis accounted for 9% and 21% of all pediatric and adult antibiotic prescriptions, respectively, written in 2002.⁶ In addition to its public health implications, rhinosinusitis has a considerable economic impact. The most recent estimates suggest that expenditures attributable to ABRS total approximately \$3.5 billion each year in the United States.⁷ In 2002, approximately \$400 to \$600 million was spent on antibiotic prescriptions for acute sinusitis.^{6,8}

Differentiating bacterial from viral rhinosinusitis often is a challenge because the clinical features of the two diseases are similar, and the common imaging modalities are not sufficiently sensitive or specific. As a result, clinicians often overtreat uncomplicated rhinosinusitis by readily prescribing antibiotics for the majority of patients with signs and symptoms of VRS (eg, headache, facial pain, nasal congestion, rhinorrhea, fever). Recent reports in the medical literature suggest that primary care physicians prescribe antibiotics for up to 85% to 98% of patients with clinically suspected rhinosinusitis.^{9,10} The practice of treating uncomplicated VRS with antibiotics has two

fundamental limitations: first, secondary bacterial infection complicates a relatively small proportion of cases and second, excessive antibiotic use is associated with consequences, both to individuals and to society as a whole.

As the total number of antibiotic prescriptions increased throughout the 1990s, antimicrobial resistance among respiratory tract pathogens emerged as a significant public health issue. Excessive antibiotic use is strongly associated with the development and spread of bacterial drug resistance.¹¹⁻¹⁶ Recent strategies promoting prudent and rational antimicrobial use have been implemented over the past several years. In 2000, there were 25 million fewer antibiotic prescriptions in the ambulatory care setting compared with 1992 (17% reduction).¹⁷ The most substantial reductions in antimicrobial prescribing have occurred for respiratory tract infections among children (<15 years of age). However, there was no significant change in the population-based antibiotic prescribing rate for sinusitis among children.¹⁸

In rhinosinusitis, two features of antibiotic prescribing are of particular concern. First is the frequent treatment of uncomplicated VRS with antimicrobials. Second is the selection of antimicrobial agents without documented efficacy or that are no longer effective due to the development of resistance. The continued goal of this panel is to develop guidelines for the judicious use of antibiotics in the treatment of ABRS.

Definition and Diagnosis of ABRS

In 1997, the American Academy of Otolaryngology developed working definitions for sinusitis to clarify communications among healthcare providers and researchers.¹⁹ Sinusitis is generally preceded by rhinitis and rarely occurs without concurrent rhinitis; therefore, sinusitis is best described as rhinosinusitis. The terms acute, subacute, recurrent acute, and chronic rhinosinusitis were also reviewed and defined. This terminology was subsequently adopted by the Agency for Health Care and Policy Research in the development of their 1999 document on the Diagnosis and Treatment of Acute Bacterial Rhinosinusitis.²⁰

Pathophysiology of ABRS

ABRS is most often preceded by a viral upper respiratory tract infection (URI). Allergy, trauma, or other environmental factors that lead to inflammation of the nose and paranasal sinuses may also predispose individuals to developing ABRS. Approximately 50% of common colds are caused by the human rhinovirus. Other viruses that cause rhinosinusitis include coronavirus, influenza A and B viruses, parainfluenza virus, respiratory syncytial virus, adenovirus, and enterovirus. Most of these viral infections occur in the early fall to early spring, and the incidence of sinusitis follows a similar pattern.

Human rhinovirus and coronavirus do not cause major epithelial damage, but influenza virus and adenovirus cause significant damage the nasal epithelium.^{21,22} Human rhinovirus, for example, enters via the nose or lacrimal duct and attaches to ICAM-1 receptors on epithelial cells in the posterior nasopharynx.²³ There is upregulation of the production of histamine, bradykinin, and various cytokines, including interleukin-1, interleukin-6, interleukin-8, tumor necrosis factor- α , and leukotriene C4. Viruses also have a substantial suppressive effect on neutrophil, macrophage and lymphocyte function. Effects on neutrophil function include diminished adherent, chemotactic, phagocytic, oxidative, secretory, and bactericidal functions. Viruses also suppress macrophage and lymphocyte function, resulting in patients with viral URIs being generally more vulnerable to secondary overgrowth and subsequent bacterial infection by pathogens residing in the nasopharynx, such as *S pneumoniae* and *H influenzae*. An animal model of nontypeable *H influenzae* adherence to respiratory epithelium was studied in the cotton rat with respiratory syncytial virus (RSV) infection.²⁴ Colonization with nontypeable *H influenzae* increased to a maximum within 4 days of RSV infection compared to RSV negative controls and then declined over the subsequent 10 days. Systemic immunity to nontypeable *H influenzae* as measured by IgG-specific antibody to the outer membrane complex and bactericidal antibody did not influence colonization. These data suggest that colonization with nontypeable *H influenzae* is significantly affected by a concurrent infection with RSV²⁴; however, the site of bacterial attachment is

not known. The mechanism of attachment involves upregulation of expression of epithelial cell surface receptors including CEACAM1, ICAM-1, and PAF-r.²⁵

Subsequent activation of inflammatory pathways and the parasympathetic nervous system generates the symptoms of rhinosinusitis. Fever, myalgia, and pharyngitis frequently associated with a viral URI tend to resolve after 5 days, whereas nasal congestion and cough may persist into the second and third week (Figure 1).²⁶ Fever alone at day 10 is not suggestive of ABRS. The causes of secondary bacterial invasion of the sinuses are unknown, but a combination of factors such as nose blowing,²⁷ local/systemic immunity, the virulence of the virus, colonization of the nasopharynx with potential bacterial pathogens (eg, *S pneumoniae*) and various environmental factors may lead to conditions that are conducive for bacterial entry and growth in the sinuses.

Because children experience an average of 3 to 8 viral URIs per year, the potential for inappropriate antibiotic use is high in this population.²⁸ The mean duration of a viral URI ranges between 6.6 days (1- to 2-year-old children in home care) and 8.9 days (children <1-year-old in day care). Upper respiratory tract symptoms may, however, last more than 15 days in approximately 7% (1- to 3-year-old children in home care) to 13% (2- to 3-year-old children in day care) of cases. Children in day care are more likely to have protracted respiratory symptoms.²⁹

Clinical Diagnosis of ABRS

Patients with a common cold usually report some combination of the following symptoms: sneezing, rhinorrhea, nasal congestion, hyposmia/anosmia, facial pressure, postnasal drip, sore throat, cough, ear fullness, fever, and myalgia. Contrary to popular belief, a change in the color or the characteristic of the nasal discharge is not a specific sign of bacterial infection because after a few days of a viral infection, mucopurulent nasal secretions may occur due to an influx of neutrophils.³⁰⁻³⁵ In a recent study,³⁵ the clinical signs and symptoms significantly associated in a multivariate model with the presence of bacteria included colored nasal discharge, facial pain, and radiologically determined maxillary sinusitis

Duration of Symptoms in URIs

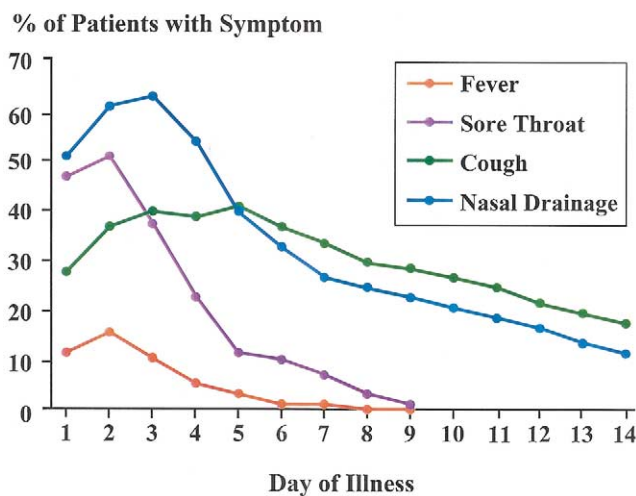


Fig 1. Duration of symptoms in rhinovirus URIs. There are three patterns of symptoms and resolution: (1) fever and myalgia; (2) sneezing and sore throat; and (3) cough and rhinorrhea, which are common and persistent in a significant proportion of patients. Persistence of these last two symptoms is entirely consistent with an uncomplicated rhinovirus infection.²⁶

(complete opacity, air-fluid level, or mucosal thickening >10 mm). The model only had a sensitivity of 69% and a specificity of 64% and therefore could not be used either as a screening tool or as a diagnostic criterion for bacterial rhinosinusitis. The authors of this study concluded that the signs and symptoms of acute rhinosinusitis in patients with mild-to-moderate clinical presentations are poor predictors of the presence of bacteria.³⁵

In a study by Gwaltney et al⁴ (n = 31), 87% of adults with acute onset of URI symptoms demonstrated inflammation within the nose and viscous secretions, sometimes with air bubbles, in the sinuses on CT scan. After 2 weeks without antibiotic therapy, repeat CT scans in 14 subjects revealed that 79% showed either disappearance or marked improvement in the previously identified abnormalities. The point at which a viral URI becomes superinfected with pathogenic bacteria may be determined with repeated sinus aspiration studies. Sinus aspiration studies in adults demonstrate significant bacterial growth in approximately 60% of patients with URI symptoms for 10 days or more.³⁶ While duration of symptoms beyond 7 days is a moderately sensitive predictor of ABRS, it is relatively nonspecific because duration of symptoms does not reliably distinguish

prolonged viral infection from ABRS.³⁷ Individual cases may fall out of the “norm” of this typical progression and have specific findings suggesting bacterial infection (fever, facial erythema and swelling, and severe pain); therefore, clinicians need to rely on clinical judgment when using these guidelines. In general, a diagnosis of ABRS may be made in adults or children with a viral URI that has not resolved after 10 days or worsens after 5 to 7 days and is accompanied by some or all of the following signs or symptoms: nasal drainage, nasal congestion, facial pressure/pain (especially when unilateral and focused in the region of a particular sinus), postnasal drainage, hyposmia/anosmia, fever, cough, fatigue, maxillary dental pain, and ear pressure/fullness (Table 1).

Diagnostic Modalities

Physical examination provides limited information in the diagnosis of ABRS. Several studies have evaluated whether certain signs or symptoms are specific to bacterial infection; however, these studies have methodologic limitations in that sinus aspiration was not used to document the presence or absence of bacterial infection.³⁷ Unlike acute otitis media, in which the tympanic membrane and middle ear space are readily available for direct

Table 1. Symptoms associated with acute bacterial rhinosinusitis*†

Nasal drainage
Nasal congestion
Facial pain/pressure (especially when unilateral and focused in the region of a particular sinus group)
Postnasal drip
Hyposmia/anosmia
Fever
Cough
Fatigue
Maxillary dental pain
Ear fullness/pressure

*A diagnosis of ABRS may be made in adults or children with a viral URI that is no better after 10 days (or worsens after 5-7 days) and is accompanied by some or all of these symptoms.

†Modified from ref. 19.

examination, the paranasal sinuses are hidden within the skull. Anterior rhinoscopy, with or without topical decongestant, allows examination of the mucosa of the inferior turbinate, secretions within the anterior nose, and the orientation of the nasal septum. Fiberoptic endoscopy allows visualization of the middle meatus, and direct culture of purulence in this region may correlate with cultures from maxillary sinus aspirates.^{38,39} In a recent review of the literature, Benninger et al⁴⁰ reported that there is 60% to 85% concordance between culture material obtained from endoscopically guided middle meatal swabs and maxillary sinus puncture. These studies, however, are limited by small sample sizes, and are therefore inadequate to make recommendations regarding the role of endoscopically guided middle meatal cultures as a formal method of identifying pathogens in ABRS at this time. A prospective study is currently underway to better answer this question. Other diagnostic modalities include transillumination, ultrasound, and radiological imaging. Transillumination has a 60% and 90% reproducibility rate for assessing disease within the maxillary sinuses and the frontal sinuses, respectively, but this does not differentiate bacterial from viral infection.⁴¹ B-mode ultrasound has replaced A-mode ultrasound for the diagnosis of diseases within the paranasal sinuses. However, because only the maxillary sinus can be adequately assessed, B-mode ultrasound has limited utility. A study correlating CT scan and B-mode ultrasound findings demonstrated a sensitivity of roughly

73% for the maxillary sinuses, 23% for the frontal sinuses and 11% for the ethmoids.⁴² Compared with clinical evaluation, the sensitivity of B-mode ultrasound was 36% and the specificity was 90%.⁴³ Because ultrasound is technique-sensitive, there may be marked variations in the reliability of the information provided.⁴⁴ Ultrasound cannot distinguish between viral and bacterial rhinosinusitis.

Plain film radiographs primarily reveal pathologic findings in the maxillary and frontal sinuses, whereas the ethmoids are poorly visualized using this imaging technique. Additionally, plain radiographs are imprecise at determining the extent of disease.⁴⁵ A meta-analysis of six studies demonstrated that positive plain film radiographs have moderate sensitivity (76%) and specificity (79%) compared to maxillary sinus puncture,²⁰ and a negative radiograph has more diagnostic value than either a negative clinical examination or ultrasound. CT scans clearly detect abnormalities within the sinuses; however, as previously noted, abnormalities are frequently found on CT scans of patients with viral respiratory disease.⁴ Magnetic resonance imaging (MRI), without exposing patients to ionizing radiation, distinctly reveals mucosal thickening and fluid within the paranasal sinuses. In patients with maxillary sinusitis, serial MRI scans demonstrate mucosal thickening persisting for up to 8 weeks.⁴⁶ Significant mucosal changes seen on CT or MRI may therefore persist significantly beyond microbiologic resolution of bacterial or viral disease. CT and MRI scans are not recommended for the routine management of ABRS, but they may be helpful in guiding the management for more complex cases.

Puncture of the maxillary sinus through the canine fossa or the inferior meatus provides material that may be cultured to identify bacterial isolates. Technical expertise is required to minimize complications, and the procedure is somewhat uncomfortable for the patient. Maxillary sinus puncture is not routinely used in cases of suspected ABRS. It is usually reserved for the research setting or for patients with more complicated infections. A novel technique—serial sinus aspirate sampling—devised by Anon, Ambrose, Jones et al, involves placing an indwelling catheter into the maxillary sinus. This technique has pro-

vided a means to determine actual time to eradication of various pathogens, compare change in symptoms as the bacterial population decreases, and evaluate antibiotic concentrations within the sinus fluid.⁴⁷

SELECTION OF ANTIMICROBIAL THERAPY FOR ABRS

The primary reason for recommending antibiotic therapy for ABRS is because withholding the benefits of treatment unnecessarily exposes patients to unreasonable morbidity, particularly for those with more severe symptoms. However, the routine use of antimicrobial therapy for patients who experience mild sinus symptoms for a short duration (indicative of self-limiting viral rhinosinusitis) is generally not a reasonable option because of the risks associated with promoting resistance. Unfortunately, not all cases are straightforward, and the decision of whether—and when—to initiate antimicrobial therapy for an individual patient with signs and symptoms consistent with ABRS often requires consideration of potential risks and benefits of treatment. For example, there is a subset of patients who may experience prolonged, moderate to relatively severe symptoms that are more attributable to host factors (eg, immune response, anatomic abnormalities) rather than bacterial infection. For these patients, the benefits of initiating an earlier course of antimicrobial therapy might be appropriate.

The primary goal of antibiotic therapy for ABRS is to eradicate the bacterial pathogens from the site of infection,⁴⁸ which helps (1) decrease the duration of symptoms to allow patients to resume daily activities more quickly; (2) return the sinuses back to health; (3) prevent severe complications (eg, meningitis and brain abscess); and (4) decrease the likelihood of developing chronic disease. Severe or life-threatening infections with or without complications are rare, and are not addressed in these guidelines.

Clinical trials conducted in this era of widespread antimicrobial resistance are just beginning to provide some evidence to use as the basis for recommending specific antimicrobial treatment options but, in general, they are not sufficiently powered. In lieu of adequate evidence, several factors may be helpful to clinicians in selecting

therapy for individual patients. These factors include pathogen distribution in ABRS, pharmacokinetic and pharmacodynamic principles of antimicrobial activity, mechanisms of antimicrobial resistance, and data from in vitro surveillance studies. Other factors, including symptom severity, the likelihood of infection with a resistant pathogen, and the likelihood of spontaneous resolution (based on the infecting pathogen) were included in the methodology used by the panel to objectively evaluate various antimicrobial options for ABRS. Each of these factors will be discussed in detail below.

MICROBIOLOGY OF ABRS

Bacteria are broadly classified into groups based on their cell-wall composition, morphologic characteristics, and metabolic requirements. The cell wall, an important determinant of inherent susceptibility or resistance for any bacterium to many antimicrobial agents, consists primarily of proteins, lipids, and a peptidoglycan layer. The peptidoglycan layer is composed of oligosaccharide chains cross-linked by short peptides that serve as the major structural component for maintaining cell-wall integrity. Although gram-positive and gram-negative bacteria share many common structural elements in their cell walls, the organization and content of these elements vary between these two bacterial classes (Figure 2). The cell wall of gram-positive bacteria consists almost entirely of a thick peptidoglycan layer fused to the outside of the cytoplasmic membrane. Gram-negative bacteria, however, have cell walls composed of a hydrophobic lipopolysaccharide capsule surrounding a lipoprotein-phospholipid membrane that contains small channels called porins. A thin peptidoglycan layer lies between the outer membrane and the inner cytoplasmic membrane. These two biological layers are separated by the periplasmic space. This space is an important site for degradation of antibiotics by drug-inactivating enzymes, such as β -lactamases, in gram-negative bacteria. Penicillin-binding proteins (PBPs), enzymes essential for cell-wall synthesis, are located in the cytoplasmic membrane. PBPs are found in gram-negative and -positive organisms. Altered PBPs, which have decreased affinity for β -lac-

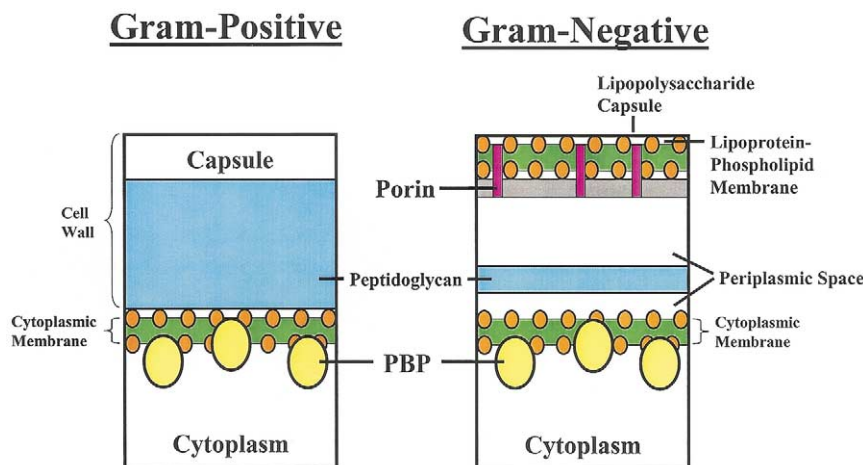


Fig 2. Gram-positive and gram-negative bacteria have different configurations of their cell walls, as noted in this illustration. Penicillin binding proteins (PBPs) play an important role in cell wall synthesis.

tams, have been identified in a variety of organisms.

The most common bacterial isolates recovered from the maxillary sinuses of patients with ABRS are *S pneumoniae*, *H influenzae*, other streptococcal species, and *Moraxella catarrhalis*. A review of sinus aspiration studies performed in adults with ABRS suggests that *S pneumoniae* is isolated in approximately 20% to 43%, *H influenzae* in 22% to 35%, and *M catarrhalis* in 2% to 10% of aspirates (Figure 3).^{2,36,49-52} In children with ABRS, *S pneumoniae* is isolated in approximately 35% to 42%, while *H influenzae* and *M catarrhalis* each are recovered from about 21% to 28% of aspirates. *Streptococcus pyogenes* and anaerobes account for 3% to 7% (Figure 4).^{36,49,50,53,54} Other bacterial isolates found in patients with ABRS include *Staphylococcus aureus* and anaerobes.^{36,49,50}

Nasopharyngeal Flora

Starting soon after birth, the nasopharynx is colonized with flora such as viridans streptococci, *Corynebacterium* species, *Neisseria* species and anaerobes. Colonization with “respiratory pathogens” occurs intermittently as discussed above, and by 12 months of age 70% of children are colonized by at least one of the three major respiratory pathogens: *S pneumoniae*, *H influenzae*, or *M catarrhalis*. Each pneumococcal strain persists in the nasopharynx for between 1 and 12 months, and point prevalence surveys have demonstrated

that as many as two thirds of children have nasopharyngeal carriage of pneumococci.⁵⁵ More than 90% of children are colonized with *S pneumoniae* by 3 years of age; the frequent serotypes/serogroups colonizing infants are 6, 9, 14, 19, and 23.⁵⁶ Pneumococci also have a high frequency of genetic recombination, and strains carried in the nasopharynx may change serotype.⁵⁷ Strains of nontypeable *H influenzae* also sequentially colonize the nasopharynx; this process starts in infancy. By 2 years of age, 44% of children have been colonized, with each strain being carried for 1 to 7 months (mean 2.2 months).⁵⁸ Production of *H influenzae*-specific IgA results in eradication of carriage of a strain, which is followed by acquisition of a new strain with different surface proteins.

As is the case with *S pneumoniae* and *H influenzae*, *M catarrhalis* colonizes the nasopharynx, in early childhood; 78% of children are colonized by 2 years of age.⁵⁹ Each child is sequentially colonized with different strains of *M catarrhalis*. Otitis-prone children are more frequently colonized than otherwise healthy children.

Colonization with “respiratory pathogens” increases considerably during winter and during periods of viral URI, which often results in these organisms causing bacterial otitis media and sinusitis.⁵⁵ Pelton et al⁶⁰ have recently reported that *S pneumoniae* was recovered from approximately 21% of nasopharyngeal cultures performed on healthy children versus 32% of cultures on the same children

Microbiology of Acute Bacterial Rhinosinusitis (Adults)

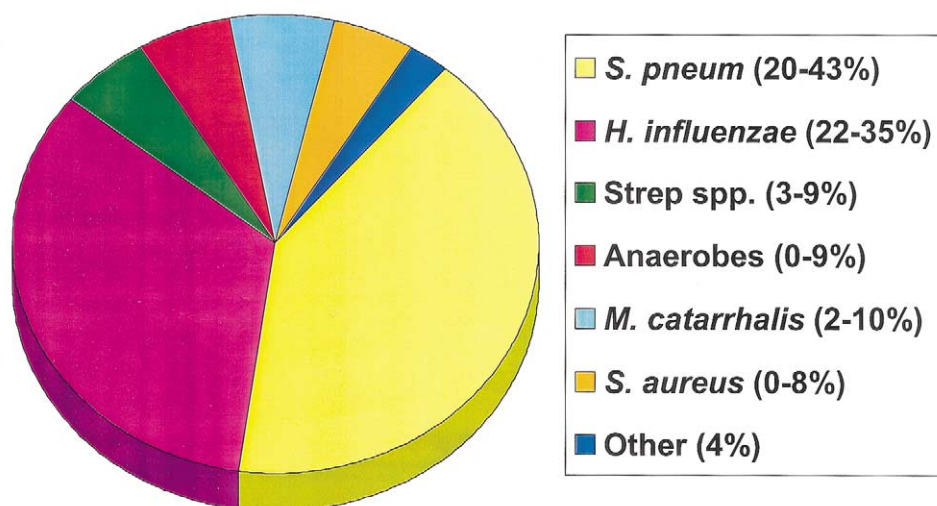


Fig 3. Prevalence of predominant pathogens associated with acute bacterial rhinosinusitis in adults.^{2,36,49-52}

Microbiology of Acute Bacterial Rhinosinusitis (Children)

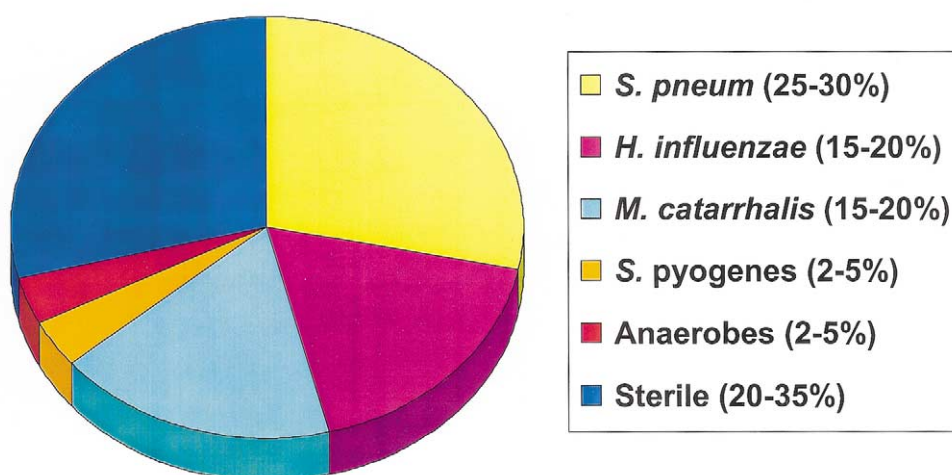


Fig 4. Prevalence of predominant pathogens associated with acute bacterial rhinosinusitis in children.^{36,49,50,53,54}

when presenting with acute otitis media (AOM). Further, a study Bernstein et al⁶¹ suggests there is a “to-and-fro” exchange of these organisms between the nasopharynx and the lateral nasal wall. Bacterial pathogens were isolated from 79% of adenoids and 46% of lateral walls of the nose in children undergoing adenoidectomy. Molecular typing of pairs of nontypeable *H influenzae*, *S pneumoniae*, and *M*

catarrhalis revealed that in 16 of 18 pairs (89%) the identical strain was present in both sites simultaneously. In addition, administration of antimicrobials increases carriage of antimicrobial-resistant strains of these bacterial pathogens.⁶² Adults also have colonization of the nasopharynx, but duration of carriage is shorter than in children.⁶³ A recent study⁶⁴ demonstrated that one of the primary respiratory

pathogens was recovered from the nasopharynx of approximately 75% of adults.

S pneumoniae

Pneumococci are gram-positive, catalase-negative, facultatively anaerobic spherical bacteria that are typically seen in pairs or chains. They are nutritionally fastidious, requiring complex media containing blood or serum for growth, and growth is often enhanced by a carbon dioxide-enriched atmosphere. *S pneumoniae* belongs to the α -hemolytic group of streptococci, and is distinguished from the viridans group by occurring in pairs, by the requirement for carbon dioxide for primary isolation, and for autolyzing in the presence of bile salts (bile solubility) and optochin (inhibition by optochin-containing disks). Pneumococci are usually encapsulated and the capsular polysaccharides are used for serological classification. There are 90 antigenically distinct capsular serotypes in 42 distinct serogroups. Some of the serotypes have common antigens and are grouped together in serogroups accounting for the designations of “6A” and “6B,” for example, in serogroup 6.

The incidence of invasive pneumococcal disease varies with serotype, and the likelihood of infection with any given serotype is largely dependent on the virulence factors expressed by the bacteria. Pneumolysin and the polysaccharide capsule are two of the most widely known virulence factors for *S pneumoniae*. Infection caused by serotype 14 and serogroups 6, 9, 18, 19, and 23 is highest in children, while that caused by serotypes 3 and 8 is highest in adults. Serotypes 1, 5, and 7 and serogroup 4 tend to cause disease at similar frequency in all age groups. Further, it has been found that 12 serogroups account for about 80% of infections.⁶⁵ Seven serotypes, 14, 6B, 19F, 18C, 23F, 4, and 9V (in order of decreasing frequency), accounted for 78% of isolates from blood, cerebrospinal fluid and middle ear sources of children in the United States.⁶⁶ These are present in the 7-valent conjugated pneumococcal vaccine currently available in the United States.

Antimicrobial resistance is observed primarily in serotypes 6A, 6B, 9, 14, 19F, and 23F, which are the serotypes most frequently colonizing children. Because these are exposed to antimicrobial

agents more commonly, they are the most likely to develop resistance.⁶⁷ Serotypes 1, 3, 4, 5, 7, 11, 15, and 18 rarely acquire antibiotic-resistant genes.

The incidence of invasive pneumococcal infections is dependent on the time of year.⁶⁸ Furthermore, the incidence of infection caused by resistant strains also may increase during winter months.⁶⁹

Mechanisms of Resistance Among *S pneumoniae*. Resistance to β -lactams results following a stepwise alteration in PBPs, which leads to a decrease in the binding affinities of β -lactams.⁷⁰ Varying degrees of resistance to penicillin and other β -lactams develop because changes can occur in multiple PBPs to alter the affinity for β -lactams.⁷¹ There are six known PBPs in *S pneumoniae*—1a, 1b, 2b, 2x, 2z, 3—and alterations in 1a, 2b, and 2x are most often associated with resistance to penicillin (penicillin minimum inhibitory concentrations [MICs] range from 0.25 μ g/mL to >8 μ g/mL compared to ≤ 0.06 μ g/mL for susceptible strains).⁷²

Macrolide resistance results primarily from alterations in ribosomal binding sites (due to a ribosomal methylase) or expression of an efflux mechanism.^{73,74} There are two important genes responsible for macrolide-resistant strains that are most commonly encountered in the clinical setting: *erm* genes, which code for a ribosomal methylase and *mef* genes, which code for a macrolide-specific cell membrane-based efflux mechanism. The efflux mechanism confers a relatively moderate degree of resistance, compared to the high level of resistance seen in strains with altered ribosomal binding sites. The efflux mechanism is generally more common in the United States and is relatively uncommon in most other parts of the world. Recently, mechanisms of macrolide resistance were identified that could not be explained by any of the known resistance determinants.⁷⁵ These novel mechanisms of macrolide resistance involve mutations in genes encoding ribosomal proteins (L4 or L22) or ribosomal RNA (23S rRNA). Mutations in genes for L22 and 23S rRNA result in increased macrolide MICs; however, the effect is variable (MIC range 0.25 μ g/mL to >64 μ g/mL). Mutations in genes for L4 generally confer high-level resistance (MICs >64 μ g/mL).^{72,76}

Isolates of *S pneumoniae* expressing these mutant genes are rare but have been identified in several surveillance studies,⁷⁶⁻⁷⁹ and there have been several recent reports of macrolide treatment failures resulting from development of these mutations during therapy with macrolides.⁸⁰⁻⁸⁴ Ribosomal methylase also confers cross-resistance to clindamycin. Macrolide usage, particularly azithromycin, has been associated with the recent increase in *S pneumoniae* resistance to macrolides in the United States.¹⁵

Fluoroquinolone resistance results following mutations in targets binding sites of these agents, DNA gyrase and topoisomerase IV, rather than requiring the acquisition of foreign genes. Mutations in the *parC* gene that encodes for topoisomerase IV or in the *gyrA* gene encoding for the Gyr A subunit of DNA gyrase results in low-level quinolone resistance. Mutations in both genes results in the expression of high-level quinolone resistance. Although cross-resistance commonly occurs among the fluoroquinolones, the newest agents often remain active against some strains that have become resistant to older agents. A fluoroquinolone efflux mechanism (*pmrA*) also has been described for *S pneumoniae*.⁸⁵

Resistance to trimethoprim and sulfonamides are also primarily a result of mutations in the target binding sites of these agents, dihydropteroate synthase and dihydrofolate reductase.

H influenzae

This organism belongs to the genus *Haemophilus*, which consists of small, pleomorphic, and facultatively anaerobic gram-negative bacilli. Most species have complex nutritional requirements, and growth is enhanced by a carbon dioxide-enriched atmosphere. *H influenzae* is characterized by its requirement for both hemin (X factor) and NAD (V factor). Strains of *H influenzae* may be either encapsulated or unencapsulated; encapsulated strains include six serotypes (serotypes a to f). However, nontypeable strains typically cause URIs such as otitis media, sinusitis, and acute exacerbations of chronic bronchitis; accordingly, the occurrence of these infections has not been affected by the use of type b vaccines.

Mechanisms of resistance among *H influ-*

***enzae*.** The primary mechanism of resistance to β -lactams is through the production of β -lactamases,⁸⁶ which hydrolyze the amide bond of the β -lactam ring, thus inactivating the antibiotic.

To overcome the effects of β -lactamase-mediated resistance, β -lactams that are less susceptible to hydrolysis, and specific β -lactamase inhibitors have been developed. Third-generation cephalosporins (eg, ceftriaxone and cefixime) are stable in the presence of β -lactamases, whereas clavulanic acid is a broad-spectrum irreversible inhibitor of β -lactamases. Because clavulanic acid is destroyed in the process of β -lactamase inhibition, it is often described as a "suicide inhibitor." Combinations of β -lactams and β -lactamase inhibitors (eg, amoxicillin/clavulanic acid) often are useful for the treatment of many β -lactamase-producing bacteria including, *H influenzae* and *M catarrhalis*. Other β -lactamase inhibitors include tazobactam and sulbactam. It is important to note that β -lactamase inhibitors only serve to increase the amount of active β -lactam compound at the target site to exert its activity against otherwise susceptible bacteria. Therefore, if the bacteria are not inherently susceptible to β -lactam in the absence of β -lactamases, addition of a β -lactamase inhibitor will not make the organism susceptible. Alterations in PBPs also have been reported occasionally among strains of *H influenzae*, and these strains are referred to as β -lactamase-negative ampicillin-resistant (BLNAR). Resistance among BLNAR strains is attributable to alterations in PBPs 3a and 3b.⁸⁷

Most gram-negative organisms have multiple efflux pumps to remove waste and foreign material; one efflux pump for *H influenzae* is chromosomally mediated via *acrAB* genes. Macrolides and azalides are substrates for these pumps and, as a result, these agents have intrinsically poor activity against *H influenzae*.⁸⁸

M catarrhalis

This species consists of aerobic, oxidase-positive, gram-negative diplococci. It has much less fastidious growth requirements than either pneumococci or *Haemophilus* species, and will grow on simple media without blood or serum. The primary mechanism of β -lactam resistance expressed by *M catarrhalis* is β -lactamase produc-

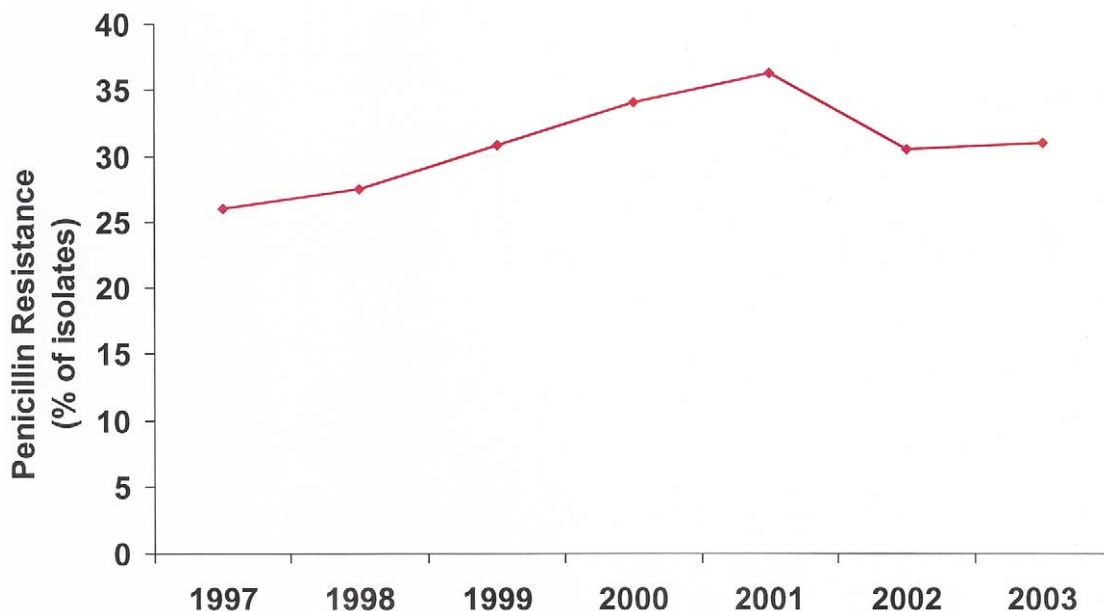


Fig 5. The prevalence of nonsusceptible (intermediate + resistant) *S pneumoniae* over the past several years in the United States.⁹⁰

tion; however, the β -lactamases produced by *M catarrhalis* are different from those produced by *H influenzae*. As a result, some agents (eg, cefpodoxime proxetil, cefuroxime axetil) are less active against *M catarrhalis* than *H influenzae* (see Table 3). *M catarrhalis* is also intrinsically resistant to trimethoprim.^{86,89}

Prevalence of Antimicrobial Resistance Among Isolates of *S pneumoniae*

Isolates of *S pneumoniae* with penicillin MICs ≤ 0.06 $\mu\text{g/mL}$ are defined as penicillin-susceptible, whereas penicillin-intermediate strains have penicillin MICs of 0.12 to 1.0 $\mu\text{g/mL}$, and penicillin-resistant isolates of *S pneumoniae* have a penicillin MIC of ≥ 2 $\mu\text{g/mL}$. The latter two groups are often referred to as “penicillin-nonsusceptible,” and the clinical significance of these varies with different β -lactams as will be discussed. Drug-resistant *S pneumoniae* (DRSP) connotes strains with penicillin MICs of ≥ 0.12 $\mu\text{g/mL}$ and/or resistance to other classes of antibiotics. Multidrug-resistant *S pneumoniae* are defined as organisms resistant to three or more classes of antibiotics.

The increasing prevalence of isolates of *S pneumoniae* that are penicillin nonsusceptible has been

a concern in the United States (Figure 5).⁹⁰ In the late 1980s and early 1990s penicillin-nonsusceptible *S pneumoniae* became a major concern in the United States.^{91,92} The Alexander Project is a worldwide surveillance study that collects respiratory tract isolates from community-based physicians and utilizes PK/PD susceptibility breakpoints to evaluate the in vitro activity of various antimicrobial agents.⁸⁹ Recent data from the US component of the Alexander project demonstrated that 12% of isolates were penicillin-intermediate and 25% were penicillin-resistant.

The prevalence of penicillin-nonsusceptibility appears to have peaked in 2001 at 36%, and has decreased to 31% in 2002.⁹² Resistance to other antimicrobial classes has also decreased. This trend may be attributable to several factors, including widespread use of the pneumococcal conjugate vaccine in children since 2000 as well as less overall antimicrobial use.

The overall US prevalence of resistance to trimethoprim/sulfamethoxazole (TMP/SMX), macrolides, doxycycline, and clindamycin was 37%, 29%, 21%, and 10%, respectively.⁸⁹ Typically, resistance to these classes of antimicrobials is higher among penicillin-nonsusceptible isolates (Figure 6).⁸⁹ The respiratory fluoroquinolones (ie,

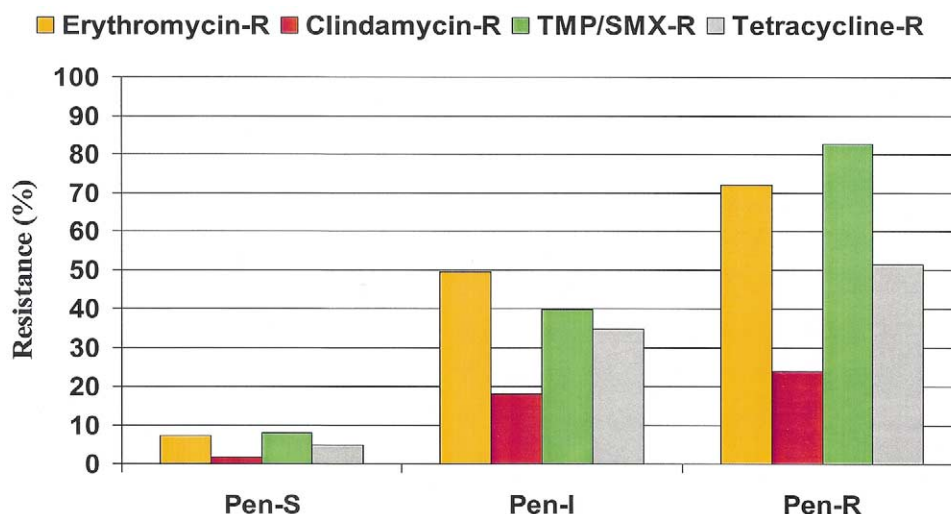


Fig 6. As resistance of *S pneumoniae* to penicillin rises, resistance to other antibiotics also increases. Drug-resistant *S pneumoniae* (DRSP) is an isolate with a penicillin MIC $>0.06 \mu\text{g/mL}$ and/or resistance to other classes of antibiotics.⁸⁹

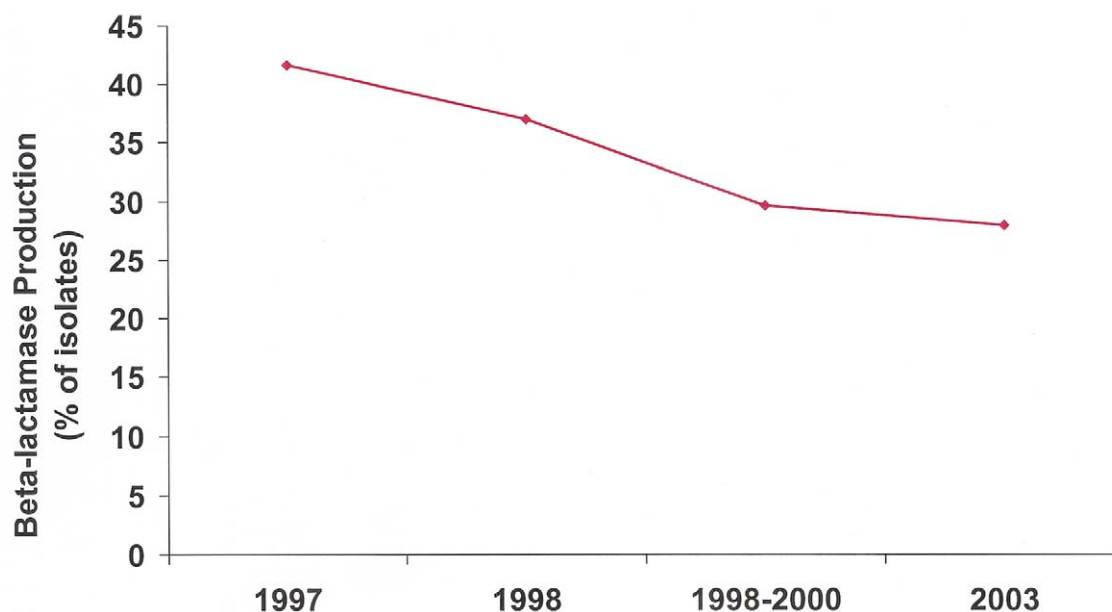


Fig 7. The prevalence of β -lactamase production by *H influenzae* over the past several years in the United States.⁸⁹⁻⁹¹

gatifloxacin, levofloxacin, moxifloxacin) remain active against *S pneumoniae*, with fewer than 2% of all isolates being resistant.⁸⁹ Data from the US component of the Alexander Project 1998-2000 demonstrate that 26% of *S pneumoniae* isolates were resistant to penicillin and two other classes of agents, and approximately 16% of isolates were resistant to any four classes of agents.⁸⁹

Prevalence of Antimicrobial Resistance Among Isolates of *H influenzae* and *M catarrhalis*

The prevalence of β -lactamase-producing isolates of *H influenzae* varies slightly according to the particular study, ranging from 30% to 40% (Figure 7).⁸⁹⁻⁹¹ However, essentially all *H influenzae* isolates were susceptible to high-dose amoxicillin/clavulanate and cefixime.⁸⁹ While

BLNAR strains of *H influenzae* are rare in the United States,⁸⁹ they are more prevalent in other countries (eg, Japan).⁹³

Based on PK/PD susceptibility breakpoints, <1%, <1%, and approximately 3% of *H influenzae* isolates were susceptible to erythromycin, clarithromycin, and azithromycin, respectively.⁸⁹ Approximately 22% of recent US *H influenzae* isolates were resistant to TMP/SMX. Data from the US component of the Alexander Project demonstrated that 92% of *M catarrhalis* isolates produced β -lactamases.⁸⁹

Antimicrobial Use and Bacterial Resistance

The extensive use of antibiotics may be associated with the development and spread of resistant microorganisms.¹¹⁻¹⁶ Nasopharyngeal carriage of resistant isolates of *S pneumoniae* is related to recent antimicrobial use as well as to living in a geographic region with a high volume of antibiotic use in children,^{12,94} and exposure to young children.⁹⁵ The prevalence of β -lactamase-producing isolates of *M catarrhalis* was found to increase in proportion with cephalosporin use.¹¹ In Finland, consumption of erythromycin was related to an increase in the prevalence of erythromycin-resistant group A streptococci.¹³ Furthermore, a steady and statistically significant decline in macrolide-resistant group A streptococci occurred after reducing the use of macrolide antibiotics for 2 years, which reinforces the rationale for judicious use of antibiotics.¹⁴

ASSESSMENT OF ANTIMICROBIAL ACTIVITY

Numerous methods may be utilized to assess the in vitro activity of an antibiotic. Tests such as the minimal inhibitory concentration (MIC), minimal bactericidal concentration (MBC), and time-kill testing are valid methods for the assessment of antimicrobial activity. It is, however, important to understand the usefulness and limitations of each of these tests.

Antimicrobial activity is commonly evaluated by determining the MIC of a particular antibiotic against a specific bacterial strain (Figure 8). Therefore, if an MIC is reported as 2 $\mu\text{g/mL}$, the true inhibitory concentration is somewhere be-

tween 1 $\mu\text{g/mL}$ and 2 $\mu\text{g/mL}$. Two other terms used are: MIC₅₀, the lowest concentration that inhibits 50% of the isolates tested and MIC₉₀, the lowest concentration that inhibits 90% of the isolates tested. It is extremely important to remember that the MIC is an in vitro characteristic of the antimicrobial and is determined under strictly adhered to conditions. Because environmental conditions at the site of infection rarely correspond to in vitro susceptibility test conditions, effects of elements such as oxygen tension, pH, and protein binding on the activity of the antimicrobial of interest need to be considered. Therefore, even if an organism appears susceptible in vitro, clinical failure may occur if in vivo conditions detract from the activity of the drug. Similarly, some host factors may actually improve the in vivo activity of an antimicrobial. Macrophages, opsonic factors, and complement may all act synergistically with an antibiotic and thus provide enhanced antibacterial activity over that which would be predicted in vitro. Additionally, many bacterial infections resolve spontaneously without the use of antimicrobial agents.

While the MIC defines the amount of an antimicrobial necessary to inhibit the growth of a microbe, the MBC provides information regarding the concentration of drug required to kill the organism. The MBC, like the MIC, is an in vitro test that is subject to similar limitations in relation to clinical effectiveness. The MBC is calculated by determining concentrations of bacteria incubated in the presence of varying drug concentrations at time 0 and after 24 hours and is defined as the lowest concentration that results in a 99.9% reduction in viable count at 24 hours compared to the initial inoculum. The MBC values generally range from 0 to 2, doubling dilutions higher than MIC values. Because MICs are better standardized, less costly, and less labor intensive, they are used more often than are MBCs. However, if the MBC is much higher than the MIC (unless the drug is known to be bacteriostatic), the organism is said to display tolerance to the antimicrobial.

Pharmacokinetic/Pharmacodynamic Principles

While MICs and MBCs are commonly utilized to describe the in vitro potency of antimicrobial

MIC – the lowest concentration of antibiotic that inhibits bacterial growth

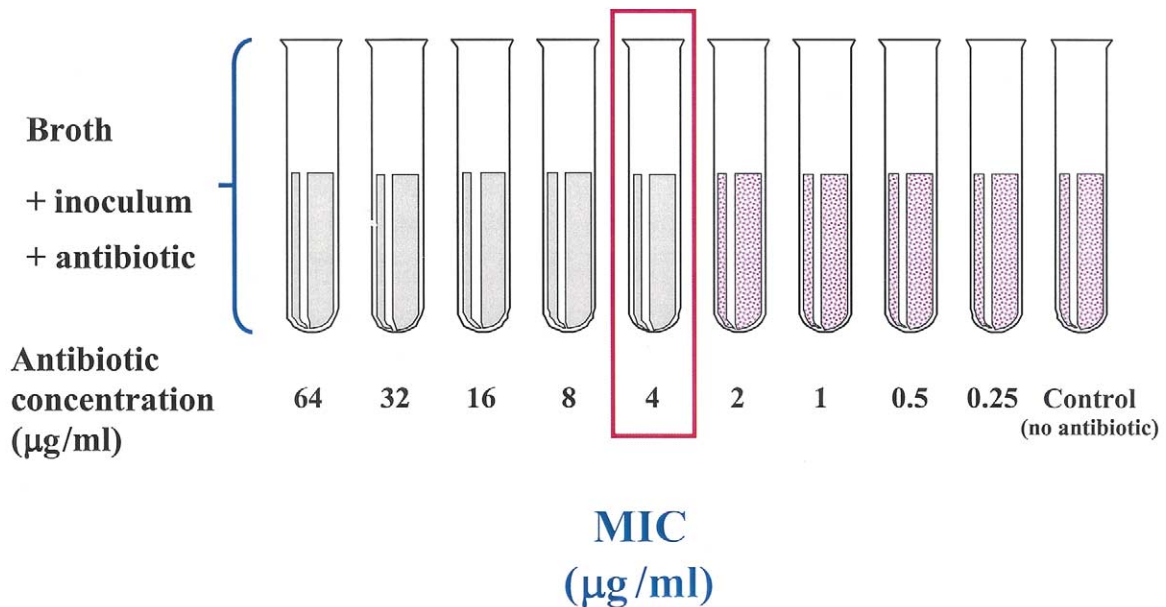


Fig 8. The MIC is the lowest concentration of the antimicrobial that results in the inhibition of growth of a microorganism. MICs are generally performed by placing a known inoculum of bacteria into media containing a range of doubling concentrations of the antimicrobial (ie, 0.5 µg/mL, 1 µg/mL, 2 µg/mL, 4 µg/mL, etc.). The MIC in this figure is 4 µg/mL.

agents, these measurements do not account for the pharmacokinetic properties of antimicrobial agents; therefore, their ability to predict therapeutic efficacy is limited.

The pharmacokinetics (ie, absorption, distribution, metabolism, and excretion) of many antimicrobials have been well established; however, the discipline of pharmacodynamics has only recently emerged. Pharmacodynamics describes the relationship between drug concentration and pharmacologic effect. For an antibiotic, it describes the relationship that exists between the drug concentration to which the bacteria is exposed at various sites of infection and bacterial killing. Pharmacodynamics attempts to integrate both microbiologic and pharmacokinetic data into more clinically relevant relationships. The evolution of this science has augmented the body of knowledge about how antimicrobials best treat infections. In addition, pharmacodynamics can be utilized to determine the impact of antimicrobial resistance. Consideration of pharmacodynamics can help define the

MIC limit at which the pharmacokinetics of a specific antimicrobial drug would not be expected to result in treatment success. Pharmacodynamics has also established rational scientific principles that provide the basis for developing dosing strategies that optimize clinical outcomes.

Pharmacodynamically, in vivo bacterial killing may be described as a function of the duration of antimicrobial drug concentration over time relative to the MIC of that agent against a particular pathogen. The product of these pharmacokinetic parameters (drug concentration and time of drug exposure) in the bloodstream over the dosing interval is expressed as the AUC (Figure 9). Outcome of infection in animal models and human studies usually correlates with one of three pharmacodynamic parameters: (1) time of exposure of a bacteria to concentrations of the antibiotic exceeding the MIC of the agent against the pathogen (time above the MIC [T > MIC]); (2) ratio of peak serum concentration of the antimicrobial agent to the MIC of the agent against the pathogen (peak:

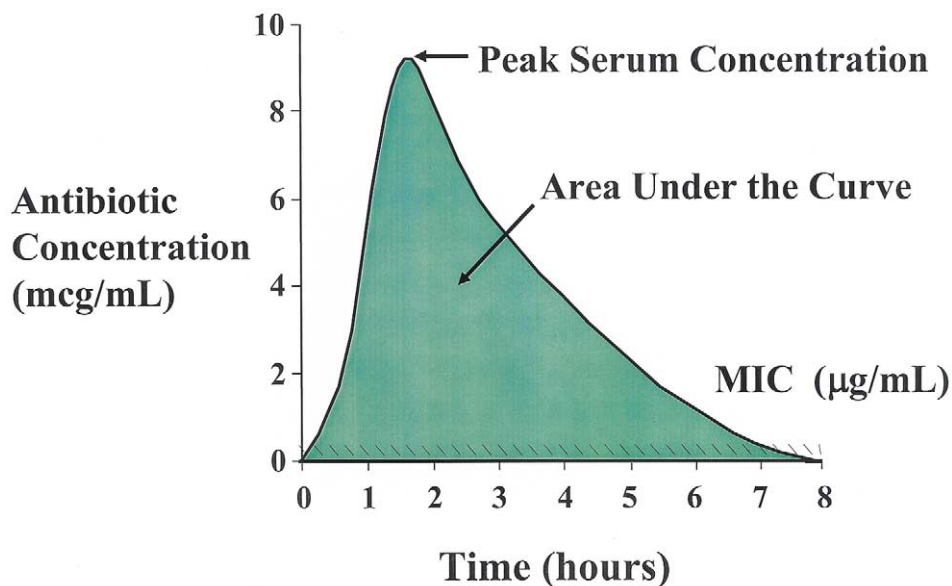


Fig 9. Pharmacodynamically, in vivo bacterial killing may be described as a function of the duration of an antimicrobial's drug concentration over time relative to the MIC of that agent against a particular pathogen. The product of these pharmacokinetic parameters (drug concentration and time of drug exposure) over the dosing interval is expressed as the area under the concentration-time curve (AUC).

MIC ratio), and (3) ratio of the AUC to the MIC of the agent against the pathogen (AUC:MIC ratio). Antimicrobial agents can thus be classified based on the pharmacodynamic parameter that best describes their in vivo pattern of bactericidal activity (Table 2).

Antimicrobials exhibiting time-dependent killing. β -Lactams are agents commonly used for respiratory tract infections that exhibit time-dependent killing. These agents do not kill more efficiently when the concentration exceeds a critical value. While a concentration that is two- to fourfold higher than the MIC is generally regarded as being optimal (ie, greatest likelihood of clinical success), further increasing the drug concentration beyond this magnitude does not improve the rate or extent of bacterial killing. These antibiotics exhibit time-dependent killing, and the best predictor of clinical outcome is the duration of time the concentration at the site of infection remains above the MIC ($T > MIC$) for the bacteria. In simplistic terms, the antibiotic needs to be at a high-enough concentration for a long-enough period of time at the site of infection. For β -lactams and extracellular pathogens, the free-drug concentration in serum is generally proportional to that in the interstitial fluid bathing the organism (protein-

bound drug lacks antimicrobial activity). Therefore, the proportion of the dosing interval that the free-drug concentration in serum exceeds the antimicrobials MIC against a pathogen also reflects this parameter at most sites of infection. The amount of time that the free-drug concentration of a time-dependent antibiotic remains above the MIC ($T > MIC$) generally does not vary with the pathogen or the immunocompetence of the host. Data from in vitro pharmacokinetic simulations, animal models, and human clinical studies suggest that the $T > MIC$ needed to achieve bacterial eradication should generally be $>40\%$ to 50% of the dosing interval for time-dependent antibiotics.^{96,97} The optimal PK/PD parameter varies somewhat for β -lactams because of variability in the bacterial killing rate. For example, the $T > MIC$ that correlates with optimal outcomes with carbapenems (15% to 25%) is slightly lower than with penicillins (30% to 40%) and cephalosporins (40% to 50%) because carbapenems have a more rapid bacterial killing effect.⁹⁸

The relationship between the $T > MIC$ and efficacy has been evaluated in patients with acute otitis media caused by *S pneumoniae* and *H influenzae*. Bacteriologic cure rates of 80% to 85% were observed when the $T > MIC$ for various

Table 2. Antimicrobial agents classified by pattern of bactericidal activity

Drug class	Pharmacodynamic class	Therapeutic goal (for <i>S pneumoniae</i>)
β -Lactams Penicillins Cephalosporins	Time-dependent	Time above MIC >40%-50% of the dosing interval
Macrolides Erythromycin Clarithromycin Azithromycin	Time-dependent (with moderate to prolonged persistent effect)	AUC-to-MIC ratio of 25-35
Ketolides Telithromycin	Concentration-dependent	Unknown*
Fluoroquinolones Gatifloxacin Levofloxacin Moxifloxacin	Concentration-dependent (with prolonged persistent effect)	AUC-to-MIC ratio of 25-35

*Further research is needed.

β -lactams were >40% to 50% of the dosing interval.^{99,100} Moreover, in hospitalized patients with community-acquired pneumonia, no differences in clinical outcome were observed between patients receiving cefuroxime sodium as a 1500 mg per day continuous infusion ($T > MIC = 100\%$) compared to 750 mg intermittently three times daily (estimated $T > MIC = 50\%$ to 60%).¹⁰¹ Thus, a serum concentration which is present for 40% to 50% of the dosing interval may be used to determine the susceptibility limit or "breakpoint" of an organism for a given dosing regimen. Additionally, the proportion of bacteria that are therefore susceptible can be based on the proportion of isolates with MICs at or below these susceptibility limits or breakpoints.

Antimicrobials exhibiting time-dependent killing with moderate to prolonged persistent effects. *Macrolides/azalides.* Macrolides (eg, erythromycin and clarithromycin) and azalides (eg, azithromycin) exhibit time-dependent killing; however, because of the prolonged postantibiotic effect against gram-positive cocci and *H influenzae*¹⁰², the pharmacodynamic parameter for these agents that correlates with efficacy is the AUC to MIC ratio rather than $T > MIC$. The AUC to MIC ratio that yields maximal efficacy with drugs from the macrolide and azalide class in animal models is approximately 25.¹⁰³

Concern has been raised regarding the propen-

sity of azithromycin to select for bacteria that are macrolide-resistant.¹⁰⁴ The impact of community-based azithromycin use on the carriage and resistance of *S pneumoniae* has been prospectively studied.¹⁰⁵ Single-dose azithromycin (20 mg/kg) was given to children with trachoma (a chronic disease caused by *Chlamydia trachomatis*) and to their household contacts who were children. Carriage rates of azithromycin-resistant *S pneumoniae* immediately before treatment and 2 to 3 weeks, 2 months, and 6 months after treatment were 2%, 55%, 35%, and 6%, respectively. The selective pressure of azithromycin may have allowed the growth and transmission of preexisting azithromycin-resistant strains.

One possible explanation for this observation relates to the long serum half-life of azithromycin and the long duration of subinhibitory concentrations of the drug.¹⁰⁶ If the serum AUC for two antimicrobials, one with a short and the other with a long serum half-life, are compared with MIC values superimposed, a period or "window" for potential Darwinian selection can be plotted (Figure 10). For the antimicrobial with a short half-life, the duration of time between the drug concentration falling below the MIC and its total elimination from the body is relatively short compared to that of the antimicrobial with the longer half-life. For an antimicrobial with a 68-hour half-life (eg, azithromycin), total elimination from the

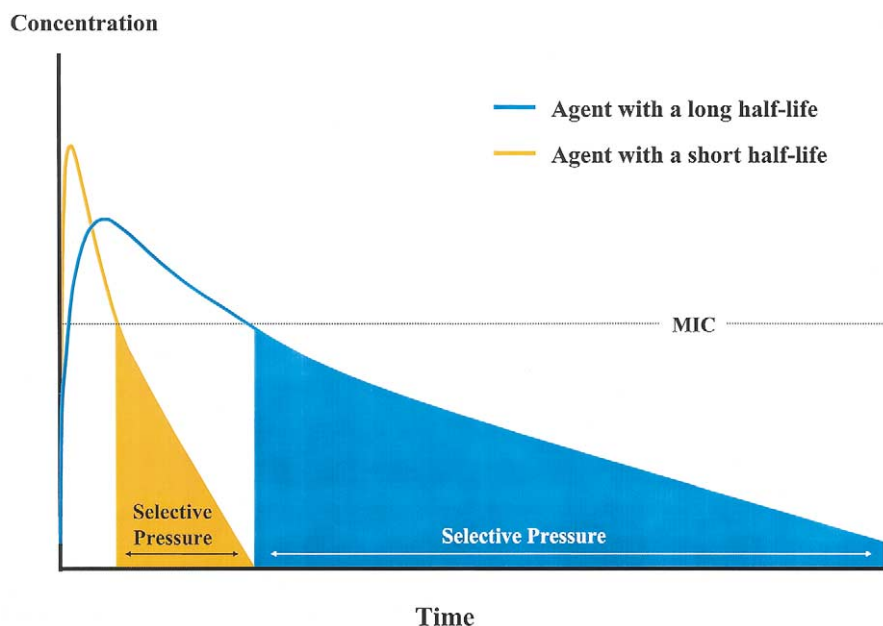


Fig 10. If the serum concentration-time curves (AUC) for two antimicrobials, one with a short and the other with a long serum half-life, are compared with MIC values superimposed, a period or “window” for potential Darwinian selection develops as illustrated in this plot.

body does not occur for 5 to 7 half-lives or 14 to 20 days. This period of subinhibitory concentrations of drug may be the pharmacodynamic explanation for the aforementioned observations. This concept is controversial and requires validation in future studies, but similar findings have recently been reported in a study from Israel.⁹⁴

Antimicrobials exhibiting concentration-dependent killing and prolonged persistent effects. Fluoroquinolones and ketolides exhibit a concentration-dependent mechanism of bacterial killing, in which they kill most efficiently when their concentrations are appreciably above the MIC of the pathogen.^{97,107,108} The goal of dosing regimen is to maximize drug concentration at the site of infection. The AUC:MIC ratio and the peak:MIC ratio are the major parameters correlating with efficacy. Fluoroquinolones eradicate organisms best at levels 10- to 12-fold higher than the MIC for the pathogen. Increases between 1 and 10 times the MIC of the *S pneumoniae* organism, the rate and extent of killing is increased, but the rate and extent of killing do not improve if the organism is initially susceptible to quinolones. If the organism has a range of susceptibilities, however, the rate and extent of killing favors the more potent in vitro agents.¹⁰⁷⁻¹¹⁰ If the optimal peak-

to-MIC ratio is obtained, most bacteria die rapidly and consequently, the period of time over which the bacteria is exposed to the drug exposure is minimal.

Although peak-to-MIC ratios of >10:1 to 12:1 correlate with optimal bactericidal activity,¹¹¹ the AUC to MIC ratio is a better parameter for determining efficacy of fluoroquinolones for moderately susceptible bacteria, such as *S pneumoniae*.¹¹¹ In fact, in most fluoroquinolone dose-fractionation studies, the AUC to MIC ratio has a better correlation with efficacy than peak to MIC ratio. Data obtained from several sources including animal models of sepsis, in vitro pharmacodynamic experiments, and clinical outcome studies indicate that the magnitude of the AUC to MIC ratio can be utilized to predict outcomes. Forrest et al¹¹² demonstrated that an AUC to MIC ratio of ≥ 125 was associated with the highest bacterial eradication rates in the treatment of infections caused by gram-negative enteric pathogens. However, for gram-positive bacteria, it appears that effective AUC to MIC ratios can be appreciably lower. For instance, against *S pneumoniae*, an in vitro model of infection demonstrated that for levofloxacin and ciprofloxacin an AUC to MIC ratio of approximately 30 was associated with a

4-log reduction in bacterial titers; while ratios <30 were associated with significantly reduced rates of bacterial killing and in some instances bacterial regrowth.¹¹³ Similarly, Lister and Sanders¹¹⁴ reported that for levofloxacin and ciprofloxacin an AUC-to-MIC ratio of 32 to 44 was associated with maximal eradication of *S pneumoniae* in an in vitro model of infection. These observations are supported by data from non-neutropenic animal models of infection, in which survival was associated with an AUC-to-MIC ratio of 25 to 30 against the pneumococcus.¹¹⁵

Moreover, these observations from in vitro models of infection are further supported by clinical data. The relationship between microbiologic response and the AUC-to-MIC ratio for gatifloxacin and levofloxacin was recently evaluated in patients with pneumococcal respiratory tract infections.¹¹⁶ This analysis demonstrated that for gatifloxacin and levofloxacin, AUC-to-MIC ratios of at least 33.7 correlated with the eradication of *S pneumoniae*. AUC-to-MIC ratios >33.7 were associated with 100% of patients having a positive microbiologic response to therapy, while those patients with AUC-to-MIC ratios <33.7 had only a 64% response to therapy. The probability of attaining an AUC-to-MIC ratio exceeding 30 with currently approved doses varies among fluoroquinolones (moxifloxacin $\geq$ gatifloxacin $\geq$ levofloxacin).

Ketolides have not yet been approved for use in the United States, and their optimal PK/PD parameters have not yet been clearly established. Certain animal models of infection (eg, mouse thigh infection) suggest that the AUC-to-MIC ratio that correlates with efficacy against *S pneumoniae* for most ketolides is 25 to 50,^{103,117} whereas higher ratios (up to 100) improve survival.¹¹⁷ For one of the ketolides, telithromycin, the AUC-to-MIC ratio that correlates with efficacy for *S pneumoniae* may be much higher (between 50 and >200).¹¹⁸⁻¹²⁰ Based on this uncertainty, we have considered telithromycin to be considered equivalent to currently available macrolides/azalides until subsequent data proves otherwise. Bacteriologic eradication rates in clinical trials to date with telithromycin suggest this agent may be valuable for the management of community-acquired respiratory tract infections, although the value of such

studies is limited, as most bacteriologic outcomes are presumed outcomes based on clinical outcome.¹²¹

The PK/PD goals identified using animal models generally correlate with those in humans, and despite PK differences between animals and humans, the PD target is similar. This should not be surprising because the antimicrobial target is within the bacterial pathogen and not the mammalian host. However, the animal models often exclude host defenses (ie, neutrophils) to more clearly delineate the effects of antimicrobial therapy, and there are data to suggest that the PK/PD goal may be lower for certain agents (eg, ketolides) in the presence of adequate host defenses.^{122,123} Furthermore, the PK/PD goals from animal models are calculated based on the assumption that serum concentrations approximate concentrations at the site of infection. However, certain agents (eg, macrolides) tend to accumulate at various sites of infection (eg, epithelial lining fluid), which may affect the PK/PD goal for these agents.¹²⁴

Pharmacokinetic and pharmacodynamic principles play an important role in the evaluation and selection of antimicrobial therapy for ABRS and bacterial infections, in general. Once the PK/PD parameter that best predicts antimicrobial activity in vivo (ie, $T > MIC$, AUC:MIC ratio) is identified and the magnitude of the PK/PD parameter required for efficacy is determined (ie, PK/PD goal), resistance can be defined for situations in which the PK/PD goal cannot be achieved. The PK/PD goal generally does not change based on the site of infection, it is not affected by the dosing regimen or the infecting pathogen (including resistant strains), or the use of other agents in the same drug class (as long as free-drug concentrations are used).

Current NCCLS breakpoints¹²⁵ for the same agent vary considerably, depending on the pathogen, whereas PK/PD breakpoints are the same for all pathogens. For *S pneumoniae*, PK/PD breakpoints are generally the same as, or within one-doubling-dilution of, NCCLS susceptibility breakpoints. As a result, both NCCLS and PK/PD breakpoints are similar at characterizing the activity of various agents against *S pneumoniae*.

However, there are significant differences be-

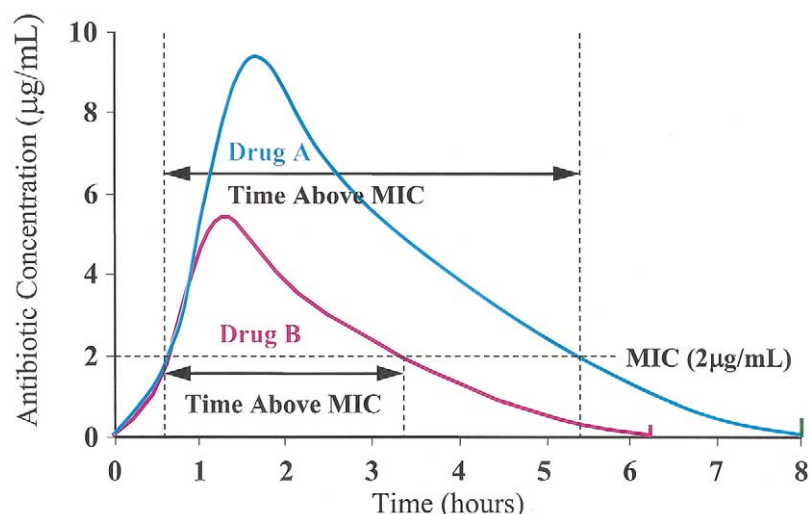


Fig 11. Determining PK/PD breakpoints: Time above the MIC. Schematic illustration of the serum pharmacokinetic profile of two time-dependent oral drug regimens over an 8-hour dosing interval. Drug A is present at 2 µg/mL for >50% of the dosing interval. Drug B is present at 2 µg/mL for approximately 35% of the dosing interval, but at 1 µg/mL for >50% of the dosing interval. Therefore, infections caused by a pathogens for which the MICs of both drugs are 2 µg/mL are more likely to be cured by Drug A rather than Drug B. Drug B would, however, be effective against strains where the MIC is ≤1 µg/mL, as Drug B is present at 1 µg/mL for >50% of the dosing interval. Drugs A and B can be two different time-dependent drugs, or two different dosing regimens of the same agent. A similar process can be done to determine the PK/PD breakpoint for concentration-dependent agents, in which the AUC (for the unbound serum fraction) is divided by 25 or 30.

tween NCCLS and PK/PD susceptibility breakpoints for several antimicrobial agents against *H influenzae*, and the breakpoints used (NCCLS vs. PK/PD) can affect the interpretation of findings from surveillance studies.^{89,126} As PK/PD breakpoints are based on the PK/PD relationships of the agents that result in successful clinical outcomes, rather than on MIC distributions of various species, the use of PK/PD breakpoints overcomes most of the limitations associated with use of NCCLS breakpoints.

Defining Antimicrobial Susceptibility Breakpoints

As previously discussed, pharmacokinetic/pharmacodynamic PK/PD parameters can be used to define susceptibility breakpoints for antibiotics. Defining susceptibility breakpoints for antimicrobial agents does not require special data sets or extensive in vitro or clinical studies. In fact, in most cases, PK/PD breakpoints can be determined from previously published data (ie, plasma concentration vs. time curves). For time-dependent agents (eg, β-lactams), the PK/PD breakpoint can

be determined by identifying the timeframe (X-axis) that corresponds with 40% to 50% of the dosing interval and extrapolating that to the concentration (Y-axis) (Figure 11). A similar process can be used to determine the PK/PD breakpoint for concentration-dependent agents, in which the AUC (for the unbound serum fraction) is divided by 25 or 30.

Table 3 compares the susceptibility of isolates of *S pneumoniae*, *H influenzae*, and *M catarrhalis* to various antibiotics according to their PK/PD breakpoints.⁸⁹ The panel used PK/PD breakpoints in preference to NCCLS¹²⁵ or FDA breakpoints to allow unbiased comparisons of sinusitis pathogens using one breakpoint for each agent.

Monte Carlo Simulations

As discussed in the previous section, two of the most important factors that influence the effectiveness of a particular antibiotic regimen are the drug exposure in the individual, which is reflected by the pharmacokinetics and pharmacodynamics of the drug, and the susceptibility of the infecting pathogen to the anti-infective agent selected for

Table 3. Susceptibility of respiratory tract isolates (1998 to 2000) to antimicrobial agents at PK/PD breakpoints^{89,90}

Agent	Percentage of isolates susceptible at PK/PD breakpoint						
	Susceptibility breakpoint (μg/mL) (PK/PD)	<i>S pneumoniae</i> (all) (n = 2901)	Penicillin-susceptible <i>S pneumoniae</i> (n = 1845)	Penicillin-intermediate <i>S pneumoniae</i> (n = 382)	Penicillin-resistant <i>S pneumoniae</i> (n = 674)	<i>H influenzae</i> (n = 1919)	<i>M catarrhalis</i> (n = 204)
Amoxicillin	≤2	91.6	100	100	63.6	70.2	7.3
Amoxicillin HD*	≤4	95.2	100	100	79.4	70.2	7.3
Amox/Clav†	≤2	92.1	100	99.7	66.3	98.3	100
Amox/Clav HD/extended release*†	≤4	95.2	100	100	79.4	99.8	100
Cefaclor	≤0.5	19.7	30.3	2.9	0.1	3.7	8.7
Cefuroxime axetil	≤1	72.6	99.9	68.8	0.0	82.8	50.5
Cefixime	≤1	66.3	96.7	35.3	0.4	>99.9	100
Ceftriaxone	≤1	96.3	100	99.5	84.6	>99.9	93.6
Cefprozil	≤1	71.8	99.7	63.1	0.4	23.2	9.2
Cefpodoxime‡	≤0.5	75.4	99.7	67.4	0.7	100	85.0
Cefdinir	≤0.25	68.8	98.4	49.2	0.5	78.2	77.6
Loracarbef	≤0.5	7.6	10.3	6.5	0	9.6	
Erythromycin	≤0.25	72.0	92.6	49.7	28.0	0.0	100
Clarithromycin	≤0.25	72.3	92.8	51.0	28.2	0.0	100
Azithromycin	≤0.12	71.0	91.8	48.4	27.2	2.3	100
Clindamycin	≤0.25	90.6	97.9	81.4	75.8	0	0
Ciprofloxacin	≤1	§	§	§	§	100	100
Levofloxacin	≤2	99.1	99.0	99.7	99.1	100	100
Gatifloxacin	≤1	99.1	99.0	99.7	99.1	100	100
Moxifloxacin	≤1	99.2	99.0	100	99.3	100	100
Doxycycline	≤0.25	80.4	95.2	65.2	48.7	25.1	96.3
TMP/SMX¶	≤0.5	63.7	86.4	46.1	11.3	78.1	19.3

The activity of telithromycin against *S pneumoniae*, *H influenzae*, and *M catarrhalis* depends on its PK/PD breakpoint, which is uncertain at this time. The activity of telithromycin is assumed to be similar to that of macrolides/azalides until further information becomes available.

Amox/clav, amoxicillin/clavulanate; NA, not applicable; PD, pharmacodynamic; PK, pharmacokinetic; TMP/SMX, trimethoprim/sulfamethoxazole. All values are based on PK/PD breakpoints, except for *S pneumoniae*, in which values are shown as PK/PD and new (Jan 2000) NCCLS breakpoints and for clindamycin and TMP/SMX, in which NCCLS breakpoints are used. Data are adapted from reference 88.

*High-dose amoxicillin or amoxicillin-clavulanate as defined in text.

†Shown as amoxicillin component.

‡Susceptibility data for cefpodoxime were obtained from the SENTRY database.⁹⁰

§The MICs of ciprofloxacin against some isolates of *S pneumoniae* are above the PK/PD breakpoint; therefore, ciprofloxacin does not reliably cover this organism.

¶Shown as TMP component.

therapy, which is reflected by the MIC of the agent against the pathogen.

However, because of natural differences in biological systems, both MICs and human pharmacokinetic curves in serum distribute across a range of values.^{127,128} Consequently, some bacterial strains are less susceptible to an antimicrobial agent than others and some are more susceptible than others. Similarly, some people absorb, metabolize, distribute, and excrete a drug more rapidly than others, and some more slowly, leading to

considerable variations in pharmacokinetic parameters.¹²⁹ As a result of these variations, antimicrobial-agent efficacy in vivo may differ from the in vitro prediction of drug susceptibility in some patients. To determine the true efficacy of an agent in every patient, the MIC of the causative organism against the agent used and the serum pharmacokinetics of the agent would need to be determined in each patient. This is, of course, physically impossible, and has only been performed on a small scale for both practical and

ethical reasons.¹¹¹ Pharmacokinetic/pharmacodynamic breakpoints are, therefore, currently determined from mean serum pharmacokinetic values, which do not reflect variations in pharmacokinetics from patient to patient, so that some patients will not achieve the target needed, while others will exceed the target.¹³⁰ An example of this using susceptibility of gatifloxacin and levofloxacin against *S pneumoniae* is shown in Figure 12.¹³¹ The susceptibility breakpoints for standard dosing regimens of these agents, based on unbound serum AUC divided by 30, is 1 µg/mL for gatifloxacin and 2 µg/mL for levofloxacin, and virtually all isolates are “susceptible” at these breakpoints (Figure 12, panels A and B). However, the modal MIC of gatifloxacin is 0.25 µg/mL, or one quarter of the breakpoint, whereas that of levofloxacin is 1 µg/mL or one half of the breakpoint.¹³² Variations in pharmacokinetics between patients are therefore more likely to result in levofloxacin not achieving its target more often than gatifloxacin, as gatifloxacin has a wider “safety margin” than does levofloxacin between MIC values and breakpoints. The variability in pharmacokinetics of these agents in patients enrolled in clinical trials, using dosing regimens of 400 mg once daily for gatifloxacin and 500 mg once daily for levofloxacin, is illustrated in panels C and D of Figure 12. AUC values for gatifloxacin varied from 8 to 500 (mean 64), while values for levofloxacin varied from 17 to 389 (mean 70). The “average” AUC and modal MIC values for these two agents would therefore result in “average” AUC:MIC ratios of 256 for gatifloxacin and 70 for levofloxacin. However, the variations in AUCs between patients and in MICs between isolates could result in AUC:MIC ratios varying from 1.5 to 6667 for gatifloxacin and from 3 to 2783 for levofloxacin.¹³¹

Monte Carlo simulation is a statistical method for estimating the probability of obtaining a desired target, which, in this case, is the pharmacokinetic/pharmacodynamic parameter needed to eradicate an infection, such as an AUC:MIC ratio of 30. Monte Carlo methods randomly select values from within a fixed range and selected to fit a probability distribution (eg, bell curve). Monte Carlo simulation can use individual values in two data sets, in this case MICs and AUCs, to generate random AUC:MIC ratios from randomly chosen

MIC and AUC values. This can be done thousands of times, and the distribution of these results can be plotted.

The results of this simulation performed 5000 times on the data from panels A to D are shown in panels E and F of Figure 12. Based on these analyses, the AUC:MIC target value of ≥ 30 was achieved with 99% certainty for gatifloxacin and 82% for levofloxacin.¹³¹ Although the clinical implications of these findings have yet to be fully explored, such analyses provide further insight into optimal patient management. The FDA advisory committee on anti-infective drug products found Monte Carlo simulation, as presented by Drusano in October 1998, to be a reasonable approach to addressing these issues. Further study of these problems is needed, particularly to address variations in pharmacokinetics between each dose of an agent during a course of therapy in an individual patient as most data collected to date only reflected pharmacokinetics determined over one dosing interval in each patient.

Antimicrobial Activity According to Pharmacokinetic/Pharmacodynamic Breakpoints

Of oral agents, the respiratory fluoroquinolones have the greatest in vitro activity against the predominant pathogens. However, parenterally administered ceftriaxone may assure adequate concentration and provide better bacteriologic outcomes compared with oral antimicrobial therapy.

The relative antimicrobial activity against isolates of *S pneumoniae* based on PK/PD breakpoints,⁸⁹ can be listed as: gatifloxacin / levofloxacin / moxifloxacin (>99%); ceftriaxone / high-dose amoxicillin ($\pm$ clavulanate [extended-release or extra strength]) (95% to 97%); amoxicillin ($\pm$ clavulanate) / clindamycin (90% to 92%) ; cefpodoxime proxetil / cefuroxime axetil / cefdinir / erythromycin / clarithromycin / azithromycin / telithromycin / cefprozil / TMP/SMX / cefixime (63% to 75%); loracarbef / cefaclor (<20%).

The relative antimicrobial activity against *H influenzae* based on PK/PD breakpoints is: gatifloxacin / moxifloxacin / ceftriaxone / cefixime / cefpodoxime proxetil / extended-release and extra strength amoxicillin/clavulanate / amoxicillin/clavulanate (95% to 100%); cefuroxime axetil / cefdinir / TMP/SMX /

amoxicillin (70% to 85%); cefprozil / cefaclor / loracarbef / doxycycline / erythromycin / clarithromycin / azithromycin / telithromycin (<25%).^{89,90}

The relative antimicrobial activity against *M. catarrhalis* is: gatifloxacin / levofloxacin / moxifloxacin / cefixime / extended-release and extra strength amoxicillin/clavulanate / telithromycin / erythromycin / clarithromycin / azithromycin (100%); doxycycline/ceftriaxone / cefpodoxime proxetil / cefdinir (78% to 96%); cefuroxime axetil (50%); cefprozil / amoxicillin/ TMP/SMX / cefaclor/loracarbef (<20%).^{89,90}

Antimicrobial Classes

Currently, the oral antimicrobial classes used to treat ABRs include: β -lactams, fluoroquinolones, macrolides/azalides, lincosamides, tetracyclines, and sulfonamides/trimethoprim, while one ketolide has undergone clinical study but has not yet been approved for clinical use by the FDA.

β -Lactams. This class of antimicrobials—which are characterized by the presence of a β -lactam ring—includes numerous compounds, many with different spectra of activity. The β -lactams exert their antibacterial effect by inhibiting cell-wall synthesis and producing autolysis. This action is accomplished through the binding of the antimicrobial to the various PBPs in the cell wall.

Orally available agents include the penicillins (with and without β -lactamase-inhibitor compounds) and the cephalosporins. Cephalosporins have been modified to broaden the spectrum of antimicrobial activity, and increase stability in the presence of β -lactamases. The physicochemical properties of many oral cephalosporins make them less suitable than penicillin/amoxicillin when *S. pneumoniae* is the infecting pathogen. Cephalosporins are inherently less active than penicillin/amoxicillin against *S. pneumoniae*—many of these agents have baseline MICs that are fourfold higher than that of amoxicillin. Furthermore, cephalosporins are actively absorbed in the gastrointestinal tract, which limits the concentration that can be achieved, regardless of the magnitude of dose administered.

Amoxicillin and amoxicillin/clavulanate. A less potent but better-absorbed derivative of ampicillin, amoxicillin is relatively safe and well tolerated. Given its intrinsic activity and excellent bio-

availability, amoxicillin is generally considered the most active of all oral β -lactams against streptococci, including pneumococci. While the addition of clavulanate to amoxicillin does not affect the intrinsic activity against *S. pneumoniae*, clavulanate does preserve the activity of amoxicillin in the presence of β -lactamases.

Resistance to penicillin in isolates of *S. pneumoniae* is relative and may be overcome by using higher doses of amoxicillin. While the “typical” adult amoxicillin dose is 1.5 to 1.75 g/day and the “typical” pediatric amoxicillin dose is 40 to 45 mg/kg per day, pharmacokinetic and pharmacodynamic research indicates that higher daily doses may be necessary to eradicate *S. pneumoniae* with high MICs. Serum levels of amoxicillin increase linearly with the dose (ie, gastrointestinal absorption is not a limiting factor), and the difference in the incidence of adverse effects between lower and higher doses is negligible.

For the purposes of these guidelines, high-dose amoxicillin is defined as 4 g/day for adults and 90 mg/kg per day for children. High-dose amoxicillin/clavulanate is defined as 4 g of amoxicillin with 250 mg of clavulanate per day for adults, and 90 mg/kg per day of amoxicillin with 6.4 mg/kg per day of clavulanate (in two divided doses) for children. The only formulations of high-dose amoxicillin approved by the FDA are in combination with clavulanate, with separate formulations for adults and children. The adult formulation uses a modified-release mechanism to provide a pharmacokinetically enhanced version of amoxicillin/clavulanate. The pediatric formulation provides a 14:1 ratio of amoxicillin to clavulanate in an oral suspension.

High-dose amoxicillin (with or without clavulanate), appears to be safe and promising for respiratory tract pathogens, including penicillin-nonsusceptible *S. pneumoniae* and β -lactamase-producing organisms (in combination with clavulanate).^{52,133-136}

The intrinsic activity of amoxicillin against β -lactamase-negative strains of *H. influenzae* is fair to good. Amoxicillin is 20 to 50 times less potent than third-generation cephalosporins (ie, cefixime, cefpodoxime), and occasional failures may be expected in infections caused by β -lactamase-negative strains of *H. influenzae* treated with

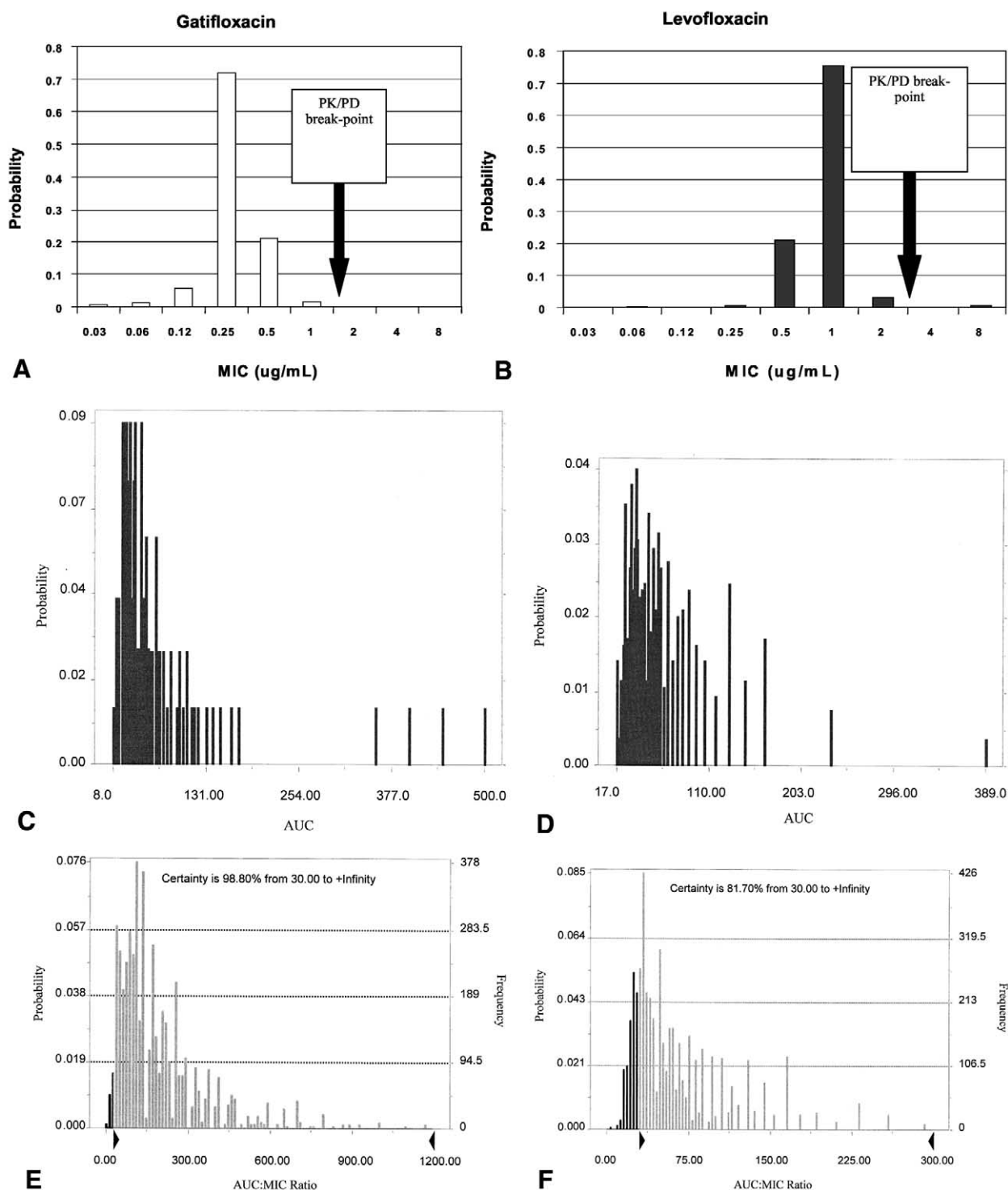


Fig 12. Monte Carlo simulation. **(A,B)** Distribution of gatifloxacin and levofloxacin MICs against *S pneumoniae* from the 1999-2000 SENTRY Respiratory Surveillance Program study. **(C)** Distribution of gatifloxacin free-drug area under the concentration-time curve (AUC)₀₋₂₄ ($\mu\text{g} \cdot \text{h/mL}$) ratio in the patient population. **(D)** Distribution of levofloxacin free-drug area under the concentration-time curve (AUC)₀₋₂₄ ($\mu\text{g} \cdot \text{h/mL}$) ratio in the patient population. **(E)** Results of a 5000-patient Monte Carlo simulation for gatifloxacin based on MIC and AUC distributions presented in **(A)** and **(C)**. The dark bars represent the number of simulated patients with AUC:MIC ratios <30 , whereas the light bars represent patients with AUC:MIC ratios of ≥ 30 . The probability of gatifloxacin attaining an AUC:MIC ratio of at least 30 is 98.80%. **(F)** Results of a 5000-patient Monte Carlo simulation for levofloxacin based on MIC and AUC distributions presented in **(B)** and **(D)**. The dark bars represent the number of simulated patients with AUC:MIC ratios <30 , whereas the light bars represent patients with AUC:MIC ratios of ≥ 30 . The probability of levofloxacin attaining an AUC:MIC ratio of at least 30 is 81.7%. Reprinted with permission from reference.¹³¹

standard doses of amoxicillin. While the addition of clavulanate enhances the activity against β -lactamase-producing strains of *H influenzae*, drugs or formulations that optimize PK/PD performance help prevent treatment failures that occur when patients concentrate the drug at the site of infection (for varying reasons) to a less than average degree, especially when the average tissue concentration is close to the MIC of the pathogen (see discussion on Monte Carlo analyses). This is the reason why recent studies show that high-dose amoxicillin ($\pm$ clavulanate) has significantly fewer bacteriologic failures against β -lactamase-negative *H influenzae* than lower doses, even though the in vitro susceptibility rate for regular doses of amoxicillin-clavulanate is 98%.

The addition of clavulanate does not appear to be a driving force in the development of resistance. When administered three times a day, amoxicillin/clavulanate has been associated with a high incidence of gastrointestinal side effects compared to most of its alternatives. The incidence is significantly less with twice-a-day dosing. In general, when the clavulanate dose exceeds approximately 10 mg/kg per day, diarrhea can become a problem.

Cefaclor. Cefaclor has poor activity against *H influenzae*, fair activity against penicillin-susceptible pneumococci, and no activity against DRSP. Therefore, cefaclor has poor overall efficacy against bacterial respiratory tract pathogens.

Cefdinir. Cefdinir is an extended-spectrum semisynthetic cephalosporin, for oral administration with activity against *S pneumoniae* that is comparable to second-generation agents (eg, cefuroxime axetil, cefpodoxime proxetil).¹³⁷ Its activity against *H influenzae* is similar to cefuroxime axetil, but lower than that of cefpodoxime proxetil. Cefdinir is not appreciably metabolized and is eliminated principally via renal excretion. This agent is generally well tolerated, and the suspension formulation is very well accepted among children.^{138,139}

Cefixime. As the prototype oral third-generation oral cephalosporin, cefixime has potent activity against *H influenzae* but provides limited gram-positive coverage including *S pneumoniae*. Cefixime has no activity against staphylococci, may occasionally fail against even penicillin-suscepti-

ble pneumococci, and has no clinically significant activity against DRSP.

Cefpodoxime proxetil. Cefpodoxime proxetil, a third-generation oral cephalosporin, is a structural analog of ceftriaxone, and has similar activity to cefixime against respiratory pathogens. The activity of cefpodoxime proxetil is similar to that of cefuroxime axetil and cefdinir against *S pneumoniae*, but greater against *H influenzae*. Because of its spectrum of activity, cefpodoxime proxetil often is regarded as the preferred treatment for patients in whom treatment with high-dose amoxicillin or amoxicillin/clavulanate fails (or is intolerable). However, the clinical utility (ie, adherence) of the suspension formulation for children is often limited by its poor taste.

Cefprozil. Cefprozil is another good-tasting and well-tolerated broad-spectrum cephalosporin that has activity against *S pneumoniae* similar to cefdinir and cefuroxime axetil.¹³⁷ However, cefprozil is markedly less active against *H influenzae*.

Ceftriaxone. Ceftriaxone is a semisynthetic, broad-spectrum cephalosporin antibiotic for intravenous (IV) or intramuscular (IM) administration. Ceftriaxone sodium is completely absorbed following IM administration with mean maximum plasma concentrations occurring between 2 and 3 hours post dosing. Multiple intravenous or IM doses ranging from 0.5 to 2 g at 12- to 24-hour intervals resulted in 15% to 36% accumulation of ceftriaxone above single-dose values.

Cefuroxime axetil. Parenteral cefuroxime sodium has a long-established history in the treatment of moderate-to-severe lower respiratory infections caused by *H influenzae* and *S pneumoniae*. An oral formulation, cefuroxime axetil, was introduced in the 1980s, it has demonstrated good potency, efficacy, and side effect profiles. The activity of cefuroxime axetil against *S pneumoniae* is similar to cefpodoxime and cefdinir. Cefuroxime axetil is less active than cefpodoxime against *H influenzae*.

Loracarbef. Loracarbef is comparable to cefaclor in its activity against pathogens in respiratory tract infections.

Fluoroquinolones: *Gatifloxacin*, *levofloxacin*, and *moxifloxacin*. Fluoroquinolones exert their bactericidal activity by binding to DNA gyrase and topoisomerase IV. This impedes the formation

of supercoiled DNA, inhibits the relaxation of supercoiled DNA, and promotes double-strand DNA breakage. Ciprofloxacin has excellent activity against *H influenzae* and *M catarrhalis*, but the AUC-to-MIC ratio against *S pneumoniae* is only 10 to 20, whereas the target AUC-to-MIC ratio of fluoroquinolones for *S pneumoniae* is approximately 25 to 30.^{97,140} Ciprofloxacin in combination with adequate gram-positive therapy (eg, clindamycin) could be used for patients with rhinosinusitis. The newer fluoroquinolones (gatifloxacin, levofloxacin, and moxifloxacin) have remarkable potency against *H influenzae* and *M catarrhalis* and, unlike ciprofloxacin, potency against gram-positive pathogens, including *S pneumoniae*.¹⁴¹ Gemifloxacin is another quinolone that is active against respiratory pathogens, but this agent is not currently approved for the management of sinusitis.

While the gastrointestinal absorption of these agents is inhibited by the coadministration of foods or supplements with certain multivalent cations (magnesium, aluminium, iron, $\pm$ calcium), they generally lack the safety concerns (ie, phototoxicity) observed with some other quinolones. Achilles tendon rupture (and other tendinopathies) is likely a class effect of the fluoroquinolones, and is a particular concern among patients with renal dysfunction/failure.¹⁴² The use of gemifloxacin in women for longer than 5 days is associated with an increased likelihood of rash. The fluoroquinolones are currently not approved for use in children in the United States.

The predominant concern surrounding fluoroquinolone use pertains to the selection of class resistance in organisms such as gram-negatives (especially *Pseudomonas aeruginosa*), staphylococci, and pneumococci. Recent data evaluating fluoroquinolones and the propensity to select resistant pathogens, especially *S pneumoniae*, suggest that the differences in pharmacodynamics are related to the frequency of resistance selection. While the specific pharmacodynamic criteria for resistance prevention are still to be established, it appears that the most potent agents are least likely to promote/select resistance.

Fluoroquinolones are increasingly being used as empiric therapy for the management of community-acquired respiratory tract infections, in part be-

cause of prevalent resistance to more traditional agents. As with most antimicrobial agents, development of resistance among *S pneumoniae* strains to one fluoroquinolone generally leads to cross-resistance to all members of the fluoroquinolone class, and there is evidence that inappropriate use of pharmacodynamically inferior fluoroquinolones is linked to the development of resistance and to clinical failures.¹⁴³⁻¹⁴⁶ Because of this, fluoroquinolones should not be used indiscriminately, and the most pharmacodynamically potent fluoroquinolones should be used to treat the suspected pathogen. When the decision is made to use a fluoroquinolone, preference should be given to agents that are most likely to achieve optimal PK/PD parameters. The relative in vitro potency (based on PK/PD parameters) for several fluoroquinolones was moxifloxacin > gatifloxacin > levofloxacin. Higher doses of levofloxacin (750 mg/day) improve its PK/PD profile.

Macrolides/azalides: *Erythromycin, clarithromycin, and azithromycin.* The macrolides include agents such as erythromycin and clarithromycin, whereas azithromycin, an azalide, is a closely related agent. These agents are active against gram-positive and some gram-negative bacteria. Bacterial ribosomes consist of a 50s subunit (comprised of a 23S and a 5S rRNA), a 30s subunit, and approximately 50 proteins. The mechanism of action of macrolides/azalides involves inhibition of RNA-dependent protein synthesis by binding to the 50S subunit of the bacterial ribosome—specifically at the polypeptide exit region. Although they are generally considered to be bacteriostatic, they are bactericidal against autolytic species such as pneumococci.

Macrolides exhibit better antibacterial activity in an environment with a neutral to basic pH. This physicochemical characteristic is due to the fact that at a low pH macrolides become positively charged and do not readily cross biological membranes. This effect is most pronounced for azithromycin because it carries a double-positive charge at a low pH.

All of the macrolides have good activity against macrolide susceptible pneumococci. However, the increasing prevalence of macrolide resistance to *S pneumoniae* is associated with a significant likelihood of clinical failure.¹⁴⁷ Furthermore, resistance

to macrolides has been correlated with increased macrolide use,¹⁵ and of these agents, azithromycin use is more likely to select for resistant strains than clarithromycin use.¹⁴⁸

While clarithromycin and azithromycin have slightly greater activity against *H influenzae* than erythromycin, most of the available eradication and efficacy studies suggest an activity that is similar to or marginally higher than that of placebo. There is some controversy surrounding the antimicrobial activity of metabolites (14-OH clarithromycin), the intracellular concentrations of the newer agents, and the effects of pH on MIC results, none of which impact the foregoing conclusions about the activity of these drugs for extracellular pathogens (ie, *S pneumoniae* and *H influenzae*). Macrolides/azalides are active against *M catarrhalis*.

Lincosamides: *Clindamycin*. Clindamycin, which is structurally different from the macrolides, also acts by binding the 50S ribosomal subunit of susceptible bacteria thereby suppressing protein synthesis. Clindamycin has a concentration-dependent mechanism of antimicrobial activity,¹⁴⁹ and this agent is used clinically for the treatment of susceptible gram-positive aerobes and anaerobes as well as many gram-negative anaerobes. It is not, however, active against *H influenzae* and *M catarrhalis*.

Tetracyclines: *Doxycycline*. These antibiotics inhibit bacterial growth via inhibition of RNA-dependent protein synthesis by reversibly binding to the 30S ribosomal subunit and prevent binding of t-RNA. A derivative of tetracycline, doxycycline has adequate activity against penicillin-susceptible pneumococci. Like other oral non- β -lactams, the likelihood of nonsusceptibility to doxycycline rises in pneumococcal strains exhibiting any degree of penicillin resistance.⁸⁹ Doxycycline also has activity against *M catarrhalis*, but its activity against *H influenzae* is limited by its pharmacokinetics. Clinicians should be aware of the possibility of photosensitivity and infrequent esophageal caustic burns. Like the other tetracyclines, usage in children <8 years of age is contraindicated because of the possibility of tooth enamel discoloration.

Rifamycins: *Rifampin*. The prototype agent in this class is rifampin, which is a semisynthetic

derivative of rifamycin B. Rifampin binds to the β subunit on RNA polymerase, which blocks RNA transcription (suppresses the initiation of chain formation), resulting in a bactericidal effect. Rifampin is active against a variety of intracellular and extracellular microorganisms, including gram-positive and -negative bacteria, fungi, and parasites. Recent surveillance studies^{150,151} demonstrate that rifampin is active against approximately 99%, 96%, and 100% of *S pneumoniae*, *H influenzae*, and *M catarrhalis* isolates, respectively. While rifampin has been available for decades, the PK/PD profile of this agent is not known. Despite its activity against predominant respiratory pathogens, rifampin should not be used indiscriminately as monotherapy or for a prolonged duration because resistance to this agent develops rapidly.

At usual doses, the antimicrobial effect of rifampin is relatively specific to microorganisms (ie, mammalian RNA synthesis is not affected). Rifampin distributes widely throughout the body, and it is a well-known inducer of several cytochrome p450 isoenzymes and therefore has a high potential for drug interactions.

Folate inhibitors: *Trimethoprim-sulfamethoxazole*. Sulfonamides disrupt bacterial folic acid synthesis by inhibiting dihydropteroate synthase; this results in their bacteriostatic activity. TMP is a pyrimidine analog that inhibits dihydrofolate reductase. Because sulfonamides and trimethoprim block folic acid synthesis at different sites, they potentiate each other's antimicrobial activity producing synergistic activity. High rates of resistance to these drugs are now present in pneumococci and *H influenzae* (~25% to 30%).⁸⁹ *M catarrhalis* is intrinsically resistant to trimethoprim. In addition, these agents can cause skin rash, erythema multiforme, and toxic epidermal necrolysis, which can be potentially fatal.

New antibiotics. Ketolides are a new class of semisynthetic antibiotics closely related to macrolides, designed, theoretically, to provide greater activity against respiratory tract pathogens, particularly against macrolide-resistant strains of *S pneumoniae*.¹²¹ The mechanism of action of ketolides is similar to that of macrolides; however, ketolides have a higher affinity for the target binding sites on 23S rRNA of the 50S ribosomal subunit, which is partly responsible for the greater

in vitro activity against respiratory tract pathogens.^{152,153} Ketolides have a concentration-dependent mechanism of antimicrobial killing.¹⁵⁴ The structural modifications do not induce the ribosomal methylase-mediated resistance among pneumococcal strains with *erm* determinants that is common with macrolides and azalides.¹⁵⁵ Furthermore, ketolides may retain activity against strains in which ribosomal methylase-mediated or efflux-mediated resistance mechanisms are present.^{156,157}

Andes et al¹²² evaluated the impact of neutrophils on the bacteriostatic activity of telithromycin against *S pneumoniae* in the murine thigh model and reported enhanced potency (1.8- to 24-fold increase) for the ketolides in the presence of neutrophils. Tessier et al¹⁵⁸ studied 10 pneumococcal isolates in a murine thigh infection model and observed that telithromycin AUC/MIC ratios of approximately 200 correlated with bacteriostatic activity, whereas ratios of ≥ 1000 were needed to obtain bactericidal activity of the compound in this model.

Drusano and Preston¹⁵⁹ have evaluated the pharmacodynamic profile of telithromycin 800 mg once daily in patients with community-acquired pneumonia. In this clinical study involving infected patients both microbiologic and clinical outcome were correlated with AUC/MIC ratios. The authors report that an AUC/MIC ratio of ≥ 3.375 resulted in 91% eradication or presumed eradication of the infecting pathogen. At the time of this writing, further research is needed to determine if these AUC/MIC ratios in patients with community-acquired pneumonia are relevant to sinusitis. As with the macrolides and azalides, ketolides have limited activity against *H influenzae* due to an efflux pump.

Oxazolidinones are a new class of antibiotics with a unique mechanism of action (protein synthesis inhibition) against gram-positive pathogens. Linezolid, the prototype agent from this class, is currently approved for more complicated infections but the emergence of linezolid-resistant gram-positive cocci has been reported. Glycylcyclines are advanced-generation tetracycline derivatives designed to overcome mechanisms of resistance to this class of antibiotics, and agents from

this class are still in clinical development (at the time of this writing).

The Poole Therapeutic Outcome Model

Evidence from controlled clinical trials represents the optimal basis for recommending antimicrobial therapy for ABRS. However, many of the current clinical trials evaluating antimicrobial therapy have methodologic limitations (eg, diagnostic criteria, comparators, endpoints, outcomes measures) that preclude them from being considered as evidence. Furthermore, the trends in antimicrobial resistance have changed dramatically over the past 10 years, which has affected the applicability of evidence from older clinical trials. While a large meta-analysis²⁰ recently was conducted to evaluate the role of antimicrobial therapy (in general, and the role of specific agents/classes) in ABRS, many of the individual trials were conducted prior to the widespread resistance that is currently reported in *S pneumoniae* and *H influenzae*. As a result, the findings from this meta-analysis may not be applicable to the current treatment of ABRS.¹⁶⁰ The methodology used in the present guidelines for evaluating antimicrobial therapy for ABRS does, however, take into account the current high levels of antibiotic-resistant organisms. In the absence of current evidence, it becomes more challenging to identify optimal therapy for ABRS. Rather than subjectively compiling a rank order of antimicrobial agents based on in vitro activity data and expert consensus, we utilized a more objective methodology to assessing treatment options. This approach involved the use of a mathematical model—the Poole therapeutic outcomes model—to predict treatment outcomes in ABRS.

The therapeutic outcomes model was extrapolated from work originally conducted by Marchant et al,¹⁶¹ involving the correlation between in vivo potency of various antimicrobial agents with clinical outcomes using double-tympanocentesis methodology in otitis media. In these studies, Marchant et al observed that nonbacterial factors can result in discrepancies between bacteriologic and clinical outcomes. For example, an agent with a 100% bacteriologic cure rate will not necessarily have a 100% clinical cure rate because some patients will continue to experience symptoms re-

sulting from nonbacterial factors (eg, viral infection, persistent middle ear effusion). Conversely, antimicrobial agents with relatively poor bacteriologic cure rates often appear to be more effective than expected because of the high rate of spontaneous resolution of symptoms. As a result, highly efficacious agents generally have only slightly better impact on clinical outcomes (ie, symptoms) compared with less-efficacious agents, despite more dramatic differences in bacteriologic outcomes.

The therapeutic outcomes model is a tool to help predict the likelihood of bacteriologic success with particular antimicrobial agents by accounting for various factors including: (1) the proportion of patients with a clinical diagnosis of acute bacterial rhinosinusitis and a positive sinus aspirate; (2) the clinical resolution of disease in the culture-negative patient group; (3) the distribution of pathogens frequently encountered in ABRS; (4) the spontaneous resolution rate associated each pathogen; and (5) the in vitro susceptibility of the predominant sinusitis pathogens to antimicrobial agents at PK/PD breakpoints (Figure 13). The therapeutic outcomes model also can predict overall clinical outcomes for the total patient group (ie, those with either bacterial or nonbacterial disease).

The first component of the mathematical model involves the process of accounting for nonbacterial disease. Among patients with nasal/sinus symptoms (who undergo sinus tap), approximately 35% will have negative bacterial cultures, with symptoms usually due to a primary viral process. The majority of these patients will achieve complete resolution of symptoms without antibiotic therapy. An additional 8% to 14% of patients will have persistent nasal/sinus symptoms, regardless of any antibiotic therapy prescribed. These persistent symptoms are likely due to nonbacterial causes of facial pain, nasal obstruction, or rhinorrhea (eg, allergy, headaches, and anatomic factors). The next component accounts for the distribution of pathogens in ABRS and the likelihood of spontaneous resolution associated with each of these pathogens (based on placebo-controlled trials in acute otitis media). Among bacterial infections—as mentioned above—the pathogen distribution in adults is *S pneumoniae* (33% to 41%), *H influenzae* (29% to 35%), and *M catarrhalis* (4%

to 8%). Most studies suggest that 10% to 20% of the bacterial sinus infections are caused by pathogens other than *S pneumoniae*, *H influenzae*, or *M catarrhalis*. For this model, the percentages used for the pathogen distribution have been modified to yield a total of 100%. Also, “miscellaneous” pathogens are omitted from the model in this guideline revision because (1) the FDA does not typically consider them to be important pathogens, (2) adequate susceptibility data against these pathogens is lacking, and (3) the activity of a given antimicrobial agent against miscellaneous pathogens is likely to be close to the average of its activity against the three usual pathogens. The overall susceptibility pattern of a given agent is not substantially affected by the exclusion of these miscellaneous pathogens.

The pathogen distribution in children is *S pneumoniae* (25% to 30%), *H influenzae* (15% to 20%), and *M catarrhalis* (15% to 20%). Modifications of these values are made in the model to give a total of 100%. Spontaneous resolution rates used in this model were 30% for *S pneumoniae*, 60% for *H influenzae*, 80% for *M catarrhalis* and 50% for other pathogens. Spontaneous resolution rates will vary depending on duration of clinical observation, age, and status of mucosal health.

Based on these values, spontaneous resolution of symptoms would be expected in 47% of adults with documented bacterial infection (62% of the total, clinically diagnosed patient group). Among untreated children, spontaneous resolution of symptoms would be expected in 50% among those with bacterial infection (63% of the clinically defined pediatric sinusitis group).

The model also accounts for the effects of antimicrobial therapy on achieving clinical outcomes by using current susceptibility data for each organism at PK/PD breakpoints, because PK/PD susceptibility breakpoints for given dosing regimens have been shown to correlate with bacteriologic cure rates.^{97,99} Resolution rates for the bacterially infected group and the total patient group are shown in a Marchant plot (Figures 14 and 15).^{89,90} These data sets were used because complete MIC distributions were available and the proportion of isolates inhibited at PK/PD breakpoints could be determined. The outcomes of these calculations are shown as Marchant plots, showing predicted bacte-

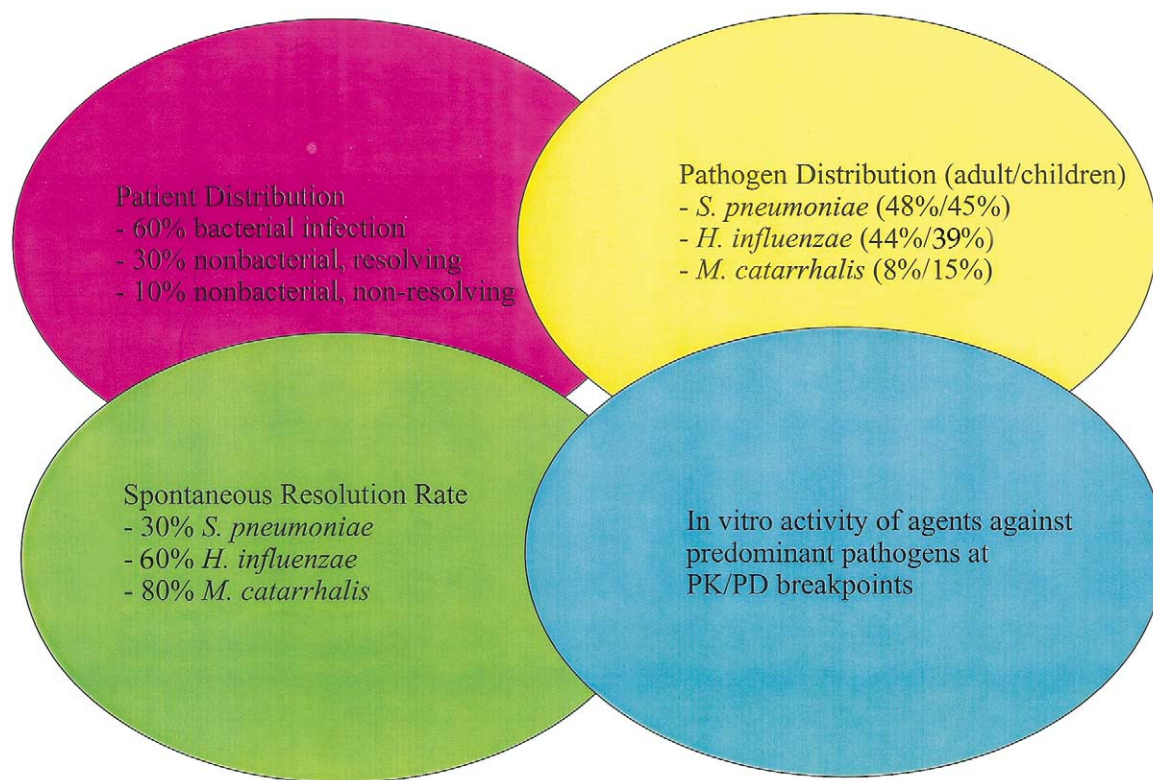


Fig 13. Factors incorporated in the Poole therapeutic outcome model.

riological outcomes in the bacterial infection group and the total patient group. The Marchant plot is only a relative rank order for the data used. Other surveillance data may, therefore, alter this relative rank order. The resolution rates are based on in vitro microbiologic efficacy and do not guarantee clinical outcome. However, in the absence of other evidence, the therapeutic outcomes model was used, as it was regarded as the best method available for objectively predicting clinical outcomes.

A more detailed description of the therapeutic outcomes model is provided elsewhere in this supplement.¹⁶²

ANTIMICROBIAL TREATMENT GUIDELINES

These recommendations are based on the therapeutic outcome model described below. Tables 4 and 5 summarize the panel's antimicrobial treatment guidelines for adults and children, respectively. Multiple factors played a role in the antimicrobial selection process. Because serious intracranial and extracranial complications associ-

ated with ABRS usually arise secondary to *S pneumoniae* infection, it is important for initial therapy to adequately cover *S pneumoniae*. Gram-negative coverage for *H influenzae* and *M catarrhalis* (in children) cannot be ignored, however. A rational approach to the treatment of ABRS should consider the aforementioned concerns along with the logical application of microbiology and the pharmacodynamic/pharmacokinetic principles.

The panel's guidelines for adults and children with ABRS characterize two groups of patients: (1) those with mild disease who have not received antibiotics within the previous 4 to 6 weeks; and (2) those with mild disease who have received antibiotics within the prior 4 to 6 weeks and those with moderate disease (regardless of recent antibiotic exposure).

As mentioned previously, the primary reason why antimicrobial therapy is recommended for ABRS is to improve patient health. The terms mild and moderate have been integrated into the decision-making process to reflect the degree of pa-

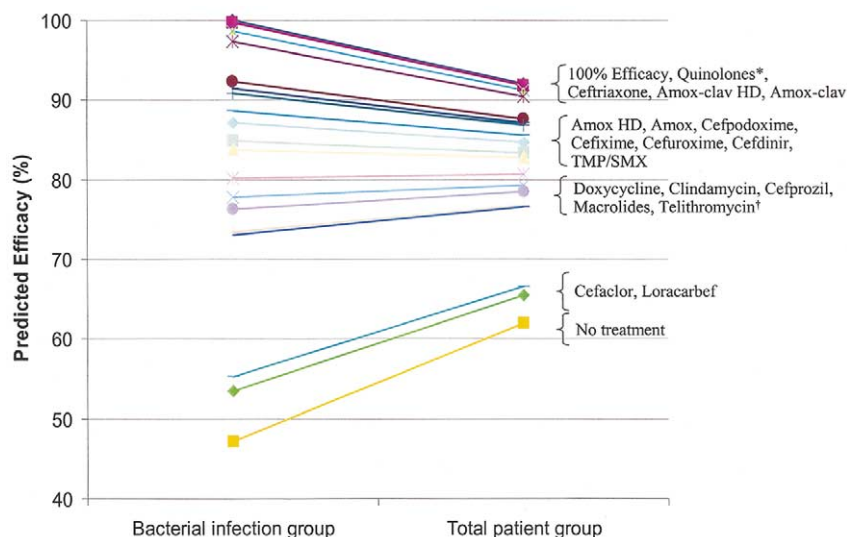


Fig 14. "Marchant" plot for antibiotics used to treat adult acute bacterial rhinosinusitis.^{89,90} (*Respiratory quinolone (ie, gatifloxacin, levofloxacin, moxifloxacin). †The activity of telithromycin against *S pneumoniae*, *H influenzae*, and *M catarrhalis* depends on its PK/PD breakpoints, which is uncertain at this time. The activity of telithromycin is assumed to be similar to that of macrolides/azalides until further information becomes available.)

tient discomfort (as evidenced by the symptom complex and the time course of the disease) and the likelihood of experiencing spontaneous resolution of those symptoms. In other words, patients with moderate disease are more likely to require therapeutic intervention to achieve resolution of their symptoms, and these patients are less likely to tolerate treatment failures. The differences in disease severity do not imply the presence or absence of antimicrobial resistance. Patients, however, may not always be neatly categorized based on this classification. An evaluation of disease severity requires clinical judgment gained only by the clinician familiar with the patient. Severe life-threatening infection with or without complications is not addressed in these guidelines.

Recent antibiotic use is a major risk factor associated with infection caused by resistant pathogens.^{163,164} Other risk factors include age <5 years and attendance in day-care centers. Because recent antimicrobial exposure increases the risk of carriage and infection due to resistant organisms, antimicrobial therapy should be based on the patient's history of recent antibiotic use. The panel's guidelines stratify patients according to antibiotic exposure within the previous 4 to 6 weeks.

Lack of response to therapy at ≥ 72 hours is an arbitrary timeframe established to define treatment failures. Clinicians should monitor the patient's response to antibiotic therapy, which may include instructing the patient to call the office or clinic if there is persistence or worsening of symptoms over the next few days.

The current recommendations for the duration of antimicrobial treatment for ABRS is 10 to 14 days, which is based on results of clinical trials that performed pre- and posttreatment sinus aspirates.³⁶ The new technique of serial sinus sampling⁴⁷ is designed to better define the optimal duration of treatment for ABRS.

Allergies to antibiotics (ie, β -lactams) or age limitations for certain antimicrobials (ie, fluoroquinolones) may preclude the use of optimal antimicrobials, and clinicians should be aware of the potential for treatment failure in these situations.

The panel used the therapeutic outcomes model as a tool in developing its antimicrobial recommendations. While the most recent and best data were used for this model, the panel realizes that resistance rates may change over time and may vary from community to community. The panel, therefore, will continue to revise the guidelines as resistance rates change and new antibiotics are introduced.

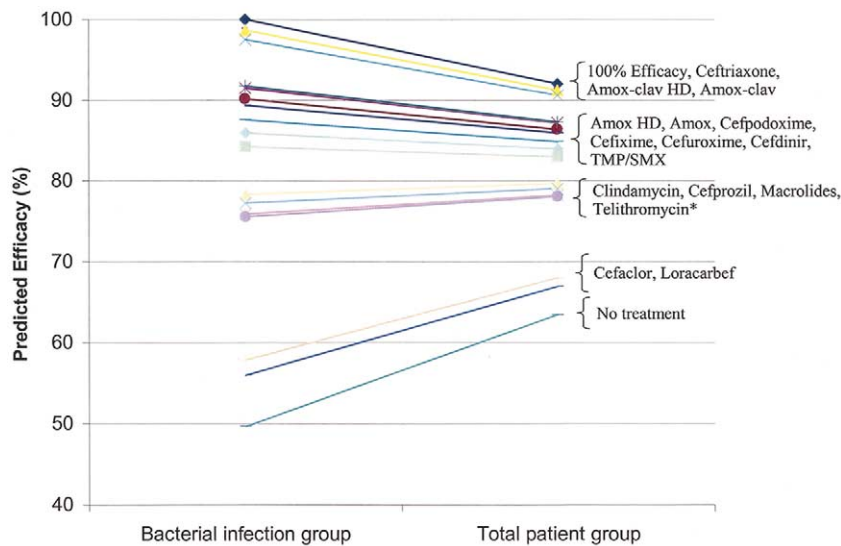


Fig 15. "Marchant" plot for antibiotics used to treat pediatric acute bacterial rhinosinusitis.^{89,90} (*The activity of telithromycin against *S pneumoniae*, *H influenzae*, and *M catarrhalis* depends on its PK/PD profile, which is uncertain at this time. The activity of telithromycin is assumed to be similar to that of macrolides/azalides until further information becomes available.)

Antimicrobial Choices

The following values calculated using the therapeutic outcomes model represent predicted clinical outcome in clinically diagnosed sinusitis. Clinical criteria were used in place of bacteriologic criteria (ie, bacteriologic outcome in patients with bacterial infection) because clinical outcomes are more consistent with what is encountered in everyday practice. While predicting bacteriologic outcomes in patients with bacterial infection may be ideal, the values obtained using the therapeutic outcomes model may be inconsistent with clinical experience. As mentioned previously, antibiotics should be reserved for patients with bacterial infection, with the primary goal of eradicating the pathogen from the site of infection. However, the limitations associated with differentiating bacterial from nonbacterial disease inevitably result in patients with nonbacterial disease receiving antibiotic therapy. Using antibiotics for patients with nonbacterial disease often dilutes or reduces the perceived bacteriologic efficacy of the antibiotic. This often is the case with bacteriologic findings from clinical trials that have methodologic limitations (eg, inclusion criteria, diagnostic criteria).

According to the therapeutic outcomes model, antibiotics can be placed into the following relative rank order of predicted clinical efficacy for

adult patients: 90% to 92% = respiratory quinolones (gatifloxacin, levofloxacin, moxifloxacin), ceftriaxone, amoxicillin/clavulanate (4 g/250 mg per day), and amoxicillin/clavulanate (1.75 g/250 mg per day); 83% to 88% = high-dose amoxicillin (4 g/day), amoxicillin (1.5 g/day), cefpodoxime proxetil, cefixime (based on *H influenzae* and *M catarrhalis* coverage only), cefuroxime axetil, cefdinir, and TMP/SMX; 77% to 81% = doxycycline, clindamycin (based on gram-positive coverage only), cefprozil, azithromycin, clarithromycin, erythromycin, and telithromycin; 65% to 66% = cefaclor and loracarbef. The predicted spontaneous resolution rate for clinically diagnosed sinusitis in untreated adults with ABRS is 62%.

According to the Poole therapeutic outcomes model, antibiotics can be placed into the following relative rank order of predicted clinical efficacy in children: 91% to 92% = ceftriaxone, high-dose amoxicillin/clavulanate (90 mg/6.4 mg per kg per day), and amoxicillin/clavulanate (45 mg/6.4 mg per kg per day); 82% to 87% = high-dose amoxicillin (90 mg/kg per day), amoxicillin (45 mg/kg per day), cefpodoxime proxetil, cefixime (based on *H influenzae* and *M catarrhalis* coverage only), cefuroxime axetil, cefdinir, and TMP/SMX; 78% to 80% = clindamycin (based on gram-positive coverage only), cefprozil, azithromycin, clarithro-

mycin, and erythromycin; 67% to 68% = cefaclor and loracarbef. The predicted spontaneous resolution rate in untreated children with ABRS is 63%.

The recommendations for patients who are not improving or are worsening at ≥ 72 hours of treatment are provided based on spectrum of activity of initial therapy against the major sinusitis pathogens. The estimated likelihood of a particular pathogen being encountered in patient failures with each type of initial therapy was utilized in lieu of obtaining a culture to guide "switch" therapy at 72 hours.

The recommendations for selecting antimicrobial therapy in the current guidelines are more focused compared with the previous guidelines. The decision to recommend fewer antimicrobial options, particularly for patients with moderate disease, was based on an evaluation of antimicrobial efficacy.

Recommendations for adult patients (see Table 4). Recommendations for initial therapy for adult patients with mild disease and who have not received antibiotics in the previous 4 to 6 weeks include the following choices: amoxicillin/clavulanate (1.75 to 4 g/250 mg per day), amoxicillin (1.5 to 4 g/day), cefpodoxime proxetil, cefuroxime axetil, or cefdinir. While TMP/SMX, doxycycline, azithromycin, clarithromycin, erythromycin, or telithromycin may be considered for patients with β -lactam allergies, bacteriologic failure rates of 20% to 25% are possible. Failure to respond to antimicrobial therapy after 72 hours should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 4). When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent.

Recommendations for initial therapy for adults with mild disease who have received antibiotics in the previous 4 to 6 weeks or adults with moderate disease include the following choices: respiratory fluoroquinolone (gatifloxacin, levofloxacin, moxifloxacin) or high-dose amoxicillin/clavulanate (4 g/250 mg per day). The widespread use of respiratory fluoroquinolones for patients with milder disease may promote resistance (especially of gut organisms) to this class of agents. Ceftriaxone or combination therapy with adequate gram-positive and -negative coverage may also be considered.

Examples of appropriate regimens of combination therapy include high-dose amoxicillin or clindamycin plus cefixime, or high-dose amoxicillin or clindamycin plus rifampin. When ceftriaxone is selected, a dose of 1 g/day IM or IV should be used for 5 days. This duration of therapy was arbitrarily extrapolated by the committee based on data from acute otitis media studies. Rifampin should not be used as monotherapy, casually, or for longer than 10 to 14 days, as resistance emerges rapidly to this agent.

Failure to respond to antimicrobial therapy after 72 hours should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 4). When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent. Patients who have received effective antibiotic therapy and continue to be symptomatic need further evaluation. A CT scan, fiberoptic endoscopy, or sinus aspiration for culture may be necessary.

When amoxicillin ($\pm$ clavulanate) is selected for patients at risk for infection with penicillin-resistant *S pneumoniae* or DRSP (eg, recent antimicrobial use, immunodeficiency, frequent exposure to children attending day care, etc.), the high-dose regimen (ie, 4 g/250 mg) should be used.⁵²

Recommendations for pediatric patients (See Table 5). Recommendations for initial therapy for children with mild disease and who have not received antibiotics in the previous 4 to 6 weeks include the following: high-dose amoxicillin/clavulanate (90 mg/6.4 mg per kg per day), high-dose amoxicillin (90 mg/kg per day), cefpodoxime proxetil, cefuroxime axetil, or cefdinir. TMP/SMX, azithromycin, clarithromycin, or erythromycin is recommended if the patient has a history of immediate Type I hypersensitivity reaction to β -lactams. These antibiotics have limited effectiveness against the major pathogens of ABRS and bacterial failure is possible. The clinician should differentiate an immediate hypersensitivity reaction from other less dangerous side effects. Children with immediate hypersensitivity reactions to β -lactams may need: desensitization, sinus cultures, or other ancillary procedures and studies. Children with other types of reactions and side effects may tolerate one specific β -lactam, but not another.

Table 4. Recommended antibiotic therapy for adults with ABRS

Initial therapy	Calculated clinical efficacy (%) [*]	Calculated bacteriologic efficacy (%) [*]	Switch therapy options (no improvement or worsening after 72 hours) [†]
Mild disease‡ with no recent antimicrobial use (past 4-6 weeks)§			
Amoxicillin/clavulanate (1.75-4 g/250 mg/d)¶	90-91	97-99	
Amoxicillin (1.5-4 g/d)	87-88	91-92	Gatifloxacin, levofloxacin, moxifloxacin
Cefpodoxime proxetil	87	91	Amoxicillin/clavulanate 4g/250 mg
Cefuroxime axetil	85	87	Ceftriaxone
Cefdinir	83	85	Combination Therapy¶¶
β-Lactam allergic#			
TMP/SMX	83	84	
Doxycycline	81	80	Gatifloxacin, levofloxacin, moxifloxacin
Azithromycin, clarithromycin, erythromycin	77	73	Rifampin plus clindamycin
Telithromycin**	77	73	
Mild disease‡ with recent antimicrobial use (past 4-6 weeks) or moderate disease‡			
Gatifloxacin/levofloxacin/moxifloxacin	92	100	
Amoxicillin/clavulanate (4 g/250 mg)	91	99	Reevaluate patient‡‡
Ceftriaxone	91	99	
(Combination therapy)¶¶			
β-Lactam allergic#			
Gatifloxacin, levofloxacin, moxifloxacin	92	100	Reevaluate patient††
Clindamycin and rifampin††			Reevaluate patient††

^{*}Clinical and bacterial efficacy (ie, clinical and microbiologic adequacy) is represented by the calculation from the Poole Therapeutic outcome model (see text) using the mean values of two surveillance data sets: the US component of the Alexander project (1998 to 2001) and SENTRY surveillance data. These values do not guarantee clinical success or failure.

[†]When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial antibiotic. The respiratory fluoroquinolones (gatifloxacin, levofloxacin, and moxifloxacin), ceftriaxone, and amoxicillin/clavulanate (4 g/250 mg) currently have the best coverage for both *S pneumoniae* and *H influenzae*. The terms mild and moderate are designed to aid in selecting antibiotic therapy.

[‡]The difference in severity of disease does not imply the presence or absence of antimicrobial resistance. Rather, this terminology indicates the relative degree of acceptance of possible therapeutic failure, and the likelihood of achieving spontaneous resolution of symptoms. The determination of disease severity lies with the clinician's evaluation of the patient's history and clinical presentation. Severe, life-threatening infection, with or without complications, is not addressed in these guidelines.

[§]Prior antibiotic therapy within 4 to 6 weeks is a risk factor for infection with resistant organisms. Antibiotic choices should be based on this and other risk factors.

[¶]The total daily dose of amoxicillin and the amoxicillin component of amoxicillin/clavulanate can vary from 1.5 to 4 g/day. Lower daily doses (1.5 g/day) are more appropriate in mild disease in patients with no risk factors for infection with a resistant pathogen (including recent antibiotic use). Higher daily doses (4 g/day) may be advantageous in areas with a high prevalence of penicillin-resistant *S pneumoniae* or DRSP, for patients with moderate disease, for patients who may need better *H influenzae* coverage or for patients with risk factors for infection with a resistant pathogen. There is a greater potential for treatment failure or resistant pathogens in these patient groups.

^{¶¶}Based on in vitro spectrum of activity; combination therapy using appropriate gram-positive and -negative coverage may be appropriate. Examples of combination therapy regimens include high-dose amoxicillin (4 g/day) or clindamycin plus cefixime, or high-dose amoxicillin (4 g/day) or clindamycin, plus rifampin. There is no clinical evidence at this time, however, of the safety or efficacy of these combinations.

[#]Cephalosporins should be considered initially for patients with penicillin intolerance/non-Type I hypersensitivity reactions (eg, rash). TMP/SMX, doxycycline, macrolides, azalides, and ketolides are not recommended unless the patient is β-lactam allergic. Their effectiveness against the major pathogens of ABRS is limited, and bacterial failure of 20% to 25% is possible. A respiratory fluoroquinolone (eg, gatifloxacin, levofloxacin, moxifloxacin) is recommended for patients who have allergies to β-lactams or who have recently failed other regimens.

^{**}Telithromycin is not approved for use by the FDA (at the time of writing).

^{††}Reevaluation is necessary because the antibiotics recommended for initial therapy provide excellent activity against the predominant ABRS pathogens, including *S pneumoniae* and *H influenzae*. Additional history, physical examination, cultures, and/or CT scan may be indicated, and the possibility of other less common pathogens considered.

^{‡‡}Rifampin is a well-known inducer of several cytochrome p450 isoenzymes and therefore has a high potential for drug interactions.

Table 5. Recommended antibiotic therapy for children with ABRs

Initial therapy	Calculated clinical efficacy (%) [*]	Calculated bacteriologic efficacy (%) [*]	Switch therapy options (no improvement or worsening after 72 hours) [†]
Mild disease‡ with no recent antimicrobial use (past 4 to 6 weeks)§			
Amoxicillin/clavulanate (90 mg/6.4 mg/kg per day)	91-92	97-99	Amoxicillin clavulanate (90 mg/6.4 mg/kg per day)
Amoxicillin	86-87	90-92	Ceftriaxone
Cefpodoxime proxetil	87	92	Combination therapy¶
Cefuroxime axetil	85	88	
Cefdinir	84	86	
β-Lactam allergic#			
TMP/SMX	83	84	Re-evaluate patient**
Azithromycin, clarithromycin, erythromycin	78	76	Combination therapy¶
Mild disease‡ with recent antimicrobial use (past 4 to 6 weeks) or moderate disease‡			
Amoxicillin/clavulanate (90 mg/6.4 mg/kg per day)	92	99	Reevaluate patient**
Ceftriaxone	91	99	
β-Lactam allergic#			
TMP/SMX	83	84	Reevaluate patient**
Azithromycin, clarithromycin, erythromycin	78	76	Combination therapy¶ (clindamycin or TMP/SMX plus rifampin)
Clindamycin††	79	78	

*Clinical and bacterial efficacy (ie, clinical and microbiologic adequacy) is represented by the calculation from the Poole therapeutic outcome model (see text) using the mean values of two surveillance data sets: the US component of the Alexander project (1998 to 2001) and SENTRY surveillance data. These values do not guarantee clinical success or failure.

†When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial antibiotic. Ceftriaxone and high-dose amoxicillin/clavulanate currently have the best coverage for both *S pneumoniae* and *H influenzae*.

‡The terms mild and moderate are designed to aid in selecting antibiotic therapy. The difference in severity of disease does not imply the presence or absence of antimicrobial resistance. Rather, this terminology indicates the relative degree of acceptance of possible therapeutic failure, and the likelihood of achieving spontaneous resolution of symptoms. The determination of disease severity lies with the clinician's evaluation of the patient's history and clinical presentation. Severe, life-threatening infection, with or without complications, is not addressed in these guidelines.

§Prior antibiotic therapy within 4 to 6 weeks is a risk factor for infection with resistant organisms. Antibiotic choices should be based on this and other risk factors.

||The total daily dose of amoxicillin and the amoxicillin component of amoxicillin/clavulanate can vary from 45 to 90 mg/kg per day. Lower daily doses (45 mg/kg per day) are more appropriate in mild disease in patients with no risk factors for infection with a resistant pathogen (including recent antibiotic use). Higher daily doses (90 mg/kg per day) may be advantageous in areas with a high prevalence of penicillin-resistant *S pneumoniae* or DRSP, for patients with moderate disease, for patients who may need better *H influenzae* coverage or for patients with risk factors for infection with a resistant pathogen. There is a greater potential for treatment failure or resistant pathogens in these patient groups.

¶Based on in vitro spectrum of activity, combination therapy using appropriate gram-positive and -negative coverage may be appropriate. Examples of combination therapy regimens include high-dose amoxicillin (90 mg/kg per day) or clindamycin plus cefixime, or high-dose amoxicillin (90 mg/kg per day) or clindamycin, plus rifampin. Other combination therapy regimens may be appropriate for patients with β-lactam allergy. There is no clinical evidence at this time, however, of the safety or efficacy of these combinations.

#Cephalosporins should be considered for patients with penicillin intolerance/non-Type I hypersensitivity reactions (eg, rash). TMP/SMX, macrolides, and azalides are not recommended unless the patient is β-lactam allergic. Their effectiveness against the major pathogens of ABRs is limited, and bacterial failure of 20% to 25% is possible.

**Reevaluation is necessary because the antibiotics recommended for initial therapy provide excellent activity against the predominant ABRs pathogens, including *S pneumoniae* and *H influenzae*. Additional history, physical examination, cultures, and/or CT scan may be indicated, and the possibility of other less common pathogens considered.

††Excluding β-lactams, clindamycin is the most active oral agent currently available with activity against approximately 90% of *S pneumoniae* isolates. It has no activity, however, against *H influenzae* or *M catarrhalis*.

The recommended initial therapy for children with mild disease who have received antibiotics in the previous 4 to 6 weeks or children with moderate disease is high-dose amoxicillin/clavulanate (90mg/6.4 mg per kg per day). Cefdinir, cefpodoxime proxetil, or cefuroxime axetil may be considered for patients with nonserious hypersensitivity reactions to penicillin. In such instances, cefdinir is the preferred agent based on patient acceptance.^{138,139} TMP/SMX, azithromycin, clarithromycin, or erythromycin are recommended if the patient is β -lactam allergic (Type I hypersensitivity reaction). Ceftriaxone or combination therapy with adequate gram-positive and -negative coverage may also be considered. Examples of appropriate regimens of combination therapy include high-dose amoxicillin or clindamycin plus cefixime, or high-dose amoxicillin or clindamycin plus rifampin. When ceftriaxone is selected, a dose of 50 mg/kg per day IM or IV should be used for 5 days. This duration of therapy was arbitrarily extrapolated by the committee based on data from acute otitis media studies. Rifampin should not be used as monotherapy, casually, or for longer than 10 to 14 days as resistance emerges rapidly to this agent. Monotherapy with clindamycin for β -lactam-allergic patients is appropriate if *S pneumoniae* is identified as a pathogen.

Failure to respond to antimicrobial therapy after 72 hours should prompt either a switch to alternate antimicrobial therapy or reevaluation of the patient (see Table 4). When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent.

When amoxicillin ($\pm$ clavulanate) is selected for patients at risk for infection with penicillin-resistant *S pneumoniae* or DRSP (eg, recent antimicrobial use, day-care attendance, etc.), the high-dose regimen should be used. This recommendation is based on data from acute otitis media studies.¹⁶⁵

CONCLUSIONS

These guidelines have been updated to provide the most recent information on management principles, antimicrobial susceptibility patterns, and therapeutic options. The treatment recommendations for ABRS in this document are based on a

mathematical model using pathogen distribution and spontaneous resolution data and pharmacodynamically derived susceptibility values of the major ABRS pathogens, from which bacteriologic outcome can be predicted. The panel hopes these guidelines will continue to provide a rational approach to the need for antimicrobial therapy in bacterial rhinosinusitis, reduction in the use of antibiotics for nonbacterial infections, and the appropriate use antibiotics when bacterial disease is likely. These recommendations should help clinicians select antimicrobial therapy for patients with ABRS until more evidence from adequately designed clinical trials becomes available.

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*The information contained in these guidelines does not necessarily reflect the views of the Food and Drug Administration.

NQF Ambulatory Care 2010**Measure number: ACP-029-10****Measure title: Patient(s) treated with an antibiotic for acute sinusitis that received a first line antibiotic.****Numerator detail (2a.3):**

Patients who filled a prescription for any antibiotic (code set RX-184) during the following time period: ten days prior to the initiating acute sinusitis encounter through 21 days after the initiating acute sinusitis encounter, and whose FIRST antibiotic prescription during this time window was one of the following:

- Amoxicillin (code set RX-185)
- Amoxicillin/clavulanate (code set RX-186)
- Cefpodoxime proxetil (code set RX-187)
- Cefuroxime axetil (code set RX-188)
- Cefdinir (code set RX-189)
- Gatifloxacin (code set RX-190)
- Levofloxacin (code set RX-191)
- Moxifloxacin (code set RX-192)
- Ceftriaxone (code set RX-193)
- Trimethoprim-sulfamethoxazole (code set RX-194)

cd. set	RX cd. set descrp.	ndc
RX-184	Any Antibiotic	00002032702
RX-184	Any Antibiotic	00002032750
RX-184	Any Antibiotic	00002032902
RX-184	Any Antibiotic	00002032903
RX-184	Any Antibiotic	00002034602
RX-184	Any Antibiotic	00002034603
RX-184	Any Antibiotic	00002034624
RX-184	Any Antibiotic	00002050101
RX-184	Any Antibiotic	00002050301
RX-184	Any Antibiotic	00002050324
RX-184	Any Antibiotic	00002050901
RX-184	Any Antibiotic	00002050924
RX-184	Any Antibiotic	00002144401
RX-184	Any Antibiotic	00002144410
RX-184	Any Antibiotic	00002144425
RX-184	Any Antibiotic	00002145401
RX-184	Any Antibiotic	00002149601
RX-184	Any Antibiotic	00002149701

RX-184	Any Antibiotic	00002149725
RX-184	Any Antibiotic	00002149801
RX-184	Any Antibiotic	00002149825
RX-184	Any Antibiotic	00002149901
RX-184	Any Antibiotic	00002149925
RX-184	Any Antibiotic	00002168101
RX-184	Any Antibiotic	00002204602
RX-184	Any Antibiotic	00002205402
RX-184	Any Antibiotic	00002207502
RX-184	Any Antibiotic	00002230733
RX-184	Any Antibiotic	00002230748
RX-184	Any Antibiotic	00002230768
RX-184	Any Antibiotic	00002230789
RX-184	Any Antibiotic	00002231633
RX-184	Any Antibiotic	00002231648
RX-184	Any Antibiotic	00002231668
RX-184	Any Antibiotic	00002231689
RX-184	Any Antibiotic	00002234305
RX-184	Any Antibiotic	00002237237
RX-184	Any Antibiotic	00002306102
RX-184	Any Antibiotic	00002306115
RX-184	Any Antibiotic	00002306133
RX-184	Any Antibiotic	00002306202
RX-184	Any Antibiotic	00002306215
RX-184	Any Antibiotic	00002306233
RX-184	Any Antibiotic	00002312542
RX-184	Any Antibiotic	00002312642
RX-184	Any Antibiotic	00002317002
RX-184	Any Antibiotic	00002317030
RX-184	Any Antibiotic	00002317102
RX-184	Any Antibiotic	00002317130
RX-184	Any Antibiotic	00002505718
RX-184	Any Antibiotic	00002505768
RX-184	Any Antibiotic	00002505818
RX-184	Any Antibiotic	00002505868
RX-184	Any Antibiotic	00002510501
RX-184	Any Antibiotic	00002510516
RX-184	Any Antibiotic	00002513048
RX-184	Any Antibiotic	00002513087
RX-184	Any Antibiotic	00002513248
RX-184	Any Antibiotic	00002513287
RX-184	Any Antibiotic	00002513548
RX-184	Any Antibiotic	00002513587
RX-184	Any Antibiotic	00002513618
RX-184	Any Antibiotic	00002513648
RX-184	Any Antibiotic	00002513687

RX-184	Any Antibiotic	00002535725
RX-184	Any Antibiotic	00002535801
RX-184	Any Antibiotic	00002535810
RX-184	Any Antibiotic	00002535901
RX-184	Any Antibiotic	00002535910
RX-184	Any Antibiotic	00002536001
RX-184	Any Antibiotic	00002536010
RX-184	Any Antibiotic	00002536101
RX-184	Any Antibiotic	00002536115
RX-184	Any Antibiotic	00002536116
RX-184	Any Antibiotic	00002536225
RX-184	Any Antibiotic	00002536310
RX-184	Any Antibiotic	00002700001
RX-184	Any Antibiotic	00002700010
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RX-186	Amoxicillin/clavulanate	55045147807
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RX-186	Amoxicillin/clavulanate	55175121900
RX-186	Amoxicillin/clavulanate	55175121901
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RX-186	Amoxicillin/clavulanate	55175122000
RX-186	Amoxicillin/clavulanate	55175122001
RX-186	Amoxicillin/clavulanate	55175122002
RX-186	Amoxicillin/clavulanate	55175122005
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RX-186	Amoxicillin/clavulanate	55175174500
RX-186	Amoxicillin/clavulanate	55175185000
RX-186	Amoxicillin/clavulanate	55175602001
RX-186	Amoxicillin/clavulanate	55175602101
RX-186	Amoxicillin/clavulanate	55289024015
RX-186	Amoxicillin/clavulanate	55289024209
RX-186	Amoxicillin/clavulanate	55289024215

RX-186	Amoxicillin/clavulanate	55289024221
RX-186	Amoxicillin/clavulanate	55289029615
RX-186	Amoxicillin/clavulanate	55289029630
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RX-186	Amoxicillin/clavulanate	55289084530
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RX-186	Amoxicillin/clavulanate	57362046034
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RX-186	Amoxicillin/clavulanate	58016010612
RX-186	Amoxicillin/clavulanate	58016010615
RX-186	Amoxicillin/clavulanate	58016010620

RX-186	Amoxicillin/clavulanate	58016010621
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RX-186	Amoxicillin/clavulanate	58016010712
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RX-186	Amoxicillin/clavulanate	58016033515
RX-186	Amoxicillin/clavulanate	58016033530
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RX-186	Amoxicillin/clavulanate	58016100201
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RX-186	Amoxicillin/clavulanate	58016499001
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RX-186	Amoxicillin/clavulanate	58864076720
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RX-186	Amoxicillin/clavulanate	60505253903
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RX-186	Amoxicillin/clavulanate	60505254102
RX-186	Amoxicillin/clavulanate	63304050901
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RX-186	Amoxicillin/clavulanate	66116068130
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RX-186	Amoxicillin/clavulanate	66267099120
RX-186	Amoxicillin/clavulanate	66267099220
RX-186	Amoxicillin/clavulanate	66267100101
RX-186	Amoxicillin/clavulanate	66267100201
RX-186	Amoxicillin/clavulanate	66336007421
RX-186	Amoxicillin/clavulanate	66685100100
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RX-186	Amoxicillin/clavulanate	66685100200
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RX-186	Amoxicillin/clavulanate	66685101100
RX-186	Amoxicillin/clavulanate	66685101101

RX-186	Amoxicillin/clavulanate	66685101102
RX-186	Amoxicillin/clavulanate	66685101200
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RX-186	Amoxicillin/clavulanate	66685101202
RX-186	Amoxicillin/clavulanate	68030126103
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RX-186	Amoxicillin/clavulanate	68030604201
RX-186	Amoxicillin/clavulanate	68030605002
RX-186	Amoxicillin/clavulanate	68071006330
RX-186	Amoxicillin/clavulanate	68084023501
RX-186	Amoxicillin/clavulanate	68084023511
RX-186	Amoxicillin/clavulanate	68084023601
RX-186	Amoxicillin/clavulanate	68084023611
RX-186	Amoxicillin/clavulanate	68115038620
RX-186	Amoxicillin/clavulanate	68115046320
RX-186	Amoxicillin/clavulanate	68115048840
RX-186	Amoxicillin/clavulanate	68115099020
RX-186	Amoxicillin/clavulanate	68115099120
RX-186	Amoxicillin/clavulanate	68118038620
RX-186	Amoxicillin/clavulanate	68387058015
RX-186	Amoxicillin/clavulanate	68387058530

cd.	set RX	code set	descr.	ndc
RX-187	Cefpodoxime	proxetil	00009353101	
RX-187	Cefpodoxime	proxetil	00009353102	
RX-187	Cefpodoxime	proxetil	00009353103	
RX-187	Cefpodoxime	proxetil	00009361501	
RX-187	Cefpodoxime	proxetil	00009361502	
RX-187	Cefpodoxime	proxetil	00009361503	
RX-187	Cefpodoxime	proxetil	00009361701	
RX-187	Cefpodoxime	proxetil	00009361702	
RX-187	Cefpodoxime	proxetil	00009361703	
RX-187	Cefpodoxime	proxetil	00009361801	
RX-187	Cefpodoxime	proxetil	00009361802	
RX-187	Cefpodoxime	proxetil	00009361803	
RX-187	Cefpodoxime	proxetil	00247033920	
RX-187	Cefpodoxime	proxetil	00403069114	
RX-187	Cefpodoxime	proxetil	00403453714	
RX-187	Cefpodoxime	proxetil	00781543820	
RX-187	Cefpodoxime	proxetil	00781543901	
RX-187	Cefpodoxime	proxetil	00781543920	
RX-187	Cefpodoxime	proxetil	00781616846	
RX-187	Cefpodoxime	proxetil	00781616852	
RX-187	Cefpodoxime	proxetil	00781616946	
RX-187	Cefpodoxime	proxetil	00781616952	
RX-187	Cefpodoxime	proxetil	12280010520	

RX-187	Cefpodoxime proxetil	16714021101
RX-187	Cefpodoxime proxetil	16714021201
RX-187	Cefpodoxime proxetil	33358006820
RX-187	Cefpodoxime proxetil	52959062710
RX-187	Cefpodoxime proxetil	52959062720
RX-187	Cefpodoxime proxetil	52959065820
RX-187	Cefpodoxime proxetil	52959079610
RX-187	Cefpodoxime proxetil	54569377400
RX-187	Cefpodoxime proxetil	54569377500
RX-187	Cefpodoxime proxetil	54569405800
RX-187	Cefpodoxime proxetil	54569405801
RX-187	Cefpodoxime proxetil	54569478300
RX-187	Cefpodoxime proxetil	55045221001
RX-187	Cefpodoxime proxetil	55175010100
RX-187	Cefpodoxime proxetil	55175010101
RX-187	Cefpodoxime proxetil	55175010102
RX-187	Cefpodoxime proxetil	55175010201
RX-187	Cefpodoxime proxetil	55175010301
RX-187	Cefpodoxime proxetil	55289039002
RX-187	Cefpodoxime proxetil	55289039010
RX-187	Cefpodoxime proxetil	55289039020
RX-187	Cefpodoxime proxetil	55289039028
RX-187	Cefpodoxime proxetil	55289039079
RX-187	Cefpodoxime proxetil	60346098114
RX-187	Cefpodoxime proxetil	63304052001
RX-187	Cefpodoxime proxetil	63304052020
RX-187	Cefpodoxime proxetil	63304052101
RX-187	Cefpodoxime proxetil	63304052120
RX-187	Cefpodoxime proxetil	63304096503
RX-187	Cefpodoxime proxetil	63304096504
RX-187	Cefpodoxime proxetil	63304096603
RX-187	Cefpodoxime proxetil	63304096604
RX-187	Cefpodoxime proxetil	65862009520
RX-187	Cefpodoxime proxetil	65862009620
RX-187	Cefpodoxime proxetil	65862014001
RX-187	Cefpodoxime proxetil	65862014050
RX-187	Cefpodoxime proxetil	65862014101
RX-187	Cefpodoxime proxetil	65862014150

cd.	set RX code set descrp.	ndc
RX-188	Cefuroxime axetil	00002535725
RX-188	Cefuroxime axetil	00002535801
RX-188	Cefuroxime axetil	00002535810
RX-188	Cefuroxime axetil	00002535901
RX-188	Cefuroxime axetil	00002535910
RX-188	Cefuroxime axetil	00002536001

RX-188	Cefuroxime axetil	00002536010
RX-188	Cefuroxime axetil	00002536101
RX-188	Cefuroxime axetil	00002536115
RX-188	Cefuroxime axetil	00002536116
RX-188	Cefuroxime axetil	00002536225
RX-188	Cefuroxime axetil	00002536310
RX-188	Cefuroxime axetil	00002727101
RX-188	Cefuroxime axetil	00002727125
RX-188	Cefuroxime axetil	00002727201
RX-188	Cefuroxime axetil	00002727210
RX-188	Cefuroxime axetil	00002727301
RX-188	Cefuroxime axetil	00002727310
RX-188	Cefuroxime axetil	00002727401
RX-188	Cefuroxime axetil	00002727410
RX-188	Cefuroxime axetil	00002727501
RX-188	Cefuroxime axetil	00002727516
RX-188	Cefuroxime axetil	00002727601
RX-188	Cefuroxime axetil	00002727624
RX-188	Cefuroxime axetil	00002727701
RX-188	Cefuroxime axetil	00002727724
RX-188	Cefuroxime axetil	00002727801
RX-188	Cefuroxime axetil	00002727825
RX-188	Cefuroxime axetil	00002727901
RX-188	Cefuroxime axetil	00002727910
RX-188	Cefuroxime axetil	00002899425
RX-188	Cefuroxime axetil	00002899510
RX-188	Cefuroxime axetil	00002899519
RX-188	Cefuroxime axetil	00002950001
RX-188	Cefuroxime axetil	00093107334
RX-188	Cefuroxime axetil	00143997603
RX-188	Cefuroxime axetil	00143997691
RX-188	Cefuroxime axetil	00143997722
RX-188	Cefuroxime axetil	00143997790
RX-188	Cefuroxime axetil	00143997922
RX-188	Cefuroxime axetil	00143997990
RX-188	Cefuroxime axetil	00173035210
RX-188	Cefuroxime axetil	00173035230
RX-188	Cefuroxime axetil	00173035231
RX-188	Cefuroxime axetil	00173035332
RX-188	Cefuroxime axetil	00173035410
RX-188	Cefuroxime axetil	00173035434
RX-188	Cefuroxime axetil	00173035435
RX-188	Cefuroxime axetil	00173035632
RX-188	Cefuroxime axetil	00173038700
RX-188	Cefuroxime axetil	00173038701
RX-188	Cefuroxime axetil	00173038706

RX-188	Cefuroxime axetil	00173038742
RX-188	Cefuroxime axetil	00173039400
RX-188	Cefuroxime axetil	00173039401
RX-188	Cefuroxime axetil	00173039442
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RX-188	Cefuroxime axetil	00173039502
RX-188	Cefuroxime axetil	00173040000
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RX-188	Cefuroxime axetil	00173040601
RX-188	Cefuroxime axetil	00173040604
RX-188	Cefuroxime axetil	00173042400
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RX-188	Cefuroxime axetil	00173074000
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RX-188	Cefuroxime axetil	00182268915
RX-188	Cefuroxime axetil	00182268926
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RX-188	Cefuroxime axetil	00182269026
RX-188	Cefuroxime axetil	00209113022
RX-188	Cefuroxime axetil	00209113142
RX-188	Cefuroxime axetil	00209113222
RX-188	Cefuroxime axetil	00209113342
RX-188	Cefuroxime axetil	00209113452
RX-188	Cefuroxime axetil	00247026202
RX-188	Cefuroxime axetil	00247026204
RX-188	Cefuroxime axetil	00247026208
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RX-188	Cefuroxime axetil	00247026220
RX-188	Cefuroxime axetil	00247094120
RX-188	Cefuroxime axetil	00247116401
RX-188	Cefuroxime axetil	00247116405
RX-188	Cefuroxime axetil	00264311211
RX-188	Cefuroxime axetil	00264311411
RX-188	Cefuroxime axetil	00338204341
RX-188	Cefuroxime axetil	00338204348
RX-188	Cefuroxime axetil	00364288134
RX-188	Cefuroxime axetil	00364288593
RX-188	Cefuroxime axetil	00403244314

RX-188	Cefuroxime axetil	00403244320
RX-188	Cefuroxime axetil	00403464518
RX-188	Cefuroxime axetil	00403464718
RX-188	Cefuroxime axetil	00409080201
RX-188	Cefuroxime axetil	00409080301
RX-188	Cefuroxime axetil	00440724503
RX-188	Cefuroxime axetil	00440724504
RX-188	Cefuroxime axetil	00591322415
RX-188	Cefuroxime axetil	00591322515
RX-188	Cefuroxime axetil	00686113022
RX-188	Cefuroxime axetil	00686113222
RX-188	Cefuroxime axetil	00781391870
RX-188	Cefuroxime axetil	00781391896
RX-188	Cefuroxime axetil	00781392046
RX-188	Cefuroxime axetil	00781392280
RX-188	Cefuroxime axetil	00781392296
RX-188	Cefuroxime axetil	00781392446
RX-188	Cefuroxime axetil	00781392646
RX-188	Cefuroxime axetil	00781392695
RX-188	Cefuroxime axetil	00781506520
RX-188	Cefuroxime axetil	00781506620
RX-188	Cefuroxime axetil	00781920570
RX-188	Cefuroxime axetil	00781920596
RX-188	Cefuroxime axetil	00781920680
RX-188	Cefuroxime axetil	00781920696
RX-188	Cefuroxime axetil	00781920746
RX-188	Cefuroxime axetil	00781920795
RX-188	Cefuroxime axetil	00904595761
RX-188	Cefuroxime axetil	00904595861
RX-188	Cefuroxime axetil	10019062001
RX-188	Cefuroxime axetil	10019062010
RX-188	Cefuroxime axetil	10019062103
RX-188	Cefuroxime axetil	10019062120
RX-188	Cefuroxime axetil	10019062205
RX-188	Cefuroxime axetil	10019062211
RX-188	Cefuroxime axetil	10119062205
RX-188	Cefuroxime axetil	10515012405
RX-188	Cefuroxime axetil	10515012501
RX-188	Cefuroxime axetil	10515012502
RX-188	Cefuroxime axetil	10515012503
RX-188	Cefuroxime axetil	10515012504
RX-188	Cefuroxime axetil	16714023201
RX-188	Cefuroxime axetil	16714023202
RX-188	Cefuroxime axetil	16714023301
RX-188	Cefuroxime axetil	16714023302
RX-188	Cefuroxime axetil	21695015020

RX-188	Cefuroxime axetil	23490524301
RX-188	Cefuroxime axetil	23490524401
RX-188	Cefuroxime axetil	23490707508
RX-188	Cefuroxime axetil	25021011810
RX-188	Cefuroxime axetil	25021011920
RX-188	Cefuroxime axetil	25021012059
RX-188	Cefuroxime axetil	49999030920
RX-188	Cefuroxime axetil	49999030930
RX-188	Cefuroxime axetil	49999078520
RX-188	Cefuroxime axetil	51079001601
RX-188	Cefuroxime axetil	51079001620
RX-188	Cefuroxime axetil	51079001701
RX-188	Cefuroxime axetil	51079001720
RX-188	Cefuroxime axetil	52959002920
RX-188	Cefuroxime axetil	52959002924
RX-188	Cefuroxime axetil	52959093920
RX-188	Cefuroxime axetil	52959093930
RX-188	Cefuroxime axetil	53002026720
RX-188	Cefuroxime axetil	53002027520
RX-188	Cefuroxime axetil	54124054614
RX-188	Cefuroxime axetil	54124054620
RX-188	Cefuroxime axetil	54569179100
RX-188	Cefuroxime axetil	54569179101
RX-188	Cefuroxime axetil	54569179200
RX-188	Cefuroxime axetil	54569179202
RX-188	Cefuroxime axetil	54569179203
RX-188	Cefuroxime axetil	54569179204
RX-188	Cefuroxime axetil	54569179205
RX-188	Cefuroxime axetil	54569179206
RX-188	Cefuroxime axetil	54569179207
RX-188	Cefuroxime axetil	54569179208
RX-188	Cefuroxime axetil	54569247900
RX-188	Cefuroxime axetil	54569277800
RX-188	Cefuroxime axetil	54569277801
RX-188	Cefuroxime axetil	54569277802
RX-188	Cefuroxime axetil	54569327900
RX-188	Cefuroxime axetil	54569359900
RX-188	Cefuroxime axetil	54569392900
RX-188	Cefuroxime axetil	54569473700
RX-188	Cefuroxime axetil	54569538600
RX-188	Cefuroxime axetil	54569538601
RX-188	Cefuroxime axetil	54569538603
RX-188	Cefuroxime axetil	54569541800
RX-188	Cefuroxime axetil	54868108000
RX-188	Cefuroxime axetil	54868108001
RX-188	Cefuroxime axetil	54868108002

RX-188	Cefuroxime axetil	54868108003
RX-188	Cefuroxime axetil	54868171000
RX-188	Cefuroxime axetil	54868171001
RX-188	Cefuroxime axetil	54868280500
RX-188	Cefuroxime axetil	54868498700
RX-188	Cefuroxime axetil	54868498701
RX-188	Cefuroxime axetil	54868502200
RX-188	Cefuroxime axetil	54868502201
RX-188	Cefuroxime axetil	54868502202
RX-188	Cefuroxime axetil	54868502203
RX-188	Cefuroxime axetil	54868598100
RX-188	Cefuroxime axetil	55045154602
RX-188	Cefuroxime axetil	55045154603
RX-188	Cefuroxime axetil	55045154605
RX-188	Cefuroxime axetil	55045154607
RX-188	Cefuroxime axetil	55045348302
RX-188	Cefuroxime axetil	55175176300
RX-188	Cefuroxime axetil	55175176302
RX-188	Cefuroxime axetil	55175176304
RX-188	Cefuroxime axetil	55175176400
RX-188	Cefuroxime axetil	55175176401
RX-188	Cefuroxime axetil	55175176402
RX-188	Cefuroxime axetil	55175526502
RX-188	Cefuroxime axetil	55175526601
RX-188	Cefuroxime axetil	55175526605
RX-188	Cefuroxime axetil	55289003210
RX-188	Cefuroxime axetil	55289037210
RX-188	Cefuroxime axetil	55289037214
RX-188	Cefuroxime axetil	55289037220
RX-188	Cefuroxime axetil	55289037297
RX-188	Cefuroxime axetil	55289038504
RX-188	Cefuroxime axetil	55289054210
RX-188	Cefuroxime axetil	55887024420
RX-188	Cefuroxime axetil	55887024430
RX-188	Cefuroxime axetil	55887065220
RX-188	Cefuroxime axetil	55887065230
RX-188	Cefuroxime axetil	57362066509
RX-188	Cefuroxime axetil	58016011410
RX-188	Cefuroxime axetil	58016011414
RX-188	Cefuroxime axetil	58016011415
RX-188	Cefuroxime axetil	58016011420
RX-188	Cefuroxime axetil	58016011430
RX-188	Cefuroxime axetil	58016011460
RX-188	Cefuroxime axetil	58016011510
RX-188	Cefuroxime axetil	58016011514
RX-188	Cefuroxime axetil	58016011520

RX-188	Cefuroxime axetil	58016011530
RX-188	Cefuroxime axetil	58016011560
RX-188	Cefuroxime axetil	58864069020
RX-188	Cefuroxime axetil	59762108101
RX-188	Cefuroxime axetil	59762108102
RX-188	Cefuroxime axetil	59762108301
RX-188	Cefuroxime axetil	59762108302
RX-188	Cefuroxime axetil	59772655001
RX-188	Cefuroxime axetil	59772655002
RX-188	Cefuroxime axetil	59772655101
RX-188	Cefuroxime axetil	59772655102
RX-188	Cefuroxime axetil	59772656901
RX-188	Cefuroxime axetil	60346036906
RX-188	Cefuroxime axetil	60346036910
RX-188	Cefuroxime axetil	60346036914
RX-188	Cefuroxime axetil	60346036920
RX-188	Cefuroxime axetil	60346036925
RX-188	Cefuroxime axetil	60505120100
RX-188	Cefuroxime axetil	60505120103
RX-188	Cefuroxime axetil	60505120200
RX-188	Cefuroxime axetil	60505120203
RX-188	Cefuroxime axetil	60505268102
RX-188	Cefuroxime axetil	60505268106
RX-188	Cefuroxime axetil	60505268202
RX-188	Cefuroxime axetil	60505268206
RX-188	Cefuroxime axetil	61703033311
RX-188	Cefuroxime axetil	61703033433
RX-188	Cefuroxime axetil	63304075120
RX-188	Cefuroxime axetil	63304075160
RX-188	Cefuroxime axetil	63304075220
RX-188	Cefuroxime axetil	63304075260
RX-188	Cefuroxime axetil	63304094625
RX-188	Cefuroxime axetil	63304094725
RX-188	Cefuroxime axetil	63304094810
RX-188	Cefuroxime axetil	63304096304
RX-188	Cefuroxime axetil	63304096403
RX-188	Cefuroxime axetil	63304096404
RX-188	Cefuroxime axetil	63323030110
RX-188	Cefuroxime axetil	63323031220
RX-188	Cefuroxime axetil	63323031361
RX-188	Cefuroxime axetil	63323035210
RX-188	Cefuroxime axetil	63323035320
RX-188	Cefuroxime axetil	63323035461
RX-188	Cefuroxime axetil	64679092101
RX-188	Cefuroxime axetil	64679092102
RX-188	Cefuroxime axetil	64679092201

RX-188	Cefuroxime axetil	64679092202
RX-188	Cefuroxime axetil	65862003420
RX-188	Cefuroxime axetil	65862003460
RX-188	Cefuroxime axetil	65862003520
RX-188	Cefuroxime axetil	65862003560
RX-188	Cefuroxime axetil	65939038700
RX-188	Cefuroxime axetil	65939038701
RX-188	Cefuroxime axetil	65939038742
RX-188	Cefuroxime axetil	65939039400
RX-188	Cefuroxime axetil	65939039401
RX-188	Cefuroxime axetil	65939039442
RX-188	Cefuroxime axetil	65939039501
RX-188	Cefuroxime axetil	65939040600
RX-188	Cefuroxime axetil	65939055400
RX-188	Cefuroxime axetil	65939055500
RX-188	Cefuroxime axetil	66288207501
RX-188	Cefuroxime axetil	66288222501
RX-188	Cefuroxime axetil	66336036920
RX-188	Cefuroxime axetil	66814060120
RX-188	Cefuroxime axetil	66814060160
RX-188	Cefuroxime axetil	66814060220
RX-188	Cefuroxime axetil	66814060260
RX-188	Cefuroxime axetil	66860003003
RX-188	Cefuroxime axetil	66860003103
RX-188	Cefuroxime axetil	66860003202
RX-188	Cefuroxime axetil	66860073003
RX-188	Cefuroxime axetil	66860073103
RX-188	Cefuroxime axetil	66860073202
RX-188	Cefuroxime axetil	67253078002
RX-188	Cefuroxime axetil	67253078102
RX-188	Cefuroxime axetil	68084021801
RX-188	Cefuroxime axetil	68084021811
RX-188	Cefuroxime axetil	68084021901
RX-188	Cefuroxime axetil	68084021911
RX-188	Cefuroxime axetil	68180030220
RX-188	Cefuroxime axetil	68180030260
RX-188	Cefuroxime axetil	68180030320
RX-188	Cefuroxime axetil	68180030360
RX-188	Cefuroxime axetil	68722035210
RX-188	Cefuroxime axetil	68722035320

cd. set RX code set descrp. ndc

RX-189	Cefdinir	00071006720
RX-189	Cefdinir	00071200616
RX-189	Cefdinir	00071200618
RX-189	Cefdinir	00074376910

RX-189	Cefdinir	00074376930
RX-189	Cefdinir	00074376960
RX-189	Cefdinir	00074377113
RX-189	Cefdinir	00074377160
RX-189	Cefdinir	00074615113
RX-189	Cefdinir	00074615160
RX-189	Cefdinir	00093316006
RX-189	Cefdinir	00093413664
RX-189	Cefdinir	00093413673
RX-189	Cefdinir	00093413764
RX-189	Cefdinir	00093413773
RX-189	Cefdinir	00781217660
RX-189	Cefdinir	00781217664
RX-189	Cefdinir	00781217669
RX-189	Cefdinir	00781607746
RX-189	Cefdinir	00781607761
RX-189	Cefdinir	00781607846
RX-189	Cefdinir	00781607861
RX-189	Cefdinir	35356003820
RX-189	Cefdinir	35356011960
RX-189	Cefdinir	35356019000
RX-189	Cefdinir	52959013420
RX-189	Cefdinir	54569487700
RX-189	Cefdinir	54569521400
RX-189	Cefdinir	54569521401
RX-189	Cefdinir	54569521500
RX-189	Cefdinir	54569564900
RX-189	Cefdinir	54569565000
RX-189	Cefdinir	54868073700
RX-189	Cefdinir	54868073701
RX-189	Cefdinir	54868436600
RX-189	Cefdinir	54868436601
RX-189	Cefdinir	54868468200
RX-189	Cefdinir	54868468201
RX-189	Cefdinir	54868576700
RX-189	Cefdinir	54868576701
RX-189	Cefdinir	54868576800
RX-189	Cefdinir	54868576801
RX-189	Cefdinir	54868576900
RX-189	Cefdinir	54868576901
RX-189	Cefdinir	55289008120
RX-189	Cefdinir	55289083120
RX-189	Cefdinir	55887018760
RX-189	Cefdinir	59762218001
RX-189	Cefdinir	65862017760
RX-189	Cefdinir	65862021801

RX-189	Cefdinir	65862021860
RX-189	Cefdinir	65862021901
RX-189	Cefdinir	65862021960
RX-189	Cefdinir	66336010406
RX-189	Cefdinir	66336010420
RX-189	Cefdinir	67253000760
RX-189	Cefdinir	67253000841
RX-189	Cefdinir	67253000846
RX-189	Cefdinir	67253000941
RX-189	Cefdinir	67253000946
RX-189	Cefdinir	68180071160
RX-189	Cefdinir	68180072210
RX-189	Cefdinir	68180072220
RX-189	Cefdinir	68180072310
RX-189	Cefdinir	68180072320
RX-189	Cefdinir	68820006306
RX-189	Cefdinir	68820006309
RX-189	Cefdinir	68820006319
RX-189	Cefdinir	68820006417
RX-189	Cefdinir	68820006437
RX-189	Cefdinir	68820006517
RX-189	Cefdinir	68820006537

cd. set RX code set descrp. ndc

RX-190	Gatifloxacin	00015111750
RX-190	Gatifloxacin	00015111780
RX-190	Gatifloxacin	00015117719
RX-190	Gatifloxacin	00015117721
RX-190	Gatifloxacin	00015117760
RX-190	Gatifloxacin	00015117780
RX-190	Gatifloxacin	00015117880
RX-190	Gatifloxacin	00015117980
RX-190	Gatifloxacin	00015118078
RX-190	Gatifloxacin	00015118079
RX-190	Gatifloxacin	00015118080
RX-190	Gatifloxacin	00015118178
RX-190	Gatifloxacin	00015118179
RX-190	Gatifloxacin	00015118180
RX-190	Gatifloxacin	49999036601
RX-190	Gatifloxacin	49999036610
RX-190	Gatifloxacin	54569492100
RX-190	Gatifloxacin	54569492101
RX-190	Gatifloxacin	54569492102
RX-190	Gatifloxacin	54569492103
RX-190	Gatifloxacin	54569519900
RX-190	Gatifloxacin	54868433000

RX-190	Gatifloxacin	54868433001
RX-190	Gatifloxacin	54868433002
RX-190	Gatifloxacin	54868448300
RX-190	Gatifloxacin	55045344905
RX-190	Gatifloxacin	55289070910
RX-190	Gatifloxacin	55289070915
RX-190	Gatifloxacin	55887037503
RX-190	Gatifloxacin	55887037506
RX-190	Gatifloxacin	55887037520
RX-190	Gatifloxacin	55887037530
RX-190	Gatifloxacin	58864074210
RX-190	Gatifloxacin	58864079010
RX-190	Gatifloxacin	58864081110
RX-190	Gatifloxacin	66116027507
RX-190	Gatifloxacin	66116027510

cd. set RX code set descrp. ndc

RX-191	Levofloxacin	00045006555
RX-191	Levofloxacin	00045006601
RX-191	Levofloxacin	00045006701
RX-191	Levofloxacin	00045006801
RX-191	Levofloxacin	00045006951
RX-191	Levofloxacin	00045006955
RX-191	Levofloxacin	00045151501
RX-191	Levofloxacin	00045152010
RX-191	Levofloxacin	00045152050
RX-191	Levofloxacin	00045152510
RX-191	Levofloxacin	00045152550
RX-191	Levofloxacin	00045153005
RX-191	Levofloxacin	00045153010
RX-191	Levofloxacin	00045153020
RX-191	Levofloxacin	00045153050
RX-191	Levofloxacin	00440772405
RX-191	Levofloxacin	00440772407
RX-191	Levofloxacin	00440772503
RX-191	Levofloxacin	00440772507
RX-191	Levofloxacin	00440772510
RX-191	Levofloxacin	00440772514
RX-191	Levofloxacin	00440772602
RX-191	Levofloxacin	00440772603
RX-191	Levofloxacin	00440772607
RX-191	Levofloxacin	00440772610
RX-191	Levofloxacin	00440772614
RX-191	Levofloxacin	12280003150
RX-191	Levofloxacin	13411011203
RX-191	Levofloxacin	13411015403

RX-191	Levofloxacin	16590055914
RX-191	Levofloxacin	16590055920
RX-191	Levofloxacin	16590055930
RX-191	Levofloxacin	16590057805
RX-191	Levofloxacin	18837020014
RX-191	Levofloxacin	21695046407
RX-191	Levofloxacin	21695051907
RX-191	Levofloxacin	23490703202
RX-191	Levofloxacin	23490926000
RX-191	Levofloxacin	23490926001
RX-191	Levofloxacin	23490926003
RX-191	Levofloxacin	23490926005
RX-191	Levofloxacin	33358020200
RX-191	Levofloxacin	33358020210
RX-191	Levofloxacin	33358020230
RX-191	Levofloxacin	33358020260
RX-191	Levofloxacin	43063011303
RX-191	Levofloxacin	49999041710
RX-191	Levofloxacin	49999041802
RX-191	Levofloxacin	49999041807
RX-191	Levofloxacin	49999041810
RX-191	Levofloxacin	49999041830
RX-191	Levofloxacin	49999041850
RX-191	Levofloxacin	50458016420
RX-191	Levofloxacin	50458016530
RX-191	Levofloxacin	50458017001
RX-191	Levofloxacin	50458092010
RX-191	Levofloxacin	50458092050
RX-191	Levofloxacin	50458092510
RX-191	Levofloxacin	50458092550
RX-191	Levofloxacin	50458093010
RX-191	Levofloxacin	50458093020
RX-191	Levofloxacin	52959049201
RX-191	Levofloxacin	52959049202
RX-191	Levofloxacin	52959049204
RX-191	Levofloxacin	52959049206
RX-191	Levofloxacin	52959049207
RX-191	Levofloxacin	52959049210
RX-191	Levofloxacin	52959049212
RX-191	Levofloxacin	52959049214
RX-191	Levofloxacin	52959049230
RX-191	Levofloxacin	52959069003
RX-191	Levofloxacin	52959069005
RX-191	Levofloxacin	52959069007
RX-191	Levofloxacin	52959069014
RX-191	Levofloxacin	52959069030

RX-191	Levofloxacin	52959078207
RX-191	Levofloxacin	52959078220
RX-191	Levofloxacin	54569448900
RX-191	Levofloxacin	54569448901
RX-191	Levofloxacin	54569448902
RX-191	Levofloxacin	54569448903
RX-191	Levofloxacin	54569448904
RX-191	Levofloxacin	54569448905
RX-191	Levofloxacin	54569467700
RX-191	Levofloxacin	54569491500
RX-191	Levofloxacin	54569491501
RX-191	Levofloxacin	54569491502
RX-191	Levofloxacin	54569555701
RX-191	Levofloxacin	54868392300
RX-191	Levofloxacin	54868392301
RX-191	Levofloxacin	54868392302
RX-191	Levofloxacin	54868392303
RX-191	Levofloxacin	54868392304
RX-191	Levofloxacin	54868392305
RX-191	Levofloxacin	54868417500
RX-191	Levofloxacin	54868417501
RX-191	Levofloxacin	54868417502
RX-191	Levofloxacin	54868417503
RX-191	Levofloxacin	54868417504
RX-191	Levofloxacin	54868417505
RX-191	Levofloxacin	54868497100
RX-191	Levofloxacin	54868497101
RX-191	Levofloxacin	55045259701
RX-191	Levofloxacin	55045259702
RX-191	Levofloxacin	55045259703
RX-191	Levofloxacin	55045259705
RX-191	Levofloxacin	55045259706
RX-191	Levofloxacin	55045259708
RX-191	Levofloxacin	55175190001
RX-191	Levofloxacin	55289039405
RX-191	Levofloxacin	55289039407
RX-191	Levofloxacin	55289071107
RX-191	Levofloxacin	55289071110
RX-191	Levofloxacin	55289071114
RX-191	Levofloxacin	55289084103
RX-191	Levofloxacin	55289084110
RX-191	Levofloxacin	57866658401
RX-191	Levofloxacin	57866658402
RX-191	Levofloxacin	57866658403
RX-191	Levofloxacin	57866658501
RX-191	Levofloxacin	57866658502

RX-191	Levofloxacin	57866658503
RX-191	Levofloxacin	58016057300
RX-191	Levofloxacin	58016057307
RX-191	Levofloxacin	58016057310
RX-191	Levofloxacin	58016057320
RX-191	Levofloxacin	58016057330
RX-191	Levofloxacin	58016057360
RX-191	Levofloxacin	58016057390
RX-191	Levofloxacin	58016092400
RX-191	Levofloxacin	58016092430
RX-191	Levofloxacin	58016092460
RX-191	Levofloxacin	58016092490
RX-191	Levofloxacin	58016097500
RX-191	Levofloxacin	58016097530
RX-191	Levofloxacin	58016097560
RX-191	Levofloxacin	58016097590
RX-191	Levofloxacin	58864003410
RX-191	Levofloxacin	58864003414
RX-191	Levofloxacin	62682103903
RX-191	Levofloxacin	66105047705
RX-191	Levofloxacin	66105047805
RX-191	Levofloxacin	66116020007
RX-191	Levofloxacin	66116020107
RX-191	Levofloxacin	66116020114
RX-191	Levofloxacin	66267036307
RX-191	Levofloxacin	66267036310
RX-191	Levofloxacin	66336038607
RX-191	Levofloxacin	66336038610
RX-191	Levofloxacin	66336083005
RX-191	Levofloxacin	68030658401
RX-191	Levofloxacin	68030658402
RX-191	Levofloxacin	68030658403
RX-191	Levofloxacin	68030658501
RX-191	Levofloxacin	68030658502
RX-191	Levofloxacin	68030658503
RX-191	Levofloxacin	68115019610
RX-191	Levofloxacin	68115019710

cd. set RX code set descrp. ndc

RX-192	Moxifloxacin	00026858141
RX-192	Moxifloxacin	00026858169
RX-192	Moxifloxacin	00026858188
RX-192	Moxifloxacin	00026858231
RX-192	Moxifloxacin	00085173301
RX-192	Moxifloxacin	00085173302
RX-192	Moxifloxacin	00085173303

RX-192	Moxifloxacin	00085173305
RX-192	Moxifloxacin	00085173701
RX-192	Moxifloxacin	00490008500
RX-192	Moxifloxacin	00490008530
RX-192	Moxifloxacin	00490008560
RX-192	Moxifloxacin	00490008590
RX-192	Moxifloxacin	13411010803
RX-192	Moxifloxacin	49999045505
RX-192	Moxifloxacin	49999045510
RX-192	Moxifloxacin	49999045530
RX-192	Moxifloxacin	52959000405
RX-192	Moxifloxacin	54569492200
RX-192	Moxifloxacin	54569492201
RX-192	Moxifloxacin	54569514900
RX-192	Moxifloxacin	54868436700
RX-192	Moxifloxacin	54868436701
RX-192	Moxifloxacin	54868436702
RX-192	Moxifloxacin	54868436703
RX-192	Moxifloxacin	54868436704
RX-192	Moxifloxacin	55045284304
RX-192	Moxifloxacin	55045284305
RX-192	Moxifloxacin	55289007710
RX-192	Moxifloxacin	58864062105
RX-192	Moxifloxacin	58864062110
RX-192	Moxifloxacin	58864062130
RX-192	Moxifloxacin	58864088307
RX-192	Moxifloxacin	68115092505

cd. set RX code set descrp. ndc

RX-193	Ceftriaxone	00004196201
RX-193	Ceftriaxone	00004196202
RX-193	Ceftriaxone	00004196301
RX-193	Ceftriaxone	00004196302
RX-193	Ceftriaxone	00004196401
RX-193	Ceftriaxone	00004196402
RX-193	Ceftriaxone	00004196403
RX-193	Ceftriaxone	00004196404
RX-193	Ceftriaxone	00004196405
RX-193	Ceftriaxone	00004196439
RX-193	Ceftriaxone	00004196501
RX-193	Ceftriaxone	00004196502
RX-193	Ceftriaxone	00004196503
RX-193	Ceftriaxone	00004196505
RX-193	Ceftriaxone	00004197101
RX-193	Ceftriaxone	00004199578
RX-193	Ceftriaxone	00004199678

RX-193	Ceftriaxone	00004200278
RX-193	Ceftriaxone	00004200378
RX-193	Ceftriaxone	00004201392
RX-193	Ceftriaxone	00004201492
RX-193	Ceftriaxone	00069448003
RX-193	Ceftriaxone	00069448010
RX-193	Ceftriaxone	00069448103
RX-193	Ceftriaxone	00069448110
RX-193	Ceftriaxone	00069448203
RX-193	Ceftriaxone	00069448210
RX-193	Ceftriaxone	00069448303
RX-193	Ceftriaxone	00069448310
RX-193	Ceftriaxone	00143976801
RX-193	Ceftriaxone	00143985625
RX-193	Ceftriaxone	00143985725
RX-193	Ceftriaxone	00143985825
RX-193	Ceftriaxone	00143985925
RX-193	Ceftriaxone	00247033101
RX-193	Ceftriaxone	00247033110
RX-193	Ceftriaxone	00264315311
RX-193	Ceftriaxone	00264315511
RX-193	Ceftriaxone	00338500241
RX-193	Ceftriaxone	00338500341
RX-193	Ceftriaxone	00403185118
RX-193	Ceftriaxone	00403185318
RX-193	Ceftriaxone	00403185518
RX-193	Ceftriaxone	00403418118
RX-193	Ceftriaxone	00403419318
RX-193	Ceftriaxone	00409733201
RX-193	Ceftriaxone	00409733261
RX-193	Ceftriaxone	00409733304
RX-193	Ceftriaxone	00409733349
RX-193	Ceftriaxone	00409733410
RX-193	Ceftriaxone	00409733503
RX-193	Ceftriaxone	00409733561
RX-193	Ceftriaxone	00409733604
RX-193	Ceftriaxone	00409733649
RX-193	Ceftriaxone	00409733701
RX-193	Ceftriaxone	00409733801
RX-193	Ceftriaxone	00517871110
RX-193	Ceftriaxone	00517872210
RX-193	Ceftriaxone	00517872510
RX-193	Ceftriaxone	00517875010
RX-193	Ceftriaxone	00703031503
RX-193	Ceftriaxone	00703032503
RX-193	Ceftriaxone	00703033501

RX-193	Ceftriaxone	00703033504
RX-193	Ceftriaxone	00703034603
RX-193	Ceftriaxone	00703035901
RX-193	Ceftriaxone	00781320685
RX-193	Ceftriaxone	00781320695
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RX-193	Ceftriaxone	00781320795
RX-193	Ceftriaxone	00781320885
RX-193	Ceftriaxone	00781320895
RX-193	Ceftriaxone	00781320990
RX-193	Ceftriaxone	00781320995
RX-193	Ceftriaxone	00781321046
RX-193	Ceftriaxone	00781932695
RX-193	Ceftriaxone	00781932795
RX-193	Ceftriaxone	00781932885
RX-193	Ceftriaxone	00781932895
RX-193	Ceftriaxone	00781932990
RX-193	Ceftriaxone	00781932995
RX-193	Ceftriaxone	00781933046
RX-193	Ceftriaxone	10019009801
RX-193	Ceftriaxone	10019009871
RX-193	Ceftriaxone	10019068501
RX-193	Ceftriaxone	10019068571
RX-193	Ceftriaxone	10019068602
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RX-193	Ceftriaxone	10019068703
RX-193	Ceftriaxone	10019068771
RX-193	Ceftriaxone	10019068804
RX-193	Ceftriaxone	10019068827
RX-193	Ceftriaxone	10019068905
RX-193	Ceftriaxone	10019068911
RX-193	Ceftriaxone	12280007310
RX-193	Ceftriaxone	21695020210
RX-193	Ceftriaxone	21695035210
RX-193	Ceftriaxone	25021010410
RX-193	Ceftriaxone	25021010510
RX-193	Ceftriaxone	25021010610
RX-193	Ceftriaxone	25021010720
RX-193	Ceftriaxone	25021010899
RX-193	Ceftriaxone	35356026701
RX-193	Ceftriaxone	43063000210
RX-193	Ceftriaxone	49999058601
RX-193	Ceftriaxone	49999058610
RX-193	Ceftriaxone	54569137700
RX-193	Ceftriaxone	54569138600
RX-193	Ceftriaxone	54569180201

RX-193	Ceftriaxone	54569320700
RX-193	Ceftriaxone	54569347700
RX-193	Ceftriaxone	54569347800
RX-193	Ceftriaxone	54569347900
RX-193	Ceftriaxone	54569441500
RX-193	Ceftriaxone	54569572000
RX-193	Ceftriaxone	54569572100
RX-193	Ceftriaxone	54569572200
RX-193	Ceftriaxone	54569572300
RX-193	Ceftriaxone	54569572400
RX-193	Ceftriaxone	54569572500
RX-193	Ceftriaxone	54868093400
RX-193	Ceftriaxone	54868093401
RX-193	Ceftriaxone	54868248800
RX-193	Ceftriaxone	54868248801
RX-193	Ceftriaxone	54868322100
RX-193	Ceftriaxone	54868322101
RX-193	Ceftriaxone	54868553300
RX-193	Ceftriaxone	54868558900
RX-193	Ceftriaxone	55045350301
RX-193	Ceftriaxone	55045351101
RX-193	Ceftriaxone	55045351102
RX-193	Ceftriaxone	55045351601
RX-193	Ceftriaxone	55081106300
RX-193	Ceftriaxone	55081106400
RX-193	Ceftriaxone	55390030910
RX-193	Ceftriaxone	55390031010
RX-193	Ceftriaxone	55390031110
RX-193	Ceftriaxone	55390031210
RX-193	Ceftriaxone	55390031601
RX-193	Ceftriaxone	57866979701
RX-193	Ceftriaxone	58016478601
RX-193	Ceftriaxone	58016479001
RX-193	Ceftriaxone	58016483401
RX-193	Ceftriaxone	58016487301
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RX-193	Ceftriaxone	58016955101
RX-193	Ceftriaxone	60505067905
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RX-193	Ceftriaxone	60505067909
RX-193	Ceftriaxone	60505075000
RX-193	Ceftriaxone	60505075004
RX-193	Ceftriaxone	60505075100
RX-193	Ceftriaxone	60505075104
RX-193	Ceftriaxone	60505075200

RX-193	Ceftriaxone	60505075204
RX-193	Ceftriaxone	60505075300
RX-193	Ceftriaxone	60505075304
RX-193	Ceftriaxone	63323034410
RX-193	Ceftriaxone	63323034510
RX-193	Ceftriaxone	63323034610
RX-193	Ceftriaxone	63323034720
RX-193	Ceftriaxone	63323034861
RX-193	Ceftriaxone	64679070101
RX-193	Ceftriaxone	64679070102
RX-193	Ceftriaxone	64679070103
RX-193	Ceftriaxone	64679070201
RX-193	Ceftriaxone	64679070202
RX-193	Ceftriaxone	64679070301
RX-193	Ceftriaxone	64679070302
RX-193	Ceftriaxone	64679098301
RX-193	Ceftriaxone	64679098302
RX-193	Ceftriaxone	66288610001
RX-193	Ceftriaxone	66860007102
RX-193	Ceftriaxone	66860007202
RX-193	Ceftriaxone	66860007302
RX-193	Ceftriaxone	66860007402
RX-193	Ceftriaxone	68030713901
RX-193	Ceftriaxone	68030721001
RX-193	Ceftriaxone	68030737201
RX-193	Ceftriaxone	68180061101
RX-193	Ceftriaxone	68180061110
RX-193	Ceftriaxone	68180062201
RX-193	Ceftriaxone	68180062210
RX-193	Ceftriaxone	68180063301
RX-193	Ceftriaxone	68180063310
RX-193	Ceftriaxone	68180064401
RX-193	Ceftriaxone	68180064410
RX-193	Ceftriaxone	68330000101
RX-193	Ceftriaxone	68330000110
RX-193	Ceftriaxone	68330000201
RX-193	Ceftriaxone	68330000210
RX-193	Ceftriaxone	68330000301
RX-193	Ceftriaxone	68330000310
RX-193	Ceftriaxone	68330000401
RX-193	Ceftriaxone	68330000410
RX-193	Ceftriaxone	68330000501
RX-193	Ceftriaxone	68330000601

cd. set RX code set descrp.

ndc

RX-194 Trimethoprim-Sulfamethoxazole

00003013850

RX-194	Trimethoprim-Sulfamethoxazole	00003013860
RX-194	Trimethoprim-Sulfamethoxazole	00003017150
RX-194	Trimethoprim-Sulfamethoxazole	00003017160
RX-194	Trimethoprim-Sulfamethoxazole	00003087250
RX-194	Trimethoprim-Sulfamethoxazole	00003087260
RX-194	Trimethoprim-Sulfamethoxazole	00003087350
RX-194	Trimethoprim-Sulfamethoxazole	00003087360
RX-194	Trimethoprim-Sulfamethoxazole	00003120110
RX-194	Trimethoprim-Sulfamethoxazole	00004005001
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RX-194	Trimethoprim-Sulfamethoxazole	00004005049
RX-194	Trimethoprim-Sulfamethoxazole	00004011701
RX-194	Trimethoprim-Sulfamethoxazole	00004011704
RX-194	Trimethoprim-Sulfamethoxazole	00004011714
RX-194	Trimethoprim-Sulfamethoxazole	00004011749
RX-194	Trimethoprim-Sulfamethoxazole	00004011754
RX-194	Trimethoprim-Sulfamethoxazole	00004101528
RX-194	Trimethoprim-Sulfamethoxazole	00004103301
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RX-194	Trimethoprim-Sulfamethoxazole	00047290523
RX-194	Trimethoprim-Sulfamethoxazole	00054480025
RX-194	Trimethoprim-Sulfamethoxazole	00054480125
RX-194	Trimethoprim-Sulfamethoxazole	00054880025
RX-194	Trimethoprim-Sulfamethoxazole	00054880125
RX-194	Trimethoprim-Sulfamethoxazole	00081085255
RX-194	Trimethoprim-Sulfamethoxazole	00081085256
RX-194	Trimethoprim-Sulfamethoxazole	00081085270
RX-194	Trimethoprim-Sulfamethoxazole	00081085275
RX-194	Trimethoprim-Sulfamethoxazole	00081085320
RX-194	Trimethoprim-Sulfamethoxazole	00081085352
RX-194	Trimethoprim-Sulfamethoxazole	00081085355
RX-194	Trimethoprim-Sulfamethoxazole	00081085356
RX-194	Trimethoprim-Sulfamethoxazole	00081085365
RX-194	Trimethoprim-Sulfamethoxazole	00081085496

RX-194	Trimethoprim-Sulfamethoxazole	00081085501
RX-194	Trimethoprim-Sulfamethoxazole	00081085502
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RX-194	Trimethoprim-Sulfamethoxazole	00093018805
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RX-194	Trimethoprim-Sulfamethoxazole	00093019162
RX-194	Trimethoprim-Sulfamethoxazole	00093056216
RX-194	Trimethoprim-Sulfamethoxazole	00093547616
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RX-194	Trimethoprim-Sulfamethoxazole	00094510801
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RX-194	Trimethoprim-Sulfamethoxazole	00094510869
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RX-194	Trimethoprim-Sulfamethoxazole	00143162525
RX-194	Trimethoprim-Sulfamethoxazole	00150040516
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RX-194	Trimethoprim-Sulfamethoxazole	00150272540
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RX-194	Trimethoprim-Sulfamethoxazole	00157072105
RX-194	Trimethoprim-Sulfamethoxazole	00173085255

RX-194	Trimethoprim-Sulfamethoxazole	00173085355
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RX-194	Trimethoprim-Sulfamethoxazole	00173085496
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RX-194	Trimethoprim-Sulfamethoxazole	00173085596
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RX-194	Trimethoprim-Sulfamethoxazole	00182140889
RX-194	Trimethoprim-Sulfamethoxazole	00182147801
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RX-194	Trimethoprim-Sulfamethoxazole	00185011205
RX-194	Trimethoprim-Sulfamethoxazole	00223661201
RX-194	Trimethoprim-Sulfamethoxazole	00223661301
RX-194	Trimethoprim-Sulfamethoxazole	00228239316
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RX-194	Trimethoprim-Sulfamethoxazole	00247006328
RX-194	Trimethoprim-Sulfamethoxazole	00247006330

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RX-194	Trimethoprim-Sulfamethoxazole	00247006398
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RX-194	Trimethoprim-Sulfamethoxazole	00247009605
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RX-194	Trimethoprim-Sulfamethoxazole	00247009652
RX-194	Trimethoprim-Sulfamethoxazole	00247009659
RX-194	Trimethoprim-Sulfamethoxazole	00247009660
RX-194	Trimethoprim-Sulfamethoxazole	00247009677
RX-194	Trimethoprim-Sulfamethoxazole	00247009678
RX-194	Trimethoprim-Sulfamethoxazole	00247009679
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RX-194	Trimethoprim-Sulfamethoxazole	00332610032
RX-194	Trimethoprim-Sulfamethoxazole	00332610038
RX-194	Trimethoprim-Sulfamethoxazole	00349233600
RX-194	Trimethoprim-Sulfamethoxazole	00349233601

RX-194	Trimethoprim-Sulfamethoxazole	00349233605
RX-194	Trimethoprim-Sulfamethoxazole	00349233698
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