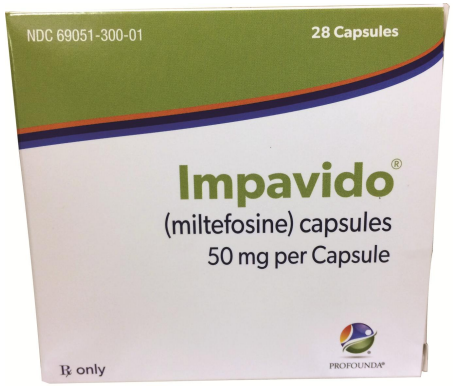
Impavido

(miltefosine)



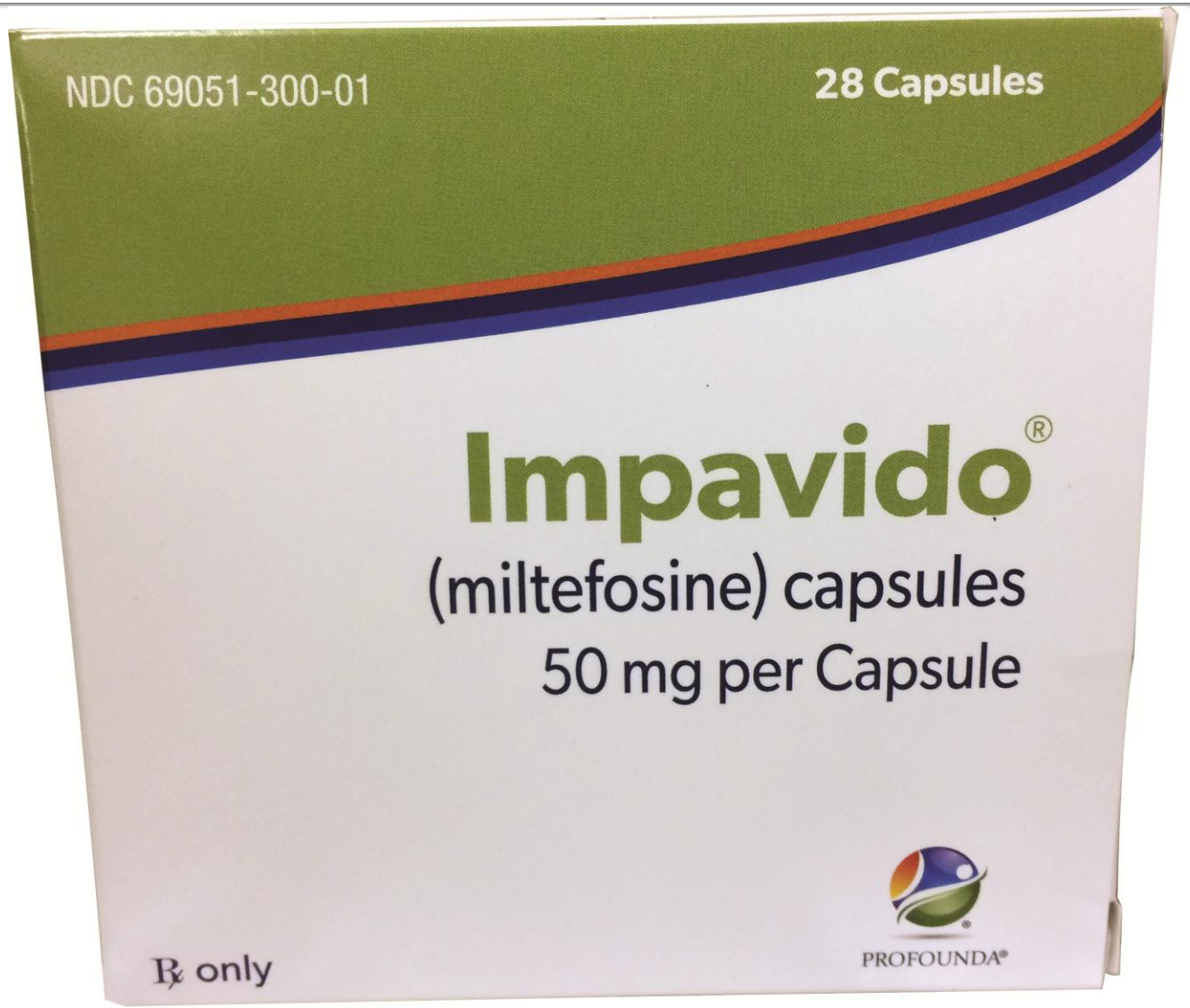
New Product Slideshow

MPR

Introduction

- **Brand name:** Impavido
- **Generic name:** Miltefosine
- **Pharmacological class:** Antileishmanial agent
- **Strength and Formulation:** 50mg; hard gel capsules
- **Manufacturer:** Profounda
- **How supplied:** Blister cards—28 (2 x 14)
- **Legal Classification:** Rx

IMPAVIDO


NDC 69051-300-01
28 Capsules
Impavido®
(miltefosine) capsules
50 mg per Capsule
℞ only
PROFOUNDA®

Indications

- Treatment of visceral (due to *Leishmania donovani*), cutaneous (due to *L. braziliensis*, *L. guyanensis*, *L. panamensis*), and mucosal (due to *L. braziliensis*) **leishmaniasis**

- **Limitations of use:**
  - Not evaluated in treatment of other *Leishmania* species
  - *Leishmania* species studied in clinical trials were based on epidemiologic data; geographic variation in clinical response of the same *Leishmania* species may exist

Dosage & Administration

- Swallow whole
- Take with food
- Treat for 28 consecutive days
- ≥12yrs:
  - 30–44kg: 50mg twice daily (breakfast and dinner)
  - ≥45kg: 50mg three times daily (breakfast, lunch, and dinner)

Considerations for Special Populations

- **Pregnancy:** Category D
- **Nursing mothers:** Not recommended (during and for 5 months after therapy)
- **Pediatric:** <12yrs: not established
- **Geriatric:** Insufficient number studied
- **Renal impairment:** SCr or BUN ≥1.5xULN excluded from studies
- **Hepatic impairment:** ALT or AST ≥3xULN and bilirubin ≥2xULN excluded from studies

Contraindications

- Pregnancy (Category D)
- Sjögren-Larsson-Syndrome

Warnings/Precautions

- **Embryo-fetal toxicity**; obtain a serum or urine pregnancy test in females of reproductive potential prior to prescribing
- Use effective contraception during therapy and for 5 months after completion; use additional non-hormonal or alternative methods of contraception if vomiting/ diarrhea occur during therapy
- Possible reproductive effects (eg, impaired fertility)

Warnings/Precautions

- **Monitor** renal function weekly during therapy and for 4 weeks after completion
- **Monitor** platelets (for visceral leishmaniasis), ALT, AST, and bilirubin during therapy
- Maintain adequate **hydration**
- **Discontinue** if exfoliative or bullous rash develops

Adverse Reactions

- Nausea
- Vomiting
- Diarrhea
- Headache
- Decreased appetite
- Dizziness
- Abdominal pain
- Pruritus
- Somnolence
- Elevated transaminases
- Elevated creatinine
- Thrombocytopenia
- Stevens-Johnson Syndrome

Mechanism of Action

- The exact mechanism of action of miltefosine against *Leishmania* species is unknown
- It is likely to involve interaction with phospholipids and sterols, including membrane lipids, inhibition of cytochrome c oxidase (mitochondrial function), and apoptosis-like cell death

Clinical Trials

- The efficacy of Impavido in the treatment of visceral leishmaniasis was studied in a randomized, open-label, active-controlled trial in India where *L. donovani* is prevalent
- Patients either received Impavido 50mg twice a day (once daily if <25kg) or amphotericin B deoxycholate 1mg/kg IV every other day for 15 doses

Clinical Trials

- The **primary endpoint** was final cure, defined as initial cure at end of therapy plus absence of signs and symptoms of visceral leishmaniasis at 6 months follow up
- The **final cure rate** for Impavido was 94% vs. 97% for amphotericin B (95% CI: −3%, 6.8%)

Clinical Trials

- Treatment of cutaneous leishmaniasis with Impavido was studied in a randomized, placebo-controlled trial in Colombia and Guatemala where *L. panamensis* and/or *L. braziliensis* are prevalent
- Patients either received Impavido 50mg three times a day (twice a day if <45kg) or placebo

Clinical Trials

- The **primary endpoint** was definite cure, defined as apparent (complete epithelialization of all lesions) or partial cure (incomplete epithelialization, no enlargement by>50% in lesions, no appearance of new lesions, and negative parasitology if done) at 2 weeks after end of therapy and complete epithelialization of all ulcers at 6 months after end of therapy

Clinical Trials

- Results demonstrated that the **definite cure rate** for Impavido was statistically significantly higher than placebo, at 66% vs. 30% respectively ($P<0.0001$)

Clinical Trials

- A single arm trial was conducted to evaluate the efficacy of Impavido for the treatment of mucosal leishmaniasis in Bolivia, where *L. braziliensis* is prevalent
- Patients received Impavido at a target dose of 2.5mg/kg/day for 28 days

Clinical Trials

- By 12 months after the end of therapy, 62% of patients had complete resolution of edema, erythema, infiltration, and erosion from the involved mucosal site.

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/impavido/drug/34473/