

Tolsura (itraconazole)



NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Tolsura
- **Generic name:** Itraconazole
- **Pharmacological class:** Azole antifungal
- **Strength and Formulation:** 65mg; capsules
- **Manufacturer:** Mayne Pharma US
- **How supplied:** Caps—60
- **Legal Classification:** Rx

Tolsura



Indication

- Blastomycosis
- Histoplasmosis
- Aspergillosis in patients who are intolerant of or refractory to amphotericin B

Limitations of Use

- **Not for treating** onychomycosis
- **Not interchangeable or substitutable** with other itraconazole products due to dosing differences

Dosage & Administration

- Swallow whole
- Take with food
- Doses >130mg should be given in 2 divided doses
- **Blastomycosis, histoplasmosis:** 130mg once daily, may increase by 65mg increments; max 260mg/day

Dosage & Administration

- **Aspergillosis:** 130mg once daily; max 260mg/day
- **Life-threatening conditions:** give loading dose of 130mg three times daily for first 3 days, followed by the appropriate treatment dose; continue for at least 3 months until resolved

Considerations for Special Populations

- **Pregnancy:** No data on exposure to itraconazole during pregnancy for approved indications
- **Nursing mothers:** Consider benefits of breastfeeding with potential adverse effect on infant
- **Pediatric:** Not established
- **Elderly:** Insufficient number studied; reversible or permanent hearing loss reported
- **Hepatic or renal impairment:** Monitor carefully

Contraindications

- Concomitant methadone, disopyramide, dofetilide, dronedarone, quinidine, isavuconazole, ergots, irinotecan, lurasidone, oral midazolam, pimozide, triazolam, felodipine, nisoldipine, ivabradine, ranolazine, eplerenone, naloxegol, lomitapide, lovastatin, simvastatin, avanafil, ticagrelor

Contraindications

- Concomitant colchicine, fesoterodine, or solifenacin in renal/hepatic impairment
- Concomitant eliglustat in poor or intermediate CYP2D6 metabolizers or those taking strong or moderate CYP2D6 inhibitors

Boxed Warning

- Congestive heart failure (CHF)
- Drug interactions

Warnings/Precautions

- **CHF risk** (eg, ischemic/valvular disease, COPD, renal failure, edema); monitor and reassess treatment if occurs
- Monitor for signs/symptoms of **liver dysfunction**; discontinue and perform LFTs if develop

Warnings/Precautions

- **Discontinue** if neuropathy, hearing loss or hypersensitivity occurs
- **Elevated liver enzymes, active liver disease, previous hepatotoxicity:** not recommended unless serious or life-threatening situation

Interactions

- See **Contraindications**
- Serious cardiac effects with pimozide, methadone, quinidine, others
- Concomitant alfuzosin, silodosin, tamsulosin, fentanyl, apixaban, rivaroxaban, vorapaxar, antineoplastics (see full labeling), simeprevir, aliskiren, riociguat, sildenafil or tadalafil (for PAH), everolimus, sirolimus, IV temsirolimus, salmeterol, darifenacin, vardenafil, colchicine, conivaptan, tolvaptan, regorafenib, *saccharomyces boulardii*: not recommended **during and 2 weeks after** itraconazole

Interactions

- **Avoid** itraconazole for more than 2 weeks during bedaquiline therapy
- Rifabutin, carbamazepine, lumacaftor/ivacaftor: **avoid** 2 weeks before, during, and 2 weeks after itraconazole
- **Avoid** isoniazid, rifampicin, phenobarbital, phenytoin, efavirenz, nevirapine 2 weeks before and during itraconazole therapy

Interactions

- **Potentiates** alfentanil, buprenorphine, oxycodone, sufentanil, digoxin, clarithromycin, trimetrexate, cilostazol, dabigatran, warfarin, repaglinide, saxagliptin, praziquantel, eletriptan, certain antineoplastics, antipsychotics, anxiolytics, hypnotics, zopiclone, daclatasvir, indinavir, maraviroc, nadolol, diltiazem, other dihydropyridines, verapamil, bosentan, guanfacine, aprepitant, loperamide, budesonide, ciclesonide, dexamethasone, fluticasone, methylprednisolone, cyclosporine, tacrolimus, atorvastatin, venlafaxine, fesoterodine, solifenacin, dutasteride, oxybutynin, sildenafil, tadalafil, tolterodine, eliglustat, oral alitretinoin, cabergoline, cannabinoids, cinacalcet, ivacaftor; monitor, may need to **reduce dose** of these

Interactions

- **Potentiated** by ciprofloxacin, erythromycin, clarithromycin, idelalisib, cobicistat, protease inhibitors, diltiazem, gastric acid suppressants (eg, antacids, H₂ blockers, PPIs), other CYP3A4 inhibitors; monitor, may need to reduce itraconazole dose
- **Tinnitus** or hearing impairment with quinidine
- Increased risk of **CHF** with concomitant CCBs

Interactions

- Concomitant artemether-lumefantrine, quinine, cobicistat, elvitegravir (ritonavir-boosted), ritonavir, saquinavir (unboosted), tenofovir disoproxil fumarate, dienogest, ulipristal, netupitant; monitor for adverse events
- **Antagonizes** meloxicam; increase dose if necessary

Adverse Reactions

- Nausea
- Rash
- Vomiting
- Edema
- Headache
- Diarrhea
- Fatigue
- Fever
- Pruritus
- Hypertension
- Abnormal hepatic function
- Abdominal pain
- Dizziness
- Hypokalemia
- Anorexia
- Malaise
- Decreased libido
- Somnolence
- Albuminuria
- Impotence
- Hepatotoxicity
- CHF
- Neuropathy
- Hearing loss
- Hypersensitivity

Mechanism of Action

- Itraconazole inhibits the CYP450-dependent ^{14}C -demethylation of ergosterol, a vital component of fungal cell membranes
- Tolsura utilizes a proprietary technology that improves the bioavailability of poorly soluble drugs

Clinical Studies

- The approval of Tolsura was supported by data from clinical studies in invasive mycoses conducted with itraconazole 100mg capsules
- Dosage for Tolsura is different from that of other itraconazole formulations
- Tolsura is **not interchangeable or substitutable** with other itraconazole products

New Product Monograph

- For more information view the product monograph available at:

<https://www.empr.com/drug/tolsura/>