Prescribing Protocol SESLHDPR/672

Bedaquiline fumarate for resistant pulmonary tuberculosis

Health
South Eastern Sydney
Local Health District

Areas where Protocol/Guideline applicable	Inpatient ward areas and outpatients seen by Respiratory tuberculosis (TB) clinic or Infectious Disease (ID) clinic
Authorised Prescribers:	Respiratory specialist, Infectious Diseases specialist Please note this medication will require an SAS form (Category A) to be completed for the entire course of therapy
Indication for use	Multidrug-resistant pulmonary tuberculosis (MDR-TB) or extensively drug resistant pulmonary tuberculosis (XDR-TB)
Clinical condition Patient selection: Inclusion criteria	Pulmonary tuberculosis in adults (≥18 years) – resistant to standard therapy but sensitive to bedaquiline. Used in combination with at least 3 other drugs to which the patient's MDR-TB isolate has been shown to be susceptible.
Contra-indications	Known hypersensitivity Pregnancy and breastfeeding Men should agree to use highly effective method of birth control and not to donate sperm during treatment and for 3 months after receiving the last dose Children <18 year of age
Precautions	An increased risk of death was observed in the bedaquiline treatment group in one placebo-controlled trial. The imbalance of deaths is unexplained. Should only be used when an effective treatment regimen cannot otherwise be provided. QT prolongation – see monitoring requirements and caution when used with other QT prolonging medications (e.g. fluoroquinolones, macrolides, clofazimine). Caution if history of: Torsade de Points, congenital long QT syndrome, hypothyroidism and bradyarrhythmia's, uncompensated heart failure. Patients >65 (lack of data) Extra pulmonary TB (lack of data) Patients should be advised to avoid alcohol while on therapy
Proposed Place in Therapy	Used as part of combination therapy for pulmonary multi-drug resistant tuberculosis.
Dosage	Weeks 1-2: 400mg orally, once daily with food Weeks 3-24: 200mg orally, three times per week with food (with at least 48 hours between doses) (for a total dose of 600mg per week)
Duration of therapy	The total duration of therapy is 24 weeks.

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Important Drug Interactions	Bedaquiline is metabolized by CYP3A4. Therapeutic effect may be reduced when administered with inducers of CYP3A4. Avoid concomitant administration with strong CYP 3A4 inducers (e.g. rifampicin) Therapeutic exposure to bedaquiline may increase with strong CYP3A4 inhibitors and increase risk of adverse reaction. Avoid use of strong CYP3A4 inhibitors for more than 14 consecutive days while on bedaquiline unless benefit of treatment outweighs the risk.
Administration Instructions	Orally with food
Monitoring requirements	Baseline ECG and ECG at least at 2, 12 and 24 weeks after starting treatment. EUC - Serum potassium, calcium, magnesium at baseline and corrected if abnormal. Follow up monitoring of electrolytes if QT prolongation is detected. Monitor for symptoms of hepatic-related adverse effects and ALT, AST, alkaline phosphatase, bilirubin at baseline, monthly while on treatment and as needed. Monitor weekly for nausea, headache, hemoptysis, chest pain, arthralgia and rash.
Management of Complications	**QT prolongation** Discontinue if patient develops clinically significant ventricular arrhythmia, QTcF interval of >500ms (confirmed by repeat ECG) If syncope occurs obtain and ECG to detect QT prolongation **Hepatic complications** Increase of serum aminotransferases to >3x ULN should be followed by repeat testing within 48 hours. Test for viral hepatitis and discontinue other hepatotoxic medications. Discontinue bedaquiline if: - Aminotransferase elevations are accompanied by total bilirubin elevation >2x ULN - Aminotransferase elevations are >8x ULN - Aminotransferase elevations persist beyond 2 weeks
Basis of Protocol/Guideline: (including sources of evidence, references)	Provisional CDC Guidelines for the Use and safety monitoring of bedaquiline fumarate for the treatment of multidrug-resistant tuberculosis. MMWR, 2013; 62(9); 1-12. SIRTURO PI

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	Sanford Guide 51st Ed. 2021. Nahid P et al. Treatment of Drug-Resistant Tuberculosis. An Offical ATS/CDC/ERS/IDSA Clinical Practice Guideline. AM J Respir Crit Care Med 2019; 200(10): e93-e142. WHO consolidated guidelines on drug-resistant tuberculosis treatment. 2019
Groups consulted in development of this guideline	AMS pharmacist, ID Department, Respiratory Specialist, Antimicrobial Stewardship Committee for Prince of Wales Hospital and St George Hospital, Guidance Management Committee

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GOVERNANCE	
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