
Title: Oral Anti-infective Agents

Policy #: Rx.01.66

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, quantity, or formulary restrictions (ie limits on non-preferred drugs). 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. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. 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.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **bedaquiline (Sirturo®), isavuconazonium (Cresemba®), tedizolid (Sivextro®), and Pretomanid** as provided under the member's prescription drug benefit.

Description:

BEDAQUILINE (SIRTURO®)

Bedaquiline (Sirturo®) is indicated as part of combination therapy in adults and pediatric patients (5 years and older and weighing at least 15 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve Sirturo® for use when an effective treatment regimen cannot otherwise be provided

Bedaquiline (Sirturo®) is a diarylquinoline antimycobacterial drug that inhibits mycobacterial ATP synthase, an enzyme that is essential for the generation of energy in Mycobacterium tuberculosis.

Isavuconazonium (Cresemba®) is indicated for the treatment of invasive aspergillosis and invasive mucormycosis.

Isavuconazonium (Cresemba®) is the prodrug of isavuconazole, an azole antifungal. Isavuconazole inhibits the synthesis of ergosterol, a key component of the fungal cell membrane, through the inhibition of cytochrome P-450 dependent enzyme lanosterol 14-alpha-demethylase. This enzyme is responsible for the conversion of lanosterol to ergosterol. An accumulation of methylated sterol precursors and a depletion of ergosterol within the fungal cell membrane weakens the membrane structure and function.

TEDIZOLID (SIVEXTRO®)

Tedizolid (Sivextro®) is indicated for the treatment of adult and pediatric patients 12 years of age and older for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria.

Tedizolid (Sivextro®) binds to the 50S bacterial ribosomal subunit. This prevents the formation of a functional 70S initiation complex that is essential for the bacterial translation process and subsequently inhibits protein synthesis. Tedizolid is bacteriostatic against enterococci, staphylococci, and streptococci.

PRETOMANID

Pretomanid is indicated for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB) as part of a combination regimen with bedaquiline and linezolid. Pretomanid is indicated for use in a limited and specific population of patients

Pretomanid is a nitroimidazooxazine antimycobacterial drug. Pretomanid kills actively replicating *M. tuberculosis* by inhibiting mycolic acid biosynthesis, thereby blocking cell wall production. Under anaerobic conditions, against non-replicating bacteria, Pretomanid acts as a respiratory poison following nitric oxide release.

Policy:

BEDAQUILINE (SIRTURO®)

Bedaquiline (Sirturo®) is approved when ALL of the following are met:

1. Diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB), for which an effective treatment regimen cannot otherwise be established; and
2. Member is 5 years of age or older and weighing at least 15kg; and
3. Prescribed by or in consultation with an infection disease specialist or pulmonologists; and
4. Bedaquiline is used as combination therapy as defined by ONE of the following:
 - a. With at least 3 other drugs to which the member's MDR-TB isolate has been shown to be susceptible in vitro; or
 - b. With at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible

Authorization duration: 24 weeks

ISAVUCONAZONIUM (CRESEMBA®)

Isavuconazonium (Cresemba®) is approved when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Prescribed by or in consultation with an infectious diseases specialist; and
3. Diagnosis of ONE of the following:
 - a. Treatment of invasive aspergillosis and inadequate response or inability to tolerate voriconazole; or
 - b. Treatment of invasive mucormycosis

Authorization duration: 12 months

TEDIZOLID (SIVEXTRO®)

Tedizolid (Sivextro®) is approved when ALL of the following are met:

1. Member is 12 years of age or older; and
2. Prescribed by or in consultation with an infectious disease specialist; and
3. Documentation of use for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of Gram-positive microorganisms and ONE of the following:
 - a. Inadequate response or inability to tolerate ALL antibiotics to which the organism is susceptible; or
 - b. Tedizolid is the only antibiotic to which the organism is susceptible

Authorization duration: 4 weeks

PRETOMANID

Pretomanid is approved when ALL of the following are met:

1. Diagnosis of pulmonary extensively drug resistant (XDR), treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB); and
2. Medication will be used as part of combination regimen with bedaquiline (Sirturo®) and linezolid; and
3. Member is 18 years of age or older; and
4. Prescribed by or in consultation with an infectious disease specialist

Authorization duration: 26 weeks

Black Box Warning as shown in the drug Prescribing Information:

BEDAQUILINE (SIRTURO®)

An increased risk of death was seen in the bedaquiline group (11.4%) compared with the placebo group (2.5%) in 1 placebo-controlled trial. Only use SIRTURO in patients 5 years of age and older when an effective treatment regimen cannot otherwise be provided..

QT prolongation can occur with bedaquiline. Use with drugs that prolong the QT interval may cause additive QT prolongation. Monitor ECGs. Discontinue SIRTURO if significant ventricular arrhythmia or QTcF interval >500 ms develops.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Pretomanid [prescribing information]. India: Mylan, Laboratories Limited; April 2019. Available from: https://www.tballiance.org/sites/default/files/assets/Pretomanid_Full-Prescribing-Information.pdf. Accessed July 13, 2022.

Cresemba® (isavuconazonium) [package insert]. Northbrook, IL. Astellas Pharma US. December 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=8f7f73b8-586a-4df0-935f-fecd4696c16c&type=display>. Accessed July 13, 2022.

Sirturo® (bedaquiline) [package insert]. Janssen Therapeutics; Titusville, NJ. May 2020. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1534c9ae-4948-4cf4-9f66-222a99db6d0e&type=display>. Accessed July 13, 2022.

Sivextro® (tedizolid) [package insert]. White House Station, NJ: Merc and Co, Inc. June 2020. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=75672079-589f-451a-bdbf-eaebcfcc80a9&type=display>. Accessed July 13, 2022.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Cresemba®	isavuconazonium
Sirturo®	bedaquiline
Sivextro®	tedizolid
	pretomanid

Cross References:

Rx.01.33 Off Label Use

Rx.01.76 Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit

Policy Version Number:

20.00

P&T Approval Date:

June 09, 2022

Policy Effective Date:

October 01, 2022

Next Required Review Date:

June 09, 2023

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

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