Tolsura™ (itraconazole) – New drug approval

- On December 12, 2018, Mayne Pharma announced the FDA approval of Tolsura (itraconazole) capsules, for the treatment of the following fungal infections in immunocompromised and non-immunocompromised adult patients: blastomycosis, pulmonary and extrapulmonary; histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis; and aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.
    - Tolsura is not indicated for the treatment of onychomycosis.
    - Tolsura is NOT interchangeable or substitutable with other itraconazole products due to the differences in the dosing between Tolsura and other itraconazole products. Therefore, follow the specific dosage recommendations for Tolsura.
- Blastomycosis, histoplasmosis, and aspergillosis are serious infections that most commonly occur in vulnerable or immunocompromised patients (eg, history of cancer, transplants, human immunodeficiency virus/acquired immunodeficiency syndrome, chronic rheumatic disorders), and are often associated with high mortality rates or long-term health issues.
- Tolsura is an azole antifungal that incorporates Mayne Pharma's proprietary SUBA technology, which improves the bioavailability of poorly soluble drugs.
    - Itraconazole is also available generically as a capsule and an oral solution.
- The approval of Tolsura was based upon efficacy studies conducted for itraconazole 100 mg capsules and pharmacokinetic studies comparing itraconazole capsules to Tolsura.
- Tolsura carries a boxed warning for congestive heart failure and drug interactions.
- Tolsura is contraindicated in co-administration with certain drugs that either affect metabolism of itraconazole or whose metabolism is affected by itraconazole.
- Additional warnings and precautions of Tolsura include hepatotoxicity, cardiac dysrhythmias, peripheral neuropathy, hearing loss, and hypersensitivity reactions.
- The most common adverse reactions (≥ 1%) with Tolsura use were nausea, rash, vomiting, edema, headache, diarrhea, fatigue, fever, pruritus, hypertension, abnormal hepatic function, abdominal pain, dizziness, hypokalemia, anorexia, malaise, decreased libido, somnolence, albuminuria, and impotence.
- The recommended dose of Tolsura depends on the indication and Tolsura is given orally with food.

Indication	Daily dosing
Treatment of blastomycosis and histoplasmosis	
Recommended dose	130 mg (2 x 65 mg capsules) once daily If no obvious improvement, or there is evidence of progressive fungal disease, the dose should be increased in 65 mg increments to a maximum of 260 mg/day (130 mg twice daily). Doses above 130 mg/day should be given in two divided doses.

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Treatment of aspergillosis	
Recommended dose	130 mg once daily; or 260 mg/day (130 mg twice daily)
Treatment in life-threatening situations	
Although clinical studies did not provide for a loading dose, it is recommended, based on pharmacokinetic data, that a loading dose should be used	A loading dose of 130 mg three times daily (390 mg/day) is recommended to be given for the first 3 days, followed by the appropriate recommended dosing based on indication. Treatment should be continued for a minimum of three months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection.

- Mayne Pharma plans to launch Tolsura in January 2019. Tolsura will be available as 65 mg capsules.