Overview

This policy supports medical necessity review for miltefosine (Impavido®).

Medical Necessity Criteria

Miltefosine (Impavido) is considered medically necessary when ONE of the following is met (1 or 2):

1. **Leishmaniasis, Visceral, Cutaneous, or Mucosal.** Individual meets the following criteria:
   A. Treatment of infection due to *Leishmania donovani*, *Leishmania braziliensis*, *Leishmania guyanensis*, or *Leishmania panamensis*

2. **Ameba Related Infections.** Individual meets the following criteria:
   A. Treatment of infection due to *Acanthamoeba*, *Balamuthia mandrillaris*, or *Naegleria fowleri* [for example, keratitis, granulomatous amebic encephalitis, primary amebic meningoencephalitis (PAM)]
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.

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

**Reauthorization Criteria**

Not applicable for continuation beyond initial approval duration.

**Authorization Duration**

Initial approval duration: up to 28 days

Reauthorization approval duration: not applicable

**Conditions Not Covered**

Miltefosine (Impavido) is considered experimental, investigational or unproven for ANY other use.

**Background**

**OVERVIEW**

Impavido, an anti-leishmanial agent, is indicated in patients ≥ 12 years of age weighing ≥ 30 kg for the treatment of visceral leishmaniasis caused by Leishmania donovani; cutaneous leishmaniasis caused by L. braziliensis, L. guyanensis, and L. panamensis; and 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). 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**

In March 2011, Impavido was added to the World Health Organization (WHO) Essential Medicines List as an anti-leishmanial medicine. The current WHO recommendations for the treatment of leishmaniasis include Impavido, liposomal amphotericin B, amphotericin B deoxycholate, paromomycin (not available in the US), pentavalent antimonial compounds (not available in the US) with or without pentoxifylline, systemicazole therapies, and thermotherapy.

The Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH) released guidelines for the management of persons with leishmaniasis in 2016. Systemic therapies, including Impavido, are recommended for the treatment of patients with cutaneous, mucosal, or visceral leishmaniasis.

According to CDC guidelines, miltefosine may be used as part of a multiple-drug regimen for the treatment of infections related to free-living ameba (including the following: Acanthamoeba, Balamuthia mandrillaris, Naegleria fowleri).
Miltefosine has been used in some patients for the treatment of free-living ameba infections, including primary amebic meningoencephalitis caused by *Naegleria fowleri* and granulomatous amebic encephalitis or other infections caused by *Balamuthia mandrillaris* or *Acanthamoeba*.

CNS infections caused by free-living ameba have a high mortality rate, and only a very limited number of cases have been successfully treated. Early diagnosis and treatment of these infections may increase the chance of survival. Although data are limited, most reported cases of *N. fowleri*, *B. mandrillaris*, or *Acanthamoeba* infection have been treated empirically with multiple-drug regimens which typically include several anti-infectives and may include miltefosine.

References