RXADVANCE
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Clinical Policy Title: **Bedaquiline (Sirturo)**
Policy Number: **RxA.490**
Drug(s) Applied: **Bedaquiline (Sirturo®)**
Last Review Date: **01/2020**
Line of Business: **Commercial, HIM, Medicaid**

Background

Bedaquiline (Sirturo®) is a diarylquinoline antimycobacterial drug. It is indicated as part of combination therapy in the treatment of adult and pediatric patients (12 to less than 18 years of age and weighing at least 30 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve Sirturo for use when an effective treatment regimen cannot otherwise be provided.
Limitation(s) 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.

Indication	Dosing Regimen	Maximum Dose
MDR TB	400 mg PO QD for the first 2 weeks, followed by 200 mg PO three times per week (with at least 48 hours between doses) for 22 weeks (total duration of 24 weeks). Situro should be administered by directly observed therapy (DOT)	400 mg/dose

Tablet: 100 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Multi-Drug Resistant Tuberculosis (must meet all)**:**

1. Diagnosis of MDR-TB;
2. Prescribed by or in consultation with an infectious disease specialist or a pulmonologist;
3. Age ≥ 12 years;
4. Prescribed in combination with at least 3 other anti-tuberculosis agents (*see Appendix B*);
5. Documented resistance to fluoroquinolones, unless contraindicated or clinically significant

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adverse effects are experienced;
6. Dose does not exceed 400 mg per day for the first 2 weeks, followed by 200 mg three times per week.

Approval duration: 24 weeks

II. Continued Therapy

A. Multi-Drug Resistant Tuberculosis (must meet all)**:**

1. Currently receiving medication via RxAdvance or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 200 mg three times per week.

Approval duration: up to a total duration of 24 weeks

III. Appendices

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MDR-TB: multi-drug resistant tuberculosis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
amikacin/kanamycin	15 mg/kg IM or IV QD or 25 mg/kg PO 3 times weekly	15 mg/kg/day
capreomycin	15 mg/kg IM or IV QD or 25 mg/kg PO 3 times weekly	1,000 mg/day
cycloserine	10 to 15 mg/kg PO QD or BID	1,000 mg/day
ethambutol	Follow weight-based dosing in prescribing information	4,000 mg/dose
ethionamide	10 to 20 mg/kg PO QD or BID	1,000 mg/day
imipenem-cilastatin*	1,000 mg IV BID	2,000 mg/day
levofloxacin	500 to 1,000 mg PO or IV QD	1,000 mg/day
linezolid	600 mg PO or IV QD	600 mg/day
meropenem*	2,000 mg IV BID or TID	6,000 mg/day
moxifloxacin	400 mg PO or IV QD	400 mg/day
para-aminosalicylic acid	8 to 12 g PO BID or TID	12 g/day

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pyrazinamide	Follow weight-based dosing in prescribing information	4,000 mg/dose
streptomycin	15 mg/kg IM or IV QD or 25 mg/kg PO 3 times weekly	20 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Amoxicillin-clavulanic acid should be coadministered with every dose of imipenem-cilastatin or meropenem but is not counted as a separate agent and should not be used as a separate agent.*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Increased mortality
  - QT prolongation

Appendix D: General Information

- Sirturo should only be used in combination with at least 3 other drugs to which the patient's MDR-TB isolate has been shown to be susceptible *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 susceptible.
- Sirturo was approved under accelerated approval based on time to sputum culture conversion. Continued approval for its indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- Laboratory confirmation of multi-drug resistant TB must show TB with an isolate showing genotypic or phenotypic resistance to isoniazid and rifampin.

References

1. Sirturo Prescribing Information. Titusville, NJ: Janssen Therapeutics; August 2019. Available at: https://www.sirturo.com/. Accessed August 16, 2019.
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3. 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. 2013; 62(RR09):1-12. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6209a1.htm?s_cid=rr6209a1_e. Accessed August 5, 2019.
4. World Health Organization. The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: interim policy guidance 2013. Available at: https://www.ncbi.nlm.nih.gov/books/NBK154134/pdf/Bookshelf_NBK154134.pdf. Accessed August 5, 2019.
5. World Health Organization. WHO consolidated guidelines on drug-resistant tuberculosis treatment. 2019. Available at: https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf?ua=1. Accessed August 5, 2019.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	03/06/2020

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