Drug Coverage Policy

Effective Date……7/15/2026
Coverage Policy Number…… IP0210
Policy Title…… Impavido

Infectious Disease – Impavido

- Impavido® (miltefosine capsules – Profounda)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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 recommends 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 *Acanthomeoba* keratitis.[4] The Centers for Disease Control and Prevention (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 more than five 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 (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.

Safety
Impavido is contraindicated in pregnancy; it may cause fetal harm based on animal data.[1] Pregnancy status should be verified prior to initiating. Females of reproductive potential should use effective contraception during treatment and for 5 months after the last dose.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for 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.

Impavido is considered medically necessary when the following criteria are met:

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) Treatment of infection due to *Acanthamoeba*, *Balamuthia mandrillaris*, or *Naegleria fowleri* [for example, keratitis, granulomatous amebic encephalitis, primary amebic meningoencephalitis (PAM)]; AND
   B) The medication is prescribed by or in consultation with an infectious diseases specialist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Impavido for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Impavido® capsules [prescribing information]. Orlando, FL: Profounda; March 2025.
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 Diseases 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/oopd/listResult.cfm. Accessed on April 9, 2025.
5. CDC at Work: Naegleria fowleri. Available at: https://archive.cdc.gov/www_cdc_gov/parasites/naegleria/cdc-at-work.html. Accessed April 9, 2025.
6. Marie C and Petri WA. Granulomatous amebic encephalitis. In: Merk Manual 2024. Available at: https://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/granulomatous-amebic-encephalitis. Accessed on April 9, 2025.
7. Marie C and Petri WA. Primary amebic meningoencephalitis. In: Merk Manual 2024. Available at: https://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/primary-amebic-meningoencephalitis. Accessed on April 9, 2025.

Revision Details

Summary of Changes	Review Date	Effective Date
Policy Name Change: Updated Policy Name from "Miltefosine" to "Infectious Disease – Impavido." **Leishmaniasis: Removed** the criteria specifying treatment for infections caused by specific Leishmania species. **Added** the requirement for medication to be prescribed by or in consultation with an infectious disease specialist. **Ameba Related Infections: Added** the requirement for medication to be prescribed by or in consultation with an infectious disease specialist.	5/30/2024	08/15/2024
No criteria changes.	5/15/2025	06/15/2025
No criteria changes.	5/21/2026	7/15/2026

The policy effective date is in force until updated or retired.

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