Pharmacy Policy Bulletin: J-0231 Pretomanid – Commercial and Healthcare Reform	
Number: J-0231	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Drugs = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0231-009	**Original Date:** 11/06/2019
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Pretomanid
FDA-Approved Indication(s):	• Indicated as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary tuberculosis (TB) that is resistant to isoniazid, rifamycins, a fluoroquinolone and a second line injectable antibacterial drug OR adults with pulmonary TB resistant to isoniazid and rifampin, who are treatment-intolerant or nonresponsive to standard therapy.

Background:	• Pretomanid is a nitroimidazooazine antimycobacterial drug that inhibits mycolic acid biosynthesis, blocking cell wall production and killing replicating Mycobacterium tuberculosis (*M. tuberculosis*). • According to the Centers for Disease Control and Prevention (CDC), multi-drug resistant tuberculosis (MDR TB) is TB that is resistant to at least isoniazid and rifampin. Two more serious forms of MDR TB are called pre-extensively drug resistant TB (pre-XDR TB) and extensively drug resistant TB (XDR-TB). Pre-XDR and XDR TB are rare types of TB disease that are resistant to nearly all medicines used to treat TB disease. Pre-XDR TB is defined as TB that is resistant to isoniazid, rifampin, and a fluoroquinolone OR by an organism that is resistant to isoniazid, rifampin, and a second-line injectable (amikacin, capreomycin, and kanamycin). XDR-TB is caused by an organism that is resistant to isoniazid, rifampin, a fluoroquinolone, and a second-line injectable (amikacin, capreomycin, and kanamycin) OR by an organism that is resistant to isoniazid, rifampin, a fluoroquinolone, and bedaquiline or linezolid. • In 2024 provisional guidance from the CDC for the use of pretomanid for treatment of drug-resistant TB, pretomanid is recommended for the treatment of pre-XDR TB and MDR TB. • The recommended treatment duration for tuberculosis should be individualized to each patient. There are several treatment regimens recommended in the United States for TB disease. TB disease treatment can take 4, 6, or 9 months depending on the regimen. In some cases, treatment can last much longer. For example, multidrug-resistant TB might require 18 to 24 months or longer to treat.

	If treatment is cut short, the remaining bacilli may develop drug resistance, and TB disease may re-occur. • CDC recommends video DOT (directly observed therapy; vDOT) as equivalent to in-person DOT for persons undergoing treatment for diagnosed tuberculosis. • Approval of this indication is based on limited clinical safety and efficacy data. This drug is indicated for use in a limited and specific population of patients. • Prescribing Considerations: o Pretomanid tablets are given once daily in a combination regimen with bedaquiline and linezolid for 26 weeks. o Safety and effectiveness of pretomanid tablets have not been established for its use in combination with drugs other than bedaquiline and linezolid. o Pretomanid should be taken with food and water. o Doses of the regimen missed for safety reasons can be made up at the end of treatment; doses of linezolid alone missed due to linezolid adverse reactions should not be made up. The combination regimen has been extended to 9 months in clinical trials. o Pretomanid tablets are not indicated for patients with drug-sensitive tuberculosis, latent infection due to *M. tuberculosis*, extra-pulmonary infection due to *M. tuberculosis*, and MDR TB that is not treatment-intolerant or nonresponsive to standard therapy. o Pretomanid is not recommended for use in breastfeeding populations. o Administer the combination regimen of pretomanid, bedaquiline, and linezolid by directly observed therapy (DOT).

Approval Criteria

I. Initial Authorization

A. Pre-Extensively Drug Resistant (XDR) or XDR Tuberculosis

When a benefit, coverage of pretomanid may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member has a diagnosis of pulmonary tuberculosis (ICD-10: A15.0), classified as one (1) of the following **(a. or b)**:
- **a.** Pre-extensively drug resistant (pre-XDR)
- **b.** Extensively drug resistant (XDR)

2. The member has experienced therapeutic failure, contraindication, or intolerance to all of the following **(a. and b.)**:
- **a.** isoniazid
- **b.** A rifamycin antibiotic (for example rifampin, rifabutin, or rifapentine)

3. The member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following **(a. or b.)**:
- **a.** A fluoroquinolone antibiotic (for example levofloxacin, moxifloxacin)
- **b.** amikacin, kanamycin, or capreomycin

4. The member is taking pretomanid as part of a combination regimen with both of the following medications **(a. and b.)**:
- **a.** bedaquiline
- **b.** linezolid

B. Treatment Intolerant or Nonresponsive Multidrug Resistant (MDR) Tuberculosis

When a benefit, coverage of pretomanid may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member has a diagnosis of pulmonary tuberculosis (ICD-10: A15.0), classified as one (1) of the following **(a. or b.)**:
- **a.** Treatment intolerant
- **b.** Nonresponsive multidrug resistant (MDR)

2. The member has experienced therapeutic failure, contraindication, or intolerance to all of the following **(a. and b.)**:
   a. isoniazid
   b. A rifamycin antibiotic (for example rifampin, rifabutin, or rifapentine)
3. The member is taking pretomanid as part of a combination regimen with both of the following medications **(a. and b.)**:
   a. bedaquiline
   b. linezolid

II. Reauthorization

When a benefit, reauthorization of pretomanid may be approved when the following criterion is met **(A.)**:

A. The member has experienced positive clinical response and requires additional antimicrobial therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Pretomanid tablets will not be covered for drug-sensitive tuberculosis, latent infection due to *M. tuberculosis*, extra-pulmonary infection due to *M. tuberculosis*, or MDR TB that is not treatment-intolerant or is responsive to standard therapy.

II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

III. For Commercial and HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Pretomanid [package insert]. Hyderabad, India: Mylan Laboratories Limited; November 2024.
2. Centers for Disease Control and Prevention. About Drug-Resistant Tuberculosis Disease. Available at: https://www.cdc.gov/tb/about/drug-resistant.html?CDC_AAref_Val. Accessed: January 6, 2025.
3. World Health Organization Consolidated Guidelines on Tuberculosis Treatment. Available at: https://www.who.int/publications/i/item/9789240063129. Accessed: January 6, 2025.
4. Centers for Disease Control and Prevention. Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease. Available at: https://www.cdc.gov/tb/topic/drtb/bpal/default.htm. Accessed January 6, 2025.
5. CDC. Clinical Overview of Drug-Resistant Tuberculosis Disease. Tuberculosis (TB). Published January 6, 2025. https://www.cdc.gov/tb/hcp/clinical-overview/drug-resistant-tuberculosis-disease.html

6. Mangan JM, Woodruff RS, Winston CA, et al. Recommendations for Use of Video Directly Observed Therapy During Tuberculosis Treatment - United States, 2023. MMWR Morb Mortal Wkly Rep. 2023;72(12):313-316. Published 2023 Mar 24.
7. Saukkonen JJ, Duarte R, Munsiff S, et al. Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. Am J Respir Crit Care Med 2025:211 (2):15-33.
8. CDC. Length of TB Disease Treatment. Available at: https://www.cdc.gov/tb/webcourses/TB101/page16411.html. Accessed February 24, 2025.