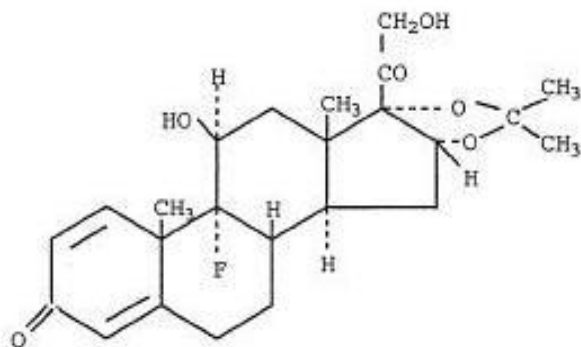


## OZURDEX<sup>®</sup> (dexamethasone) 700 µg implant

### NAME OF THE MEDICINE

The active constituent of OZURDEX<sup>®</sup> intravitreal implant is dexamethasone.

Chemical structure:



### Chemical name:

pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-(11 $\beta$ ,16 $\alpha$ )

**Molecular weight:** 392.47

**Empirical formula:** C<sub>22</sub>H<sub>29</sub>FO<sub>5</sub>

### DESCRIPTION

Dexamethasone is a white to cream-coloured crystalline powder with not more than a slight odour, and is practically insoluble in water and very soluble in alcohol.

OZURDEX<sup>®</sup> is a biodegradable intravitreal implant containing 700 µg dexamethasone in a solid polymer drug delivery system (DDS). OZURDEX<sup>®</sup> is preloaded into a single-use, specially designed DDS applicator to facilitate injection of the rod-shaped implant directly into the vitreous. The polymer DDS contains polyglactin [poly (D,L-lactide-coglycolide)] PLGA biodegradable polymer matrix. OZURDEX<sup>®</sup> is preservative-free.

### PHARMACOLOGY

#### Mechanism of action

Dexamethasone, a potent corticosteroid, has been shown to suppress inflammation by inhibiting multiple inflammatory cytokines resulting in decreased oedema, fibrin deposition, capillary leakage, and migration of the inflammatory cells. Vascular endothelial growth factor (VEGF) is a cytokine which is expressed at increased concentrations in the setting of macular oedema. It is a potent promoter of vascular permeability. Corticosteroids have been shown to inhibit the expression of VEGF and modulate VEGF-mediated responses. Additionally, corticosteroids prevent the release of prostaglandins, some of which have been identified as mediators of cystoid macular oedema.

OZURDEX<sup>®</sup> contains 700 µg micronised dexamethasone in a biodegradable polymer matrix that is injected directly into the posterior segment of the eye with an applicator. The polymer

degrades into water and carbon dioxide over time, gradually releasing dexamethasone to the vitreous, allowing for sustained drug levels in the target area with a smaller total amount of drug administered than via other routes of corticosteroid administration. Furthermore, delivery of OZURDEX<sup>®</sup> 700 µg directly into the vitreous cavity reduces the potential for systemic effects compared to other routes of administration. The dose of dexamethasone delivered by OZURDEX<sup>®</sup> 700 µg every 6 months is less than the usual single daily physiologic replacement dose (0.75 mg).

### **Pharmacokinetics**

***Absorption and Distribution:*** In two Phase 3 diabetic macular oedema studies, adult patients with a diagnosis of type 1 or type 2 diabetes mellitus and clinically observable macular oedema associated with diabetic retinopathy were randomised in a 1:1:1 ratio to 700 µg OZURDEX<sup>®</sup>, 350 µg OZURDEX<sup>®</sup>, or Sham DEX PS DDS needleless applicator. Blood samples were obtained from a subgroup of patients at predose, days 1, 7, and 21, and months 1.5 and 3 to determine plasma dexamethasone concentrations. In both studies, the majority of concentrations were below the lower limit of quantitation (LLOQ) of 0.05 ng/mL. Plasma dexamethasone concentrations from 5 of 52 samples in the OZURDEX<sup>®</sup> 700 µg group and from 0 of 60 samples in the OZURDEX<sup>®</sup> 350 µg group were above the LLOQ, ranging from 0.0599 ng/mL to 0.102 ng/mL. The highest plasma concentration value of 0.102 ng/mL was observed in one subject from the 0.7 mg group. Plasma dexamethasone concentration did not appear to be related to age, body weight, or sex of patients.

In monkeys, following single bilateral intravitreal implantation of OZURDEX<sup>®</sup> 700 µg, dexamethasone was released in two phases. The first phase provided high concentrations of dexamethasone, with peak concentrations of dexamethasone observed in the vitreous humour and retina 60 days post-injection. This was followed by a second phase in which low concentrations of dexamethasone were released, extending the therapeutic period to 6 months.

***Metabolism:*** In an *in vitro* metabolism study, following the incubation of [<sup>14</sup>C]-dexamethasone with human cornea, iris-ciliary body, choroid, retina, vitreous humour, and sclera tissues for 18 hours, no metabolites were observed. This is consistent with results from rabbit and monkey ocular metabolism studies. Systemically, dexamethasone is subject to metabolism by CYP3A4 in the liver.

***Excretion:*** Dexamethasone is predominantly cleared from the vitreous humour by diffusion in to the retina/choroid/sclera membrane. Dexamethasone is ultimately metabolised to lipid and water soluble metabolites that can be excreted in bile and urine.

**Renal impairment:** No formal studies have been conducted to examine the pharmacokinetics of OZURDEX<sup>®</sup> in patients with renal impairment.

**Hepatic impairment:** No formal studies have been conducted to examine the pharmacokinetics of OZURDEX<sup>®</sup> in patients with hepatic impairment.

### **CLINICAL TRIALS**

The clinical efficacy of OZURDEX<sup>®</sup> was assessed in two Phase 3 randomised, masked, Sham-controlled studies in patients with diabetic macular oedema. A total of 1,048 patients

(351 OZURDEX<sup>®</sup> 700 µg, 347 OZURDEX<sup>®</sup> 350 µg, and 350 Sham) were evaluated as the ITT population and received up to 7 treatments during the 3-year study period.

The primary endpoint in both studies was best corrective visual acuity (BCVA) using early treatment diabetic retinopathy study (ETDRS) method in the study eye at the qualification/baseline visit and each follow-up visit.

Patients were eligible for retreatment based upon central subfield retinal thickness >175 microns by optical coherence tomography (OCT) or upon physician's interpretation for any evidence of residual retinal oedema consisting of intraretinal cysts or any regions of increased retinal thickening within or outside of the central subfield.

#### BCVA Average Change from Baseline (AUC approach)

In study 1, the mean BCVA average change from baseline during the study was significantly greater with OZURDEX<sup>®</sup> compared to Sham (4.1 letters versus 1.9 letters,  $p = 0.016$ ).

In study 2, the mean BCVA average change from baseline during the study was 2.9 letters with OZURDEX<sup>®</sup> compared to 2.0 letters with Sham; the difference was not statistically significant ( $p = 0.366$ ).

In the pooled analysis, the mean BCVA average change from baseline during the study was significantly greater with OZURDEX<sup>®</sup> compared to Sham (3.5 letters versus 2.0 letters,  $p = 0.023$ ).

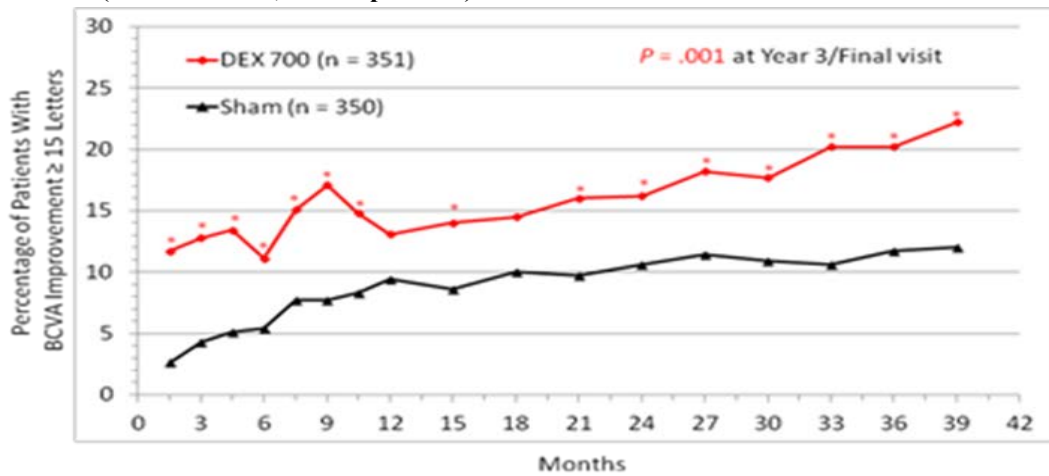
#### BCVA Improvement $\geq$ 15 Letters from Baseline

In Study 1, the proportion of patients with 15 or more letters improvement in BCVA from baseline was significantly higher with OZURDEX<sup>®</sup> (22.1%) compared with Sham (13.3%) at the year 3 final visit,  $p = 0.038$ .

In Study 2, the proportion of patients with 15 or more letters improvement in BCVA from baseline was significantly higher with OZURDEX<sup>®</sup> (22.3%) compared with Sham (10.8%) at the year 3 final visit,  $p = 0.003$ .

In the pooled analysis, the proportion of patients with 15 or more letters improvement from baseline was significantly higher with OZURDEX<sup>®</sup> (22.2%) compared to Sham (12.0%) at the year 3 final visit ( $p < 0.001$ ) and significantly higher with OZURDEX<sup>®</sup> compared to Sham at 15 of the 17 study visits. The treatment benefit of OZURDEX<sup>®</sup> in vision improvement was seen throughout the 3-year study period.

Figure 1 Percent of Patients with  $\geq 15$  Letters Improvement from Baseline BCVA in the Study Eye (Pooled Studies, ITT Population)



\* indicates statistically significant ( $p \leq 0.05$ ) difference between OZURDEX<sup>®</sup> versus Sham  
 Note: Missing values are imputed by last observation carried forward at the follow-up visits.

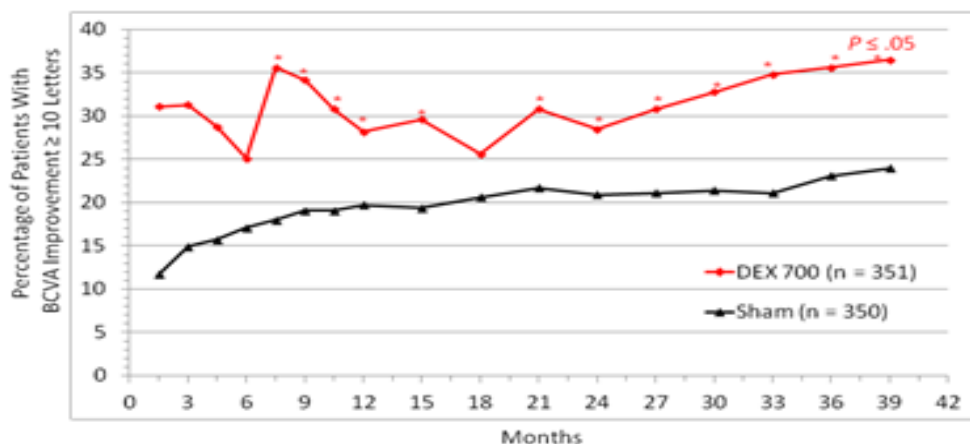
#### BCVA Improvement of 10 or More Letters from Baseline

In study 1, the proportion of patients with 10 or more letters improvement in BCVA was significantly higher with OZURDEX<sup>®</sup> compared to Sham at 14 of the 17 study visits. At the end of the study, significantly greater proportions of patients receiving OZURDEX<sup>®</sup> (38.7%) showed a 10-letter improvement compared to Sham (23.0%),  $p = 0.002$ .

In study 2, the proportion of patients with 10 or more letters improvement in BCVA was significantly higher with OZURDEX<sup>®</sup> compared to Sham at 10 of the 17 study visits. At the end of the 3-year study, a significantly greater proportion of patients receiving OZURDEX<sup>®</sup> (34.6%) showed a  $\geq 10$ -letter improvement compared to Sham (24.9%),  $p = 0.040$ .

In the pooled analysis, the proportion of patients with 10 or more letters improvement in BCVA was significantly higher with OZURDEX<sup>®</sup> compared with Sham at 16 of the 17 study visits. By the end of the 3-year study, 36.5% of patients receiving OZURDEX<sup>®</sup> showed a 10-letter improvement compared to 24.0% of patients receiving Sham ( $p < 0.001$ ).

**Figure 2** Percent of Patients with  $\geq 10$  Letters Improvement from Baseline BCVA in the Study Eye (Pooled Studies, ITT Population)



\* indicates statistically significant ( $p \leq 0.05$ ) difference between OZURDEX<sup>®</sup> versus Sham  
 Note: Missing values are imputed by last observation carried forward at the follow-up visits

#### BCVA 20/40 or Better

In the pooled analysis, the proportion of patients achieving a BCVA of 20/40 or better in the study eye was significantly greater with OZURDEX<sup>®</sup> compared to Sham at 10 of the 17 study visits. At the year 3/final visit, the proportion of patients achieving BCVA 20/40 or better was significantly higher with OZURDEX<sup>®</sup> (28.8% [101/351]) compared to Sham (21.4% [75/350]),  $p = 0.025$ .

#### Time to BCVA $\geq 15$ Letters Improvement

In each of the phase 3 studies and the pooled analysis, OZURDEX<sup>®</sup> was shown to have a rapid onset of action, as demonstrated by the time to BCVA 15-letter improvement from baseline in the study eye. The response time distributions in the OZURDEX<sup>®</sup> group was significantly earlier compared with Sham, indicating an earlier onset of BCVA improvement in the OZURDEX<sup>®</sup> group, with separation of curves at the first efficacy visit and no crossover during the study.

#### Retinal Thickness in the Center Subfield using OCT

In study 1, the mean average decrease from baseline during the study in central subfield retinal thickness was significantly greater with OZURDEX<sup>®</sup> (101.1  $\mu\text{m}$ ) versus Sham (37.8  $\mu\text{m}$ ),  $p < 0.001$ .

In study 2, the mean average decrease from baseline during the study in central subfield retinal thickness was significantly greater with OZURDEX<sup>®</sup> (120.7  $\mu\text{m}$ ) versus Sham (45.8  $\mu\text{m}$ ),  $p < 0.001$ .

In the pooled studies, the improvement in vision with OZURDEX<sup>®</sup> during the 3-year study was associated with a rapid and sustained improvement in anatomical outcomes, as demonstrated by OCT. The mean average decrease from baseline during the study in the central subfield retinal thickness was significantly greater with OZURDEX<sup>®</sup> (111.6  $\mu\text{m}$ ) compared to Sham (41.9  $\mu\text{m}$ ),  $p < 0.001$ .

Mean decreases in retinal thickness at the center subfield were consistently greater with OZURDEX<sup>®</sup> than with Sham throughout the study. Statistically significant mean

improvements with OZURDEX<sup>®</sup> compared to Sham were observed at every visit during the 3-year study.

#### Retreatment intervals

In the pooled phase 3 studies, during the course of the 3-year study period, a total of 1080 study retreatments for OZURDEX<sup>®</sup> were administered. Approximately 80% of the retreatments were administered between 5 to 7 months after the prior treatment and 19.9% were after 7 months.

#### Discontinuations

A total of 35.9% of OZURDEX<sup>®</sup> treated patients discontinued study participation for any reason during the study compared with 56.6% of Sham patients. Discontinuation rates due to adverse events were similar across treatment and Sham groups (12.8% vs 11.1%). Discontinuation due to lack of efficacy was higher in the Sham group (6.6% vs 24.0%).

### **INDICATIONS**

OZURDEX<sup>®</sup> is indicated for the treatment of diabetic macular oedema (DME).

### **CONTRAINDICATIONS**

OZURDEX<sup>®</sup> is contraindicated in the following:

- patients with active or suspected ocular or periocular infection, including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.
- patients with advanced glaucoma
- aphakic eyes with rupture of the posterior lens capsule
- eyes with an anterior chamber intraocular lens (ACIOL), iris or transscleral fixated IOLs, and rupture of the posterior lens capsule
- patients with hypersensitivity to dexamethasone or to any other components of the product

### **PRECAUTIONS**

Treatment with OZURDEX<sup>®</sup> is for intravitreal injection only.

Intravitreal injections, including those with OZURDEX<sup>®</sup>, have been associated with endophthalmitis, intraocular inflammation, increased IOP, and retinal detachment. Proper aseptic injection techniques must always be used. In addition, patients should be monitored following the injection to permit early treatment if an infection or increased IOP occur. Monitoring may consist of a check for perfusion of the optic nerve head immediately after the injection, tonometry within 30 minutes following the injection, and biomicroscopy between two and seven days following the injection.

Patients should be instructed to report any symptoms suggestive of endophthalmitis or any of the above-mentioned events without delay.



Patients who had a tear in the posterior lens capsule (e.g. due to cataract surgery), or who had an iris opening to the vitreous cavity (e.g. due to iridectomy) are at risk of implant migration into the anterior chamber. Implant migration to anterior chamber might lead to corneal oedema. Persistent severe corneal oedema could progress to the need of corneal transplantation. Regular monitoring of such patients allows for early diagnosis and management of device migration.

Use of corticosteroids, including those with OZURDEX<sup>®</sup>, have been associated with posterior subcapsular cataracts, increased IOP, glaucoma, and may enhance the establishment of secondary ocular infections for due to bacteria, fungi, or viruses.

In the 3 year DME clinical studies, 59% of patients with a phakic study eye treated with OZURDEX<sup>®</sup> underwent cataract surgery in the study eye (see **ADVERSE EFFECTS**).

As expected with ocular steroid treatment and intravitreal injections, IOP increases may be seen. The rise in IOP is normally manageable with IOP lowering medication (see **ADVERSE EFFECTS**). Of the patients experiencing an increase of IOP of  $\geq 10$  mmHg from baseline, the greatest proportion showed this IOP increase between 45 and 60 days following an injection. Therefore, regular monitoring of IOP, irrespective of baseline IOP, is required and any elevation should be managed appropriately post-injection as needed.

Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex. Corticosteroids should not be used in active ocular herpes simplex.

The safety and efficacy of OZURDEX<sup>®</sup> administered to both eyes on the same day has not been studied.

A limited number of subjects with Type 1 diabetes were investigated in the Phase 3 studies, and the response to OZURDEX<sup>®</sup> in these subjects was not significantly different to those subjects with Type 2 diabetes.

In DME, anti-coagulant therapy was used in 8% of patients. Among patients who used anti-coagulant therapy, the frequency of haemorrhagic adverse events was similar in the OZURDEX<sup>®</sup> and sham groups (29% vs 32%). Among patients who did not use anti-coagulant therapy, 27% of OZURDEX<sup>®</sup> treated patients reported haemorrhagic adverse events compared to 20% in the sham group. Vitreous haemorrhage was reported in a higher proportion of patients treated with OZURDEX<sup>®</sup> who received anti-coagulant therapy (11%) compared with those not receiving anticoagulant therapy (6%).

Anti-platelet medicinal products, such as clopidogrel, were used at some stage during the clinical studies in up to 56% of patients. For patients using concomitant and anti-platelet medication, haemorrhagic adverse events were reported in a slightly higher proportion of patients injected with OZURDEX<sup>®</sup> (up to 29%) compared with the sham group (up to 23%), irrespective of indication or number of treatments. The most common haemorrhagic adverse event reported was conjunctival haemorrhage (up to 24%). OZURDEX<sup>®</sup> should be used with caution in patients taking anti-coagulant or anti-platelet medicinal products.

**Effects on Fertility:**

There are no fertility data available.

**Use in Pregnancy:**

Category B3.

Studies in animals have shown teratogenic effects following topical ophthalmic administration. There are no adequate data from the use of intravitreally administered dexamethasone in pregnant women. Long-term systemic treatment with glucocorticoids during pregnancy increases the risk for intra-uterine growth retardation and adrenal insufficiency of the newborn child. Therefore, although the systemic exposure of dexamethasone would be expected to be very low after local, intraocular treatment, OZURDEX<sup>®</sup> is not recommended during pregnancy unless the potential benefit justifies the potential risk to the foetus.

**Use in Lactation:**

Dexamethasone is excreted in breast milk. No effects on the child are anticipated due to the route of administration and the resulting systemic levels. OZURDEX<sup>®</sup> should not be used by a breastfeeding women unless clearly necessary.

**Paediatric Use:**

The safety and efficacy of OZURDEX<sup>®</sup> in paediatric patients has not been established.

**Use in the Elderly:**

No overall differences in safety and efficacy have been observed between elderly and younger patients.

**Renal impairment**

OZURDEX<sup>®</sup> has not been studied in patients with renal impairment; however no special considerations are needed in this population.

**Hepatic impairment**

OZURDEX<sup>®</sup> has not been studied in patients with hepatic impairment; however no special considerations are needed in this population

**Genotoxicity:**

Studies evaluating the mutagenic potential of dexamethasone in bacteria and mammalian cells *in vitro* have been negative. Assays for clastogenicity conducted *in vitro* and *in vivo* (mouse bone marrow micronucleus test) have returned mixed results, but the observed positive findings are considered likely to be confounded by the drug's pharmacological activity. The available data support that dexamethasone, as well as the polymeric component of OZURDEX<sup>®</sup>, do not pose a genotoxic hazard to patients.

**Carcinogenicity:**

No studies on the carcinogenic potential of OZURDEX<sup>®</sup> have been conducted.



### Effects on Ability to Drive:

Patients may experience temporary visual blurring after receiving OZURDEX<sup>®</sup> by intravitreal injection. They should not drive or use machines until this has resolved.

### INTERACTIONS WITH OTHER MEDICINES

No interaction studies have been performed.

### ADVERSE EFFECTS

#### Clinical Trials

The clinical safety of OZURDEX<sup>®</sup> was assessed in 2 Phase 3 randomised, masked, Sham-controlled studies in patients with diabetic macular oedema. In both studies, a total of 347 patients were randomised and received OZURDEX<sup>®</sup> and 350 received Sham.

The most frequent adverse reactions (dexamethasone or injection procedure) were defined as adverse reactions that occurred with a higher frequency in the OZURDEX<sup>®</sup> group compared to the Sham group and had a plausible mechanism of action as shown in Table 1:

**Table 1 Summary of Adverse Reactions in Phase 3 Studies in ≥ 1% of Patients – Entire Study Period**

	<b>OZURDEX<sup>®</sup></b> <b>N = 347</b>	<b>Sham</b> <b>N = 350</b>
<i>Eye Disorders (Study Eye)</i>		
Cataract	131 (37.8)	34 (9.7)
Cataract subcapsular	41 (11.8)	12 (3.4)
Cataract nuclear	18 (5.2)	8 (2.3)
Lenticular opacities	16 (4.6)	4 (1.1)
Intraocular pressure increased	107 (30.8)	12 (3.4)
Ocular hypertension	21 (6.1)	5 (1.4)
Conjunctival haemorrhage*	73 (21.0)	45 (12.9)
Vitreous haemorrhage*	24 (6.9)	25 (7.1)
Eye pain*	18 (5.2)	13 (3.7)
Vitreous detachment*	17 (4.9)	8 (2.3)
Vitreous floaters*	17 (4.9)	7 (2.0)
Conjunctival oedema*	15 (4.3)	4 (1.1)
Vitreous opacities*	11 (3.2)	3 (0.9)
Anterior chamber inflammation*	6 (1.7%)	0 (0.0)
Visual acuity reduced	29 (8.4%)	14 (4.0%)

Note: “\*” indicates adverse drug reactions considered to be related to the intravitreal injection procedure.

Uncommon adverse reactions included endophthalmitis (0.6% - injection procedure related), glaucoma (0.9%) and necrotising retinitis (0.3%).

### **Cataract and Raised Intraocular Pressure**

The most frequently reported adverse reactions across the entire study period in the study eye of patients who received OZURDEX<sup>®</sup> were cataract and elevated IOP (see below).

In the 3 year DME clinical studies, at baseline, 87% of patients with a phakic study eye treated with OZURDEX<sup>®</sup> had some degree of lens opacification/ early cataract. The incidence of all observed cataract types (i.e. cataract cortical, cataract diabetic, cataract nuclear, cataract subcapsular, cataract lenticular, cataract) was 68% in OZURDEX<sup>®</sup> treated patients with a phakic study eye across the 3 year studies. 59% of patients with a phakic study eye required cataract surgery by the 3 year final visit, with the majority performed in the 2nd and 3rd years.

Mean IOP in the study eye at baseline was the same in both treatment groups (15.3 mmHg). The mean increase from baseline IOP did not exceed 3.2 mmHg across all visits in the OZURDEX<sup>®</sup> group with the mean IOP peaking at the 1.5 month visit post injection, and returning to approximately baseline levels by month 6 following each injection. The rate and magnitude of IOP elevation following OZURDEX<sup>®</sup> treatment did not increase upon repeated injection of OZURDEX<sup>®</sup>.

28% of patients treated with OZURDEX<sup>®</sup> had a  $\geq 10$  mm Hg IOP increase from baseline at one or more visits during the study. At baseline 3% of patients required IOP-lowering medication(s). Overall, 42% of patients required IOP-lowering medications in the study eye at some stage during the 3 year studies, with the majority of these patients requiring more than one medication. Peak usage (33%) occurred during the first 12 months and remained similar from year to year.

A total of 4 patients (1%) treated with OZURDEX<sup>®</sup> had procedures in the study eye for the treatment of IOP elevation. One patient treated with OZURDEX<sup>®</sup> required incisional surgery (trabeculectomy) to manage the steroid-induced IOP elevation, 1 patient had a trabeculectomy owing to anterior chamber fibrin blocking the aqueous outflow leading to increased IOP, 1 patient had an iridotomy for narrow angle glaucoma and 1 patient had iridectomy due to cataract surgery. No patient required removal of the implant by vitrectomy to control IOP.

### **Postmarketing Experience**

The following adverse reactions have been identified during postmarketing use of OZURDEX<sup>®</sup> in clinical practice. Because postmarketing reporting of these reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate the frequency of these reactions. The reactions have been chosen for inclusion due to a combination of the frequency of reporting and/or possible causal connection to OZURDEX<sup>®</sup>.

#### ***Eye disorders***

Endophthalmitis

Hypotony of eye (associated with vitreous leakage due to injection)

Retinal Detachment

***General disorders and administration site conditions***

Complication of device insertion (implant misplacement)  
Device dislocation with or without corneal oedema

**DOSAGE AND ADMINISTRATION**

The safety and efficacy of OZURDEX<sup>®</sup> administered to both eyes on the same day has not been studied; and is not recommended.

OZURDEX<sup>®</sup> must be administered by a qualified ophthalmologist, experienced in intravitreal insertions.

Treatment with OZURDEX<sup>®</sup> for diabetic macular oedema is 700 µg per eye (entire contents of a single-use OZURDEX<sup>®</sup> device).

Patients treated with OZURDEX<sup>®</sup> who have experienced an initial response and in the physician's opinion may benefit from retreatment without being exposed to significant risk should be considered for retreatment.

In clinical trials, the majority of retreatments were administered between 5 and 7 months after a prior treatment (see **CLINICAL TRIALS**). Patients in the OZURDEX<sup>®</sup> arm of the pivotal trials received an average of 4 implants over 3 years. The protocol in the pivotal trials specified a 6-monthly dosing interval. There is currently no experience of the efficacy and safety of repeat administrations in DME beyond 7 implants.

The intravitreal injection procedure should be carried out under aseptic conditions, which include the use of surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). The patient's medical history for hypersensitivity reactions should be carefully evaluated before performing the intravitreal procedure. The periocular skin, eyelid and ocular surface should be disinfected and adequate local anaesthesia and a broad-spectrum topical microbicide should be administered before the injection. Aseptic technique should be maintained at all times before and during the injection procedure.

Remove the foil pouch from the carton and examine for damage. Then, in a sterile field, open the foil pouch and gently place the applicator on a sterile tray. Carefully remove the cap from the applicator. Hold the applicator in one hand and pull the safety tab straight off the applicator. Do not twist or flex the tab.

With the long axis of the applicator parallel to the limbus, enter the sclera at a shallow oblique angle with the bevel of the needle up (away from the sclera) to create a partial thickness tract 1-2 mm in length parallel to the limbus (no more than the length of the needle bevel). Re-direct the needle perpendicularly towards the center of the vitreous cavity; this creates a bi-planar self-sealing scleral puncture.

Advance the needle until the vitreous cavity is entered and the silicone sleeve is against the conjunctiva. Do not advance the needle past the point where the sleeve touches the conjunctiva. When re-directing into the vitreous cavity, allow for the fact that the DDS can be up to 6.5 mm long. Slowly depress the actuator button on the applicator until an audible or palpable click is noted (on occasion, a smaller, softer click is heard or felt while the button is only partially depressed).

**Attachment 1: Product information for AusPAR OZURDEX - dexamethasone - Allergan Australia Pty Ltd PM-2014-00332-1-5 Final 25 October 2016. This Product Information was approved at the time this AusPAR was published.**

Before withdrawing the applicator from the eye, ensure the button is fully depressed and has locked flush with the applicator surface. The speed of the DDS injection is proportional to the speed that the button is depressed. Withdraw the needle from the eye back-tracking along the original entry path if possible.

Following the intravitreal injection, patients may be treated with antibiotics.

Patients should be monitored. Monitoring may consist of a check for perfusion of the optic nerve head immediately after the injection, tonometry within 30 minutes following the injection, and biomicroscopy between 2 and 7 days following the injection.

Each applicator can only be used for the treatment of a single eye.

#### **OVERDOSAGE**

Overdosage with OZURDEX<sup>®</sup> has not been reported in clinical trials and would not be expected due to its method of administration.

#### **PRESENTATION AND STORAGE CONDITIONS**

1 pack contains: 1 sustained release sterile implantable rod shaped implant containing 700 µg of dexamethasone, located in the needle (stainless steel) of a disposable applicator.

The applicator containing the implant is packaged in a sealed foil pouch containing desiccant.

OZURDEX<sup>®</sup> has a shelf life of 36 months. Store below 25°C. Protect from excessive heat.

#### **NAME AND ADDRESS OF THE SPONSOR**

Allergan Australia Pty Ltd  
810 Pacific Highway  
Gordon NSW 2072  
ABN: 85 000 612 831

**POISON SCHEDULE OF THE MEDICINE:** S4 Prescription Only Medicine

**DATE OF FIRST INCLUSION IN THE ARTG:** 04 June 2015

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