

PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

SIRTURO
(bedaquiline)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 923-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Sirturo is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in the treatment of adult 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.

This indication is approved under accelerated approval based on time to sputum culture conversion. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitations of Use:

- Do not use Sirturo for the treatment of:
 - Latent infection due to *Mycobacterium tuberculosis*
 - Drug-sensitive tuberculosis
 - Extra-pulmonary tuberculosis
 - Infections caused by non-tuberculous mycobacteria
- The safety and efficacy of Sirturo in the treatment of HIV infected patients with MDR-TB have not been established as clinical data are limited

Off Label Uses

Combination regimen with pretomanid and linezolid for the treatment of pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB)^{5,6}

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed as part of combination therapy in a patient with pulmonary multi-drug resistant tuberculosis (MDR-TB)

AND

- Another effective treatment regimen cannot be used instead of Sirturo (bedaquiline)

OR

- The requested drug is being prescribed for pulmonary extensively drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis

AND

- The requested drug is being prescribed as part of a combination regimen with Pretomanid and Zyvox (linezolid)

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Sirturo is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in the treatment of adult 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.

Sirturo should only be initiated as part of combination therapy with at least 3 drugs to which the patient's MDR-TB isolate has been shown to be effective in vitro. If in vitro testing results are unavailable, Sirturo treatment may be initiated in combination with at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible. The recommended dosage of Sirturo is 400 mg orally once daily for 2 weeks, then 200 mg orally 3 times weekly (with at least 48 hours between doses) for 22 weeks. The total duration of treatment with Sirturo is 24 weeks.

Pretomanid is indicated as part of a combination regimen with bedaquiline (Sirturo) and linezolid (Zyvox) for the treatment of pulmonary XDR-TB or treatment-intolerant or nonresponsive MDR-TB; the recommended dosage and duration for this combination regimen are as follows⁵:

- Pretomanid Tablet 200 mg orally (1 tablet of 200 mg), once daily, for 26 weeks. Swallow Pretomanid Tablets whole with water
- Bedaquiline 400 mg orally once daily for 2 weeks followed by 200 mg 3 times per week, with at least 48 hours between doses, for 24 weeks for a total of 26 weeks
- Linezolid starting at 1,200 mg orally per day for 26 weeks, with dose adjustments to 600 mg daily and further reduction to 300 mg daily or interruption of dosing as necessary for known linezolid adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy
- Take the combination regimen of Pretomanid Tablets, bedaquiline, and linezolid with food
- If the combination regimen of Pretomanid Tablets, bedaquiline, and linezolid is interrupted by a healthcare provider for safety reasons, missed doses can be made up at the end of the treatment; doses of linezolid alone missed due to linezolid adverse reactions should not be made up

Dosing of the combination regimen of Pretomanid Tablets, bedaquiline, and linezolid can be extended beyond 26 weeks, if necessary.⁵ Additionally, the Centers for Disease Control and Prevention (CDC) provisional guidelines for the use of bedaquiline for the treatment of multidrug-resistant tuberculosis, go beyond current FDA-approved labeling for bedaquiline.⁴ The guidelines state the following: Bedaquiline may be used for 24 weeks of treatment in adults with laboratory-confirmed pulmonary MDR-TB (TB with an isolate showing genotypic or phenotypic resistance to both isoniazid and rifampin) when an effective treatment regimen cannot otherwise be provided; bedaquiline may be used on a case-by-case basis in children, HIV-infected persons, pregnant women, persons with extrapulmonary MDR-TB, and patients with comorbid conditions on concomitant medications when an effective treatment regimen cannot otherwise be provided; and bedaquiline may be used on a case-by-case basis for durations longer than 24 weeks when an effective treatment regimen cannot be provided otherwise.^{4,7} Additionally, new evidence is available from the World Health Organization (WHO) on the use of bedaquiline longer than six months duration for MDR/Rifampin Resistant (RR)-TB, concurrent use of bedaquiline and delamanid for MDR/RR-TB, and use of bedaquiline, pretomanid and linezolid in combination for patients with extensively drug resistant tuberculosis (XDR-TB).^{6,8,9} Therefore, the duration of approval is set at 12 months.

REFERENCES

1. Sirturo [package insert]. Titusville, New Jersey: Janssen Therapeutics; May 2020.
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5. Pretomanid [package insert]. Morgantown, WV: Mylan Specialty L.P.; April 2020.
6. Update of WHO guidelines on the programmatic management of drug resistant TB. Geneva: World Health Organization; 2019. https://www.who.int/tb/features_archive/Update-WHO-guidelines-programmatic-management-of-drug/en/. Accessed January 2021.
7. WHO consolidated guidelines on drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2019. <https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf?ua=1>. Accessed January 2021.
8. Rapid communication: key changes to treatment of drug-resistant tuberculosis. Geneva: World Health Organization; December 2019. https://www.who.int/tb/publications/2019/WHO_RapidCommunicationMDRTB2019.pdf?ua=1. Accessed January 2021.
9. WHO Global Tuberculosis Report 2020. Geneva: World Health Organization; 2020. <https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf>. Accessed January 2021.

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CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed as part of combination therapy in a patient with pulmonary multi-drug resistant tuberculosis (MDR-TB)? [If no, then skip to question 3.]	Yes	No
2	Can another effective treatment regimen be used instead of Sirturo (bedaquiline)? [No further questions.]	Yes	No
3	Is the requested drug being prescribed for pulmonary extensively drug resistant (XDR) or treatment-intolerant/nonresponsive multidrug-resistant (MDR) tuberculosis? [If no, then no further questions.]	Yes	No
4	Is the requested drug being prescribed as part of a combination regimen with Pretomanid and Zyvox (linezolid)?	Yes	No

Mapping Instructions

	Yes	No	DENIAL REASONS – DO NOT USE FOR MEDICARE PART D
1.	Go to 2	Go to 3	
2.	Deny	Approve, 12 months	You do not meet the requirements of your plan. Your plan covers this drug when other drugs cannot be used for the infection. Your request has been denied based on the information we have. [Short Description: Another effective treatment regimen can be used]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is used with other drugs for a certain infection in the lungs that is resistant to multiple drugs. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is used with Pretomanid and Zyvox (linezolid) for the infection. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis/combination regimen]