

Package leaflet: information for the user

OZURDEX 700 micrograms intravitreal implant in applicator dexamethasone

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor. See section 4.

What is in this leaflet

1. What OZURDEX is and what it is used for
2. What you need to know before you are given OZURDEX
3. How OZURDEX is used
4. Possible side effects
5. How to store OZURDEX
6. Contents of the pack and other information

1. What OZURDEX is and what it is used for

The active substance in OZURDEX is dexamethasone. Dexamethasone belongs to a group of medicines called corticosteroids.

OZURDEX is used to treat adult patients with:

- Vision loss due to diabetic macular oedema (DME), if you have already had an operation for cataract, or if you have not previously responded to, or are not suitable for, other types of treatment. Diabetic macular oedema is a swelling of the light-sensitive layer at the back of the eye called the macula. DME is a condition that affects some people with diabetes.
- Vision loss caused by a blockage of veins in the eye. This blockage leads to a build up of fluid causing swelling in the area of the retina (the light-sensitive layer at the back of the eye) called the macula.

Swelling of the macula may lead to damage which affects your central vision which is used for tasks like reading. OZURDEX works by reducing this swelling of the macular which helps to lessen or prevent more damage to the macula.

- Inflammation of the back of the eye. This inflammation leads to a decrease of vision and/or the presence of floaters in the eye, (black dots or wispy lines that move across the field of vision). OZURDEX works by reducing this inflammation.

2. What you need to know before you are given OZURDEX

You must not be given OZURDEX

- if you are allergic to dexamethasone or any of the other ingredients of this medicine (listed in section 6)
- if you have an infection of any kind in or around your eye (bacterial, viral or fungal)
- if you have glaucoma or high pressure inside your eye which is not controlled properly with the medicines you may be using
- if the eye to be treated does not have a lens and the back of the lens capsule (“the bag”) has been ruptured

- if the eye to be treated has undergone cataract surgery and has a man-made lens, which was implanted in the front compartment of the eye (anterior chamber intraocular lens) or was fixed to the white portion of the eye (sclera) or to the coloured part of the eye (iris), and the back of the lens capsule (“the bag”) has been ruptured

Warnings and precautions

Before your OZURDEX injection tell your doctor if:

- You have had cataract surgery, iris surgery (the coloured part of the eye that controls the amount of light that enters into the eye) or surgery to remove the gel (called the vitreous) from within the eye
- You are taking any medicines to thin the blood
- You are taking any steroid or non-steroidal anti-inflammatory medicines by mouth or applied to the eye
- You have had a herpes simplex infection in your eye in the past (an ulcer on the eye that has been there a long time, or sores on the eye)

Occasionally the injection of OZURDEX may cause an infection inside the eye, pain or redness in the eye, or a detachment or tear of the retina. It is important to identify and treat these as soon as possible. Please tell your doctor immediately if you develop increased eye pain or increased discomfort, worsening redness of your eye, flashing lights and sudden increase in floaters, partially blocked vision, decreased vision or increased sensitivity to light after your injection.

In some patients the eye pressure may increase with the possible development of glaucoma. This is something you may not notice so your doctor will monitor you regularly and, if necessary provide treatment to lower the eye pressure.

In the majority of patients who have not yet had an operation for cataract, a clouding of the eye's natural lens (a cataract) may occur after repeated treatment with OZURDEX. If this occurs your vision will decrease, and you are likely to need an operation to remove the cataract. Your doctor will help you to decide when is the most appropriate time to perform this operation, but you should be aware that until you are ready for your operation your vision may be as bad or worse than it was before you started receiving your OZURDEX injections.

The implant can move from the back to the front of the eye in patients with a tear in the back of the lens capsule and/or those who have an opening in the iris. This can lead to swelling of the clear layer in the front of the eye and cause blurred vision. If this continues for a long time and is left untreated, it may require tissue transplantation.

The injection of OZURDEX into both eyes at the same time has not been studied and is not recommended. Your doctor should not inject OZURDEX into both eyes at the same time.

Children and adolescent (below 18 years of age)

The use of OZURDEX in children and adolescents has not been studied and is therefore not recommended.

Other medicines and OZURDEX

Tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

There is no experience of using OZURDEX in pregnant women or during breast-feeding. OZURDEX should not be used during pregnancy or breast-feeding unless your doctor thinks it is clearly necessary. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, discuss this with your doctor before OZURDEX treatment. Ask your doctor for advice before taking any medicine.

Driving and using machines

After OZURDEX treatment you may experience some reduced vision for a short time. If this happens, do not drive or use any tools or machines until your vision improves.

3. How OZURDEX is used

All OZURDEX injections will be given by an appropriately qualified eye doctor.

The recommended dose is one implant to be given by injection into your eye. If the effect of this injection wears off and your doctor recommends it, another implant may then be injected into your eye.

Your doctor will ask you to use antibiotic eye drops daily for 3 days before and after each injection to prevent any eye infection. Please follow these instructions carefully.

On the day of the injection, your doctor may use antibiotic eye drops to prevent infection. Before the injection, your doctor will clean your eye and eyelid. Your doctor will also give you a local anaesthetic to reduce or prevent any pain you might have with the injection. You may hear a 'click' during the injection of OZURDEX; this is normal.

Detailed instructions for your doctor on how to carry out the OZURDEX injection are provided in the medicine carton.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects may be seen with OZURDEX:

Very common (may affect more than 1 in 10 people):

Increased pressure in the eye, clouding of the lens (cataract), bleeding on the surface of the eye*

Common (may affect up to 1 in 10 people):

High pressure in the eye, clouding at the back of the lens, bleeding into the inside of the eye*, worsening of vision*, difficulties in seeing clearly, detachment of the jelly inside the eye from the light-sensitive layer at the back of the eye (vitreous detachment)*, a feeling of spots in front of the eye (including 'floaters')*, a feeling of looking through mist or fog*, inflammation of the eyelid, eye pain*, seeing flashes of light*, swelling of the layer over the white part of the eye*, redness of the eye*, headache

Uncommon (may affect up to 1 in 100 people):

A severe inflammation at the back of the eye (usually due to viral infection), serious infection or inflammation inside the eye*, glaucoma (an eye disease in which increased pressure in the eye is associated with damage to the optic nerve), detachment of the light-sensitive layer from the back of the eye* (retinal detachment), tear of the light-sensitive layer at the back of the eye (retinal tear)*, a decrease in the eye pressure which is associated with leakage of the jelly (vitreous) from inside the eye*, inflammation inside the front part of the eye*, increased protein and cells in the front of the eye due to inflammation*,

abnormal feeling in the eye * itchiness of the eyelid, redness of the white of the eye*, migration of the OZURDEX implant from the back to the front of the eye causing blurred or decreased vision and which may or may not cause swelling of the clear part of the eye (cornea)*, accidental incorrect placement of the OZURDEX implant*, migraine

**These side effects may be caused by the injection procedure and not the OZURDEX implant itself. The more injections you have the more these effects can occur.*

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

Malta

ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store OZURDEX

Keep this medicine out of the sight and reach of children.

Do not use OZURDEX after the expiry date which is stated on the carton and the pouch after EXP:. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What OZURDEX contains

- The active substance is dexamethasone.
- Each implant contains 700 micrograms of dexamethasone.
- The other ingredients are: Ester terminated 50:50 poly D,L-lactide-co-glycolide and Acid terminated 50:50 poly D,L-lactide-co-glycolide.

What OZURDEX looks like and contents of the pack

OZURDEX is a rod-shaped implant which is stored inside the needle of an applicator. The applicator and a packet of drying material are sealed in a foil pouch which is inside a carton. One carton contains one applicator with one implant which will be used once and thrown away.

Marketing Authorisation Holder and Manufacturer

Allergan Pharmaceuticals Ireland
Castlebar Road
Westport
Co. Mayo
Ireland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Ireland/Malta

Allergan Pharmaceuticals Ireland
Tel: 1800 931 787 (IE)
+356 27780331 (MT)

United Kingdom

Allergan Ltd
Tel: +44 (0) 1628 494026

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu/>.

Version 12

[To be provided in the carton]

The following information is intended for medical or healthcare professionals only, and includes the numbered sections of the SmPC which provide practical information for use of the medicinal product. Please refer to the SmPC for full product information.

INFORMATION FOR THE HEALTHCARE PROFESSIONAL

1. NAME OF THE MEDICINAL PRODUCT

OZURDEX 700 micrograms intravitreal implant in applicator

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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) (see SmPC section 5.1)
- inflammation of the posterior segment of the eye presenting as non-infectious uveitis

4.2 Posology and method of administration

OZURDEX must be administered by a qualified ophthalmologist experienced in intravitreal injections.

Posology

The recommended dose is one OZURDEX implant to be administered intra-vitreally to the affected eye. Administration to both eyes concurrently is not recommended (see SmPC section 4.4).

Patients should be monitored following the injection to permit early treatment if an infection or increased intraocular pressure occurs (see SmPC section 4.4).

Special populations

Elderly (≥65 years old)

No dose adjustment is required for elderly patients.

Method of administration

OZURDEX is a single-use intravitreal implant in applicator for intravitreal use only.

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

The intravitreal injection procedure should be carried out under controlled aseptic conditions which include the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent).

The patient should be instructed to self-administer broad spectrum antimicrobial drops daily for 3 days before and after each injection. Before the injection, the periocular skin, eyelid and ocular surface should be disinfected (using for example drops of povidone iodine 5% solution on the conjunctiva as it was done in the clinical trials for the approval of OZURDEX) and adequate local anaesthesia should be administered. Remove the foil pouch from the carton and examine for damage (see SmPC section 6.6). 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. Once the foil pouch is opened the applicator should be used immediately. Hold the applicator in one hand and pull the safety tab straight off the applicator. Do not twist or flex the tab. With the bevel of the needle up away from the sclera, advance the needle

about 1 mm into the sclera then redirect toward the centre of the eye into the vitreous cavity until the silicone sleeve is against the conjunctiva. Slowly press the actuator button until an audible click is noted. Before withdrawing the applicator from the eye, make sure that the actuator button is fully pressed and has locked flush with the applicator surface. Remove the needle in the same direction as used to enter the vitreous.

For instructions on the administration of the intravitreal implant, see section 6.6

Immediately after injecting OZURDEX, use indirect ophthalmoscopy in the quadrant of injection to confirm successful implantation. Visualisation is possible in the large majority of cases. In cases in which the implant cannot be visualised, take a sterile cotton bud and lightly depress over the injection site to bring the implant into view.

Following the intravitreal injection patients should continue to be treated with a broad spectrum antimicrobial.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients as listed in SmPC section 6.1.
- 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.
- Advanced glaucoma which cannot be adequately controlled by medicinal products alone.
- Aphakic eyes with ruptured posterior lens capsule.
- Eyes with Anterior Chamber Intraocular Lens (ACIOL), iris or transscleral fixated intraocular lens and ruptured posterior lens capsule.

4.4 Special warnings and precautions for use

Intravitreal injections, including those with OZURDEX, can be associated with endophthalmitis, intraocular inflammation, increased intraocular pressure 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 intraocular pressure occurs. 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 must be instructed to report any symptoms suggestive of endophthalmitis or any of the above mentioned events without delay, e.g. eye pain, blurred vision etc. (see SmPC section 4.8).

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) where OZURDEX should not be used, 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.

Use of corticosteroids, including OZURDEX, may induce cataracts (including posterior subcapsular cataracts), increased IOP, steroid induced glaucoma and may result in secondary ocular infections.

In the 3 year DME clinical studies, 59% of patients with a phakic study eye treated with OZURDEX underwent cataract surgery in the study eye (see SmPC section 4.8).

After the first injection the incidence of cataract appears higher in patients with non-infectious uveitis of the posterior segment compared with BRVO/CRVO patients. In BRVO/CRVO clinical studies, cataract was reported more frequently in patients with phakic lens receiving a second injection (see SmPC section 4.8). Only 1 patient out of 368 required cataract surgery during the first treatment and 3 patients out of 302 during the second treatment. In the non-infectious uveitis study, 1 patient out of the 62 phakic patients underwent cataract surgery after a single injection.

The prevalence of conjunctival haemorrhage in patients with non-infectious uveitis of the posterior segment appears to be higher compared with BRVO/CRVO and DME. This could be attributable to the intravitreal injection procedure or to concomitant use of topical and/or systemic corticosteroid or Non-steroidal anti-inflammatory medications. No treatment is required since spontaneous resolution occurs.

As expected with ocular steroid treatment and intravitreal injections, increases in intraocular pressure (IOP) may be seen. The rise in IOP is normally manageable with IOP lowering medication (see section 4.8). Of the patients experiencing an increase of IOP of ≥ 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. Patients of less than 45 years of age with macular oedema following Retinal Vein Occlusion or inflammation of the posterior segment of the eye presenting as non-infectious uveitis are more likely to experience increases in IOP.

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

The safety and efficacy of OZURDEX administered to both eyes concurrently have not been studied. Therefore administration to both eyes concurrently is not recommended.

OZURDEX has not been studied in patients with macular oedema secondary to RVO with significant retinal ischemia. Therefore OZURDEX is not recommended.

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

In RVO, anti-coagulant therapy was used in 2% of patients receiving OZURDEX; there were no reports of haemorrhagic adverse events in these patients. 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 and sham groups (29% vs 32%). Among patients who did not use anti-coagulant therapy, 27% of OZURDEX 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 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 anti-platelet medication, haemorrhagic adverse events were reported in a slightly higher proportion of patients injected with OZURDEX (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 should be used with caution in patients taking anti-coagulant or anti-platelet medicinal products.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, consider evaluating for possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
Systemic absorption is minimal and no interactions are anticipated.

4.6 Fertility, pregnancy and lactation

Pregnancy

Studies in animals have shown teratogenic effects following topical ophthalmic administration (see SmPC section 5.3). 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 is not recommended during pregnancy unless the potential benefit justifies the potential risk to the foetus.

Breast-feeding

Dexamethasone is excreted in breast milk. No effects on the child are anticipated due to the route of administration and the resulting systemic levels. However OZURDEX is not recommended during breast feeding unless clearly necessary.

Fertility

There are no fertility data available.

4.7 Effects on ability to drive and use machines

OZURDEX may have a moderate influence on the ability to drive and use machines. Patients may experience temporarily reduced vision after receiving OZURDEX by intravitreal injection (see SmPC section 4.8). They should not drive or use machines until this has resolved.

4.8 Undesirable effects

Summary of the safety profile

The most commonly-reported adverse events reported following treatment with OZURDEX are those frequently observed with ophthalmic steroid treatment or intravitreal injections (elevated IOP, cataract formation and conjunctival or vitreal haemorrhage respectively).

Less frequently reported, but more serious, adverse reactions include endophthalmitis, necrotizing retinitis, retinal detachment and retinal tear.

With the exception of headache and migraine, no systemic adverse drug reactions were identified with the use of OZURDEX.

Tabulated list of adverse reactions

The adverse reactions considered related to OZURDEX treatment from the Phase III clinical trials (DME, BRVO/CRVO and uveitis) and spontaneous reporting are listed by MedDRA System organ class in the table below using the following convention:

Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1 Adverse reactions

System organ class	Frequency	Adverse reaction
Nervous system disorders	Common	Headache
	Uncommon	Migraine
Eye disorders	Very common	Intraocular pressure increased**, cataract**, conjunctival haemorrhage*
	Common	Ocular hypertension, cataract subcapsular, vitreous haemorrhage**, visual acuity reduced*, visual impairment/ disturbance, vitreous detachment*, vitreous floaters*, vitreous opacities*, blepharitis, eye pain*, photopsia*, conjunctival oedema* conjunctival hyperaemia*
	Uncommon	Necrotizing retinitis, endophthalmitis*, glaucoma, retinal detachment*, retinal tear*, hypotony of the eye*, anterior chamber inflammation*, anterior chamber cells/ flares*, abnormal sensation in eye*, eyelids pruritus, scleral hyperaemia*
General disorders and administration site conditions	Uncommon	Device dislocation* (migration of implant) with or without corneal oedema (see also section 4.4), complication of device insertion resulting in ocular tissue injury* (implant misplacement)

* indicates adverse reactions considered to be related to the intravitreal injection procedure (the frequency of these adverse reactions is proportional to the number of treatments given).

** in a 24-month real world observational study in the treatment of macular oedema following RVO and non-infectious uveitis affecting the posterior segment of the eye these adverse events were reported more frequently among patients who received >2 injections vs patients who received ≤2 injections; cataract formation (24.7% vs 17.7%), cataract progression (32.0% vs 13.1%), vitreous haemorrhage (6.0% vs 2.0%), and increased IOP (24.0% vs 16.6%).

Description of selected adverse reactions

Diabetic Macular Oedema

The clinical safety of OZURDEX in patients with diabetic macular oedema was assessed in two phase 3 randomized, double-masked, sham-controlled studies. In both studies, a total of 347 patients were randomized and received OZURDEX and 350 patients received sham.

The most frequently reported adverse reactions across the entire study period in the study eye of patients who received OZURDEX 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 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 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 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 treatment did not increase upon repeated injection of OZURDEX.

28% of patients treated with OZURDEX had a ≥ 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 had procedures in the study eye for the treatment of IOP elevation. One patient treated with OZURDEX 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.

BRVO/CRVO

The clinical safety of OZURDEX in patients with macular oedema following central or branch retinal vein occlusion has been assessed in two Phase III randomised, double-masked, sham-controlled studies. A total of 427 patients were randomised to receive OZURDEX and 426 to receive sham in the two Phase III studies. A total of 401 patients (94 %) randomised and treated with OZURDEX completed the initial treatment period (up to day 180).

A total of 47.3 % of patients experienced at least one adverse reaction. The most frequently reported adverse reactions in patients who received OZURDEX were increased intraocular pressure (24.0 %) and conjunctival haemorrhage (14.7 %).

The adverse reaction profile for BRVO patients was similar to that observed for CRVO patients although the overall incidence of adverse reactions was higher for the subgroup of patients with CRVO.

Increased intraocular pressure (IOP) with OZURDEX peaked at day 60 and returned to baseline levels by day 180. Elevations of IOP either did not require treatment or were managed with the temporary use of topical IOP-lowering medicinal products. During the initial treatment period, 0.7 % (3/421) of the patients who received OZURDEX required laser or surgical procedures for management of elevated IOP in the study eye compared with 0.2 % (1/423) with sham.

The adverse reaction profile of 341 patients analysed following a second injection of OZURDEX, was similar to that following the first injection. A total of 54 % of patients experienced at least one adverse reaction. The incidence of increased IOP (24.9 %) was similar to that seen following the first injection and likewise returned to baseline by open-label day 180. The overall incidence of cataracts was higher after 1 year compared to the initial 6 months.

Uveitis

The clinical safety of OZURDEX in patients with inflammation of the posterior segment of the eye presenting as non-infectious uveitis, has been assessed in a single, multicentre, masked, randomised study.

A total of 77 patients were randomised to receive OZURDEX and 76 to receive Sham. A total of 73 patients (95%) randomised and treated with OZURDEX completed the 26-week study.

The most frequently reported adverse reactions in the study eye of patients who received OZURDEX were conjunctival haemorrhage (30.3%), increased intraocular pressure (25.0%) and cataract (11.8%).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

If an overdose occurs, intraocular pressure should be monitored and treated, if deemed necessary by the attending physician.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at doses considered sufficiently in excess of the maximum dose for human indicating little relevance to clinical use.

No mutagenicity, carcinogenicity, reproductive or developmental toxicity data are available for OZURDEX. Dexamethasone has been shown to be teratogenic in mice and rabbits following topical ophthalmic application.

Dexamethasone exposure to the healthy/untreated eye via contralateral diffusion has been observed in rabbits following delivery of the implant to the posterior segment of the eye.

6. PHARMACEUTICAL PARTICULARS

6.6 Special precautions for disposal and other handling

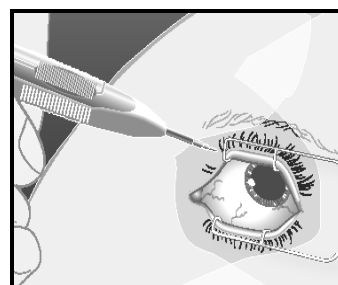
OZURDEX is for single use only.

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

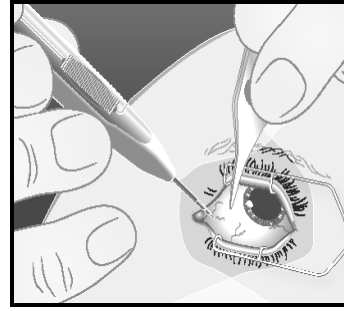
If the seal of the foil pouch containing the applicator is damaged, the applicator must not be used. Once the foil pouch is opened the applicator should be used immediately.

Administering OZURDEX

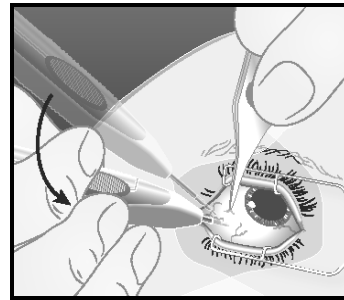
- 1) Hold the long axis of the applicator parallel to the limbus.



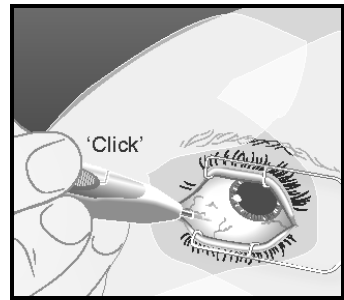
- 2) Allow the applicator to meet the sclera at an oblique angle with the bevel of the needle facing up, away from the sclera. Push the tip about 1 mm into the sclera, keeping it parallel to the limbus.



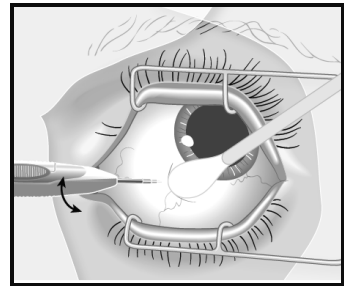
- 3) Redirect towards the centre of the eye into the vitreous cavity. This will create a shelved scleral path. Advance the needle until you enter the vitreous cavity. Do not advance the needle past the point where the sleeve of the applicator touches the conjunctiva.



- 4) Depress the actuator button slowly until you hear a click. Before withdrawing the applicator from the eye, make sure that the actuator button is fully depressed and has locked flush with the applicator surface.



- 5) Withdraw the applicator in the same direction that you used to enter the vitreous.



- 6) Dispose of the applicator safely immediately after treatment. The OZURDEX applicator is for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.