

PRIOR AUTHORIZATION POLICY

POLICY: Infectious Disease – Impavido Prior Authorization Policy

- Impavido® (miltefosine capsules – Profounda)

REVIEW DATE: 04/24/2024; selected revision 06/05/2024

OVERVIEW

Impavido, an anti-leishmanial agent, is indicated in patients ≥ 12 years of age weighing ≥ 30 kg (66 lbs) for the treatment of:¹

- **Visceral leishmaniasis** caused by *Leishmania donovani*.
- **Cutaneous leishmaniasis** caused by *L. braziliensis*, *L. guyanensis*, and *L. panamensis*.
- **Mucosal leishmaniasis** caused by *L. braziliensis*.

The treatment duration is 28 consecutive days. Limitation of use: *Leishmania* species studied in clinical trials evaluating Impavido were based on epidemiologic data; there may be geographic variation in clinical response of the same *Leishmania* species to Impavido; and the efficacy of Impavido in the treatment of other *Leishmania* species has not been evaluated.

A systematic review of four studies conducted in the Americas evaluated the efficacy of Impavido in pediatric patients ≤ 12 years of age with cutaneous leishmaniasis (n = 130).² The regimen was similar for all studies, with a target dose of 2.5 mg/kg/day (given as three times a day) for 28 days. The reported efficacy ranged from 63.1% to 82.8%.

Guidelines/Recommendations

Infectious Diseases Society of America (IDSA) guidelines for treatment of *Leishmaniasis* (2016) note that Impavido can be used as monotherapy.³ Amphotericin B is also a treatment option for Leishmaniasis. IDSA recommend minimizing exposure to and preventing sand fly bites especially for immunocompromised travelers.

The FDA has given Impavido an Orphan Drug Designation for the treatment of leishmaniasis, granulomatous amebic encephalitis (GAE), primary amebic encephalitis (PAM), and Acanthamoeba keratitis.⁴ The CDC recognizes Impavido as a treatment option for Ameba related infections cause by Naegleria fowleri, Balamuthia, and Acanthamoeba.⁵ Impavido is recommended as part of a treatment regimen of often > 5 medications that include amphotericin B, an azole, rifampin, flucytosine, pentamidine, sulfadiazine, or trimethoprim/sulfamethoxazole for GAE infections.⁶ PAM infections are treated with Impavido plus antifungals and antibiotics to include amphotericin B, rifampin, an azole, and azithromycin.⁷ Patients may require antiseizure and dexamethasone to control seizures and cerebral edema. Therapeutic hypothermia is often used and has been associated with survival and neurologic recovery.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Impavido. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Impavido as well as the monitoring required for adverse events and long-term efficacy, approval requires Impavido to be prescribed by or in consultation with a physician who specializes in the condition being treated.

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Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Impavido is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Leishmaniasis.** Approve for 1 month if the patient meets BOTH of the following (A and B):
 - A) Patient meets ONE of the following (i, ii, or iii):
 - i. Patient has cutaneous leishmaniasis; OR
 - ii. Patient has mucosal leishmaniasis; OR
 - iii. Patient has visceral leishmaniasis; AND
 - B) The medication is prescribed by or in consultation with an infectious diseases specialist.

Other Uses with Supportive Evidence

2. **Ameba Related Infections.** Approve for 1 month if the patient meets BOTH of the following (A and B):
 - A) Patient is being treated for an infection due to ONE of the following (i, ii, or iii):
 - i. Acanthamoeba; OR
 - ii. Balamuthia mandrillaris; OR
 - iii. Naegleria fowleri; AND

Note: Examples of ameba related infections are Acanthamoeba keratitis, granulomatous amebic encephalitis (GAE), and primary amebic meningoencephalitis (PAM).
 - B) The medication is prescribed by or in consultation with an infectious diseases specialist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Impavido is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Impavido® capsules [prescribing information]. Orlando, FL: Profounda; August 2023.
2. Uribe-Restrepo A, Cossio A, Desai MM, et al. Interventions to treat cutaneous leishmaniasis in children: a systematic review. *PLoS Negl Trop Dis.* 2018;12(12):e0006986.
3. Aronson N, Herwaldt BL, Libman M, et al. Diagnosis and treatment of Leishmaniasis: clinical practice guidelines by the Infectious Disease Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). *Clin Infect Dis.* 2016;63(12):e202-e264.
4. Cumulative List of Orphan Drug Designations and Approvals. Available at: <https://www.accessdata.fda.gov/scripts/opdlisting/opd/listResult.cfm>. Accessed on May 31, 2024.
5. CDC at Work: Naegleria fowleri. Available at: https://archive.cdc.gov/www_cdc.gov/parasites/naegleria/cdc-at-work.html. Accessed on May 31, 2024.
6. Marie C and Petri WA. Granulomatous amebic encephalitis. In: Merck Manual 2024. Available at: <https://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/granulomatous-amebic-encephalitis>. Accessed on May 30, 2024.
7. Marie C and Petri WA. Primary amebic meningoencephalitis. In: Merck Manual 2024. Available at: <https://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/primary-amebic-meningoencephalitis>. Accessed on May 30, 2024.

