Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a therapeutic review of Outpatient Antibiotic Stewardship and Upper Respiratory Infections (URI) at the Fall 2021 quarterly meeting. Evidence provided during the evaluation included a review of antibiotic resistance and the Centers for Disease Control & Prevention (CDC) core elements of outpatient antibiotic stewardship. Focus was given to clinical guidelines and recommended therapies for otitis media, pharyngitis (viral and bacterial), sinusitis (viral and bacterial), and cough (bronchitis specifically). Following review and deliberation, the NPTC voted to ADD both adult and pediatric oral formulations of the following: (1) amoxicillin, (2) amoxicillin and clavulanate, (3) cefdinir, (4) cephalaxin, (5) clindamycin and (6) penicillin V potassium to the National Core Formulary.

Discussion:
Antibiotic (AB) resistance is a complex global problem; thoughtful appropriate use of antibiotics is essential. A 2019 CDC report estimates in the United States each year antibiotic-resistant bacteria and fungi cause 2,868,700 infections with 35,900 deaths, and 223,900 cases and 12,800 deaths from Clostridioidious difficile1,2. In addition to antibiotic-resistant microbes, inappropriate AB use creates poor patient outcomes, severe type 1 and non-severe allergies, side effects and unnecessary cost3.

Upper respiratory infections are one of the top three diagnoses in the outpatient setting, with an estimated 10 million outpatient appointments a year4,5. This accounts for >20 million days of work lost and >20 million missed school days annually. Inappropriate AB prescribing has been identified in up to 40-50% of URI visits, with estimated annual costs for inappropriate prescribing for viral URIs at ~$3 billion and a total cost exceeding $22 billion. Improving AB stewardship is “perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections” 6,7. Basic principles of judicious use of antibiotics include (1) accurate diagnosis, (2) use of AB only when necessary, (3), choosing the correct AB, and (4) providing the antibiotic in the correct way for the correct length of time3.

Clinical Practice Guidelines for four common URIs were reviewed and are detailed below.

Acute Otitis Media (AOM) 3,8,9,10,11,12
AOM affects all ages but is predominately an illness of childhood, most common in those <5 years old. Much of the information of AOM in adults has been extrapolated from studies in children. The American Academy of Pediatrics (AAP) diagnosis, flow chart and treatment guidelines were discussed. Preferred ABs for AOM remain amoxicillin (pediatrics) and amoxicillin-clavulanate (adults). Key points include to diagnose by exam, then decide whom to treat and whom to watch.

Pharyngitis 3,9,13,14,15,16,19
Pharyngitis causes 11 million pediatric visits annually; 70-85% are viral. Group A streptococcus (GAS) accounts for 5-10% of adult sore throats and 20-30% of pediatric sore throats. Considering the high GAS carrier rate, whom to test is a critical decision13. Key points for judicious AB use in pharyngitis includes (1) test only those with appropriate indications, (2) treat only laboratory confirmed positive patients (rapid antigen test or throat culture), and (3) always use the penicillin family unless allergic to such. As a clinical pearl, amoxicillin liquid formulations can be given QD for GAS and tastes reasonable; it is much preferred over penicillin liquid formulations.

Acute Bacterial Sinusitis (ABS) 3,9,18,19,20
Sinusitis is a commonly treated adult diagnosis yet 98% are viral and do not require ABs. A diagnosis of ABS is made when one of three conditions exists; (1) persistent nasal discharge or daytime cough, (2) a worsening course, (3) temperature of >102.2° F with nasal discharge or facial pain for at least 3 days. More detailed information from the AAP’s Red Book can be found here. Recommended ABs are amoxicillin (pediatrics) and amoxicillin-clavulanate (adult).

Cough: acute viral rhino-sinusitis (“cold”), bronchitis 3,19,21,22,23
Cough is the most common symptom for which adult patients visit their provider. Bronchitis is the most common diagnosis for the cough. Nearly 90% of bronchitis is non-bacterial, yet 70% of patients receive ABs. The focus of cough/bronchitis is to determine if lower respiratory tract infections exist (pneumonia, influenza, pertussis, COPD exacerbation, other)22. For pediatric patients, non-specific cough illness does not warrant an AB prescription. For adult with bronchitis, ABs are also not recommended unless a specific treatable pathogen is identified.
Preferred antibiotic choices: these recommendations have been consistent for many years.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Preferred antibiotic</th>
<th>Alternate antibiotic if allergies exist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Otitis Media</td>
<td>Amoxicillin (pediatric) Amoxicillin-clavulanic acid (adult)</td>
<td>Cefdinir Ceftriaxone Clindamycin Doxycycline</td>
</tr>
<tr>
<td>GAS Pharyngitis</td>
<td>Penicillin family: Amoxicillin (liquid/solid) Penicillin V potassium (solid form) Penicillin G benzathine (IM)</td>
<td>Cephalexin Clindamycin Azithromycin (less preferred): Resistance well-documented</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Amoxicillin (pediatric) Amoxicillin-clavulanic acid (adult)</td>
<td>Cefdinir Ceftriaxone Clindamycin Doxycycline Levofloxacin</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>None recommended</td>
<td></td>
</tr>
</tbody>
</table>

Findings:
Antibiotics have significantly contributed to the control of infectious diseases, the leading cause of human morbidity and mortality for most of human existence. In each of the four URI categories presented, most (~90%) are of viral etiology. Proper antibiotic stewardship includes a balance between the avoidance of prescribing for common viral etiologies of URI and the judicious use of antibiotics when bacterial etiologies are suspected, based on appropriate clinical findings. The NPTC took action to add six antibiotics to the NCF (amoxicillin, amoxicillin-clavulanate, cefdinir, cephalexin, clindamycin and penicillin V potassium) based on well-established standards of care.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References: