Part VI: Summary of the Risk Management Plan

Summary of the Risk Management Plan for OZURDEX (dexamethasone intravitreal implant in applicator)

This is a summary of the Risk Management Plan (RMP) for OZURDEX. The RMP details important risks of OZURDEX, how these risks can be minimised, and how more information will be obtained about OZURDEX risks and uncertainties (missing information).

OZURDEX's Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how OZURDEX should be used.

This summary of the RMP for OZURDEX should be read in the context of all this information, including the assessment report of the evaluation and its plain-language summary, which are part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of OZURDEX's RMP.

I. The medicine and what it is used for

OZURDEX is indicated for the treatment of adult patients with:

- visual impairment due to diabetic macular oedema (DME) who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for, non-corticosteroid therapy
- macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO)
- inflammation of the posterior segment of the eye presenting as non-infectious uveitis.

It contains dexamethasone as the active substance and it is given by intravitreal injection.

Further information about the evaluation of OZURDEX ’s benefits can be found in OZURDEX’s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine’s webpage *https://www.ema.europa.eu/en/medicines/human/EPAR/ozurdex*.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of OZURDEX, together with measures to minimise such risks and the proposed studies for learning more about OZURDEX's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine’s packaging
- The authorised pack size — the amount of medicine in a pack is chosen to ensure that the medicine is used correctly

- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without a prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation measures*.

In the case of OZURDEX, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and is regularly analysed, including Periodic Safety Update Report (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of OZURDEX is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of OZURDEX are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of OZURDEX. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	• Increased intraocular pressure, Glaucoma, Ocular hypertension • Endophthalmitis • Device dislocation • Implant misplacement • Retinitis secondary to reactivation of latent viral or other ophthalmic infections
Important potential risks	None
Missing information	None

II.B Summary of important risks

Important Identified Risk: Increased intraocular pressure, Glaucoma, Ocular hypertension	
Evidence for linking the risk to the medicine	Clinical trials data, and literature
Risk factors and risk groups	A review of published literature on the intravitreal use of the corticosteroid triamcinolone revealed that steroid-induced elevation of IOP (SIOP) is a well-known side effect of intravitreal steroids (van Kooij et al. 2006). Dexamethasone, a synthetic glucocorticoid, would therefore be expected to elicit a similar response.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 PL section 2 and 4. Pack size: single-use intravitreal implant in applicator Legal status: restricted medical prescription Additional risk minimisation measures: - Patient guide - Patient audio CD (where required)

Important Identified Risk: Endophthalmitis	
Evidence for linking the risk to the medicine	Clinical trials data, Global Safety Database, and literature
Risk factors and risk groups	Endophthalmitis is a serious complication following cataract surgery and intravitreal injection and diabetes has been suggested as a risk factor (Montan et al. 1998, Fahmy1975, Skarbez et al. 2010). Endogenous endophthalmitic among diabetics is caused by bacteria such as *Klebsiella pneumonia*, *Escherichia coli*, and *Staphylococcus* (Skarbez et al. 2010, Phillips et al. 1994). It has been suggested that patients' external tissues are the source of the infecting organism in acute postoperative endophthalmitis cases (Speaker et al. 1991). Identified possible risk factors for infectious endophthalmitis in intravitreal injection of another corticosteroid, triamcinolone, include diabetes mellitus, multi-use bottles, poor sterile techniques, filtering blebs (decreased ocular barrier function), and blepharitis (Moshfeghi et al. 2003).
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2, 4.4 and 4.8 PL section 2, 3 and 4. Pack size: single-use intravitreal implant in applicator Legal status: restricted medical prescription Additional risk minimisation measures: - Patient guide - Patient audio CD (where required)

Important Identified Risk: Device dislocation	
Evidence for linking the risk to the medicine	Global Safety Database
Risk factors and risk groups	All patients with posterior capsule tear, such as those with a posterior lens (e.g., due to cataract surgery), and/or those who have an iris opening to the vitreous cavity (e.g., due to iridectomy) with or without a history of vitrectomy, are at risk of implant migration into the anterior chamber. Implant migration to the anterior chamber may lead to corneal oedema. Persistent severe corneal oedema could progress to the need for corneal transplantation. Other than those patients contraindicated (see SmPC section 4.3), OZURDEX should be used with caution and only following a careful risk benefit assessment. These patients should be closely monitored to allow for early diagnosis and management of device migration.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 PL section 2 and 4. Pack size: single-use intravitreal implant in applicator Legal status: restricted medical prescription Additional risk minimisation measures: None

Important Identified Risk: Implant Misplacement	
Evidence for linking the risk to the medicine	Global Safety Database
Risk factors and risk groups	Not applicable
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2, 4.8 and 6.6 PL section 3 and 4. Pack size: single-use intravitreal implant in applicator Legal status: restricted medical prescription Additional risk minimisation measures: None

Important Identified Risk: Retinitis secondary to reactivation of latent viral or other ophthalmic infections	
Evidence for linking the risk to the medicine	Clinical trials data, Global Safety Database, and literature
Risk factors and risk groups	Immunosuppression/Immunodeficiency; other factors unknown. Literature report of CMV retinitis following intravitreal triamcinolone treatment in 2 otherwise-immunocompetent patients with a history of type II diabetes mellitus, pseudophakia, and vitrectomy (Delyfer et al., 2007). The risk of reactivation of latent ophthalmic infections increases with immunosuppressive therapy and immunodeficiency. In addition, the risk of reactivation of infection has been observed to be highest immediately after the immune recovery seen with initiation or re-initiation of highly active antiretroviral therapy (HAART). (Holland, 2008)
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 PL section 2 and 4. Pack size: single-use intravitreal implant in applicator Legal status: restricted medical prescription Additional risk minimisation measures: None

II.C Post-authorisation development plan

II.C.1 Studies that are conditions of the marketing authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of OZURDEX.

II.C.2 Other studies in the post-authorisation development plan

There are no other studies required for OZURDEX.