

**Leaflet update for Impavido 10 mg/50 mg capsules (miltefosine):  
New warning about ocular leishmaniasis complications, including keratitis**

Dear Customer, Dear Doctor,

Impavido 10 mg/50 mg capsules (active substance: miltefosine) is an orphan drug for the treatment of the parasitic tropical disease leishmaniasis.

We would like to inform you about a new warning concerning ocular leishmaniasis complications, including keratitis, which has been included in the Summary of Product Characteristics and the Patient Leaflet.

Please share this information with your customers or the treating physicians.

**Updated Summary of Product Characteristics, Section 4.4:**

- **Ocular changes such as keratitis are well-known symptoms of leishmaniasis.<sup>1</sup>**
- **However, in 20 patients reported in the worldwide literature so far, particularly in the treatment of post-kala-azar dermal leishmaniasis (PKDL), ocular complications occurred after miltefosine had been administered for several weeks.** In most of these cases, miltefosine had been administered for longer than the recommended therapy duration of 28 days.
- In published case reports, patients who developed ocular complications under miltefosine and who were therefore **treated with topical glucocorticoids** showed an improvement of symptoms.<sup>2,3,4</sup>
- If ocular complications occur and a connection with miltefosine cannot be excluded, **miltefosine should be discontinued immediately** and an alternative treatment for leishmaniasis should be initiated if necessary.
- Since miltefosine has a very long half-life, it is possible that ocular changes will not heal without treatment even after discontinuation of miltefosine. Therefore, an **eye specialist** should be consulted in such cases to avoid possible permanent damage. See also sections 4.8 and 4.9. of the Summary of Product Characteristics.

In Section 4.8 “Undesirable effects”, the eye disorders keratitis, keratopathy and acute scleritis (frequency cannot be estimated) have been included. The Package Leaflet, Sections 2 and 4, has been updated accordingly.

**Current translations available online**

The current Summary of Product Characteristics and the Package Leaflet in English, German and other languages are available online under: <http://paesel-lorei.de/en/impavido>

**Medical enquiries**

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Yours sincerely,

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**References**

- 1) ModarresZadeh, M. et al., 2006. Ocular Leishmaniasis. Iranian Journal of Ophthalmology, pp.1–5. [https://www.researchgate.net/publication/277851904\\_Ocular\\_Leishmaniasis](https://www.researchgate.net/publication/277851904_Ocular_Leishmaniasis)
- 2) **Kusumesh, R. et al., 2020. Keratitis occurring in patients treated with miltefosine for post-kala-azar dermal leishmaniasis.** The British journal of ophthalmology, 23, pp.bjophthalmol–2020–317325. <https://dx.doi.org/10.1136/bjophthalmol-2020-317325>
- 3) Maruf, S. et al., 2018. Corneal complications following Post Kala-azar Dermal Leishmaniasis treatment. PLoS neglected tropical diseases, 12(9), p.e0006781. <https://doi.org/10.1371/journal.pntd.0006781>
- 4) Khatri, A. et al., 2020. Miltefosine-related paracentral ulcerative keratolysis in a patient with active cutaneous leishmaniasis from Nepal. Tropical doctor, p.49475520929822. <https://doi.org/10.1177/0049475520929822>