Lincosamide and Oxazolidinone Anti-Infectives Summary

November 1, 2022

FDA-APPROVED INDICATIONS AND DOSAGES

Drug	Manufacturer	Indication(s)	Dosage	Availability
clindamycin HCl (Cleocin HCl®)[1] clindamycin palmitate HCl (Cleocin Pediatric®)[2]	generic, Pharmacia/Pfizer	Treatment of serious infections caused by susceptible anaerobic bacteria **Anaerobes:** Serious respiratory tract infections; serious skin and soft tissue infections; septicemia; intra-abdominal infections (typically resulting from anaerobic organisms resident in the normal gastrointestinal [GI] tract); infections of the female pelvis and genital tract Treatment of serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci; its use should be reserved for penicillin-allergic patients or other patients for whom penicillin is inappropriate **Streptococci:** Serious respiratory tract infections; serious skin and soft tissue infections **Staphylococci:** Serious respiratory tract infections; serious skin and soft tissue infections **Pneumococci:** Serious respiratory tract infections	**Adults:** *Serious infections* – 150 to 300 mg every 6 hours *More severe infections* – 300 to 450 mg every 6 hours **Pediatric Patients:** *Serious infections* – 8 to 16 mg/kg/day (4 to 8 mg/lb/day)* divided into 3 or 4 equal doses *More severe infections* – 17 to 25 mg/kg/day (8.5 to 12.5 mg/lb/day)* divided into 3 or 4 equal doses	Capsules: 75 mg, 150 mg, 300 mg Granules for oral solution (pediatric): 75 mg/5 mL

*Use total body weight

FDA-Approved Indications and Dosages (continued)

Drug	Manufacturer	Indication(s)	Dosage	Availability
linezolid (Zyvox®)[3]	generic, Pharmacia/Pfizer	Treatment of the following infections caused by susceptible Gram-positive bacteria: • Community-acquired pneumonia (CAP) • Complicated skin and skin structure infections, including diabetic foot infections without concomitant osteomyelitis • Nosocomial pneumonia • Uncomplicated skin and skin structure infections • Vancomycin-resistant *Enterococcus faecium* infections Limitations of Use: • Linezolid is not indicated for the treatment of Gram-negative infections. Gram-negative therapy should be started immediately if a Gram-negative pathogen is identified • The safety and efficacy of linezolid when given for > 28 days have not been fully evaluated in controlled clinical trials • Linezolid has not been studied for the treatment of decubitus ulcers	**CAP; Complicated skin and skin structure infections; and Nosocomial pneumonia** *Adults and adolescents:* 600 mg every 12 hours *Pediatrics:* 10 mg/kg every 8 hours Duration: 10 to 14 days **Vancomycin-resistant *E. faecium* infection** *Adults and adolescents:* 600 mg every 12 hours *Pediatrics:* 10 mg/kg every 8 hours Duration: 14 to 28 days **Uncomplicated skin and skin structure infections** *Adults:* 400 mg every 12 hours *Adolescents:* 600 mg every 12 hours *Pediatrics:* < 5 years – 10 mg/kg every 8 hours; 5 to 11 years – 10 mg/kg every 12 hours Duration: 10 to 14 days	Tablets: 600 mg Suspension: 100 mg/5 mL
tedizolid (Sivextro®)[4]	Merck Sharp & Dohme, Nabriva	Treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria	**Adults and pediatrics ≥ 12 years:** 200 mg once daily Duration: 6 days	Tablets: 200 mg

OVERVIEW[5,6,7,8]

Clindamycin (Cleocin) is a semisynthetic derivative of lincomycin and produces inhibition of bacterial protein synthesis by binding to the 50S subunit of the ribosome. It has bacteriostatic activity against Gram-positive aerobes and anaerobes, and some Gram-negative anaerobes. Clindamycin is indicated for treatment of serious infections of the respiratory tract and skin and soft tissue structures and is also widely used for the treatment of infections due to methicillin-resistant *Staphylococcus aureus* (MRSA), including community- and hospital-acquired methicillin-resistant *S. aureus* (CA-MRSA and HA-MRSA) infections. Clindamycin is extensively distributed in body fluids and tissues, including bone; however, it has low penetration into the cerebrospinal fluid.

Linezolid (Zyvox) is a synthetic oxazolidinone antibiotic which binds to the bacterial 23S ribosomal RNA resulting in inhibition of bacterial protein synthesis.[9] It is predominantly active against aerobic Gram-positive organisms and exhibits little activity against aerobic Gram-negative organisms or anaerobes *in vitro.* Linezolid is bacteriostatic against staphylococci and enterococci and is often bactericidal against streptococci. Its activity against staphylococci includes MRSA and methicillin-resistant *S. epidermidis,* penicillin-resistant pneumococci, and *S. aureus* with intermediate susceptibility to vancomycin. Linezolid has no significant Gram-negative activity. Linezolid is well distributed in body tissue and fluids.

Tedizolid (Sivextro) is an oxazolidinone antibiotic which binds to the 50S subunit of the bacterial ribosome thereby inhibiting protein synthesis. Tedizolid has activity against the following Gram-positive organisms: *S. aureus* (including MRSA and methicillin-susceptible [MSSA] isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* Group (including *Streptococcus anginosus, Streptococcus intermedius*, and *Streptococcus constellatus*), and *Enterococcus faecalis*.

A major concern with regard to the use of clindamycin for CA-MRSA infection is the possible presence of inducible resistance to clindamycin which has been identified in macrolide-resistant strains of staphylococci and beta-hemolytic streptococci.[10,11] Inducible clindamycin resistance is not detected by standard susceptibility testing; therefore, it is appropriate to perform a D-Zone test to determine if there is a macrolide-resistant strain of bacteria present when testing Gram-positive bacteria for sensitivity to clindamycin.[12] This test is essential because some bacteria express a phenotype known as MLS_B, in which susceptibility tests will indicate the bacteria are susceptible to clindamycin, but *in vitro* the pathogen shows inducible resistance. The clinical significance of inducible clindamycin resistance is unclear because the drug may still be effective for some patients with mild infections; however, the presence of inducible clindamycin resistance should preclude the use of clindamycin for more serious infections.

Linezolid resistance is rare; although reports of vancomycin-resistant *Enterococcus faecium* and MRSA developing resistance to linezolid have occurred.[13] Resistance typically occurs during prolonged use. Linezolid inhibits bacterial protein synthesis through a mechanism of action different from that of other antibacterial agents; therefore, cross-resistance between linezolid and other classes of antibiotics is unlikely.

Tedizolid inhibits bacterial protein synthesis through a mechanism of action different from that of other antibacterial agents; therefore, cross-resistance between tedizolid and other classes of antibiotics is unlikely.

To reduce the development of drug-resistant bacteria and to maintain effectiveness of the antibiotic, clindamycin, linezolid, and tedizolid should only be used to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

Clindamycin is available via oral, parenteral, topical, and vaginal routes. Linezolid and tedizolid are available for oral and parenteral administration. These agents are highly bioavailable via the oral route (clindamycin: 90%, linezolid: 100%, and tedizolid: 91%) which allows for switching from IV to oral administration or for use in patients with impaired gastrointestinal (GI) absorption or who are unable to take oral medications. Outpatient use of clindamycin, linezolid, and tedizolid oral formulations will be included in this review.

SPECIAL USAGE CONSIDERATIONS[14,15,16]

Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *Clostridium (Clostridioides) difficile*. *C. difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, linezolid, and tedizolid. Severity can range from mild to fatal. Boxed warnings advise to reserve the use of clindamycin for serious infections where less toxic antimicrobial agents are inappropriate. Clindamycin should be prescribed with caution in individuals with a history of GI disease, particularly colitis, and in elderly patients (> 60 years) since they may be more susceptible to CDAD. The occurrence of CDAD has been reported over 2 months after the administration of antibacterial agents.

Occasionally, clindamycin use has resulted in overgrowth of nonsusceptible organisms, particularly yeasts. Appropriate medical care should be provided if superinfections occur.

Prescribing clindamycin, linezolid, or tedizolid in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Myelosuppression, including anemia, leukopenia, pancytopenia, and thrombocytopenia, has been reported in patients receiving linezolid and tedizolid. Patients should be monitored appropriately while on therapy, particularly those who are receiving linezolid for > 2 weeks or tedizolid for > 6 days, those who have pre-existing myelosuppression, those who are receiving concomitant drugs associated with bone marrow suppression, or those with a chronic infection who have received previous or concomitant antibiotic therapy. Discontinue linezolid and tedizolid therapy if myelosuppression worsens.

Linezolid and tedizolid have been associated with peripheral and optic neuropathies, primarily in treatment lasting > 28 days. Although visual blurring has been reported in patients treated for < 28 days, prompt ophthalmic evaluation is recommended if changes in vision occur during treatment with either agent.

Lactic acidosis has been reported with the use of linezolid. Patients who develop recurrent nausea or vomiting, unexplained acidosis, or low bicarbonate level while receiving linezolid should receive immediate medical evaluation.

Convulsions have been reported in patients with and without a history of seizures or at risk for seizures while treated with linezolid.

Potentially clinically significant hematology laboratory abnormalities seen in patients treated with tedizolid include hemoglobin values of < 10.1 g/dL for males and < 9 g/dL for females (3.4%), platelet count of < 112 x $10^3/mm^3$ (2.1%), and absolute neutrophil count of < 0.8 x $10^3/mm^3$ (0.4%).

Postmarketing reports of adverse reactions associated with the use of linezolid have identified sideroblastic anemia and cutaneous skin disorders including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS). Postmarketing cases of hyponatremia and/or Syndrome of

Inappropriate Antidiuretic Hormone Secretion (SIADH) have also been observed with linezolid use. Patients at risk of hyponatremia and/or SIADH while taking linezolid should have serum sodium levels monitored regularly. Treatment should be discontinued, and supportive measures implemented, if signs and symptoms of hyponatremia and/or SIADH occur.

Previously Pregnancy Category B, clindamycin labeling has been updated to comply with the Pregnancy and Lactation Labeling Rule (PLLR). In clinical trials, clindamycin systemic use by pregnant women in the second and third trimesters has not been associated with an increased risk of birth defects. Clindamycin use in the first trimester has not been adequately studied and should only be used if necessary. Previously Pregnancy Category C, labeling for linezolid has been updated to comply with the PLLR and advises that available data in pregnant women have not identified a drug-related risk of major harm to the mother or fetus. While tedizolid was previously also Pregnancy Category C, product labeling has also been updated to comply with the PLLR. Although data for tedizolid in pregnant women are inadequate to determine the risk for birth defects or adverse maternal or fetal outcomes, animal studies have shown tedizolid may cause harm to the fetus when given to a pregnant woman. Safety and efficacy of clindamycin, linezolid, and tedizolid have been established in the pediatric population.

The pharmacokinetics of the parent drug, linezolid, are not altered in patients with renal impairment, but accumulation of its 2 primary metabolites may occur. However, because similar plasma concentrations of linezolid are achieved regardless of renal function, no dose adjustment is recommended for patients with renal impairment. Given the lack of information on the clinical significance of accumulation of the primary metabolites, linezolid should be used with caution in patients with renal impairment. Linezolid and its metabolites are removed by hemodialysis; therefore, it should be given after hemodialysis.

No dose adjustment of linezolid is recommended for patients with mild to moderate hepatic impairment. The pharmacokinetics of linezolid in patients with severe hepatic impairment have not been evaluated. Clindamycin dosage adjustments are not required in patients with renal or hepatic impairment; however, periodic kidney and liver function tests should be performed during prolonged therapy. Clindamycin may cause acute kidney injury and is potentially nephrotoxic. Renal function monitoring should be considered in patients with pre-existing renal dysfunction or in patients taking concomitant nephrotoxic drugs. Clindamycin should be discontinued in the setting of acute kidney injury if no other etiology is identified. Tedizolid dosage adjustments are not required in patients with renal impairment, hepatic impairment, or for patients on hemodialysis.

Tedizolid inhibits Breast Cancer Resistance Protein (BCRP). Inhibition of BCRP can result in increased bioavailability and increased toxicity of BCRP substrates, especially those with narrow therapeutic indices such as methotrexate or topotecan.

The safety and efficacy of tedizolid have not been adequately evaluated in patients with neutropenia (neutrophil counts < 1,000 cells/mm^3). Neutropenic patients with acute bacterial skin and skin structure infections should be treated with alternative therapies.

Clindamycin has been shown to have neuromuscular blocking properties and should be used with caution in patients receiving other neuromuscular blocking agents due to additive effects.

Clindamycin is metabolized predominantly by CYP3A4 and to a lesser extent by CYP3A5. Inhibitors of CYP3A4 and CYP3A5 may increase plasma concentrations and inducers of these isoenzymes may reduce plasma concentrations of clindamycin. Monitor for adverse reactions in the presence of strong CYP3A4

inhibitors and monitor for loss of effectiveness in the presence of strong CYP3A4 inducers, such as rifampin.

Linezolid is a reversible, nonselective monoamine oxidase inhibitor and most potential drug interactions with linezolid are related to this action. Use of linezolid within 2 weeks of taking monoamine oxidase inhibitors (MAOIs) is contraindicated due to the risk of severe hypertensive crisis and serotonin syndrome. Tedizolid is also a reversible inhibitor of monoamine oxidase, but the interaction with MAOIs was not evaluated in clinical trials. The product labeling for tedizolid does not include a contraindication with MAOIs, but it should be avoided in patients on concurrent MAOI therapy.

Serotonin syndrome, including fatal cases, has also been reported with the co-administration of linezolid and serotonergic agents. Serotonin syndrome is caused by excessive levels of serotonin in the central and peripheral nervous systems and is characterized by mental status and neuromuscular changes and autonomic hyperactivity. Linezolid is not recommended in patients with carcinoid syndrome and/or patients taking serotonin reuptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), meperidine, bupropion, or buspirone, unless carefully monitored for signs and symptoms of serotonin syndrome or neuroleptic malignant syndrome-like (NMS-like) reactions. Furthermore, tedizolid is structurally similar to linezolid, and patients should be monitored for signs and symptoms of serotonin syndrome and NMS-like reactions if tedizolid is used concomitantly with serotonergic agents.

Reversible enhancement of the pressor response to indirect-acting sympathomimetic agents, vasopressor agents, or dopaminergic agents can occur with concurrent use of linezolid. In clinical trials, mean increases in systolic blood pressure of 32 mm Hg and 38 mm Hg were reported with pseudoephedrine and phenylpropanolamine, respectively, when co-administered with linezolid. Therapy with adrenergic agents, such as dopamine or epinephrine, should be started at reduced dosages and titrated to achieve the desired response.

Severe hypertension can occur if linezolid is taken concomitantly with large amounts of tyramine; patients should avoid foods rich in tyramine, such as aged cheeses, fermented or air-dried meats, soy sauce, tap beers, and red wines. Tedizolid also has the potential to interact with foods containing large amounts of tyramine and these same foods and beverages should be consumed with caution while on tedizolid therapy and for 2 weeks thereafter.

Linezolid oral suspension contains 4 mg/mL of phenylalanine which can be harmful to patients with phenylketonuria (PKU).

No dose adjustment of linezolid is necessary when switching from intravenous (IV) to oral administration.

PLACE IN THERAPY

Skin and Soft Tissue Infections

Skin and soft tissue infections (SSTI) are often caused by beta-hemolytic streptococcus, *Staphylococcus aureus, or Streptococcus pyogenes.*[17] According to the Infectious Disease Society of America (IDSA) 2014 practice guidelines update on SSTI, minor infections may be empirically treated with semi-synthetic penicillin, first- or second-generation oral cephalosporins, macrolides, trimethoprim-sulfamethoxazole (TMP-SMX), or clindamycin; and for simple abscesses, incision and drainage alone may be adequate. Patients with severe infection or whose infection is progressing despite empirical antibiotic therapy should be treated more aggressively, and the treatment strategy should be based upon results of

appropriate Gram stain, culture, and drug susceptibility analyses. *S. aureus* and *S. pyogenes* frequently develop resistance to methicillin and erythromycin, respectively. Empirical choices of antimicrobials must include agents with activity against resistant strains.[18] According to the IDSA 2011 guidelines for MRSA infections in adults and children, oral options for MRSA community acquired SSTI include linezolid, clindamycin, a tetracycline (doxycycline, minocycline), or TMP-SMX. If coverage for both beta-hemolytic streptococci and CA-MRSA is needed, options include clindamycin monotherapy, linezolid monotherapy, or TMP-SMX or a tetracycline in combination with a beta-lactam, such as amoxicillin. Tedizolid was not approved at the time that the 2014 IDSA SSTI guidelines were published, but was included as a medication effective against SSTI, including those cases caused by MRSA. The 2011 IDSA guidelines for MRSA infections are no longer current but are included in this class review for historical purposes.

In a non-inferiority, randomized, double-blind comparison of IV tedizolid 200 mg once daily for 6 days versus IV linezolid 600 mg twice daily for 10 days, with optional step-down to oral therapy, tedizolid was shown to be as effective as linezolid in patients (n=666) with ABSSSI.[19]

Respiratory Tract Infections

The most common etiology of outpatient community-acquired pneumonia (CAP) is *Streptococcus pneumoniae;* other bacterial causes include *Haemophilus influenzae, Mycoplasma pneumoniae, Staphylococcus aureus, Legionella species, Chlamydia pneumoniae,* and *Moraxella catarrhalis.*[20] The joint 2019 guidelines by the American Thoracic Society (ATS) and IDSA for adults with CAP recommend that in patients without comorbidities or risk factors for antibiotic resistant pathogens, standard treatment may include monotherapy with amoxicillin, doxycycline, or a macrolide. For patients with comorbidities, treatment should include combination therapy with amoxicillin/clavulanate or a cephalosporin (e.g., cefpodoxime or cefuroxime) and a macrolide or doxycycline; these patients could also receive monotherapy with a respiratory fluoroquinolone. For MRSA pneumonia, the IDSA recommends IV vancomycin or oral or IV linezolid or clindamycin, if the strain is susceptible, for 7 to 21 days.[21] In pediatric patients with MRSA pneumonia, vancomycin is recommended, and in stable patients without ongoing bacteremia or intravascular infection, IV clindamycin can be used as empiric therapy if the clindamycin resistance rate is low, with transition to oral therapy. Linezolid via IV or oral route is an alternative. The IDSA guidelines that discuss the treatment of MRSA pneumonia have been archived and are included in this class review for historical purposes; no replacement recommendations have been published to date.

Empiric oral therapy for rhinosinusitis, administered for 7 to 14 days, includes amoxicillin, amoxicillin-clavulanate, a select cephalosporin, azithromycin, levofloxacin, TMP-SMX, doxycycline, and clindamycin.[22] Data suggest that most cases without complications will improve regardless of the treatment used, but will do so faster and will have a better chance of improvement if given antibiotics. In children, antibiotic therapy should be reserved for those with complications or concomitant diseases (e.g., asthma, chronic bronchitis) that could be exacerbated by acute bacterial rhinosinusitis. Antibiotics recommended in this situation include amoxicillin-clavulanate (preferred) and amoxicillin. Alternatives are quinolones or clindamycin or linezolid with a second- or third- generation cephalosporin. Clindamycin may provide benefit particularly if anaerobic organisms are suspected. Notably, the IDSA guidelines for rhinosinusitis have been archived. Per the IDSA, penicillin or amoxicillin is the treatment of choice for the management of Group A Streptococcal pharyngitis; however, cephalosporins, macrolides, and clindamycin are appropriate in penicillin-allergic individuals.[23] The IDSA guidelines for Group A Streptococcal pharyngitis also have been archived; this information is included for historical purposes.

Other

For treatment of MRSA native vertebral osteomyelitis, the first-choice regimen is IV vancomycin; alternatives are daptomycin, linezolid, or levofloxacin and rifampin for a duration of 6 weeks.[24]

Enterococci are Gram-positive anaerobes found in the normal intestinal flora, *Enterococcus faecalis* and *Enterococcus faecium* being the most prevalent cultured from humans.[25] Enterococci have both an intrinsic or acquired resistance to many antibiotics, such as penicillins, cephalosporins, nalidixic acid, aztreonam, macrolides, clindamycin, aminoglycosides, chloramphenicol, tetracyclines, rifampin, fluoroquinolones, and vancomycin. Vancomycin resistance by enterococci, particularly *E. faecium,* has had a great impact on the treatment and infection control of these organisms. Vancomycin resistant enterococci (VRE) strains are usually resistant to all antibiotics that are effective treatments for vancomycin-susceptible enterococci, thereby limiting therapeutic options. Agents such as linezolid and daptomycin (Cubicin®) with activity against many VRE strains have been developed; however, rare reports of resistance to these agents have occurred.

To reduce the development of drug-resistant bacteria and maintain their effectiveness, clindamycin, linezolid, and tedizolid should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. Bacteriologic susceptibility studies, including local hospitals and practice area susceptibility profiles, should be employed to guide in the selection of the most effective antimicrobial agent.

REFERENCES

1 Cleocin capsules [package insert]. New York, NY; Pfizer; May 2022.
2 Cleocin Pediatric [package insert]. New York, NY; Pfizer; August 2021.
3 Zyvox [package insert]. New York, NY; Pfizer; November 2021.
4 Sivextro [package insert]. Fort Washington, PA; Nabriva; July 2022.
5 Cleocin capsules [package insert]. New York, NY; Pfizer; May 2022.
6 Zyvox [package insert]. New York, NY; Pfizer; November 2021.
7 Sivextro [package insert]. Fort Washington, PA; Nabriva; July 2022.
8 Clinical Pharmacology. Available at: https://www.clinicalkey.com/pharmacology/. Accessed November 8, 2022.
9 Medical Letter. Available at: http://secure.medicalletter.org/TML-article-1079a. Accessed November 8, 2022.
10 Lewis JS II, Jorgensen JH. Inducible clindamycin resistance in staphylococci: should clinicians and microbiologists be concerned? Clin Infect Dis. 2005; 40:280–285. DOI: 10.1086/426894.
11 Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 (Archived); 52(3): 18-55. DOI: 10.1093/cid/ciq146. Available at http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 8, 2022.
12 Woods CR. Macrolide-inducible resistance to clindamycin and the D-test. Pediatr Infect Dis J. 2009; 28: 1115–1118. DOI: 10.1097/INF.0b013e3181c35cc5.
13 Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 (Archived); 52(3): 18-55. DOI: 10.1093/cid/ciq146. Available at http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 8, 2022.
14 Cleocin capsules [package insert]. New York, NY; Pfizer; May 2022.
15 Zyvox [package insert]. New York, NY; Pfizer; November 2021.
16 Sivextro [package insert]. Fort Washington, PA; Nabriva; July 2022.
17 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; 59(2): 10-52. DOI: 10.1093/cid/ciu444. Available at: http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 3, 2022.
18 Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 (Archived); 52(3): 18-55. DOI: 10.1093/cid/ciq146. Available at http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 3, 2022.
19 Moran GJ, Fang E, Corey GR, et al. Tedezolid for 6 days versus linezolid for 10 days for acute bacterial skin and skin-structure infections (ESTABLISH-2): a randomized, double-blind, phase 3, non-inferiority trial. Lancet Infect Dis. 2014; 14(8):696-705. DOI: 10.1016/S1473-3099(14)70737-6.
20 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; 200(7):e45–e67. DOI: 10.1164/rccm.201908-1581ST. Available at: https://www.thoracic.org/statements/tuberculosis-pneumonia.php. Accessed November 8, 2022.

21 Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 (Archived); 52(3): 18-55. DOI: 10.1093/cid/ciq146. Available at http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 8, 2022.
22 Peters AT, Spector S, Hsu J, et al. American College of Allergy, Asthma & Immunology. Diagnosis and management of rhinosinusitis: a practice parameter update. 2014. Ann Allergy Asthma Immunol. 2014;113:347-385. DOI: 10.1016/j.anai.2014.07.025. Available at: http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/2014-October_Rhinosinusitis_Update.pdf. Accessed November 8, 2022.
23 Shulman ST, Bisno AL, Glegg HW, et al. Clinical practice guideline for the diagnosis and management of Group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012 (Archived); 54(8): 72-112 DOI: 10.1093/cid/cir1043. Available at: http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 8, 2022.
24 Berbari EF, Kanj SS, Kowalski TJ, et al. 2015 Infectious Diseases Society of America clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. Clin Infect Dis. 2015; 61(6):e26-46. DOI: 10.1093/cid/civ482. Available at: http://www.idsociety.org/Templates/PracticeGuideline.aspx?id=32212270088. Accessed November 8, 2022.
25 Enterococcal infections. Medscape. Updated June 10, 2021. Available at: http://emedicine.medscape.com/article/216993-overview. Accessed November 8, 2022.