

Summary of the risk management plan (RMP) for Ikervis (ciclosporin)

This is a summary of the risk management plan (RMP) for Ikervis, which details the measures to be taken in order to ensure that Ikervis is used as safely as possible. For more information on RMP summaries, see [here](#).

This RMP summary should be read in conjunction with the EPAR summary and the product information for Ikervis, which can be found on [Ikervis' EPAR page](#).

Overview of disease epidemiology

Ikervis is a medicine used to treat severe keratitis (inflammation of the cornea, the transparent layer at the front of the eye), in patients with dry eye disease for whom treatment with artificial tears (tear substitutes) is insufficient. In dry eye disease not enough tear fluid is produced to create the protective film of moisture that normally coats the eye, or abnormalities in the tear fluid cause it to dry out too quickly. Without adequate protection from the tear fluid the surface of the eye can develop damage and become inflamed (keratitis), which can eventually lead to ulceration, infection and reduced vision. Patients typically have symptoms of discomfort including a feeling as though a foreign body is in the eye, with symptoms often becoming worse as the day progresses. Burning, sensitivity to bright light, blurred vision, and an inability to produce tears, are among other possible symptoms.

Overall, about 5% to 30% of the population are estimated to have dry eye disease and the incidence increases markedly with age. About 2% of these patients are estimated to have severe keratitis. Dry eye disease affects more women than men.

Summary of treatment benefits

Ikervis is given as eye drops that contain the active substance ciclosporin.

The benefits of Ikervis have been shown in one main study involving 246 patients with severe dry eye disease, where Ikervis was compared with the vehicle (the same eye drop formula but without any active substance). The main measure of effectiveness was the proportion of patients whose condition responded to treatment after six months, as measured by a combination of damage to the cornea and a score for the level of symptoms, including discomfort and pain. About 29% (44 of 154) of those given Ikervis responded, compared with 23% (21 of 91) given the vehicle. The proportion of patients who responded to treatment was therefore similar in the two groups, but when only the damage to the cornea was considered, Ikervis was significantly better than the vehicle at reducing it. Levels of HLA-DR (a measure of inflammation in eye cells) were also reduced in patients using Ikervis compared with the dummy treatment.

Unknowns relating to treatment benefits

In the main and supporting studies virtually all patients were Caucasian, but there is no evidence to suggest that the product will be less effective in non-Caucasian patients. Safety of the medicine has not been investigated in pregnant or breastfeeding women.

Summary of safety concerns

Important identified risks

None identified.

Important potential risks

Risk	What is known
Local abrasion affecting the cornea (corneal decompensation)	One case of severe abrasion of the outer layer of the cornea, which resolved without long-term consequences, was reported during Ikervis clinical studies.
Medication errors	<p>The medicine is supplied in single-dose containers sufficient to supply both eyes with the daily dose of one drop. To allow for any spillage each container contains extra volume, corresponding to approximately 10 drops, but only a single drop is supposed to be given.</p> <p>There is a potential risk that patients might try to use the remaining liquid for subsequent doses. Because it is no longer guaranteed to be sterile once opened, this could lead to infection. Any unused liquid should be discarded once the dose has been given.</p>
Use for non-approved conditions or patient groups (off-label use)	There is a potential risk that Ikervis may be used by doctors for eye conditions in which it is not authorised or in non-authorised patient groups such as children. Ikervis is only recommended for use in adult patients with dry eye disease being treated for severe keratitis that does not improve despite treatment with tear substitutes. Use in other populations with a different eye disease or in children has not been investigated and so the safety and effectiveness of the medicine in these cases is not known.
Allergy	Allergic (hypersensitivity) reactions could occur after application of Ikervis in patients who are allergic to ciclosporin or any of the other ingredients. These could potentially be severe or even life threatening. Although this has not occurred so far in studies with Ikervis it is considered a potential risk.
Development/ worsening of eye infection	Ciclosporin belongs to a group of medicines known as immunosuppressive agents (agents that suppress or reduce the strength of the immune system, the body's natural defences). There is therefore a potential risk that it could encourage or worsen eye infections. Ikervis must not be given to patients with known or suspected eye infection.
Cancer of the eye or skin around the eye (periocular skin cancer, conjunctival)	Ciclosporin belongs to a group of medicines known as immunosuppressive agents (agents that suppress or reduce the strength of the immune system, the body's natural defences). There is therefore a potential risk that cancers could develop in or around the eye. Although the potential risk is considered

Risk	What is known
or corneal tumour)	low, the effects of the medicine will be carefully monitored.

Missing information

Risk	What is known
Safety in pregnant and breastfeeding women	Ikervis has not been investigated in pregnant women or in breastfeeding women, therefore its safety and effectiveness in these groups are not known. Studies in animals given ciclosporin systemically (into the body) in higher doses than recommended have shown effects on the developing young. The medicine should therefore not be used in pregnant women. If a woman could become pregnant she must use contraception while using this medicine. Ciclosporin is likely to be present in breast milk in very small amounts after using Ikervis. Women who are breastfeeding should talk to their doctor to decide whether to stop breastfeeding or stop Ikervis treatment.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Ikervis can be found on [Ikervis' EPAR page](#).

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

Not applicable.

Summary of changes to the risk management plan over time

Not applicable.

This summary was last updated in 02-2015.