Policies Repository

Independence Blue Cross

Policy Title	Oral Anti-infective Agents
Policy Number	FS.CLIN.8

Application of Pharmacy Policy is determined by benefits and contracts. Benefits may vary based on product line, group or contract. Some medications may be subject to precertification, age, gender or quantity edits. Individual member benefits must be verified.

This Pharmacy Policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety or FDA approval may have changed. If the Medical/Pharmacy Reviewer is aware of any new information on the subject of this document, please provide it promptly to the Medical/Pharmacy Policy Department. This information may include new FDA approved indications, withdrawals or other FDA alerts. This type of information is relevant not only when considering whether this Policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Policy

AZITHROMYCIN (ZMAX®)
Azithromycin (Zmax®) is indicated for the treatment of mild-to-moderate infections that are caused by susceptible strains of the designated micro-organisms in specific conditions such as: acute bacterial sinusitis due to Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae; and community-acquired pneumonia due to Chlamydophila pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, or Streptococcus pneumoniae.

The use of azithromycin (Zmax®) requires a prior authorization (ie, clinical pharmacy and/or Medical Director review).

LINEZOLID (ZYVOX®)
Linezolid (Zyvox®) formulations are indicated for the treatment of the following infections that are caused by susceptible strains of the designated micro-organisms:

- Vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia.
- Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant strains) or Streptococcus pneumoniae (penicillin-susceptible strains only). Combination therapy may be clinically indicated if the documented or presumptive pathogens include gram-negative organisms.
- Complicated skin and skin structure infections, including diabetic foot infections without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and -resistant strains), Streptococcus pyogenes, or Streptococcus agalactiae. Linezolid (Zyvox®) has not been studied in the treatment of diabetic foot and decubitus ulcers. Combination therapy may be clinically indicated if the documented or presumptive pathogens include gram-

negative organisms.
- Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin-susceptible strains only) or Streptococcus pyogenes.
- Community-acquired pneumonia caused by Streptococcus pneumoniae (penicillin-susceptible strains only), including cases with concurrent bacteremia or Staphylococcus aureus (methicillin-susceptible strains only).

Due to concerns about inappropriate use of antibiotics leading to an increase in resistance, providers should carefully consider alternatives before initiating treatment with linezolid (Zyvox®) in the outpatient setting.

The use of linezolid (Zyvox®) requires a prior authorization (ie, clinical pharmacy and/or Medical Director review).

POSACONAZOLE (NOXAFIL®)
Posaconazole (Noxafil®) oral suspension is indicated for prophylaxis of invasive Aspergillus and Candida infections in individuals, 13 years of age or more, who are at high risk of developing these infections due to being severely immunocompromised (eg, hematopoietic stem cell transplant [HSCT] recipients with graft-versus-host disease [GVHD] or individuals with hematologic malignancies who have prolonged neutropenia from chemotherapy). Posaconazole (Noxafil®) is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.

The use of posaconazole (Noxafil®) requires a prior authorization (ie, clinical pharmacy and/or Medical Direction review).

DOXYCYCLINE (ORACEA®)
Doxycycline (Oracea®) is indicated for the treatment of inflammatory lesions (papules and pustules) contributed to rosacea in adults.

The use of doxycycline (Oracea®) requires a prior authorization (ie, clinical pharmacy and/or Medical Director review).

Policy Description

AZITHROMYCIN (ZMAX®)
Azithromycin (Zmax®) is an extended-release formulation using microsphere technology to provide a complete course of therapy in a single two-gram dose. Azithromycin (Zmax®) is similar to other azithromycin-containing drugs that inhibit messenger ribonucleic acid (RNA)-directed polypeptide and protein synthesis by binding at the 50 S ribosomal subunit.

LINEZOLID (ZYVOX®)
Linezolid (Zyvox®) is a synthetic antibacterial agent of the oxazolidinone class. Appropriate specimens for bacteriological examination should be obtained to isolate and identify the causative organisms and to determine their susceptibility to linezolid (Zyvox®). Therapy may be instituted empirically while awaiting the results of these tests. Once these results become available, antimicrobial therapy should be adjusted accordingly.

POSACONAZOLE (NOXAFIL®)
Posaconazole (Noxafil®), a triazole antifungal agent, blocks the synthesis of ergosterol, a key component of the fungal cell membrane, through the inhibition of the enzyme lanosterol 14a-demethylase and accumulation of methylated sterol precursors. Posaconazole (Noxafil®) has shown in vitro activity against Aspergillus fumigatus and

Candida albicans, including C. albicans, isolates from individuals refractory to itraconazole or fluconazole or both drugs.

Posaconazole (Noxafil®) interpretive criteria have not been established for any fungi. In immunocompetent and/or immunocompromised mice and rabbits with pulmonary or disseminated infection with A. fumigatus, posaconazole (Noxafil®) administered prophylactically was effective in prolonging survival and reducing mycological burden. Prophylactic posaconazole (Noxafil®) also prolonged survival of immunocompetent mice challenged with C. albicans or A. flavus.

DOXYCYCLINE (ORACEA®)
Doxycycline (Oracea®) is a member of the tetracycline class of antibacterial drugs. Doxycycline interferes with the third stage of bacterial protein synthesis. After amino acids are activated and attached to t-RNA (transfer RNA), the resulting amino acyl-t-RNA migrates to the bacterial ribosome for synthesis of proteins. Doxycycline binds to the 30 S subunit on the ribosome and inhibits binding of the aminoacyl-t-RNA molecules. Doxycycline (Oracea®) capsules 40 mg are hard gelatin capsule shells filled with two types of doxycycline beads (30 mg immediate release and 10 mg delayed release) that together provide a dose of 40 mg of anhydrous doxycycline. Doxycycline (Oracea®) should not be used for: treating bacterial infections, providing antibacterial prophylaxis, or reducing/eliminating microorganisms associated with any bacterial disease.

Policy Guideline Inclusion

AZITHROMYCIN (ZMAX®)

Azithromycin (ZMAX®) is approved when the following inclusion criterion is met:

- Documentation of contraindication to all other generic formulations of azithromycin

LINEZOLID (ZYVOX®)

Linezolid (Zyvox®) is approved when at least **one** of the following inclusion criteria is met:

- Documentation of a **current** diagnosis of vancomycin-resistant Enterococcus faecium (VRE) infection, methicillin-resistant Staphylococcus aureus (MRSA) or methicillin-resistant Staphylococcus epidermis (MRSE) infection prescribed by an infectious disease (ID) specialist or prescribed with ID consultation (telephone consultation is acceptable) including name of the ID specialist and date of the consultation within the last 60 days
- Documentation of a current bacterial infection with trial and failure of at least one drug from two of the following groups within the last 60 days:
    - At least one of the penicillins or cephalosporins
    - At least one of the macrolides or a ketolide
    - At least one of the fluoroquinolones
    - Trimethoprim and sulfamethoxazole
    - At least one of the tetracyclines
    - Clindamycin

The quantity limit for linezolid (Zyvox®) is 28 doses. Requests for quantities greater than 28 doses are to be reviewed by a pharmacist or physician. The infectious organism and the site of infection will determine the appropriate length of therapy.

An initial 96-hour supply (eight doses) will be covered to assure that therapy is not delayed while the prior authorization request is being reviewed.

POSACONAZOLE (NOXAFIL®)

Posaconazole (NOXAFIL®) is approved for an individual who is 13 years of age or more when **any one** of the following inclusion criteria is met:

- Use in prophylaxis of invasive Aspergillus and Candida infections due to a severe immunocompromised state
- Use in the treatment of invasive Aspergillus and Candida infections due to a severe immunocompromised state after trial and failure of voriconazole (Vfend®)
- Diagnosis of oropharyngeal candidiasis with failed trials of itraconazole and fluconazole

DOXYCYCLINE (ORACEA®)

Doxycycline (Oracea®) is approved when **all** of the following inclusion criteria are met:

- Documentation of diagnosis of Rosacea
- Documentation of trial and failure or contraindication/intolerance/allergy to topical metronidazole and one other formulation of oral doxycycline

Policy Guideline Exclusion

AZITHROMYCIN (ZMAX®)

Azithromycin (ZMAX®) is denied when the following exclusion criterion is present:

- No documentation of contraindication to all other generic formulations of azithromycin.

LINEZOLID (ZYVOX®)

Linezolid (Zyvox®) is denied when **all** of the following exclusion criteria are present:

- No documentation of a **current** diagnosis of vancomycin-resistant Enterococcus faecium (VRE) infection, methicillin-resistant Staphylococcus aureus (MRSA) or methicillin-resistant Staphylococcus epidermis (MRSE) infection prescribed by an infectious disease (ID) specialist or prescribed with ID consultation (telephone consultation is acceptable) including name of the ID specialist and date of the consultation within the last 60 days
- No documentation of a current bacterial infection with trial and failure of at least one drug from two of the following groups within the last 60 days:
    - At least one of the penicillins or cephalosporins
    - At least one of the macrolides or a ketolide
    - At least one of the fluoroquinolones
    - Trimethoprim and sulfamethoxazole
    - At least one of the tetracyclines
    - Clindamycin

POSACONAZOLE (NOXAFIL®)

Posaconazole (NOXAFIL®) is denied when **all** of the following exclusion criteria are present:

- No documentation of an individual who is 13 years of age or more
- No documentation of use in prophylaxis of invasive Aspergillus and Candida infections due to a severe immunocompromised state
- No documentation of its use in the treatment of invasive Aspergillus and Candida infections due to a severe immunocompromised state after trial and failure of voriconazole (Vfend®)
- No documentation of diagnosis of oropharyngeal candidiasis with failure of both itraconazole and fluconazole

DOXYCYCLINE (ORACEA®)

Doxycycline (Oracea®) is denied when **any** of the following exclusion criteria are present:

- No documentation of diagnosis of Rosacea
- No documentation of trial and failure or contraindication/intolerance/allergy to topical metronidazole and one other formulation of oral doxycycline

Policy List of Applicable Drugs

Brand Name	Generic Name
Zmax	azithromycin
Zyvox	linezolid
Noxafil	posaconazole
Oracea	doxycycline

Dosing and Administration

Refer to the specific manufacturer's prescribing information for administration and dosage details for each specific agent.

Policy References

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Policy Link to Related Policies

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