PRIOR AUTHORIZATION POLICY

POLICY: Infectious Disease – Impavido Prior Authorization Policy
- Impavido® (miltefosine capsules – Profounda)

REVIEW DATE: 04/23/2025

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.

CIGNA NATIONAL FORMULARY COVERAGE:

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.

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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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 COVERED

- **Impavido® (miltefosine capsules - Profounda)**

is(are) considered not medically necessary for ANY other use(s); 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/19/2023
Annual Revision	No criteria changes.	04/24/2024
Selected Revision	**Ameba-Related Infections:** This new condition was added to Other Uses with Supportive Evidence.	06/05/2024
Annual Revision	No criteria changes.	04/23/2025