

AHRQ Safety Program for Telemedicine: Improving Antibiotic Use

Antibiotics and What They Treat

Slide Title and Commentary	Slide Number and Slide
Antibiotics and What They Treat SAY: Welcome to the presentation titled, “Antibiotics and What They Treat.”	Slide 1 AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat  AHRQ Pub. No. 20271/0021 October 2018
Objectives SAY: At the end of this presentation, participants will be able to— • Describe the spectrum of activity of commonly prescribed antibiotics used in children and adults in the telemedicine setting • Describe common antibiotic-associated adverse events in children and adults • Describe common indications for oral antibiotics in children and adults in the telemedicine setting This presentation is meant to provide an overview of antibiotics commonly prescribed in the telemedicine setting. About 30 to 40 percent of patients seen in the telemedicine setting receive antibiotics, underscoring the importance of understanding appropriate antibiotic use during virtual visits. More details of use of these agents for common outpatient and telemedicine indications are provided in other presentations in the AHRQ Telemedicine Toolkit To Improve Antibiotic Use. For this presentation, generic names are generally used and not brand names.	Slide 2 Objectives By the end of this presentation, participants will be able to— • Describe the spectrum of activity of commonly prescribed antibiotics used in children and adults in the telemedicine setting¹ • Describe common antibiotic-associated adverse events in children and adults • Describe common indications for oral antibiotics in children and adults in the telemedicine setting  AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 2

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Overview of Beta-Lactam Agents SAY: Beta-lactams include four classes of drugs: penicillins, cephalosporins, aztreonam, and carbapenems. This presentation reviews antibiotics within these beta-lactam classes that are commonly prescribed in the outpatient and telemedicine setting. Both gram-positive and gram-negative bacteria have cell walls that are made of peptidoglycan chains that are cross-linked by enzymes called penicillin binding proteins. Beta-lactam antibiotics work by interfering with the function of penicillin-binding proteins. Atypical bacteria like <i>Mycoplasma pneumoniae</i>, <i>Chlamydia pneumoniae</i>, and <i>Legionella pneumophila</i> don't have cell walls, and therefore beta-lactam antibiotics are not effective for these organisms. Common adverse events to mention to patients include rashes and diarrhea. Rashes are generally maculopapular and resolve after antibiotic discontinuation. Similarly, diarrhea is generally mild, but patients should be cautioned. If a patient is being prescribed a beta-lactam, it is good practice to let the patient know that these are possible side effects. Fortunately, some of the other adverse events associated with intravenous beta-lactams, such as cytopenias and seizures, are uncommon with oral beta-lactam agents.	Slide 3 Overview of Beta-Lactam Agents - Gram-positive and gram-negative bacteria have cell walls made of peptidoglycans - Penicillin binding proteins (PBPs) cross-link peptidoglycans - Beta-lactams inhibit activity of PBPs <i>Mycoplasma pneumoniae</i>, <i>Chlamydia pneumoniae</i>, and <i>Legionella pneumophila</i> do not have a cell wall and are not inhibited by beta-lactams - Bacteria inhibits beta-lactam antibiotics by limiting their entry, actively pumping them out, altering PBPs, and producing inactivating enzymes Common adverse events - Rashes - Diarrhea - Cytopenias - Seizures  AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 3

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Penicillin SAY: There are oral, intramuscular (IM), and intravenous (IV) formulations of penicillin. The oral formulation, however, is poorly absorbed and therefore not commonly used for the treatment of active infections. Penicillins cover gram-positive bacteria such as group A <i>Streptococcus</i>, group B <i>Streptococcus</i>, and <i>Streptococcus pneumoniae</i>. If oral therapy is being considered for these infections—for example a cellulitis caused by group A <i>Streptococcus</i>—alternate beta-lactams such as amoxicillin or a first-generation cephalosporin are generally used over oral penicillin given their improved oral absorption. Intramuscular penicillin G benzathine is the preferred treatment for early and latent syphilis. This treatment will be discussed further during a separate presentation focusing on sexually transmitted infections.	Slide 4 Penicillin² • Penicillin VK (oral), penicillin G benzathine (IM), penicillin G aqueous (IV) • Oral formulation: short half-life requiring frequent administration, limited absorption • Intramuscular formulation: long half-life • Common outpatient indications of IM penicillin ◦ Early and late syphilis <table border="1"> <caption>Spectrum of Activity</caption> <tbody> <tr> <td>Gram-positive</td><td><i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i></td></tr> <tr> <td>Gram-negative</td><td><i>Neisseria meningitidis</i></td></tr> <tr> <td>Spirochetes</td><td><i>Treponema pallidum</i> (syphilis)</td></tr> </tbody> </table> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 4	Gram-positive	<i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i>	Gram-negative	<i>Neisseria meningitidis</i>	Spirochetes	<i>Treponema pallidum</i> (syphilis)
Gram-positive	<i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i>						
Gram-negative	<i>Neisseria meningitidis</i>						
Spirochetes	<i>Treponema pallidum</i> (syphilis)						

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Amoxicillin

SAY:

Amoxicillin belongs to a class of penicillins called the aminopenicillins. It covers the same gram-positive organisms as penicillin and in addition is considered a preferred treatment for *Enterococcus faecalis*. Amoxicillin, however, has broader gram-negative coverage compared with penicillin.

Amoxicillin can cover respiratory gram-negative bacteria like *Haemophilus influenzae*. However, about 25 to 30 percent of *Haemophilus influenzae* isolates produce a beta-lactamase enzyme that inactivates amoxicillin. Fortunately, amoxicillin-clavulanic acid can treat these isolates that produce a beta-lactamase. Amoxicillin used to be highly effective for the treatment of enteric gram-negative bacteria as well, such as *Escherichia coli*. Unfortunately, more than half of *E. coli* produce beta-lactamases that inactivate amoxicillin. As *E. coli* are the most common cause of urinary tract infections or UTIs, amoxicillin is not suggested as empiric treatment for UTIs. However, if a patient has a UTI with *E. coli*, amoxicillin can be considered for therapy. *Enterococcus faecalis* is another common cause of UTIs and is 100 percent susceptible to amoxicillin.

There are several common indications for which amoxicillin can be considered in the telemedicine setting. These include group A *Streptococcus pharyngitis*. Amoxicillin is always active against group A *Streptococcus*, so it can be prescribed when this organism is recovered without awaiting susceptibility testing results. Amoxicillin can be considered for a skin and soft tissue infection, but only after group A *Streptococcus* is confirmed present in the infection. Additionally, amoxicillin is a preferred treatment for community-acquired pneumonia in children and adults and acute otitis media in children. Amoxicillin can be used for UTIs if *Enterococcus faecalis* is recovered in culture even if antibiotic susceptibility data are not available. However, amoxicillin can only be used for *E. coli* UTIs if antibiotic susceptibility results indicate susceptibility. Finally, amoxicillin is a preferred treatment for children with Lyme disease and adults who have issues tolerating doxycycline for Lyme disease.

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Amoxicillin³⁻⁵

- β -lactamase production can cause resistance in gram-negative organisms
- Not appropriate empiric therapy for urinary tract infections (UTIs)
- **Common outpatient indications**
 - Group A *Streptococcus* pharyngitis
 - Group A *Streptococcus* skin and soft tissue infection (culture confirmed)
 - Community-acquired pneumonia
 - Acute otitis media
 - UTIs (antibiotic susceptibilities confirmed)
 - Lyme disease

Spectrum of Activity	
Gram-positive	<i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i> , <i>Enterococcus faecalis</i> , <i>Listeria monocytogenes</i>
Gram-negative	<i>Haemophilus influenzae</i> , enteric gram-negatives (e.g., <i>Escherichia coli</i>)
Spirochetes	<i>Borrelia burgdorferi</i> (Lyme disease)

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Amoxicillin-Clavulanic Acid

SAY:

Clavulanic acid broadens the coverage of amoxicillin to also include coverage of methicillin-susceptible *Staphylococcus aureus* (MSSA) and some gram-negative organisms.

With the addition of clavulanic acid, all *Haemophilus influenzae* isolates are covered—both those organisms that do and do not produce beta-lactamase enzymes. Therefore, as amoxicillin-clavulanate covers both *Streptococcus pneumoniae* and respiratory gram-negative bacteria, it is commonly used for infections such as sinusitis, community-acquired pneumonia, and chronic obstructive pulmonary disease (COPD). It also can be considered for the treatment of acute otitis media in children who received amoxicillin the previous 30 days or with a history of recurrent otitis media unresponsive to amoxicillin.

For *E. coli*, however, it broadens coverage to include approximately 50 percent of *E. coli*. Therefore, amoxicillin-clavulanic acid can only be used for *E. coli* UTIs if antibiotic susceptibility results indicate susceptibility to this agent. Although newer data indicate that moderate diverticulitis may not require any antibiotic therapy, for select patients if antibiotics are considered, amoxicillin-clavulanic acid remains an option. Finally, amoxicillin-clavulanic acid is a preferred treatment for skin and soft tissue infections from animal bites.

Amoxicillin-clavulanic acid can cause the same adverse events described for beta-lactams in general, but one notable side effect is diarrhea, which can occur in about 20 percent of patients, particularly with higher dosages.

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Amoxicillin-Clavulanic Acid⁵⁻⁸

- Commonly referred to as Augmentin[®]
- **Notable adverse events:** diarrhea (20%)⁹
- **Common outpatient indications**
 - Sinusitis
 - Community-acquired pneumonia
 - Moderate chronic obstructive pulmonary disease exacerbation
 - Acute otitis media (if recent use of amoxicillin)
 - Moderate diverticulitis
 - Skin infections from animal bites
 - Urinary tract infections (if antibiotic susceptibilities confirmed)

Spectrum of Activity

Gram-positive	(All the gram-positives covered by amoxicillin) as well as MSSA
Gram-negative	<i>Haemophilus influenzae</i> , <i>Moraxella catarrhalis</i> , enteric gram-negatives (e.g., <i>Escherichia coli</i>)

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First-Generation Cephalosporins

SAY:

There are two commonly prescribed oral first-generation cephalosporins: cephalexin and cefadroxil. These drugs have identical spectrums of activity, but cefadroxil can be more convenient as it is dosed twice-daily compared with cephalexin, which is dosed three to four times a day.

Of note, the cross-reactivity between penicillin and cephalosporin allergies is less than 5 percent, so cephalosporins are often safe to give patients with penicillin allergies. Please review the presentation on antibiotic allergies for more information.

Cephalexin and cefadroxil have excellent activity against MSSA as well as group A and B *Streptococcus*. In the outpatient setting they are commonly used for skin and soft tissue infections when MRSA is unlikely. Additionally, they have broader coverage against gram-negatives compared with amoxicillin and amoxicillin-clavulanic acid, so they can be considered for the treatment of UTIs caused by bacteria like *E. coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*.

Cefuroxime

SAY:

Cefuroxime is a second-generation cephalosporin available in an oral formulation. It has activity against both gram-positive and gram-negative organisms that cause respiratory infections such as sinusitis, community-acquired pneumonia, COPD exacerbations, and acute otitis media.

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First-Generation Cephalosporins¹⁰

- Cephalexin (Keflex®), and cefadroxil (Duricef®)
- Cross-allergenicity between penicillin and cephalosporins <5%
- **Common outpatient indications**
 - Skin and soft tissue infections (when MRSA unlikely)
 - UTIs

Spectrum of Activity

Gram-positive	MSSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>)
Gram-negative	Some enteric gram-negatives (e.g., <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>)

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Cefuroxime⁵⁻⁸

- Second-generation cephalosporin
- **Common outpatient indications**
 - Sinusitis (penicillin allergy)
 - Community-acquired pneumonia (penicillin allergy)
 - Moderate chronic obstructive pulmonary disease exacerbation
 - Acute otitis media (if severe penicillin allergy)

Spectrum of Activity

Gram-positives	<i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i> , MSSA
Gram-negatives	<i>Haemophilus influenzae</i> , <i>Moraxella catarrhalis</i>

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Third-Generation Cephalosporins

SAY:

Notable third-generation cephalosporins administered in the outpatient setting include IM ceftriaxone and a variety of oral cephalosporins. IM ceftriaxone is commonly administered for the treatment of gonorrhea, as discussed in the AHRQ Safety Program toolkit presentation about sexually transmitted infections.

Third-generation cephalosporins have broad gram-positive and gram-negative coverage. However, it is important to note that while ceftriaxone covers virtually all *Streptococcus pneumoniae*, the coverage of oral third-generation cephalosporins against this organism is more variable. Therefore, amoxicillin-clavulanic acid is generally preferred for common respiratory bacterial infections, except in settings of severe penicillin allergies.

Additionally, oral third-generation cephalosporins have broad gram-negative enteric coverage and can be considered for UTIs when first-generation cephalosporins are not active.

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Third-Generation Cephalosporins²

- IM ceftriaxone and several oral antibiotics
 - Examples: cefdinir (Omnicef®), cefpodoxime (Vantin®), cefixime (Suprax®)
- Ceftriaxone preferred for gonococcal infections; resistance is a concern
- **Common outpatient indications**
 - IM ceftriaxone: gonorrhea
 - Oral third-generation cephalosporins: UTIs, bacterial respiratory tract infections

Spectrum of Activity	
Gram-positives	<i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus agalactiae</i> (group B <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i>
Gram-negatives	<i>Haemophilus influenzae</i> , <i>Moraxella catarrhalis</i> , <i>Neisseria gonorrhoeae</i> , gram-negative enterics
Spirochetes	<i>Borrelia burgdorferi</i> (Lyme disease)

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Fluoroquinolones

SAY:

There are four oral fluoroquinolones: ciprofloxacin, levofloxacin, moxifloxacin, and delafloxacin. Ciprofloxacin has broad gram-negative coverage, including coverage of *Pseudomonas aeruginosa*, and is commonly prescribed for UTIs. Levofloxacin has essentially the same gram-negative coverage as ciprofloxacin but also includes coverage for *Streptococcus pneumoniae*. Therefore, levofloxacin is commonly prescribed for UTIs and for bacterial respiratory tract infections—particularly for patients with severe penicillin allergies.

Moxifloxacin has reduced gram-negative coverage compared to ciprofloxacin and levofloxacin and does not cover *Pseudomonas*, but retains coverage against respiratory gram-negatives and *Streptococcus pneumoniae*. Therefore, moxifloxacin is also generally limited to the treatment of bacterial respiratory tract infections in patients with severe penicillin allergies. Finally, delafloxacin is the newest fluoroquinolone and has similar activity as moxifloxacin but includes additional coverage of both methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*. It can be considered for the treatment of skin and soft tissue infections and bacterial respiratory tract infections.

Fluoroquinolones chelate cations, and their bioavailability is significantly reduced when administered with calcium, iron, antacids, multivitamins, milk, or yogurt. If possible, these agents should be avoided or at least adequately spaced out by several hours while receiving fluoroquinolone therapy.

The adverse event profile associated with fluoroquinolones is notable and should be discussed when these agents are prescribed. These include an increased risk of *Clostridioides difficile* infections—arguably higher than beta-lactam agents. QTc prolongation may also occur, which is generally most problematic in patients with other risk factors such as underlying arrhythmias. Other adverse events include tendonitis and very rarely tendon rupture, photosensitivity, and central nervous system toxicities such as dizziness, confusion, and hallucinations.

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Fluoroquinolones¹¹

- Calcium, magnesium, iron salts reduce absorption
- Notable adverse events (all up to 10%)**
 - Clostridioides difficile* infections
 - QTc prolongation (generally in patients with underlying arrhythmias)
 - Tendinopathy
 - CNS toxicities (dizziness, confusion, hallucinations)
- Common outpatient indications**
 - Ciprofloxacin: UTIs
 - Levofloxacin, moxifloxacin: bacterial respiratory tract infections
 - Delafloxacin: skin and soft tissue infections, bacterial respiratory tract infections

Spectrum of Activity

Ciprofloxacin	Gram-negative enteric organisms, <i>Pseudomonas aeruginosa</i> , <i>Haemophilus influenzae</i>
Levofloxacin	Gram-negative enteric organisms, <i>P. aeruginosa</i> , <i>H. influenzae</i> , <i>Streptococcus pneumoniae</i> , atypical bacteria
Moxifloxacin	Gram-negative enteric organisms, <i>Haemophilus influenzae</i> , <i>Streptococcus pneumoniae</i> , atypical bacteria, moderate activity against intestinal anaerobes
Delafloxacin	Gram-negative enteric organisms, <i>H. influenzae</i> , MRSA, MSSA, <i>S. pneumoniae</i>

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Doxycycline

SAY:

Doxycycline has a broad spectrum of activity. It covers gram-positive bacteria including MRSA. It is active against almost 90 percent of *Streptococcus pneumoniae* and about 80 percent of group A *Streptococcus*. Doxycycline covers respiratory gram-negative bacteria and several enteric gram-positive bacteria as well. It also covers a variety of other organisms.

It is important to note that doxycycline has very limited urinary excretion and is not advised for UTIs. Newer guidance from the American Academy of Pediatrics indicates doxycycline is safe to administer in children of all ages, without any restrictions on the allowable duration. Unlike tetracycline, there is no evidence that doxycycline causes any sort of enamel damage to children.

Similar to fluoroquinolones, doxycycline chelates cations, and its bioavailability is significantly reduced when administered with calcium, iron, antacids, multivitamins, milk, or yogurt. These agents should be discontinued, if possible, when administering doxycycline.

Doxycycline can cause gastrointestinal upset, and it is generally advised that it be taken with a small meal. It can cause photosensitivity, so direct sunlight should be avoided. Doxycycline can cause increased intracranial pressure, and females who are overweight appear to be at greater risk. Patients should be cautioned to return to medical care if experiencing persistent headaches or double vision while taking doxycycline. Additionally, as it can cause esophageal ulcers or what is commonly referred to as “pill esophagitis,” patients should be advised to sit up for about 30 minutes after taking doxycycline.

Doxycycline, Continued

SAY:

Common outpatient indications include skin and soft tissue infections, osteoarticular infections, bacterial respiratory tract infections, tick-borne infections like Lyme disease, Rocky Mountain spotted fever, and ehrlichiosis. It is used for both the prevention and treatment of malaria. It is also preferred therapy for chlamydia.

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Doxycycline¹²⁻¹⁴

- Calcium, magnesium, iron salts reduce absorption
- Poor urinary excretion
- **Notable adverse events (all up to 10%)**
 - Gastrointestinal upset
 - Photosensitivity
 - Increased intracranial pressure
 - Pill esophagitis
- Safe to administer in children for ≤ 21 days

Spectrum of Activity

Gram-positive	MSSA, MRSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i>
Gram-negative	<i>Haemophilus influenzae</i> , some enteric gram-negatives (e.g., <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>)
Others	<i>Mycoplasma pneumoniae</i> , <i>Chlamydia pneumoniae</i> , <i>Legionella pneumophila</i> , <i>Borrelia burgdorferi</i> (Lyme disease), <i>Rickettsia</i> (Rocky Mountain spotted fever, ehrlichiosis), <i>Plasmodium</i> species (malaria), <i>Chlamydia trachomatis</i> (chlamydia)

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Doxycycline, Continued¹²⁻¹⁴

- **Common outpatient indications**
 - Skin and soft tissue infections
 - Osteoarticular infections
 - Bacterial respiratory tract infections
 - Tick-borne illnesses
 - Malaria prophylaxis
 - Chlamydia

Spectrum of Activity

Gram-positive	MSSA, MRSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), <i>Streptococcus pneumoniae</i>
Gram-negative	<i>Haemophilus influenzae</i> , some enteric gram-negatives (e.g., <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>)
Others	<i>Mycoplasma pneumoniae</i> , <i>Chlamydia pneumoniae</i> , <i>Legionella pneumophila</i> , <i>Borrelia burgdorferi</i> (Lyme disease), <i>Rickettsia</i> (Rocky Mountain spotted fever, ehrlichiosis), <i>Plasmodium</i> species (malaria), <i>Chlamydia trachomatis</i> (chlamydia)

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Clindamycin SAY: Clindamycin is an option for skin and soft tissue infections when MRSA is a concern. However, growing resistance makes it less desirable for this indication. More specifically, although there is regional variation, in some areas of the United States, clindamycin is active against only approximately 60 percent of MRSA isolates. Data from the Centers for Disease Control and Prevention data indicate that approximately 20 percent of group A streptococcal isolates, another common cause of skin and soft tissue infections, are resistant to clindamycin. Another concern with clindamycin is its association with <i>C. difficile</i> infections. If clindamycin is prescribed, caution should be given to patients about signs and symptoms associated with <i>C. difficile</i> infection.	Slide 13 Clindamycin¹⁴⁻¹⁵ • Clindamycin-resistant streptococcal and staphylococcal species increasing ◦ Active against ~60% of MRSA isolates ◦ Active against ~80% of Group A streptococcal isolates • Notable adverse events ◦ <i>C. difficile</i> infection ◦ Gastrointestinal distress • Common outpatient indications ◦ Skin and soft tissue infections (if high suspicion for MRSA) Spectrum of Activity <table><tr><td>Gram-positives</td><td>MSSA, MRSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>)</td></tr><tr><td>Anaerobes</td><td>Oral anaerobes</td></tr></table> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 13	Gram-positives	MSSA, MRSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>)	Anaerobes	Oral anaerobes
Gram-positives	MSSA, MRSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>)				
Anaerobes	Oral anaerobes				
Trimethoprim-Sulfamethoxazole (TMP-SMX) SAY: Trimethoprim-sulfamethoxazole or “trim-sulfa” is commonly referred to as Bactrim® or Septra®. Trim-sulfa is frequently prescribed for skin and soft tissue infections given that it covers MSSA, MRSA, and <i>Strep pyogenes</i>. More recent data indicate that trim-sulfa covers over 95 percent of strep <i>pyogenes</i> isolates and for suppurative skin infections where it is not clear what the causative bacteria is or if MRSA has been cultured, trim-sulfa remains a good choice. Trim-sulfa is also commonly used for UTI treatment, although resistance to this agent is a growing problem among <i>E. coli</i>. This is discussed in the AHRQ Safety Program presentation focusing on UTIs. Trim-sulfa is associated with a number of adverse events, but the most pertinent ones for relatively short courses in the outpatient setting are hypersensitivity reactions, which can range from relatively mild such as a maculopapular rash to severe such as Stevens-Johnson Syndrome. Patients should be cautioned that if they develop a rash or new fever while taking trim-sulfa that they should stop the medication and call their healthcare provider for further guidance.	Slide 14 Trimethoprim-Sulfamethoxazole (TMP-SMX)¹⁶⁻¹⁷ • Newer data indicate TMP-SMX (Bactrim®, Septra®) against >95% of <i>S. pyogenes</i> isolates • Notable adverse events (all up to 10%) ◦ Hypersensitivity reactions ◦ Bone marrow suppression ◦ Acute kidney injury ◦ Hyperkalemia • Common outpatient indications ◦ Skin and soft tissue infections ◦ UTIs Spectrum of Activity MSSA, MRSA, <i>Streptococcus pyogenes</i> (group A <i>Streptococcus</i>), gram-negative enterics, <i>Stenotrophomonas maltophilia</i>, <i>Pneumocystis jirovecii</i>, <i>Toxoplasma gondii</i>, <i>Listeria monocytogenes</i>, <i>Nocardia</i> species AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 14				

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Linezolid SAY: Linezolid has broad gram-positive coverage including MSSA, MRSA, <i>Enterococcus</i>—including vancomycin-resistant <i>Enterococcus</i>, and <i>Pneumococcus</i>—including <i>Streptococcus pneumoniae</i>. It is most commonly prescribed for skin and soft tissue infections in the outpatient setting. Although uncommon and generally limited to patients with significant healthcare exposure, it is also used for UTIs caused by vancomycin-resistant <i>Enterococcus</i>. Linezolid is associated with a number of adverse events—particularly when taken for prolonged periods of time. Bone marrow suppression—particularly thrombocytopenia—tends to occur after 14 days of therapy. Blood counts should be monitored for courses beyond 2 weeks. Linezolid is also associated with peripheral and optic neuropathy, which typically present as a “glove and stocking” and diminished visual acuity, respectively. These symptoms may not always be reversible, but fortunately they only tend to occur in patients taking linezolid for several months. Lactic acidosis is rare and generally only occurs in patients taking more than a month of linezolid. It presents with abdominal pain, nausea, vomiting, and generalized weakness, and it can be associated with high mortality. Finally, linezolid can cause serotonin syndrome when taken with a selective serotonin reuptake inhibitor or SSRI. Even though serotonin syndrome occurs in fewer than 5 percent of patients taking both medications, if the patient can hold off on taking the SSRI while completing the linezolid course, that is preferred, but not required. Symptoms of serotonin syndrome include tachycardia, hyperthermia, agitation, and tremor. For these reasons, linezolid is not recommended for courses beyond 28 days. Fortunately, for skin and soft tissue infections, treatment courses generally range no more than 5 to 10 days.	Slide 15 Linezolid¹⁸⁻¹⁹ • Brand name Zyvox® • Broad gram-positive coverage • Notable adverse events (more commonly with >2 weeks of therapy) ◦ Myelosuppression (most commonly thrombocytopenia) ◦ Optic and peripheral neuropathy ◦ Serotonin syndrome ◦ Lactic acidosis • Common outpatient indications ◦ Skin and soft tissue infections ◦ UTIs due to vancomycin-resistant <i>Enterococcus</i> Spectrum of Activity MSSA, MRSA, <i>Streptococcus</i> spp., <i>Enterococcus</i> spp., <i>Norcardia</i>, <i>Mycobacteria</i> spp. AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 15

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Azithromycin SAY: Azithromycin is commonly considered for mild bacterial respiratory tract infections like community-acquired pneumonia when severe penicillin allergies preclude the use of a beta-lactam. Azithromycin generally provides coverage against <i>Streptococcus pneumoniae</i>—about 70 percent of isolates, respiratory gram-negative bacteria, and atypical bacteria like <i>Mycoplasma pneumoniae</i>. Other common outpatient indications include a single 1-gram dose for chlamydia for people unlikely to adhere to a 7-day course of doxycycline or pregnant women and travelers' diarrhea. In 2021, the FDA issued a warning about increased risk of acute cardiovascular death among all patients taking azithromycin based on observational studies, including one that showed increased risk of acute cardiovascular mortality with azithromycin compared with amoxicillin exposure. However, causality has not been established. Azithromycin is associated with prolonging the QTc interval; this risk appears highest in patients with known cardiovascular disease.	Slide 16 Azithromycin^{2,20-21} • Long half life ◦ A 5-day "Z-pack" lasts in the body about 10 days • Notable adverse events (both <1%) ◦ QTc prolongation (generally in patients with underlying arrhythmias) ◦ Liver dysfunction • Common outpatient indications ◦ Mild bacterial respiratory tract infections ◦ Chlamydia (if unable to take doxycycline) ◦ Travelers' diarrhea Spectrum of Activity <i>Mycoplasma pneumoniae</i>, <i>Chlamydia pneumoniae</i>, <i>Legionella pneumophila</i>, <i>Haemophilus influenzae</i>, <i>Streptococcus pneumoniae</i> (~70%), <i>Chlamydia trachomatis</i>, atypical <i>Mycobacteria</i> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 16

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Nitrofurantoin SAY: Nitrofurantoin is a preferred treatment for uncomplicated cystitis in women. In the Macrobid® formulation of the drug that is typically prescribed, it is generally taken twice a day for 5 days. Nitrofurantoin has good coverage against <i>E. coli</i> and other enteric gram-negatives that commonly cause UTIs. Nitrofurantoin should be avoided if there is suspicion for pyelonephritis, as it does not concentrate well in the kidneys. In patients with significant renal dysfunction, there may be insufficient accumulation of nitrofurantoin in the urine. Therefore, it is not suggested for such patients. The main adverse events to be aware of with nitrofurantoin are acute pneumonitis and chronic pulmonary fibrosis. Acute pneumonitis typically occurs in about 1 in 5,000 patients after their first exposure to nitrofurantoin and usually occurs about a week after initiating a course of therapy. It generally presents with cough, fever, and dyspnea. The onset can be within a day for patients who have received previous courses of nitrofurantoin. Symptoms generally resolve on their own after treatment with nitrofurantoin is discontinued. Chronic pulmonary fibrosis more commonly occurs with prolonged nitrofurantoin therapy; recovery of lung function is more limited and occurs over months to years. The risk of both types of pulmonary injury increases with prolonged nitrofurantoin use.	Slide 17 Nitrofurantoin²²⁻²⁴ • Common brand names: Macrobid® (twice daily), Macrochantin® (four times daily) • Notable adverse events (both <1%) ◦ Acute pneumonitis ◦ Chronic pulmonary fibrosis • Avoid if significant renal dysfunction • Avoid for pyelonephritis • Common outpatient indication ◦ Uncomplicated cystitis Spectrum of Activity <i>Escherichia coli</i> and other enteric gram-negatives (not <i>Pseudomonas aeruginosa</i>), <i>Staphylococcus saprophyticus</i> (cause of UTIs) AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 17
Fosfomycin SAY: Fosfomycin is dosed as 3 grams of powder mixed in water as a single oral dose for the treatment of uncomplicated cystitis in women. As it does not concentrate well in the kidneys, it should generally be avoided for patients with pyelonephritis. Susceptibility testing for fosfomycin is not routinely available in most clinical laboratories but resistance to <i>E. coli</i> remains rare. The most common adverse event with fosfomycin is diarrhea which occurs in approximately 10 percent of patients.	Slide 18 Fosfomycin²⁵ • Brand name Monurol® • Available as a powder that is added to water • Notable adverse events ◦ Diarrhea (10%) • Generally avoid for pyelonephritis • Common outpatient indication ◦ Uncomplicated cystitis Spectrum of Activity <i>Escherichia coli</i> and <i>Enterococcus faecalis</i> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 18

Slide Title and Commentary	Slide Number and Slide
Gepotidacin SAY: The FDA approved gepotidacin in 2025 for the treatment of uncomplicated UTIs as well as for the treatment of <i>Neisseria gonorrhoeae</i>. Although it is distantly related to fluoroquinolones, it belongs to a distinct antibiotic class—a triazaacenaphthylene. Gepotidacin is generally well tolerated. Fewer than 5 percent of patients in clinical trials report nausea or diarrhea. Gepotidacin covers the typical bacteria implicated in uncomplicated UTIs and is a reasonable option for the treatment of uncomplicated UTIs in women, but clinicians may wish to verify the cost of the drug.	Slide 19 Gepotidacin²⁶⁻²⁷ • Belongs to a novel antibiotic class (i.e., a triazaacenaphthylene) that inhibits bacterial DNA replication • Notable adverse events ◦ Nausea and diarrhea in <5% of patients • Common outpatient indication ◦ FDA-approved 2025 for treatment of uncomplicated UTIs (i.e., cystitis) ◦ FDA-approved for gonorrhea for patients with limited or no alternative treatment options Spectrum of Activity <i>Escherichia coli</i>, <i>Klebsiella pneumoniae</i>, <i>Citrobacter freundii</i> complex, <i>Staphylococcus saprophyticus</i> (cause of UTIs), <i>Enterococcus faecalis</i>, and <i>Neisseria gonorrhoea</i> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 19
Pivmecillinam SAY: Pivmecillinam is a semi-synthetic penicillin derivative antibiotic that became approved by the FDA in 2025 for the treatment of uncomplicated UTIs and is generally prescribed for a 3 to 7 day course. Clinical trials support dosages and durations of 200 mg three times daily for 7 days, 200 mg twice daily for 7 days, and 400 mg twice daily for 3 days. Pivmecillinam covers common causes of UTIs such as <i>E. coli</i>—including ESBL-producers, <i>Proteus mirabilis</i>, and <i>Staphylococcus saprophyticus</i>. Pivmecillinam has been used for decades in several other regions of the world and extensive safety data are available for its use in pregnant women. Although generally well tolerated, nausea and diarrhea that may result in discontinuation of pivmecillinam occur in less than 5 percent of patients. Clinicians may wish to verify the cost of the drug.	Slide 20 Pivmecillinam²⁸⁻³⁰ • Semi-synthetic penicillin derivative • Extensive safety data in pregnant women • Notable adverse events ◦ Nausea and diarrhea in <5% of patients • Common outpatient indication ◦ FDA-approved in 2025 for treatment of uncomplicated UTIs (i.e., cystitis) ◦ Expected activity against ESBL-producing <i>E. coli</i> UTIs Spectrum of Activity <i>Escherichia coli</i>, <i>Proteus mirabilis</i>, and <i>Staphylococcus saprophyticus</i> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 20
Sulopenem SAY: Sulopenem is an antibiotic belonging to a novel class called the thiopenems that is coformulated with probenecid. Sulopenem was FDA-approved in 2024 for the treatment of uncomplicated UTIs. It is generally well tolerated; less than 10 percent of patients receiving this agent experience nausea or diarrhea. Clinicians may wish to verify the cost of the drug.	Slide 21 Sulopenem³¹⁻³⁵ • Antibiotic belonging to a novel class (i.e., thiopenem) that is coformulated with probenecid • Notable adverse events ◦ Nausea and diarrhea in <10% of patients • Common outpatient indication ◦ FDA approved 2024 for treatment of uncomplicated urinary tract infections (i.e., cystitis) Spectrum of Activity <i>Escherichia coli</i>, <i>Klebsiella pneumoniae</i>, <i>Proteus mirabilis</i>, <i>Citrobacter</i> spp., <i>Enterobacter cloacae</i> complex, <i>Providencia</i> species, <i>Staphylococcus saprophyticus</i>, and <i>Streptococcus agalactiae</i> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 21

Slide Title and Commentary	Slide Number and Slide						
Metronidazole SAY: Metronidazole is known for its broad anaerobic coverage. In the outpatient setting it is commonly used for <i>Clostridioides difficile</i> infections—although it is considered an alternative treatment if oral vancomycin and oral fidaxomicin are not available. Notable adverse events associated with metronidazole include nausea, vomiting, diarrhea, and a metallic taste. Particularly for patients receiving high doses and/or prolonged durations of metronidazole therapy neurologic toxicities can be a concern including reversible peripheral neuropathy, confusion, and/or seizures and can occur in approximately 20 percent of patients. For relatively short courses neurologic toxicities occur in about 1 percent of patients.	Slide 22 Metronidazole - Broad anaerobic coverage Notable adverse events³⁶⁻³⁷ - Nausea, vomiting, diarrhea, metallic taste - Reversible peripheral neuropathy, confusion, seizures (1% for courses ~1 week; 18% for courses >4 weeks) - Interactions - Disulfiram-like reaction with alcohol consumption - Inhibits warfarin metabolism <table border="1"> <caption>Spectrum of Activity</caption> <tr> <td>Gram-positive anaerobes</td><td><i>Clostridium</i> species</td></tr> <tr> <td>Gram-negative anaerobes</td><td><i>Bacteroides</i> species, <i>Fusobacterium</i> species</td></tr> <tr> <td>Others</td><td><i>Trichomonas vaginalis</i>, <i>Entamoeba histolytica</i>, <i>Giardia lamblia</i>, <i>Helicobacter pylori</i></td></tr> </table> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 22	Gram-positive anaerobes	<i>Clostridium</i> species	Gram-negative anaerobes	<i>Bacteroides</i> species, <i>Fusobacterium</i> species	Others	<i>Trichomonas vaginalis</i> , <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> , <i>Helicobacter pylori</i>
Gram-positive anaerobes	<i>Clostridium</i> species						
Gram-negative anaerobes	<i>Bacteroides</i> species, <i>Fusobacterium</i> species						
Others	<i>Trichomonas vaginalis</i> , <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> , <i>Helicobacter pylori</i>						
Metronidazole Continued SAY: Other outpatient indications for metronidazole include peptic ulcer disease treatment, diarrhea caused by the protozoa <i>Giardia</i>, and <i>Trichomonas</i> sexually transmitted infections.	Slide 23 Metronidazole, Continued Common outpatient indications of metronidazole - Mild–moderate <i>Clostridioides difficile</i> infection - Component of peptic ulcer disease treatment <i>Giardia</i> diarrhea <i>Trichomonas</i> sexually transmitted infection <table border="1"> <caption>Spectrum of Activity</caption> <tr> <td>Gram-positive anaerobes</td><td><i>Clostridium</i> species</td></tr> <tr> <td>Gram-negative anaerobes</td><td><i>Bacteroides</i> species, <i>Fusobacterium</i> species</td></tr> <tr> <td>Others</td><td><i>Trichomonas vaginalis</i>, <i>Entamoeba histolytica</i>, <i>Giardia lamblia</i>, <i>Helicobacter pylori</i></td></tr> </table> AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 23	Gram-positive anaerobes	<i>Clostridium</i> species	Gram-negative anaerobes	<i>Bacteroides</i> species, <i>Fusobacterium</i> species	Others	<i>Trichomonas vaginalis</i> , <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> , <i>Helicobacter pylori</i>
Gram-positive anaerobes	<i>Clostridium</i> species						
Gram-negative anaerobes	<i>Bacteroides</i> species, <i>Fusobacterium</i> species						
Others	<i>Trichomonas vaginalis</i> , <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> , <i>Helicobacter pylori</i>						
Take-Home Messages SAY: In summary, while antibiotics are necessary for many bacterial infections, all antibiotics have the potential for associated harm. Although the severity of antibiotic-associated adverse events ranges from relatively mild maculopapular rashes to life-threatening conditions like Stevens-Johnson Syndrome, all adverse events can prompt a return to medical care and be associated with distress, inconvenience, and avoidable costs for patients. Up to 40 percent of patients seen via telemedicine receive antibiotics. Therefore, understanding the spectrum of activity, common antibiotic-associated adverse events, and common indications for oral antibiotics is imperative when selecting antibiotics in the telemedicine setting to optimize the safety of patients.	Slide 24 Take-Home Messages ✓ Up to 40 percent of patients seen via telemedicine receive antibiotics ✓ Although antibiotics are necessary for many bacterial infections, all antibiotics also have associated harm ✓ It's important to understand the spectrum of activity, common antibiotic-associated adverse events, and common indications for oral antibiotics in the telemedicine setting AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 24						

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Disclaimer SAY: Please review this disclaimer.	Slide 25 Disclaimer - The findings and recommendations in this presentation are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this presentation should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services. - Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications and/or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities. AHRQ Safety Program for Telemedicine: Improving Antibiotic Use Antibiotics and What They Treat 25
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