

## PRIOR AUTHORIZATION POLICY

**POLICY:** Antiparasitics – Impavido® (miltefosine capsules – Profounda, Inc.)

**DATE REVIEWED:** 04/22/2020

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### OVERVIEW

Impavido is indicated in adults and adolescents  $\geq 12$  years of age weighing  $\geq 30$  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*.<sup>1</sup>

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.

Impavido is active *in vitro* against promastigotes and amastigotes of a variety of *Leishmania* species and anti-leishmanial activity has been demonstrated in clinical infections.<sup>1</sup> The exact mechanism of action is unknown. The recommended dose of Impavido is one 50 mg capsule twice daily with food for patients who weigh between 30 kg and 44 kg, and one 50 mg capsule three times a day with food for patients who weigh  $\geq 45$  kg. The treatment duration is 28 consecutive days.

A systematic review of four studies conducted in the Americas evaluated the efficacy of Impavido in pediatric patients  $\leq 12$  years of age with cutaneous leishmaniasis (n = 130).<sup>2</sup> 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%.

### Disease Overview

Leishmaniasis is a vector-borne disease that is transmitted by sandflies.<sup>3</sup> The number of annual new cases of leishmaniasis is unknown; it is estimated there are 700,000 to 1 million new cases annually. The cases of leishmaniasis in the US reflect travel and immigration patterns; leishmaniasis is not endemic to the US.<sup>4</sup> There are three primary forms of leishmaniasis: cutaneous, mucosal, and visceral.<sup>3-5</sup> Cutaneous leishmaniasis is the most common form, both in general and in US 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-oro-pharyngeal mucosa.<sup>4</sup> 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.<sup>3,4</sup>

### Guidelines/Recommendations

In March 2011, Impavido was added to the World Health Organization (WHO) Essential Medicines List as an anti-leishmanial medicine.<sup>6</sup> 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, systemic azole therapies, and thermotherapy.<sup>6,7</sup>

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.<sup>8</sup> Systemic therapies, including Impavido, are recommended for the treatment of patients with cutaneous, mucosal, or visceral leishmaniasis.

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## **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.

**Automation:** None.

## **RECOMMENDED AUTHORIZATION CRITERIA**

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

### **FDA-Approved Indications**

1. **Leishmaniasis, Visceral, Cutaneous, or Mucosal.** Approve Impavido for 1 month if prescribed by, or in consultation with, an infectious diseases specialist.

## **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Impavido has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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, Inc.; June 2019.
  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 Dec;12:e0006986.
  3. WHO: World Health Organization: Leishmaniasis. Available at: <https://www.who.int/news-room/fact-sheets/detail/leishmaniasis>. Last updated: March 2020. Accessed on March 26, 2020.
  4. Centers for Disease Control and Prevention: Parasites – Leishmaniasis. Available at: <https://www.cdc.gov/parasites/leishmaniasis/>. Last updated: July 2018. Accessed on March 26, 2020.
  5. Centers for Disease Control and Prevention: Leishmaniasis – Resources for Health Professionals. Available at: [https://www.cdc.gov/parasites/leishmaniasis/health\\_professionals/index.html](https://www.cdc.gov/parasites/leishmaniasis/health_professionals/index.html). Last updated: October 2018. Accessed on March 26, 2020.
  6. Impavido, FDA Med Review. Available at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2014/204684Orig1s000MedR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/204684Orig1s000MedR.pdf). Accessed on March 26, 2020.
  7. WHO: World Health Organization: Recommended treatment for leishmaniasis. Available at: [http://www.who.int/leishmaniasis/research/978924129496\\_pp67\\_71.pdf?ua=1](http://www.who.int/leishmaniasis/research/978924129496_pp67_71.pdf?ua=1). Accessed on March 26, 2020.
  8. 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 Inf Dis*. 2016;63(12):e202-264.
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