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 a newly approved FDA drug 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 follows[5]:

- 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
- If either bedaquiline or Pretomanid Tablets are discontinued, the entire combination regimen should also be discontinued. 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.

If linezolid is permanently discontinued during the initial four consecutive weeks of treatment, bedaquiline and Pretomanid Tablets should also be discontinued. If linezolid is discontinued after the initial four weeks of consecutive treatment, continue administering bedaquiline and Pretomanid Tablets.[5]

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] The dosing of the combination regimen of Pretomanid, bedaquiline, and linezolid can be extended beyond 26 weeks, if necessary.[5] Therefore, the duration of approval is set at 12 months.

REFERENCES

1. Sirturo [package insert]. Titusville, New Jersey: Janssen Therapeutics; May 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed January 2020.
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4. Centers for Disease Control and Prevention. Provisional CDC Guidelines for the Use and Safety Monitoring of Bedaquiline Fumarate (Sirturo) for the Treatment of Multidrug-Resistant Tuberculosis. *MMWR*. Oct 2013; 62(9): 1-12.
5. Pretomanid [package insert]. Hyderabad, India: Mylan Laboratories Limited for The Global Alliance for TB Drug Development (TB Alliance); August 2019.
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 2020.
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
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 2020.

Written by:	UM Development (SE)
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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?	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]