trchealthcare

New Drug

Ceftobiprole Medocaril (Zevtera)

Why it matters:

Antibiotic options are limited for treating methicillin-resistant *Staphylococcus aureus* (MRSA) infections. Ceftobiprole medocaril is a prodrug of active ceftobiprole and is the second available IV cephalosporin antibiotic that can target MRSA, similar to ceftaroline.

What else to know:

Ceftobiprole may cause nausea, vomiting, anemia, or liver injury. Avoid use in ventilator-associated pneumonia since studies suggest ceftobiprole may have higher mortality.

Manufacturer	Basilea Pharmaceutica International Ltd
Approved use	• *Staphylococcus aureus* bacteremia (including MRSA) in adults. • Acute bacterial skin and skin structure infections in adults. • Community-acquired pneumonia (CAP) in ages 3 months and up.
Approval date	April 2024
Anticipated availability	Available now
Dosage and administration (adults)	• Skin infections and CAP: 667 mg IV every 8 hours. • Blood stream infections: 667 mg IV every 6 hours for 8 days, then 667 mg IV every 8 hours thereafter. • Infuse each dose over 2 hours. • Reduce dose for CrCl <50 mL/min and increase frequency to every 6 hours if CrCl >150 mL/min, regardless of indication.
Storage requirements	• Refrigerate unopened vials and prepared doses at 2 to 8°C and protect from light. • Beyond-use dates for prepared doses range from 24 to 94 hours depending on the diluent and ceftobiprole concentration. • Light protection is not required during administration.
Prescribing information	https://innovivaspecialtytherapeutics.com/products/

Article, *Clarify the Limited Role of Ceftobiprole*. *Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber Insights.* July 2025. [410663]

Ceftobiprole Medocaril (Zevtera)

References:

- Holland TL, Cosgrove SE, Doernberg SB, et al. Ceftobiprole for Treatment of Complicated Staphylococcus aureus Bacteremia. N Engl J Med. 2023 Oct 12;389(15):1390-1401.
- Overcash JS, Kim C, Keech R, et al Ceftobiprole Compared With Vancomycin Plus Aztreonam in the Treatment of Acute Bacterial Skin and Skin Structure Infections: Results of a Phase 3, Randomized, Double-blind Trial (TARGET). Clin Infect Dis. 2021 Oct 5;73(7):e1507-e1517.
- Nicholson SC, Welte T, File TM Jr, et al. A randomised, double-blind trial comparing ceftobiprole medocaril with ceftriaxone with or without linezolid for the treatment of patients with community-acquired pneumonia requiring hospitalisation. Int J Antimicrob Agents. 2012 Mar;39(3):240-6.
- Product information for ceftobiprole medocaril (Zevtera). Basilea Pharmaceutica International Ltd. 4123 Allschwil, Switzerland. April 2024.

Skin and Soft Tissue Infections

The following FAQ addresses common questions about diabetic foot infections, and antibiotic choices for cellulitis/erysipelas and necrotizing infections. A chart, *Antibiotics for MRSA Skin Infections,* is also included to help with choice of antibiotic.

--Information in chart may differ from product labelling. Information pertains to ADULTS--

Clinical Question	Pertinent Information or Suggested Approach
What are some risk factors for **foot infections in patients with diabetes**?	• Poor glycemic control[2] • Peripheral neuropathy, especially with loss of protective sensation[2] • Peripheral artery disease[2] • Foot deformity, corns, or calluses[2] • Previous foot ulceration or amputation[2] • Visual impairment[2] • Chronic kidney disease, especially for patients receiving dialysis[2] • Smoking[2]

What can be done to **prevent foot infections** in patients with **diabetes**?	• Patients should check their feet every day.[2]
	  ○ Palpate the feet.
	  ○ Visually examine all parts of the feet, using a non-breakable mirror as needed.[2]
	  ○ Enlist the help of caregivers (i.e., if the patient has visual, physical, or cognitive problems that impair their ability to assess their feet).[2]
	• Choose appropriate shoes (e.g., well-fitting walking or running shoes; no open-toe sandals).[2]
	  ○ Refer patients who may benefit for specialized shoes or orthotics (e.g., patients with plantar calluses, hammertoes, ulcers, Charcot foot, loss of protective sensation, poor circulation, history of amputation).[2]
	• Patients should avoid going barefoot.[2]
	• Advise use of a moisturizer on dry or scaly skin.[2]
	• Avoid self-treatment of ingrown toenails or calluses.[2]
	• Patients should seek urgent medical care for ulceration, redness, swelling, or skin warmth.[2]
	• Advise a comprehensive foot exam at least yearly (patients with sensory loss or prior ulceration or amputation should have their feet inspected at each visit).[2] This should include:
	  ○ documentation of risk factors.[2]
	  ○ physical exam (10 g monofilament test plus pinprick, temperature, or vibration testing; visual inspection; assessment for deformities; assessment of pulses in legs and feet).[2]
	  ○ inquiry about symptoms (e.g. pain, burning, numbness, leg fatigue, claudication).[2]

Clinical Question	Pertinent Information or Suggested Approach
What topical products have evidence for management of diabetic foot ulcers?	• Treatment of diabetic ulcers includes offloading, revascularization, debridement, treatment of infection, and physiologic wound dressings.[2] • Patients who do not achieve a 50% reduction of wound area within four weeks can be referred for "advanced" wound management.[2] o Evidence from placebo-controlled RCTs to guide selection of advanced wound therapies is lacking.[2] o Interventions with the most evidence include placental membranes, bioengineered skin substitutes, acellular matrices, and autologous platelet/leukocyte/fibrin patches.[2] Topical antibiotics or antiseptics, honey, negative pressure devices, topical or hyperbaric oxygen lack convincing evidence.[1]
How are diabetic foot infections classified?	• **Mild infections** only involve the skin or subcutaneous tissue; there are no systemic signs or symptoms.[1] Two or more of the following are present: erythema extending >0.5 to <2 cm from the wound margin; local swelling or induration; local tenderness or pain; warmth; and/or purulent discharge.[1] • **Moderate infections** have erythema extending ≥2 cm from the wound margin, and/or involve bone, joint, tendon, or muscle, without systemic symptoms.[1] • **Severe infections** are any foot infection with ≥2 of the following: temp >38°C or <36°C; heart rate >90 beats per minute; respiratory rate >20 breaths per minute or PaCO2 <32 mmHg; WBC >12,000 per mcL or <4,000 per mcL, or ≥10% bands.[1]
What are the **empiric** antibiotic choices for **diabetic foot infections**? *Continued…*	• General considerations: o Consult surgery for patients with severe infection or moderate infection with extensive gangrene, severe ischemia, necrotizing infection, deep abscess, or compartment syndrome.[1] o Choose empiric coverage based on likely organisms, cost, adverse effects, allergies, and infection severity.[1] o Switch to targeted coverage when culture and sensitivity results (of **tissue** collected aseptically with biopsy or curettage) are available.[1] o Generally use IV instead of oral antibiotics in severe infections, or unless stepping down (when improving).[1,30] o Consider hospitalization for IV antibiotics (at least initially) in moderate infections in patients with severe peripheral artery disease or problems with adherence.[1] o Dose antibiotics as for serious infection, with dose adjustment for comorbidities (e.g., kidney insufficiency).[1] o Empiric coverage of *Pseudomonas* is not routinely needed in North America.[1] o Continue antibiotics for mild cases for one to two weeks (10 days post-debridement), or two to four weeks for more severe cases (IV initially, then oral).[1] Duration will be different for patients with bone or joint involvement.[1] • For **mild** infections, usually choose oral agents that cover streptococci and staphylococci (e.g., dicloxacillin [US], cloxacillin [Canada], cephalexin).[1] o For patients who cannot take a beta-lactam, options might include clindamycin,[a] TMP/SMX, doxycycline, levofloxacin, or moxifloxacin.[1]

Clinical Question	Pertinent Information or Suggested Approach
Empiric antibiotic choices for **diabetic foot infections,** continued	• **MRSA** coverage is recommended in: o mild infection with history of MRSA infection or colonization (oral).[1] ▪ Options might include clindamycin,[a] TMP/SMX, doxycycline, linezolid, levofloxacin, or moxifloxacin.[1] o moderate or severe infection and history of MRSA infection or colonization, or MRSA risk factors (e.g., recent antibiotic use or invasive procedure, recent hospital or nursing home stay, hemodialysis, HIV, long-term central venous access, open wounds.[1] ▪ Options might include TMP/SMX, doxycycline, vancomycin, linezolid, or daptomycin.[1] • **Gram negative** coverage is recommended or should be considered in certain scenarios:[1] o moderate or severe infection with no complicating factors. Options might include amoxicillin/clavulanic acid, ampicillin/sulbactam, cefuroxime, cefotaxime, ceftriaxone.[1] o **recent antibiotic exposure** and:[1] ▪ mild infection. Oral options might include amoxicillin/clavulanic acid, TMP/SMX, levofloxacin, or moxifloxacin.[1] ▪ moderate or severe infection (consider expert consult).[1] Options might include ticarcillin/clavulanic acid, piperacillin/tazobactam, cefuroxime, cefotaxime, ceftriaxone, or ertapenem.[1] o moderate or severe infection with risk factors for ESBL-producers.[1] Consider expert consult. Options might include ertapenem, meropenem, imipenem/cilastatin, ciprofloxacin, amikacin, colistin.[1] o moderate or severe infection with suspicion of *Pseudomonas* (macerated ulcer, warm climate, water immersion).[1,30] Options might include ticarcillin/clavulanic acid, piperacillin/tazobactam, meropenem, or imipenem/cilastatin.[1] o moderate or severe infection with ischemia, limb necrosis, or gas formation (gangrene).[1] Urgent surgical consultation is recommended for extensive gangrene, deep abscess, compartment syndrome, severe ischemia.[1] Consider anerobic coverage as well.[1] (Necrotizing infections are covered in a separate section below.) Antibiotic options might include amoxicillin/clavulanic acid, ampicillin/sulbactam, ticarcillin/clavulanic acid, piperacillin/tazobactam, ertapenem, meropenem, imipenem/cilastatin, or cephalosporin (cefuroxime, cefotaxime, ceftriaxone) plus clindamycin[a] or metronidazole.[1]
What antibiotics may be appropriate for **empiric** treatment of **cellulitis** and **erysipelas** (non-necrotizing)? *Continued…*	• General considerations: o Usually choose agents that cover *Streptococcus pyogenes*, or perhaps staphylococci (e.g., for **purulent** infections).[3,5] Due to the difficulty of determining the causative bacteria in most cellulitis cases, prescribers may choose antibiotics that target both.[25] o *Streptococcus pyogenes* is susceptible to beta-lactams.[25] o Consider MRSA coverage for severe penetrating trauma, injection drug use, unhoused persons, military personnel, correctional facility residents, athletes, history of MRSA infection or colonization, prior hospitalization for skin or soft tissue infection, antibiotic use in the past six months, recent invasive procedure (e.g., dialysis), severe infections, septic shock, age <2 yrs or >65 yrs, purulent infections, or facial erysipelas.[4-6,8]

Clinical Question	Pertinent Information or Suggested Approach
Antibiotics that may be appropriate for **empiric** treatment of **cellulitis** and **erysipelas** (non-necrotizing), continued	○ Patients with diabetes may need additional coverage (e.g., for Enterobacterales and anaerobes).[5] ○ Orbital or periorbital cellulitis may also involve *Haemophilus influenzae*, *Moraxella catarrhalis*, other gram negatives (post-trauma), or anaerobes (dental source).[5] ○ Consider additional organisms in specific situations (e.g., bite wounds, fresh water [e.g., *Aeromonas* spp; may cause necrotizing infection]; sea water or seafood exposure [*Vibrio* spp. may cause necrotizing infection])[4,6,7] ○ Associated abscess (e.g., due to staph) will require incision and drainage.[5,6] • **Milder infection** ○ A 5-day course of an oral beta-lactam (penicillin VK, amoxicillin, dicloxacillin [US]. cephalexin) may be sufficient.[3-6,25] For patients who cannot take a beta-lactam, options might include azithromycin, clindamycin,[a] linezolid, tedizolid (US), or omadacycline (US).[5,25] ▪ For MRSA coverage, options include TMP/SMX, doxycycline, clindamycin,[a] minocycline, linezolid, tedizolid (US), delafloxacin (US), or omadacycline.[5,6,8,9] ○ For mild **peri**orbital cellulitis (no systemic signs of infection), expand coverage to amoxicillin/clavulanic acid, cefpodoxime, or cefdinir (plus TMP/SMX or linezolid if MRSA coverage is needed).[5] ○ For patients with **diabetes** and mild infection (outpatient treatment), TMP/SMX should be added to penicillin VK or cephalexin.[5] Omadacycline is another option.[5] • **More severe infection** (i.e., signs of systemic infection[25])(necrotizing infections are discussed in a separate section below) ○ Moderate to severe infection: options might include IV penicillin, cefazolin, ceftriaxone, nafcillin (US), oxacillin (US).[5,6] Alternatives for patients with serious beta-lactam allergy include vancomycin, linezolid, or clindamycin.[5,6,a] ▪ For **MRSA** coverage, options include vancomycin, linezolid, daptomycin, ceftaroline, telavancin, dalbavancin, and ortiavancin.[5,6,9] ○ For severe infection, consider expanding empiric coverage by using vancomycin plus piperacillin/tazobactam.[4] For information on necrotizing infections, see the section below. ○ For orbital cellulitis (consult surgery) or periorbital cellulitis, consider vancomycin **plus** piperacillin/tazobactam or ampicillin/sulbactam or ceftriaxone and metronidazole.[5] For patients with serious beta-lactam allergy, add moxifloxacin to vancomycin in place of a beta-lactam.[5] Linezolid or daptomycin are vancomycin alternatives.[5] ○ For patients with diabetes, consider coverage for Enterobacterales (carbapenem, levofloxacin, or piperacillin/tazobactam) and staph (vancomycin, linezolid, or daptomycin).[5]

Clinical Question	Pertinent Information or Suggested Approach
What antibiotics may be appropriate for **empiric** treatment of **necrotizing** infections?	• In addition to rapid introduction of appropriate IV broad-spectrum antibiotics, surgical intervention is required.[1,6,29] • **Broad spectrum antimicrobial coverage is needed empirically**, including *Streptococcus pyogenes*, MRSA, gram negatives, and anaerobes.[5,6] o Consider vancomycin, linezolid, or daptomycin **plus** piperacillin/tazobactam, a carbapenem, or ceftriaxone plus metronidazole).[4-6] Add clindamycin,[a] or include linezolid, if a toxin-producer is suspected (see below).[5,6] • Consider coverage for *Aeromonas* (e.g., doxycycline plus ciprofloxacin) in cases involving fresh or brackish water exposure, or *Vibrio* in cases involving sea water or seafood exposure.[4,6,7] o For information on *Vibrio* treatment from the CDC, see https://www.cdc.gov/vibrio/healthcare.html. • Include a protein synthesis inhibitor (e.g., clindamycin,[a] linezolid) to block bacterial toxin production if any of the following bacteria are suspected (e.g., in rapidly progressive, severe infection; suggestive gram stain):[5,6,29] o For staph coverage in staphylococcal toxic shock syndrome (e.g., hypotension, fever, organ failure, macular rash, and later desquamation of the palms and soles), consider including vancomycin plus clindamycin,[a] or linezolid.[5,6] o *S. pyogenes* may be covered with high-dose IV penicillin (24 million units/day[c]) or ampicillin, plus high-dose clindamycin[a] (900 mg IV q8h[c]).[5,6,29] For severe necrotizing fasciitis or streptococcal toxic shock syndrome (e.g., hypotension, nausea, vomiting, diarrhea, kidney and/or respiratory failure, erythroderma), consider adjunctive IVIG (0.5 g/kg x 1, then 25 g on days 2 and 3[c]).[5,6,29] o *Clostridium* may be covered with high-dose IV penicillin plus a protein synthesis inhibitor (e.g., clindamycin[a]).[4,6]
How do **antibiotics for MRSA** compare?	See the chart below, Antibiotics for MRSA Skin Infections, below.
How is **impetigo** treated?	• Antibiotic treatment, whether oral or topical, should be aimed at both *Streptococcus pyogenes* and *Staphylococcus. aureus*. Topical antibiotics may be used when there are only a few lesions, while oral antibiotics are used for multiple lesions.[26] • Topical options: mupirocin, fusidic acid [Canada], retapamulin [*Altabax*, US].[8,27] o Ozenoxacin (*Xepi* [US]; *Ozanex* [Canada]) is not first-line due to high cost and lack of head-to-head studies with older agents.[27] The tube size available in Canada may not be sufficient for more than one treatment course in the event of recurrence.[27] • Oral options: dicloxacillin, cephalexin, erythromycin (some *Streptococcus pyogenes* and *Staphylococcus aureus* may be resistant), clindamycin,[a] amoxicillin-clavulanic acid.[4]

--Continue to the section below for a chart, *Antibiotics for MRSA Skin Infections*---

Antibiotics for MRSA Skin Infections

Drug	Considerations and Dosing[b]	Cost (see footnote d)
Ceftaroline (*Teflaro* [US])	• Parenteral formulation only. • Approved for acute bacterial skin and skin structure infections caused by *Staphylococcus aureus* (including MRSA), *E. coli*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca*.[10,b] • Potential for cross-sensitivity in patients with beta-lactam allergy.[10] • Usual adult dose 600 mg IV Q12H.[10] Reduce dose for CrCl ≤50 mL/min.[10]	$490.40/day. Approved duration of therapy 5 to 14 days.[10]
Clindamycin	• Parenteral and oral formulations available. • Approved for skin and soft tissue infections with *Streptococcus pyogenes*, *Staphylococcus aureus*, and anaerobes.[11-13,b] • Usual adult PO dose: 300 to 450 mg Q6H.[4] • Adult dose for necrotizing infections: 900 mg IV Q8H.[5] • Bacteriostatic.[4] • See **footnote a** regarding resistance concerns.	**US**: ~$30/day (IV); <$10/day (PO) **Canada**: ~$75/day (IV), <$5/day (oral)
Dalbavancin (*Dalvance* [US], *Xydalba* [Canada])	• Parenteral formulation only. • A lipoglycopeptide approved for skin and soft tissue infections with Staphylococcus aureus (including MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus anginosus* group, and vancomycin-sensitive Enterococcus faecalis.[14,15,b] • Insufficient data for diabetic foot infection to recommend.[1] • 1,500 mg x 1, OR 1,000 mg on day one, then 500 mg on day eight.[14,15] Reduce dose for CrCl <30 mL/min.[14,15] • Because it can be given as a one-time infusion, could be used for moderately ill patients with cellulitis who refuse hospitalization, or for an outpatient who might be nonadherent.[5]	**US**: $5,337.39/course of therapy **Canada**: ~$3,101.22
Daptomycin (*Cubicin* [Canada], *Cubicin RF* [Canada], generics)	• Parenteral formulation only. • A cyclic lipopeptide approved for complicated skin and soft tissue infections caused by *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, (US: *Streptococcus dysgalactiae* subspecies *equisimilis*, and vancomycin-sensitive *Enterococcus faecalis*).[16,17,b] • Usual adult dose is 4 mg/kg Q24H.[16,17] Reduce dose for CrCl <30 mL/min.[16,17] • Check creatine phosphokinase weekly (more often in kidney impairment or recent statin users) and monitor for muscle pain or weakness. Also monitor for peripheral neuropathy.[16,17]	**US**: ~$55/day (for 70 kg adult); **Canada**: ~$98; Approved duration of therapy seven to 14 days.[16,17]

Drug	Considerations and Dosing[b]	Cost (see footnote d)
Delafloxacin (*Baxdela* [US])	• Parenteral and oral formulations available • A **quinolone** approved for skin and soft tissue infections with *Staphylococcus aureus* (including MRSA), *Staphylococcus haemolyticus*, *Staphylococcus lugdunensis*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group, *Enterococcus faecalis*, *E. coli*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*.[28,b] • Usual adult dose: 300 mg IV Q12H or 450 mg PO Q12H[28] • Reduce **IV** dose if eGFR <30 mL/min/1.73 m^2, due to accumulation of the IV vehicle.[16] Do not use oral or IV delafloxacin if eGFR <15 mL/min/1.73 m^2.[28] • Typical quinolone warnings: tendinitis/tendon rupture, peripheral neuropathy, central nervous system effects.[28] Interacts with di- and trivalent cations (e.g., in antacids, sucralfate, multivitamins, iron supplements).[28] • Does not appear to cause significant CYP450 drug interactions, QT prolongation, or phototoxicity.[28]	~$142/day (IV), ~$160/day (oral) Approved duration of therapy five to 14 days.[28]
Doxycycline	• Parenteral (US) and oral formulations available. • An option for MRSA coverage in diabetic foot infections or milder cellulitis.[1,6] • Usual adult dose: 100 mg PO Q12H[4]	**US**: ~$40/day (IV), <$10/day (oral) **Canada**: <$1/day (oral)
Linezolid (*Zyvox*, *Zyvoxam*, generics)	• Parenteral and oral formulations available. Approved duration of therapy 10 to 14 days (14 to 28 for VRE).[18,19] • An oxazolidinone approved for complicated skin and soft tissue infections (including diabetic foot infections without osteomyelitis) with *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*.[18,19,b] Also approved for uncomplicated infections caused by MSSA and *S. pyogenes*, and infections caused by VRE.[18,19,b] • Usual adult dose 600 mg IV or PO Q12H.[18,19] • Myelosuppressive; CBC required at least weekly.[18,19] • Linezolid is an MAO inhibitor and has serotonergic effects; screen for drug interactions.[18,19]	**US**: ~$90/day (IV); ~$15/day (oral); **Canada**: ~$230 (IV), ~$40/day (oral) Approved duration of therapy 10 to 14 days (14 to 28 days for diabetic foot infection [Canada] or VRE)[18,19]
Minocycline	• An option for MRSA coverage in milder cellulitis.[6] • Oral formulation only. • Usual adult dose 100 mg PO Q12H.[4]	US: <$10/day **Canada**: <$5/day

Drug	Considerations and Dosing[b]	Cost (see footnote d)
Omadacycline (*Nuzyra* [US])	• Parenteral and oral formulation available • An aminoethylcycline (a type of tetracycline) approved for acute bacterial skin and soft tissue infections caused by *Staphylococcus aureus* (including MRSA), *Staphylococcus lugdunensis*, *Streptococcus pyogenes*, *Streptococcus anginosu*s group, *Enterococcus faecalis*, *Enterobacter cloacae*, and *Klebsiella pneumoniae*.[20,b] • Usual adult IV dose: 200 mg on day one (200 mg x 1 or two separate 100 mg doses), then 100 mg Q24H.[20] • Usual adult PO dose: 450 mg Q24H x 2 days, then 300 mg Q24H.[20] • Potential for permanent tooth discoloration if used during the last half of gestation up to age eight years, or reversible inhibition of bone growth if used during the second or third trimesters, up to age eight years.[20] Breastfeeding is not recommended during treatment and for four days after the last dose.[20] • Nausea (incidence up to 30%) and vomiting (incidence up to 17%) appear to be more common in patients after an oral loading dose.[20] • No dosage adjustments needed in patients with kidney or liver impairment.[20]	~$437/day (IV), ~$510/day (oral). Approved duration of therapy seven to 14 days.[20]
Oritavancin (*Orbactiv* [US])	• Parenteral formulation only (single dose).[21] • Approved for skin and soft tissue infections caused by *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group, *Streptococcus dysgalactiae*, and vancomycin susceptible Enterococcus faecalis.[21,b] • Long-acting (dose is 1,200 mg x 1, over three hours[c]).[21] Could be used for moderately ill patients with cellulitis who refuse hospitalization, or for an outpatient who might be nonadherent.[5] • Insufficient data for diabetic foot infections to recommend.[1] • IV heparin contraindicated for five days after use due to artificial increases in coagulation tests. Affects aPTT for up to five days and PT/INR for up to 12 hours after administration.[21] • May cause infusion reaction (flushing, itching, rash). Stop or slow infusion if this occurs.[21]	~$3,500/dose. Single-dose treatment.[21]
Tedizolid (*Sivextro* [US])	• Parenteral and oral formulations available. • An oxazolidinone approved for skin and soft tissue infections caused by *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group, and *Enterococcus faecalis*.[22,b] • Usual adult dose: 200 mg Q24H (IV or PO).[22] • May have less tendency for interactions with MAO inhibitors and selective serotonin reuptake inhibitors (SSRIs) than linezolid.[23] • No CBC monitoring required.[22]	~$350/dose (IV) ~$420/day (oral). Approved duration of therapy six days.[22]

Drug	Considerations and Dosing[b]	Cost (see footnote d)
Telavancin (*Vibativ* [US])	• Parenteral formulation only. • A lipoglycopeptide approved for complicated skin and soft tissue infections caused by *Staphylococcus aureus* (including MRSA), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group, and vancomycin-sensitive Enterococcus faecalis.[24,b] • Usual adult dose: 10 mg/kg IV Q24H.[24] Reduce dose for CrCl ≤50 mL/min.[24] • May cause infusion reaction (flushing, itching, rash).[24] Stop or slow infusion if this occurs.[24] • May cause kidney toxicity; monitor serum creatinine.[24]	~$550/day (for 70 kg patient). Approved duration of therapy seven to 14 days.[24]
TMP/SMX	• Parenteral and oral formulations available. • An option for MRSA coverage in diabetic foot infections, and milder cellulitis.[1,5] • Usual adult PO dose: one or two double-strength tablets Q12H.[4] • Usual adult IV dose: 8 to 10 mg/kg (TMP component) divided Q8H to Q12H.[9] • Reduce for CrCl <30 mL/min.[9] • TMP may cause hyperkalemia.[9]	**US**: ~$50/day (for 320 mg IV Q12 H); <$10/day (oral) **Canada**: $80/day (for 320 mg IV Q12H [*Septra*]); <$1/day oral)
Vancomycin	• Parenteral formulation only. • An option for moderate or severe skin infections.[1,4-6] • Consider a target AUC 400 to 600 mcg/mL or trough 15 to 20 mcg/mL),[5] • May cause vancomycin infusion reaction (e.g., flushing, hypotension, itching) if infused too rapidly (e.g., >10 mg/min).[9]	**US**: <$60/day (for 1 g IV Q12 H) **Canada**: ~$40/day (for 1 g IV Q12H)

Abbreviations: CBC = complete blood count; ESBL = extended-spectrum beta-lactamase; H = hours; HIV = human immunodeficiency virus; MAO = monoamine oxidase; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*; PO = oral; Q = every; SIRS = systemic inflammatory response syndrome; TMP/SMX = trimethoprim/sulfamethoxazole; VRE = vancomycin-resistant *Enterococcus*

a. Clindamycin: *Streptococcus pyogenes* may be resistant to clindamycin; consider local resistance patterns and use with caution in severe cases.[6] MRSA resistance to clindamycin can be inducible, so some isolates that show sensitivity *in vitro* may not be clinically susceptible to clindamycin.[4] Erythromycin-resistant MRSA may also be resistant to clindamycin.[4] The lab can use the "D test" to check for inducible resistance.[5] There is also a concern for *Clostridioides difficile* colitis.[8]
b. Bacterial coverage noted in the chart may not reflect the full spectrum of coverage for each drug.
c. Dosing is for adults.
d. Wholesale acquisition cost (WAC) of adult dose denoted. US medication pricing by Elsevier, accessed January 2024.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

References

1. Senneville É, Albalawi Z, van Asten SA, et al. IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections (IWGDF/IDSA 2023). Clin Infect Dis. 2023 Oct 2:ciad527.
2. American Diabetes Association Professional Practice Committee. 12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S231-S243. doi: 10.2337/dc24-S012.
3. Brindle R, Williams OM, Barton E, Featherstone P. Assessment of Antibiotic Treatment of Cellulitis and Erysipelas: A Systematic Review and Meta-analysis. JAMA Dermatol. 2019 Sep 1;155(9):1033-1040.
4. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis. 2014 Jul 15;59(2):147-59.
5. Gilbert DN, Chambers HF, Eliopoulos GM, et al, Eds. Sanford Guide Web Edition. Sperryville, VA: Antimicrobial Therapy, Inc., 2024. http://webedition.sanfordguide.com/. (Accessed January 6, 2024).
6. Duane TM, Huston JM, Collom M, et al. Surgical Infection Society 2020 Updated Guidelines on the Management of Complicated Skin and Soft Tissue Infections. Surg Infect (Larchmt). 2021 May;22(4):383-399.
7. Naidoo S, Zwane AM, Paruk A, Hardcastle TC. Diagnosis and Management of Severe Water-Related Skin and Soft Tissue Sepsis: A Summative Review of the Literature. Diagnostics (Basel). 2023 Jun 23;13(13):2150.
8. Kosar L, Laubscher T. Management of impetigo and cellulitis: Simple considerations for promoting appropriate antibiotic use in skin infections. Can Fam Physician. 2017 Aug;63(8):615-618.
9. Clinical Pharmacology powered by ClinicaKey. Tampa (FL): Elsevier. 2024. http://clinicalkey.com (Accessed January 10, 2024).
10. Product information for *Teflaro*. Allergan USA. Madison, NJ 07940. December 2021.
11. Product information for Cleocin hydrochloride. Pfizer. New York, NY 10017. May 2022.

12. Product information for Cleocin phosphate. Pfizer. New York, NY 10017. May 2022.
13. Product monograph for Dalacin C phosphate. Pfizer Canada. Kirkland, QC H9J 2M5. January 2022.
14. Product information for Dalvance. Allergan. Madison, NJ 07940.July 2021.
15. Product monograph for Xydalba. Paladin Labs. St. Laurent, QC H4M 2P2. April 2021.
16. Product information for daptomycin. Xellia Pharmaceuticals USA. Buffalo Grove, IL 60089. January 2023.
17. Product monograph for Cubicin/Cubicin RF. Sunovion Pharmaceuticals Canada. Mississauga, ON L5N 0E8. May 15, 2020.
18. Product information for Zyvox. Pfizer. New York, NY 10017. July 2023.
19. Product monograph for Zyvoxam. Pfizer Canada. Kirkland, QC H9J 2M5. November 2022.
20. Product information for Nuzyra. Parateck Pharmaceuticals. Boston, MA 02116. May 2021.
21. Product information for Orbactiv. Melinta Therapeutics. Lincolnshire, IL 60069. January 2022.
22. Product information for Sivextro. Merck Sharp & Dohme. Rahway, NJ 07065. March 2023.
23. Durkin MJ, Corey GR. New developments in the management of severe skin and deep skin structure infections - focus on tedizolid. Ther Clin Risk Manag. 2015 May 22;11:857-62.
24. Product information for Vibativ. Cumberland Pharmaceuticals. Nashville, TN 37203. November 2023.
25. CDC. Group A Streptococcal (GAS) disease. Cellulitis. June 27, 2022. https://www.cdc.gov/groupastrep/diseases-hcp/cellulitis.html#anchor_1588878009926. (Accessed January 11, 2024).
26. CDC. Group A Streptococcal (GAS) disease. Impetigo. June 27, 2022. https://www.cdc.gov/groupastrep/diseases-hcp/cellulitis.html#anchor_1588878009926. (Accessed January 12, 2024).
27. Clinical Review Report: Ozenoxacin 1% Cream (Ozanex): (Ferrer Internacional, S.A.): Indication: The topical treatment of impetigo in patients aged two months and older [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018 Oct. PMID: 30942991.
28. Product information for Baxdela. Melinta Therapeutics. Lincolnshire, IL 60069. June 2021.
29. CDC. Group A Streptococcal 9GAS) disease. Type II necrotizing fasciitis. https://www.cdc.gov/groupastrep/diseases-hcp/necrotizing-fasciitis.html#treatment. Accessed January 12, 2024.
30. Weintrob AC, Sexton DJ. Clinical manifestations, diagnosis, and management of diabetic infections of the lower extremities. (Last updated March 7, 2023). In UpToDate, Post TW (ed), UpToDate, Waltham, MA 02013.

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Managing Community-Acquired Pneumonia and Aspiration Pneumonia in Adults

last modified June 2025

The chart below is based on the 2019 guideline for the management of community-acquired pneumonia in adults from the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA).[1] Antibiotic dosing is provided for **adults**. The second chart below provides answers to common questions about aspiration pneumonia.

Community-Acquired Pneumonia Treatment Basics
• The **need for hospitalization** should be based on clinical judgment plus results of a validated prognostic tool.[1] Use of the PSI is recommended over CURB-65.[1] PSI is better than the CURB-65 at identifying patients who can safely be treated as outpatients, but CURB-65 is easier to use.[1] PSI may underestimate severity in younger patients.[1] The PSI is available at https://www.mdcalc.com/psi-port-score-pneumonia-severity-index-cap and the CURB-65 is available at https://www.mdcalc.com/curb-65-score-pneumonia-severity.
• Patients with **severe pneumonia** are typically those requiring intensive/critical care. See **footnote b** for guideline criteria for severe pneumonia.
• Patients with CAP should be treated with antibiotics **for at least five days** (**seven days** for MRSA or *Pseudomonas*).[1] Antibiotics should not be stopped **until the patient is clinically stable**.[1] This means abnormalities in vitals (heart rate, blood pressure, respiratory rate, oxygen saturation, body temperature) and cognition have resolved, and the patient is eating.[1]
• The most common **bacterial causes** of community-acquired pneumonia in outpatients are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, *Legionella* species, *Chlamydia pneumoniae*, and *Moraxella catarrhalis*.[1]
• It is suggested that anaerobic coverage not be routinely added in cases of **aspiration pneumonia** unless lung abscess or empyema is suspected.[1] Our chart below covering aspiration pneumonia has more considerations.
• **Blood culture** yield is low in patients with nonsevere CAP.[1] Blood cultures are not recommended in outpatients, and it is suggested that they not be routinely done in the hospital setting in nonsevere CAP.[1] Blood cultures are recommended in severe CAP, and in patients being treated empirically for, or previously infected with, *Pseudomonas aeruginosa* or MRSA, or who had been hospitalized and received parenteral antibiotics within the prior 90 days.[1]
• **Sputum gram stain and culture** is recommended in severe CAP, in patients being treated empirically for, or previously infected with, *Pseudomonas aeruginosa* or MRSA, and perhaps in those hospitalized and treated with antibiotics within the prior 90 days.[1] Collection of lower respiratory tract secretions for *Legionella* culture or nucleic acid amplification testing is suggested in severe CAP.[1]
• **Urine antigen testing** for *Pneumococcus* and *Legionella* is suggested in severe CAP.[1] *Legionella* testing is also suggested if epidemiology indicates exposure (e.g., travel or overnight stay in a healthcare facility in the previous 14 days; outbreak).[1,2]
• If **influenza** is circulating in the community, testing with a rapid molecular assay (preferred over an antigen test) is suggested.[1] Coverage for influenza is suggested for outpatients who test positive, and is recommended for inpatients who test positive.[1]
• **Procalcitonin** is not recommended to determine need for initial, empiric antibiotic treatment (**see footnote g**).[1]
• Guidelines suggest not using **corticosteroids routinely** for severe CAP.[1] See **footnote f** for newer data and situations where they might be considered.

Patient Characteristics (see footnote a)	**Outpatient Oral Antibiotic Regimen (see footnote a)**

Previously healthy without comorbidities (see below) and without risk factors for *Pseudomonas aeruginosa* or MRSA (e.g., prior respiratory isolation of MRSA or *Pseudomonas aeruginosa*, or hospitalization and receipt of parenteral antibiotics within the 90 days prior. See **footnote d** for additional risk factors).	• Amoxicillin 1 g TID (high dose targets resistant *Streptococcus pneumoniae*[3])
	OR
	• Macrolide (if local pneumococcal resistance is <25% [resistance is >30% in most of US])
	  • Azithromycin 500 mg x 1, then 250 mg once daily, or
	  • Clarithromycin 500 mg BID or 1,000 mg once daily (extended-release)
	OR
	• Doxycycline 100 mg BID (less data) (consider a loading dose of 200 mg)
	
	Note: patients with risk factors for MRSA or *Pseudomonas* are not commonly managed as outpatients, but if they are, they will need coverage for these pathogens as well.

With comorbidities:
• Heart disease
• Lung disease
• Liver disease
• Kidney disease
• Diabetes
• Alcoholism
• Cancer
• Asplenia
 	
Regimens for patients with comorbidities target resistant *Streptococcus pneumoniae*, atypicals, beta-lactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis*, enteric gram negatives, and methicillin-susceptible *Staphylococcus aureus*.
	Beta-lactam
	• Amoxicillin/clavulanate (500 mg/125 mg TID or 875 mg/125 mg BID, 2,000 mg/125 mg BID)
	OR
	• Cephalosporin (cefpodoxime 200 mg BID or cefuroxime axetil 500 mg BID)
	PLUS
	Macrolide
	  • Azithromycin 500 mg x 1, then 250 mg once daily, or
	  • Clarithromycin 500 mg BID or 1,000 mg once daily (extended-release)
	OR
	Doxycycline 100 mg BID (less data) (consider a loading dose of 200 mg)
	
	OR
	
	Monotherapy with a respiratory quinolone: levofloxacin 750 mg once daily, moxifloxacin 400 mg once daily, gemifloxacin 320 mg once daily (US), delafloxacin 450 mg orally every 12 h[5] (US; new indication post-guideline publication[5]). Consider adverse effects.
	
	Note: patients with risk factors for MRSA or Pseudomonas are not commonly managed as outpatients, but if they are, they will need coverage for these pathogens as well.

a. If the patient has recently received (i.e., within the past 90 days) an antibiotic, pick an option from a different class.[1,3] Dosing is for oral tablets/capsules for **adults** with normal kidney/liver function. Based on ATS/IDSA guideline unless otherwise referenced. Information may differ from product labeling. Most antibiotics available generically, at lower cost. Brand only available for gemifloxacin (*Factive*, US).

Patient Characteristics (see footnote c)	Inpatient Antibiotic Regimen (see footnote c)
Nonsevere pneumonia without risk factors for Pseudomonas aeruginosa or MRSA (e.g., prior respiratory isolation of MRSA or Pseudomonas aeruginosa, or hospitalization and receipt of parenteral antibiotics within the 90 days prior. **See footnote d** for additional risk factors.)	**Beta-lactam** • Ampicillin/sulbactam (1.5 to 3 g every 6 h) OR • Cephalosporin (cefotaxime 1 to 2 g every 8 h, ceftriaxone 1 to 2 g once daily, or ceftaroline 600 mg every 12 h [US], or possibly ceftobiprole 667 mg every 8 h [US][19]). **PLUS** **Macrolide** • Azithromycin 500 mg once daily, or • Clarithromycin 500 mg BID OR **Doxycycline** 100 mg BID (less data) **OR** **Monotherapy with a respiratory quinolone**: levofloxacin 750 mg once daily, moxifloxacin 400 mg once daily, or delafloxacin 300 mg IV every 12 h[5] (US; new indication post-guideline publication[5]). Evidence favors beta-lactam/macrolide combination. Consider adverse effects.
Severe pneumonia without risk factors for Pseudomonas aeruginosa or MRSA (e.g., prior respiratory isolation of MRSA or Pseudomonas aeruginosa, or hospitalization and receipt of parenteral antibiotics within the 90 days prior. **See footnote d** for additional risk factors.)	Beta-lactam plus a macrolide, or a beta-lactam plus a respiratory quinolone. Dosing as above. Use of HCAP criteria (e.g., nursing home residence, recent hospitalization) should no longer be used to broaden coverage for resistant organisms (e.g., MRSA, resistant gram negatives), and use of this term is no longer recommended.[1,4]
Prior respiratory isolation of MRSA, or hospitalization and parenteral antibiotics within 90 days prior and locally validated risk factors for MRSA. **See footnote d** for additional risk factors. MRSA coverage generally not needed if nasal swab is negative, especially for nonsevere CAP. If positive, cover pending culture results.	**Prior respiratory MRSA isolation: add** MRSA coverage* to above inpatient regimen and use cultures/nasal PCR to guide need for continuation/discontinuation of MRSA coverage. **Recent hospitalization and parenteral antibiotics and locally validated risk factors for MRSA (see footnote e)** • **Severe** pneumonia: **add** MRSA coverage* to above inpatient regimen and use cultures/nasal PCR to guide need for continuation/discontinuation of MRSA coverage. • **Nonsevere: add** MRSA coverage* to above inpatient regimen only if cultures or PCR are positive. ***MRSA coverage** = linezolid 600 mg BID, or vancomycin 15 mg/kg every 12 h with dose adjusted per levels.

Patient Characteristics (see footnote c)	Inpatient Antibiotic Regimen (see footnote c)
Prior respiratory isolation of Pseudomonas aeruginosa, or hospitalization and parenteral antibiotics within 90 days prior and locally validated risk factors for Pseudomonas aeruginosa. **See footnote d** for additional risk factors to consider.	**Prior respiratory Pseudomonas aeruginosa isolation**: change beta-lactam in above inpatient regimen to one with pseudomonal coverage,** and use cultures/nasal PCR to guide need for continuation/discontinuation of pseudomonal coverage. **Recent hospitalization and parenteral antibiotics and locally validated risk factors for Pseudomonas aeruginosa** (see footnote e) • **Severe** pneumonia: change beta-lactam in above inpatient regimen to one with pseudomonal coverage** and use culture to guide need for continuation/discontinuation of pseudomonal coverage. • **Nonsevere**: change beta-lactam in above inpatient regimen to one with pseudomonal coverage** only if culture-positive. ****Pseudomonal coverage** = piperacillin/tazobactam 4.5 g every 6 h, cefepime 2 g every 8 h, ceftazidime 2 g every 8 h, imipenem 500 mg every 6 h, meropenem 1 g every 8 h, aztreonam 2 g every 8 h

b. ATS/IDSA guideline criteria for **severe pneumonia**: septic shock with need for vasopressors, respiratory failure requiring mechanical ventilation, or three or more minor criteria: respiratory rate ≥30 breaths/min., PaO2/FiO2 ratio ≤250, multilobar infiltrates, confusion or disorientation, BUN ≥20 mg/dL, white blood cell count <4,000 cells/mm^3 (not due to chemo), platelets <100,000/mm^3, core temperature <36°C, hypotension requiring aggressive fluid resuscitation.[1]

c. If the patient has recently received (i.e., within the past 90 days) an antibiotic, pick an option from a different class.[1,3] Dosing is for adults with normal kidney/liver function. Based on ATS/IDSA guideline unless otherwise referenced. Information may differ from product labeling. Most antibiotics available generically, at lower cost. Brand only available for ceftaroline (*Teflaro* [US]) and ceftobiprole (*Zevtera* [US]).

d. **Examples of additional risk factors to consider:** COPD with bronchiectasis, chronic kidney disease, antibiotic use within the past 30 to 60 days, tube feeding, nursing home residence.[7,11] Nursing home residence is not consistently a risk factor.[7]

e. **"Local validation"** means using local data to determine the prevalence of MRSA and *Pseudomonas* patients with CAP and identifying risk factors for infection locally (e.g., at your local hospital). If local data are unavailable and empiric coverage for MRSA or *Pseudomonas* is instituted on the basis of published risk factors (e.g., footnote d), continue or deescalate the regimen based on culture results.[1]

f. Role of **corticosteroids**. Corticosteroids can be considered in refractory septic shock, patients on high-flow supplemental oxygen, a pneumonia severity score over 130, and for steroid-responsive comorbidities (e.g., COPD, asthma, autoimmune disease, etc).[1,12] Corticosteroids may reduce mortality in severe CAP (NNT = 18), although mortality benefit is not consistent across studies.[1,8] Another, larger study showed reduction in mortality with early initiation of hydrocortisone in one in 17 ICU patients (N = 795).[12] Corticosteroids may reduce time to clinical stability and length of stay by about one day, and reduce the need for mechanical ventilation.[6,9] More study is needed to identify which subgroups benefit the most (e.g., patients with high inflammatory response).[10] Consider corticosteroids for patients who are clinically unstable or not responding to treatment, and perhaps those with elevated markers of inflammation (e.g., C-reactive protein).[6,9,10]

g. Empiric antibiotics should be started if CAP is clinically suspected and radiographically confirmed, regardless of **procalcitonin** level; new evidence suggests that sensitivity is inadequate to determine when initial antibiotic therapy can be safely deferred in this setting.[1]

Aspiration Pneumonia	
Question	**Answer/Pertinent Information**
What is aspiration pneumonia?	• Aspiration pneumonia is a lung infection caused by large-volume inhalation of pathologically-colonized oropharyngeal or upper GI secretions. Think of aspiration pneumonia as part of the pneumonia spectrum including community-acquired pneumonia, and hospital-acquired pneumonia, rather than its own entity.[13] • Microaspiration (small-volume aspiration) of oropharyngeal secretions is normal, especially during sleep. However, microaspiration is involved in the pathogenesis of most pneumonias.[13] • Aspiration pneumonia is DIFFERENT from chemical pneumonitis from aspiration.[13] o Chemical pneumonitis from aspiration leads to **inflammation** due to aspiration of irritating acidic gastric contents.[13] This inflammation can lead to a sudden onset (almost immediate) of symptoms that can easily be confused with pneumonia (e.g., fever, cough, elevated white blood cell count, wheezing, tachycardia).[13,14] Chemical pneumonitis can also appear like acute respiratory distress syndrome (ARDS) with bronchospasms and frothy sputum with bilateral patchy infiltrates on chest x-ray.[15] o Aspiration pneumonia is a **secondary infection** that develops over a few days due to the combination of aspirated microorganisms and damaged lung tissue.[13,14] Infiltrates on chest x-ray may not be seen early in cases of pneumonia.[13] • Aspiration pneumonia is linked to a higher mortality rate (29.4%) compared to community-acquired pneumonia (11.6%).[13]
What are **risk factors** for aspiration pneumonia?	• Patients with multiple risk factors for large-volume aspiration are at increased risk for aspiration pneumonia and death.[13] These risk factors include:[13,15,16] o alcohol use o poor dentition (increases bacterial load, not necessarily risk of aspiration) o dysphagia and gastroesophageal reflux o head, neck, and esophageal cancer o esophageal strictures o chronic obstructive pulmonary disease (COPD) o seizures o degenerative neurologic disease (e.g., multiple sclerosis, Parkinson's disease; dementia) o impaired consciousness o enteral feeding (especially if associated with impaired gastric motility, poor cough reflex, and altered mental status)
How do **chest x-rays** help diagnose aspiration pneumonia?	• Aspiration pneumonia is difficult to diagnose and differentiate from other aspiration syndromes, community-acquired pneumonia, and hospital-acquired pneumonia.[13] • Chest x-rays, along with clinical history, are used to diagnose aspiration pneumonia.[13] • Infiltrates on chest x-ray seen in gravity-dependent locations can be a clue that a patient with pneumonia has an aspiration pneumonia.[13]

Aspiration Pneumonia	
Question	**Answer/Pertinent Information**
	○ Aspiration from a supine position leads to infiltrates in the superior lower lobe or posterior upper lobes.[13] ○ Aspiration from an upright position leads to infiltrates in the basal segments of the lower lobes.[13]
What role do **proton pump inhibitors** play in aspiration pneumonia?	• PPIs reduce gastric acid and have the potential to promote an environment more favorable for bacterial growth in secretions that may be aspirated.[15] • It is not known if PPIs increase the risk of aspiration pneumonia. However, PPIs seem to **reduce** the risk of chemical pneumonitis.[13,15] • See our chart, *Proton Pump Inhibitors: Appropriate Use and Safety Concerns*, for how PPIs impact pneumonias.
What **microorganisms** are typically responsible for aspiration pneumonia?	• The bacteria most often involved in aspiration pneumonia appear to be similar to the bacteria involved in non-aspiration pneumonias.[13] ○ Bacteria associated with **community-acquired cases of aspiration pneumonia** are commonly *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, and Enterobacteriaceae.[13] ○ Bacteria associated with **hospital-acquired cases of aspiration pneumonia** are commonly gram-negative organisms, including *Pseudomonas aeruginosa*.[13] • It was previously thought (i.e., in the 1970s) that anaerobes (alone or in combination with aerobes) were involved in a large number of cases of aspiration pneumonia (45% to 48%).[13,14,17] Common anaerobes include *Bacteroides*, *Peptostreptococcus*, *Porphyromonas*, *Prevotella melaninogenica*, and *Fusobacterium* species.[15]
When should therapy be **started** after aspiration?	• Follow hospital protocols for when to initiate antibiotics with suspected pneumonias. • If it is not clear if a patient has chemical pneumonitis versus aspiration pneumonia after an acute episode of aspiration:[13] ○ Can consider waiting about 48 hours before starting antibiotics in patients who display mild to moderate symptoms if the chest x-ray is clear. ○ Can consider empirically starting antibiotics in patients with severe symptoms. Re-evaluate the need for continued antibiotics in two to three days based on clinical course and chest x-ray.

Aspiration Pneumonia	
Question	**Answer/Pertinent Information**
Which **antibiotics** are most appropriate for suspected aspiration pneumonia?	• Choice of antibiotics will depend on where the pneumonia developed (e.g., community, hospital, long-term care facility), risk factors for resistant infections, and the likelihood that anaerobes are involved.[13] • There are limited data to guide anaerobic coverage when treating pneumonia.[17] Avoid empirically covering for anaerobes in most patients with suspected aspiration pneumonia (including pneumonia patients with aspiration risks) as they may not improve clinical outcomes.[13,17] Instead, choose antibiotics based on hospital protocols for CAP, HAP, and VAP. Consider initially covering for anaerobes in patients with: o risk factors for aspiration AND highest risk for an anaerobic infection (e.g., severe gum disease or poor dentition).[13] o foul smelling sputum or drainage from an abscess or empyema.[17] **Antibiotic Selection** • Most beta-lactam/beta-lactamase inhibitor combos (e.g., piperacillin/tazobactam), carbapenems, and some fluoroquinolones (e.g., moxifloxacin), already cover many anaerobes.[13,15,18,19] (Note ceftazidime/avibactam and levofloxacin, a common formulary fluoroquinolone, should not be used for anaerobic coverage.) In addition, antibiotics used to treat CAP, HAP, or VAP can be changed to an antibiotic that covers typical CAP pathogens and anaerobes. For example, beta-lactams can be changed to ampicillin/sulbactam or amoxicillin/clavulanate.[19] • Note that data using metronidazole to treat pneumonias are very limited. However, if adding specific anaerobic coverage to existing therapy, consider metronidazole over clindamycin. **Metronidazole** has good oral bioavailability (>90%), covers anaerobes from both "**above and below the belt,**" and has a lower risk of *C. difficile* infections compared to clindamycin.[20] **Clindamycin** also has good oral bioavailability (~90%), has a higher risk of *C. difficile* infections, and only covers gram-positive organisms and anaerobes from "above the belt."[21] o If using metronidazole, be sure to combine with a beta-lactam. Metronidazole lacks coverage of organisms commonly associated with pneumonia, such as gram-positive bacteria (e.g., *S. pneumoniae*).[16,19] • Can consider a **fluoroquinolone** (e.g., moxifloxacin [covers anaerobes], levofloxacin plus metronidazole if covering for anaerobes), in patients with a severe penicillin allergy. Also, see our chart, *Managing Beta-Lactam Allergies*, when considering a beta-lactam in a patient who reports a penicillin allergy. **Assessment and Follow-up** • Promote antibiotic stewardship and adjust antibiotic therapy based on culture and sensitivity results. o Sputum cultures are easy to get (noninvasive) and inexpensive, but are often inconclusive. However, they can be used to guide therapy when organisms are able to be identified.[14] • In addition, follow hospital protocols to convert patients to oral therapy once stable, clinically improving, and able to take things by mouth. For example, patients on an intravenous beta-lactam (e.g., ampicillin/sulbactam) can usually be converted to oral amoxicillin/clavulanate.[22]

Aspiration Pneumonia	
Question	**Answer/Pertinent Information**
How long should patients with aspiration pneumonia be treated?	• Treat most patients with aspiration pneumonia like you would for CAP (at least five days) or HAP and VAP (seven days total) [Evidence Level C].[3,13,23] Can consider longer durations of treatment for patients:[13] o who are not responding well to antibiotic therapy. o with necrotizing pneumonia (destruction of the underlying lung tissue, leading to multiple small, thin-walled cavities). o with lung abscesses. o with empyema (a collection of pus in the pleural cavity). • Expect patients with an abscess or empyema to require drainage in addition to antibiotic therapy.[13]
What **prevention strategies** can be used?	• Use the following to minimize post-operative chemical pneumonitis:[13] o Ensure patients fast for at least EIGHT hours, and avoid clear liquids for at least two hours, prior to surgery. o If possible, avoid using medications that increase risk of aspiration or interfere with swallowing (e.g., sedatives, antipsychotics). • Though data are not conclusive, can consider promoting oral intake with a mechanical soft diet with thickened liquids over pureed foods to reduce the risk of aspiration pneumonia in patients with dysphagia.[13,15] • When enteral feedings are needed, ensure patients are semirecumbent, not supine to reduce the risk of gastric aspiration.[13] • Follow hospital protocols for elevating the head of the bed in ventilated patients, to reduce the risk of aspiration.[15] • For patients with swallowing disorders, promote nutritional rehab with swallowing exercises and early mobilization.[13] • The data are weak to support oral hygiene in preventing aspiration pneumonia, but these efforts are unlikely to lead to harm.[13,15] Promote good oral hygiene (e.g., tooth brushing, cleaning dentures, gargling disinfectant solution, extraction of nonviable teeth).[15,16]

Abbreviations: BID = twice daily; BUN = blood urea nitrogen; CAP = community-acquired pneumonia; COPD = chronic obstructive pulmonary disease; GI = gastrointestinal; h = hour or hours; HAP = hospital-acquired pneumonia; HCAP = healthcare-associated pneumonia; ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; PaO2/FiO2 = arterial oxygen partial pressure/fractional inspired oxygen; PCR = polymerase chain reaction; PPI = proton pump inhibitor; PSI = pneumonia severity index; TID = three times daily; VAP = ventilator-associated pneumonia.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56.
https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

References

1. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019 Oct 1;200(7):e45-e67.
2. CDC. Legionella (Legionnaire's disease and Pontiac fever). Last reviewed/updated March 25, 2021. https://www.cdc.gov/legionella/clinicians/diagnostic-testing.html. (Accessed July 18, 2023).
3. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2(Suppl 2):S27-72.
4. Ewig S, Kolditz M, Pletz MW, Chalmers J. Healthcare-associated pneumonia: is there any reason to continue to utilize this label in 2019? Clin Microbiol Infect. 2019 Oct;25(10):1173-1179.
5. Product information for Baxdela. Melinta Therapeutics. Lincolnshire, IL 60069. June 2021.
6. Briel M, Spoorenberg SMC, Snijders D, et al. Corticosteroids in Patients Hospitalized With Community-Acquired Pneumonia: Systematic Review and Individual Patient Data Metaanalysis. Clin Infect Dis. 2018 Jan 18;66(3):346-354.
7. Prina E, Ranzani OT, Polverino E, et al. Risk factors associated with potentially antibiotic-resistant pathogens in community-acquired pneumonia. Ann Am Thorac Soc. 2015 Feb;12(2):153-60.
8. Stern A, Skalsky K, Avni T, et al. Corticosteroids for pneumonia. Cochrane Database Syst Rev. 2017 Dec 13;12(12):CD007720.
9. Siemieniuk RA, Meade MO, Alonso-Coello P, et al. Corticosteroid Therapy for Patients Hospitalized With Community-Acquired Pneumonia: A Systematic Review and Meta-analysis. Ann Intern Med. 2015 Oct 6;163(7):519-28.
10. Torres A, Sibila O, Ferrer M, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. JAMA. 2015 Feb 17;313(7):677-86.
11. Webb BJ, Dascomb K, Stenehjem E, et al. Derivation and Multicenter Validation of the Drug Resistance in Pneumonia Clinical Prediction Score. Antimicrob Agents Chemother. 2016 Apr 22;60(5):2652-63.
12. Dequin PF, Meziani F, Quenot JP, et al. Hydrocortisone in Severe Community-Acquired Pneumonia. N Engl J Med. 2023 May 25;388(21):1931-1941.
13. Mandell LA, Niederman MS. Aspiration Pneumonia. N Engl J Med. 2019 Feb 14;380(7):651-663.
14. BMJ best practice. Aspiration pneumonia. Updated November 8, 2022. https://newbp.bmj.com/topics/en-us/21. (Accessed July 18, 2023).
15. DiBardino DM, Wunderink RG. Aspiration pneumonia: a review of modern trends. J Crit Care. 2015 Feb;30(1):40-8.
16. Simpson AJ, Allen JL, Chatwin M, et al. BTS clinical statement on aspiration pneumonia. Thorax. 2023 Feb;78(Suppl 1):s3-s21.
17. Yoshimatsu Y, Aga M, Komiya K, et al. The Clinical Significance of Anaerobic Coverage in the Antibiotic Treatment of Aspiration Pneumonia: A Systematic Review and Meta-Analysis. J Clin Med. 2023 Mar 2;12(5):1992.
18. Brook I, Wexler HM, Goldstein EJ. Antianaerobic antimicrobials: spectrum and susceptibility testing. Clin Microbiol Rev. 2013 Jul;26(3):526-46.
19. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2023. http://www.clinicalkey.com. (Accessed July 17, 2023).

20. Product information for Flagyl. Pfizer. New York, NY 10017. January 2023.
21. McDonald LC, Gerding DN, Johnson S, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018 Mar 19;66(7):987-994.
22. University of Rhode Island. IV to PO antibiotic step-down guidelines. https://web.uri.edu/wp-content/uploads/sites/1349/IV-to-PO-Stepdown-2019-JD.pdf. (Accessed July 18, 2023).
23. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. Erratum in: Clin Infect Dis. 2017 May 1;64(9):1298. Erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435. Erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161.

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