Pharmacy Benefit Coverage Criteria

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**Next Review Date** ................................. 2/1/2021
**Coverage Policy Number** ....................... P0019

## Miltefosine

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### 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. 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.

### Medical Necessity Criteria

Miltefosine (Impavido®) is considered medically necessary when ANY of the following criteria are met:

- Treatment of infection with *Leishmania donovani*, *Leishmania braziliensis*, *Leishmania guyanensis*, or *Leishmania panamensis*
- Treatment of infection with *Acanthamoeba*
- Treatment of infection with *Balamuthia mandrillaris*
- Treatment of infection with *Naegleria fowleri*

Authorization is up to (1) month.

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.

Miltefosine is considered experimental, investigational or unproven for any other indication.

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

Impavido (miltefosine) capsules are indicated in adults and adolescents ≥12 years of age weighing ≥ 30 kg for the treatment of:

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

Limitations 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.
- The efficacy of Impavido in the treatment of other *Leishmania* species has not been evaluated.

Recommended Dosing

FDA Recommended Dosing

The treatment duration is 28 consecutive days. Administer with food to ameliorate gastrointestinal adverse reactions.

Table 1: Miltefosine Dosage

<table>
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<th>Weight</th>
<th>Dosage and Administration</th>
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<td>30 kg to 44 kg</td>
<td>One 50 mg capsule twice daily with food (breakfast and dinner)</td>
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<tr>
<td>45 kg or greater</td>
<td>One 50 mg capsule three times daily with food (breakfast, lunch, and dinner)</td>
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Drug Availability

Supplied as a capsule containing 50 mg miltefosine.

Background

Disease Overview

Leishmaniasis is a vector-borne disease that is transmitted by sandflies. The number of annual new cases of leishmaniasis is unknown, although it is estimated that 1.3 million new cases occur annually. (WHO, 2014[a]) The cases of leishmaniasis in the United States reflect travel and immigration patterns; leishmaniasis is not endemic to the United States. (CDC, 2018[a]) There are three primary forms of leishmaniasis: cutaneous, mucosal, and visceral. (CDC, 2018[a]; CDC, 2018[b]; WHO, 2014[a]) Cutaneous leishmaniasis is the most common form, both in general and in United States travelers. Mucosal leishmaniasis is the least common form of the three and it can be a sequela of cutaneous leishmaniasis, resulting from dissemination of the parasites from the skin to the naso-oropharyngeal mucosa. (CDC, 2018[a]) Visceral leishmaniasis can affect several internal organs (usually the spleen, liver, and bone marrow) and can be life-threatening. If left untreated, visceral leishmaniasis can become fatal, either directly from the disease or indirectly from complications such as secondary bacterial infection or hemorrhage. (CDC, 2018[a]; WHO, 2014[a])

There are four genera of free-living amoebae associated with human disease: *Acanthamoeba spp., Balamuthia mandrillaris, Naegleria fowleri, Sappinia diploidea. Acanthamoeba spp.* Causes opportunistic infections of the central nervous system and can cause sight-threatening infection (*Acanthamoeba keratitis [AK]). AK occurs mostly in contact-lens wearers. *Balamuthia mandrillaris* causes granulomatous amoebic encephalitis (GAE). GAE immunocompromised individuals (for example, HIV/AIDS, diabetic, have undergone organ transplantation) and may occur at any time of the year. *Naegleria fowleri* causes primary amebic meningoencephalitis (PAM) that can lead to death in healthy individuals. *Sappinia diploidea* has been associated with causing encephalitis. (Linam, 2015; Visvesvara, 2007)

Professional Societies/Organizations

In March 2011, Impavido was added to the World Health Organization (WHO) Essential Medicines List as an
anti-leishmanial medicine. (Impavido, 2014[b]) The current WHO recommendations for the treatment of leishmaniasis include Impavido, liposomal amphotericin B, amphotericin B deoxycholate, paromomycin (not available in the United States), pentavalent antimonial compounds (not available in the United States) with or without pentoxifylline, systemic azole therapies, and thermotherapy. (Impavido, 2014[b]; WHO, 2014[a]; WHO, 2014[b])

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. (Aronson, 2016) Systemic therapies, including Impavido, are recommended for the treatment of patients with cutaneous, mucosal, or visceral leishmaniasis.

**Off Label Uses**

AHFS Drug Information 2019 Edition supports the following off-label uses: *Acanthamoeba, Balamuthia mandrillaris, Naegleria fowleri.*

**References**