Pretomanid

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: UMP080

Description

Pretomanid is an orally administered nitroimidazooxazines antimycobacterial agent.

Length of Authorization

- Initial: six months
- Renewal: N/A

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
pretomanid	200 mg tablet	Pulmonary tuberculosis that is extensively drug resistant (XDR), treatment intolerant, or nonresponsive multi-drug resistant (MDR)	30 tablets/30 days	TBD

Initial Evaluation

I. Pretomanid may be considered medically necessary when the following criteria below are met:
   A. The member is 18 years of age or older; **AND**
   B. The medication is prescribed by, or in consultation with a pulmonologist or infectious disease specialist; **AND**
   C. A diagnosis of **pulmonary extensively drug resistant (XDR), treatment-intolerant, or nonresponsive multidrug-resistant (MDR) tuberculosis (TB)** when the following are met:
      1. Documentation of resistance to isoniazid, rifamycins, a fluoroquinolone and an injectable antimicrobial (e.g., amikacin, kanamycin, or capreomycin); **AND**
      2. Documentation of intolerance to para-aminosalicyclic acid (PAS), ethionamide, aminoglycosides or fluoroquinolones; **AND**
      3. The member will be using pretomanid in combination with bedaquiline (Situro) AND linezolid (Zyvox) for the duration of therapy; **AND**
      4. The member will have directly observed treatment (DOT) plan in place

II. Pretomanid is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:
   A. The use of pretomanid in combination with drugs other than bedaquiline (Situro) and linezolid (Zyvox)

B. Drug-sensitive (DS) tuberculosis
C. Latent infection due to Mycobacterium tuberculosis
D. Extra-pulmonary infection due to Mycobacterium tuberculosis
E. Multidrug-resistant tuberculosis that is not treatment-intolerant or nonresponsive to standard therapy

Supporting Evidence

I. Pretomanid was studied in a Phase 3, open-label trial with 109 adult patients with pulmonary TB that are XDR, treatment intolerant, or non-responsive MDR. In that trial, the safety and efficacy of pretomanid in combination with bedaquline and linezolid was assessed.

Definition of TB Types	
Drug-resistant TB	TB caused by an isolate of Mycobacterium tuberculosis (M. tuberculosis) that is resistant to one or more antituberculous drugs
Multidrug-resistant TB (MDR-TB)	TB caused by an isolate of M. tuberculosis that is resistant to both isoniazid (INH) and rifampin and possibly additional agents
Extensively drug-resistant TB (XDR-TB)	TB caused by an isolate of M. tuberculosis that is resistant to at least INH, rifampin, and fluoroquinolones as well as either aminoglycosides (e.g. amikacin, kanamycin) or capreomycin or both
Totally drug-resistant TB (TDR-TB)	TB caused by an isolate of M. tuberculosis resistant to all locally tested medications

II. The primary efficacy outcome was the incidence of bacteriologic failure, relapse, or clinical failure through follow up until six months after the end of treatment; of the 107 patients assessed, 12 (11%) patients were classified as treatment failure, while 95 (89%) patients were classified as treatment success. Treatment success was defined as culture negative status at six months post treatment.
III. No pediatric patients were included in the trial.
IV. Pretomanid was only studied in combination with bedaquiline (Situro) and linezolid (Zyvox).
V. Patients that were included in the trial demonstrated resistance to isoniazid, rifamycins, a fluroquinolone and an injectable antimicrobial, and had intolerance to para-aminosalicyclic acid (PAS), ethionamide, aminoglycosides or fluoroquinolones.

Investigational or Not Medically Necessary Uses

I. Safety and efficacy has not been established for the use of pretomanid in combination with drugs other than bedaquiline (Situro) and linezolid (Zyvox).
II. Pretomanid was FDA-approved on an accelerated approval pathway under the Limited Population Pathway for Antibacterial and Antifungal Drugs. As stated in the label, the approval of this indication is based on limited clinical safety and efficacy data. Therefore, the use of this drug is indicated for a very specific population of patients, and antimicrobial stewardship practices should be applied when treating this population of patients. Therefore, the use of pretomanid in setting other than the label indication [pulmonary extensively drug resistant (XDR), treatment-intolerant, or nonresponsive multidrug-resistant (MDR) tuberculosis (TB)], is considered experimental and investigational.

References

1. Pretomanid [Prescribing Information]. Mylan: Hyderabad, India. August 2019.
2. Sirturo [Prescribing information]. Janssen Therapeutics: Titusville,NJ. December 2012.
3. Center 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. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6209a1.htm?s_cid=rr6209a1_e
4. World Health Organization: WHO Guidelines on Tuberculosis. Available at: https://www.who.int/publications/guidelines/tuberculosis/en/
5. The Food and Drug Administration: FDA Briefing Document on Pretomanid 200 mg Tablet. Meeting of the Antimicrobial Drugs Advisory Committee (AMDAC). June 2019. Available at: https://www.fda.gov/media/127592/download
6. Clinicaltrial.gov

Policy Implementation/Update:

Date Created	September 2019
Date Effective	November 2019
Last Updated	
Last Reviewed	

Action and Summary of Changes	Date