

Clinical Policy: Bedaquiline (Sirturo)

Reference Number: PA.CP.PMN.212

Effective Date: 01/2020

Last Review Date: 01/2026

Description

Bedaquiline (Sirturo[®]) is a diarylquinoline antimycobacterial drug.

FDA Approved Indication(s)

Sirturo is indicated as part of combination therapy in the treatment of adult and pediatric patients (2 years and older and weighing at least 8 kg) with pulmonary tuberculosis (TB) due to *Mycobacterium tuberculosis* resistant to at least rifampin and isoniazid.

Limitation(s) of use:

- Do not use Sirturo for the treatment of:
 - Latent infection due to *Mycobacterium tuberculosis*
 - Drug-sensitive pulmonary TB
 - Extra-pulmonary TB
 - Infections caused by non-tuberculous mycobacteria

Policy/Criteria

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

It is the policy of PA Health & Wellness[®] that Sirturo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multi-Drug Resistant Tuberculosis without Pretomanid (must meet all):

1. Diagnosis of multi-drug resistant (MDR)-TB (i.e., resistant to at least rifampin and isoniazid);
2. Prescribed by or in consultation with an infectious disease specialist or a pulmonologist or expert in the treatment of TB (e.g., state or county public health department, specialists affiliated with TB Centers of Excellence as designated by the CDC, infectious disease specialists managing TB clinics);
3. Age \geq 2 years;
4. Weight \geq 8 kg;
5. Prescribed in combination with at least 3 other anti-TB agents (*Appendix B*);
6. Dose does not exceed one of the following (a, b, c or d):
 - a. Weight \geq 30 kg: 400 mg per day for the first 2 weeks, followed by 200 mg three times per week;
 - b. Weight \geq 15 kg to < 30 kg: 200 mg per day for the first 2 weeks, followed by 100 mg three times per week;
 - c. Weight \geq 10 kg to < 15 kg: 120 mg per day for the first 2 weeks, followed by 60 mg three times per week;

- d. Weight \geq 8 kg to $<$ 10 kg: 80 mg per day for the first 2 weeks, followed by 40 mg three times per week.

Approval duration: 24 weeks

B. Multi-Drug Resistant Tuberculosis with Pretomanid (must meet all):

1. Diagnosis of pulmonary MDR-TB or extensively drug resistant (XDR)-TB;
2. Prescribed by or in consultation with an expert in the treatment of tuberculosis (e.g., state or county public health department, specialists affiliated with TB Centers of Excellence as designated by the CDC, infectious disease specialists managing TB clinics);
3. Age \geq 14 years;
4. Prescribed in combination with pretomanid and linezolid;
**Prior authorization may be required for pretomanid and linezolid.*
5. One of the following (a or b):
 - a. Prescribed in combination with moxifloxacin (off-label);
 - b. Documented resistance to fluoroquinolones, unless contraindicated or clinically significant 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: 26 weeks

C. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Multi-Drug Resistant Tuberculosis without Pretomanid (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
Member has not received more than 24 weeks of Sirturo therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, c or d):
 - a. Weight \geq 30 kg: 200 mg three times per week;
 - b. Weight 15 kg to $<$ 30 kg: 100 mg three times per week;
 - c. Weight \geq 10 kg to $<$ 15 kg: 60 mg three times per week;
 - d. Weight \geq 8 kg to $<$ 10 kg: 40 mg three times per week.

Approval duration: up to a total duration of 24 weeks

B. Multi-Drug Resistant Tuberculosis with Pretomanid (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. Member meets one of the following (a or b):

- a. Member continues to receive pretomanid and linezolid in combination with Sirturo;
- b. Member continues to receive pretomanid and has completed at least 4 weeks of linezolid therapy;
4. Member has not received more than 26 weeks of Sirturo therapy;
5. If request is for a dose increase, new dose does not exceed 200 mg three times per week.

Approval duration: up to a total treatment duration of 26 weeks

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BPaL: bedaquiline, pretomanid, and linezolid

CDC: Centers for Disease Control

DOT: directly observed therapy

FDA: Food and Drug Administration

MDR-TB: multi-drug resistant tuberculosis

TB: tuberculosis

XDR-TB: extensively drug resistant tuberculosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria.

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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
pretomanid	200 mg PO QD for 26 weeks.	200 mg/day
linezolid	600 - 1,200 mg PO QD	1,200 mg/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): QT prolongation

Appendix D: General Information

For MDR-TB:

- 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.
- Laboratory confirmation of multi-drug resistant TB must show TB with an isolate showing genotypic or phenotypic resistance to isoniazid and rifampin.

For MDR-TB or XDR-TB with pretomanid:

- CDC Centers of Excellence for TB: https://www.cdc.gov/tb/education/tb_coe/default.htm
- Pretomanid should only be used in combination with Sirturo and linezolid.
- Laboratory confirmation of multi-drug resistant TB must show TB with an isolate showing genotypic or phenotypic resistance to isoniazid and rifampin.
- Laboratory confirmation of extensively drug resistant TB must show TB with an isolate showing genotypic or phenotypic resistance to isoniazid, rifampin, fluoroquinolones, as well as second-line injectable agents such as aminoglycosides or capreomycin.
- Linezolid starting dose of 1,200 mg daily for 26 weeks may be managed as follows:
 - Adjusted to 600 mg daily and further reduced to 300 mg daily as necessary for adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy.
 - Doses of the regiment missed for safety reasons can be made up at the end of treatment; doses of linezolid alone missed due to adverse reactions should not be made up.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MDR-TB	<p>Weight \geq 30 kg: 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).</p> <p>Weight 15 to <30 kg: 200 mg PO QD for the first 2 weeks, followed by 100 mg PO three times per week (with at least 48 hours between doses) for 22 weeks (total duration of 24 weeks).</p> <p>Weight 10 to < 15 kg: 120 mg PO QD for the first 2 weeks, followed by 60 mg PO three times per week (with at least 48 hours between doses) for 22 weeks (total duration of 24 weeks).</p> <p>Weight 8 to < 10 kg: 80 mg PO QD for the first 2 weeks, followed by 40 mg PO three times per week (with at least 48 hours between doses) for 22 weeks (total duration of 24 weeks).</p> <p>Situro should be administered by directly observed therapy (DOT)</p>	<p>Weight \geq 30 kg: 400 mg/dose</p> <p>Weight 15 to 29 kg: 200 mg/dose</p>
MDR-TB or XDR-TB with pretomanid	<p>Administer in combination with pretomanid and linezolid (BPAL regimen) in a directly observed therapy (DOT) setting.</p> <ul style="list-style-type: none"> • Sirturo: 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 24 weeks (total duration of 26 weeks*). • Pretomanid: 200 mg PO QD for 26 weeks*. • Linezolid: 600 mg* PO QD for 26 weeks*. <p>Patients 17 years of age or older may continue treatment with Sirturo and pretomanid without linezolid if the patient has previously received a total daily dose of linezolid 1,200 mg for at least 4 weeks.</p>	400 mg/dose

VI. Product Availability

Tablets: 20 mg, 100 mg

VII. References

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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 October 30, 2025.
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12. WHO consolidated guidelines on tuberculosis: module 5: management of tuberculosis in children and adolescents. 18 March 2022. Available at: <https://www.who.int/publications/i/item/9789240046764>. Accessed October 30, 2025.
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<https://www.ncbi.nlm.nih.gov/books/NBK613092/>. Accessed November 24, 2025. PMID: 40163610.

Reviews, Revisions, and Approvals	Date
Policy Created	01/2020
1Q 2021 annual review: updated for pediatric extension from 12 years old or 30 kg to 5 years of age or 15 kg for MDR-TB without Pretomanid per revised prescribing information; for requests in combination with Pretomanid, revised prescriber requirement from infectious disease specialist to an expert in the treatment of tuberculosis; references reviewed and updated	01/2021
1Q 2022 annual review: clarified expert in the treatment of tuberculosis to include state or county public health department, specialists affiliated with any of the four TB Centers of Excellence as designated by the CDC, or ID specialists managing TB clinics; references reviewed and updated.	01/2022
1Q 2023 annual review: for use without Pretomanid added requirement for weight \geq 15 kg per prescribing information; for use with Pretomanid lowered age requirement from 17 to 15 years per updated WHO 2022 guidance, added alternative option if there is no documented fluoroquinolone resistance for off-label use when prescribed in combination with moxifloxacin, clarified approval duration from 6 months to 26 weeks; for continued therapy reinforced therapy duration requirements that were previously only referenced in the approval duration; references reviewed and updated.	01/2023
1Q 2024 annual review: updated linezolid dosing from 1,200 mg to 600 mg per updated CDC recommendations; references reviewed and updated.	01/2024
RT4: updated FDA approved indications to reflect changes from accelerated to full approval per updated prescribing information; removed increased mortality from boxed warnings.	07/2024
1Q 2025 annual review: for continuation of therapy added option for up to 9 month approval duration if request is for Sirturo prescribed in combination with linezolid, moxifloxacin, and pyrazinamide per World Health Organization (WHO) updates to the treatment of drug-resistant tuberculosis; references reviewed and updated.	01/2025
1Q 2026 annual review: revised age limit for use with pretomanid down to 14 years of age (from 15 years) per IDSA; removed allowance for use up to 9 months as these extended regimens only recommend bedaquiline be used for 24-26 weeks, not the entire extended treatment duration; references reviewed and updated. RT4: updated to include pediatric extension down to 2 years of age and weighing at least 8 kg for MDR-TB without pretomanid per updated prescribing information.	01/2026