Sirturo® (bedaquiline) – Expanded indication

- On May 27, 2020, the FDA approved Janssen's Sirturo (bedaquiline), as part of combination therapy in the treatment of adult and pediatric patients (5 years and older and weighing at least 15 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Sirturo should be reserved for use when an effective treatment regimen cannot otherwise be provided.
    - Sirturo was previously approved for this indication in patients 12 to less than 18 years of age and weighing at least 30 kg.
    - Sirturo is approved under accelerated approval based on time to sputum culture conversion. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.
- Sirturo should not be used 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.
- The approval of Sirturo for the expanded indication was based on a single-arm, open-label, multi-cohort study in patients 5 to less than 18 years of age with confirmed or probable pulmonary MDR-TB infection. Fifteen patients were 5 to 10 years of age. The study evaluated the pharmacokinetics, safety and tolerability of Sirturo in combination with a background regimen.
    - In the subset of patients with culture positive pulmonary MDR-TB at baseline, treatment with Sirturo resulted in conversion to a negative culture in 100% (3/3 patients) at week 24.
- Sirturo carries a boxed warning for increased mortality and QT prolongation.
- The most common adverse reaction (≥ 10%) with Sirturo use in pediatric patients 5 years to less than 12 years of age was elevation in liver enzymes.
- The recommended dose of Sirturo in pediatric patients (5 years and older and weighing at least 15 kg) is based on body weight and shown in the table below. The total duration of treatment with Sirturo in pediatric patients is 24 weeks.
    - Sirturo should be administered by directly observed therapy.
    - Refer to the Sirturo drug label for adult dosing and additional dosing recommendations.

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Body weight	Dosage recommendations	
	Weeks 1 and 2	**Weeks 3 to 24**
15 kg to < 30 kg	200 mg (2 of the 100 mg tablets OR 10 of the 20 mg tablets) orally **once daily**	100 mg (1 of the 100 mg tablets OR 5 of the 20 mg tablets) orally **three times per week**
≥ 30 kg	400 mg (4 of the 100 mg tablets OR 20 of the 20 mg tablets) orally **once daily**	200 mg (2 of the 100 mg tablets OR 10 of the 20 mg tablets) orally **three times per week**

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