

**Leaflet update for Impavido 10 mg/50 mg capsules (miltefosine):
Updated 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 an updated 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 are well-known symptoms of leishmaniasis.¹**
- **However, in case reports mainly from South Asia, predominantly in the treatment of post-kala-azar dermal leishmaniasis (PKDL), ocular complications such as unilateral or bilateral keratitis and visual impairment, sometimes permanent, occurred after miltefosine had been administered for a few days or several weeks.** In most of these cases, miltefosine had been administered for PKDL during 12 weeks, longer than the recommended therapy duration of 28 days in the treatment of VL.
- In published case reports, patients who developed ocular complications under miltefosine and who were therefore **treated with topical glucocorticoids** showed an improvement of symptoms.^{2,3,4}
- Before starting the treatment eyes examination should be considered and the history of ocular disorders should be collected. In case of current or past history of ocular disorder, the benefits and the risks of treating a patient with miltefosine should be carefully considered, and advice from an ophthalmologist should be sought if feasible. **All patients should be informed before starting the treatment that in case of eye problems (e.g. red eyes, eye pain, blurred vision) they should discontinue miltefosine and contact their healthcare professional immediately.**
- 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 following eye disorders (frequency cannot be estimated) are listed: Keratitis, keratopathy, acute scleritis, uveitis, ocular hyperaemia (increased ocular vascularity), visual impairment up to blindness. 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 and German are available online under: <http://paesel-lorei.de/en/impavido>

Medical enquiries

Paesel + Lorei GmbH & Co. KG, Nordring 11, 47495 Rheinberg. Germany
Phone: +49 228 710027-73, Email: drugsafety@paesel-lorei.de

References

- 1) ModarresZadeh, M. et al., 2006. Ocular Leishmaniasis. Iranian Journal of Ophthalmology, pp.1–5. 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>