DEXAMETHASONE

OZURDEX®

700 mcg Sustained Release Sterile Rod-Shaped Implant for Ophthalmic Intravitreal Injection

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Dexamethasone (OZURDEX) safely and effectively. See full prescribing information.

Dexamethasone (OZURDEX) (dexamethasone intravitreal implant)

----------INDICATIONS AND USAGE----------

For the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) (1) and non-infectious uveitis affecting the posterior segment of the eye, and for the treatment of diabetic macular edema (DME).

----------DOSAGE AND ADMINISTRATION----------

• For ophthalmic intravitreal injection only. (2.1)

• The intravitreal injection procedure should be carried out under controlled aseptic conditions. Following the intravitreal injection, patients should be monitored for elevation in intraocular pressure and for endophthalmitis. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

• Intravitreal implant containing dexamethasone 0.7 mg in the NOVADUR™ solid polymer drug delivery system. (3)

----------CONTRAINDICATIONS----------

• Ocular or periocular infections. (4.1)

• Advanced glaucoma. (4.2)

• Aphakic eyes with ruptured posterior lens capsule. (4.3)

• Eyes with ACIOL, iris or transscleral fixated IOLs and ruptured posterior lens capsule. (4.4)

• Hypersensitivity. (4.5)

----------WARNINGS AND PRECAUTIONS----------

• Intravitreal injections have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments. Patients should be monitored following the injection. (5.1)

• 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. (5.2)

• Use of corticosteroids may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. (5.3)

• Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex. (5.4)

----------ADVERSE REACTIONS----------

In controlled studies, the most common adverse reactions reported by 20-70% of patients were cataract, increased intraocular pressure and conjunctival haemorrhage. (7.1)

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15 PATIENT COUNSELING INFORMATION

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

Dexamethasone (OZURDEX) (dexamethasone intravitreal implant) is indicated for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) and for the treatment of non-infectious uveitis affecting the posterior segment of the eye. Dexamethasone (OZURDEX) is indicated for the treatment of diabetic macular edema (DME).

2. DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

For ophthalmic intravitreal injection only.

2.2 Administration

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's medical history for hypersensitivity reactions should be carefully evaluated before performing the intravitreal procedure. The periocular skin, eyelid and ocular surface should be dissected (for example, drops of povidone 5% solution on the conjunctiva). Adequate local anesthesia and a broad-spectrum microbicide are recommended to be given prior to the injection. Dexamethasone (OZURDEX) must be administered by a qualified ophthalmology experienced in intravitreal injections.

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.** The long axis of the applicator should be held parallel to the limbus, and the sclera should be engaged at an oblique angle with the bevel of the needle up (away from the sclera) to create a shelved scleral path. The tip of the needle is advanced within the sclera for about 1 mm (parallel to the limbus), then re-directed toward the center of the eye and advanced until penetration of the sclera is completed and the vitreous cavity is entered. The needle should not be advanced past the point where the sleeve touches the conjunctiva. When re-directing into the vitreous cavity, allow for the fact that the DDS® canbe up to 6.5 mm long.

Slowly depress the actuator button until an audible click is noted. (Note: On occasion, a smaller, softer click is heard or felt while the button is only partially depressed). Before withdrawing the applicator from the eye, make sure that the actuator 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. Remove the needle in the same direction as used to enter the vitreous.

Following the intravitreal injection, patients should be monitored for elevation in intraocular pressure and for endophthalmitis. 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 without delay.

Each applicator can only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new applicator must be used, and the sterile field, syringe, gloves, drapes, and eyelid speculum should be changed before Dexamethasone (OZURDEX) is administered to the other eye.

3. DOSAGE FORMS AND STRENGTHS

Intravitreal implant containing dexamethasone 0.7 mg in the NOVADUR™ solid polymer drug delivery system.

4. CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

Dexamethasone (OZURDEX) (dexamethasone intravitreal implant) is contraindicated in patients with active or suspected ocular or periocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

4.2 Advanced Glaucoma

Dexamethasone (OZURDEX) is contraindicated in patients with advanced glaucoma.

4.3 Aphakic eyes with ruptured posterior lens capsule

Dexamethasone (OZURDEX) is contraindicated in aphakic eyes with ruptured posterior lens capsule.

4.4 Eyes with ACIOL, iris or transscleral fixated IOLs and ruptured posterior lens capsule

Dexamethasone (OZURDEX) is contraindicated in eyes with ACIOL (Anterior Chamber Intraocular Lens), iris or transscleral fixated IOLs and ruptured posterior lens capsule.

4.5 Hypersensitivity

Dexamethasone (OZURDEX) is contraindicated in patients with known hypersensitivity to dexamethasone or to any other components of this product.

5. WARNINGS AND PRECAUTIONS

5.1 Intravitreal Injection-related Effects

Intravitreal injections, including those with Dexamethasone (OZURDEX), have been associated with endophthalmitis, eye 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 occur. Patients should be instructed to report any symptoms suggestive of endophthalmitis or any of the above-mentioned events without delay. (see **PATIENT COUNSELING INFORMATION, 15**)

5.2 Risk of Implant Migration

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 the anterior chamber might lead to corneal edema. Persistent severe corneal edema could progress to the need of corneal transplantation. Regular monitoring of such patients allows for early diagnosis of device migration.

5.3 Potential Steroid-related Effects

Use of corticosteroids, including those with Dexamethasone (OZURDEX), have been associated with posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses.

5.4 Ocular Herpes Simplex

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

5.5 Effects on Ability to drive and Use Machinery

Patient may experience temporary visual blurring after receiving an intravitreal injection. They should not drive or use machines until this has resolved.

6. DRUG INTERACTIONS

No interaction studies have been performed.

7. ADVERSE REACTIONS

7.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Treatment of Macular Edema

The following information is based on the combined clinical trial results from the initial 6 month masked period of two randomized, sham-controlled, parallel studies.

Table 1. Adverse reactions reported by greater than 2% of patients in the first six months

MeDRA Term	Dexamethasone (OZURDEX) N=421(%)	Sham N=423(%)
Intraocular pressure increased	106 (25%)	5 (1%)
Conjunctival hemorrhage	85 (20%)	63 (15%)
Eye pain	31 (7%)	16 (4%)
Conjunctival hyperemia	28 (7%)	20 (5%)
Ocular hypertension	17 (4%)	3 (1%)
Cataract	15 (4%)	6 (1%)
Vitreous detachment	12 (3%)	8 (2%)
Headache	14 (3%)	7 (2%)

Increased intraocular pressure with Dexamethasone (OZURDEX) peaked at day 60 and returned to baseline levels by day 180. During the initial treatment period, 0.7% (3/421) of the patients who received Dexamethasone (OZURDEX) required laser or surgical procedures for management of elevated intraocular pressure.

Following a second injection of Dexamethasone (OZURDEX) in cases where a second injection was indicated, the overall incidence of cataracts was higher after 1 year.

CONSTANCE 206207-025 (24-Month Post Approval Observational Study)

The clinical safety of Dexamethasone (OZURDEX) was assessed in a multicentre, 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. The most frequent adverse reactions observed in this study were consistent with the most frequent adverse reactions from clinical trials.
Stratifications by injection frequency revealed increases in the incidence of adverse reactions among patients who received >2 injections compared to patients who received ≤2 injections. The most frequent adverse reactions for patients who received >2 injections included cataract [(24.7%,

44/178) for cataract formation and (32.0%, 57/178) for cataract progression] based on eyes with phakic lens status at baseline, vitreous haemorrhage (6.0%, 17/283), and increased IOP (24.0%, 68/283).

Treatment of Uveitis

The clinical safety of Dexamethasone (OZURDEX) was assessed in a multi-center, masked, and randomized, 26-week phase 3 study in the treatment of non-infectious uveitis affecting the posterior segment of the eye. A total of 76 patients were treated with Dexamethasone (OZURDEX) and 75 were treated with sham.

Table 2. Summary of Adverse Events in Phase 3 Study 206207-014

	Dexamethasone (OZURDEX) N = 76	Sham N = 75

Eye Disorders (Study Eye)		
Intraocular pressure increased	19 (25.0%)	5 (6.7%)
Cataract	9 (11.8%)	4 (5.3%)
Myodesopsia	6 (7.9%)	5 (6.7%)
Vitreous opacities	3 (3.9%)	1 (1.3%)
Blepharitis	3 (3.9%)	0 (0.0%)
Scleral hyperaemia	2 (2.6%)	1 (1.3%)
Visual impairment	2 (2.6%)	1 (1.3%)
Abnormal sensation in eye	2 (2.6%)	0 (0.0%)
Eyelids pruritus	2 (2.6%)	0 (0.0%)
Nervous System Disorders		
Migraine	2 (2.6%)	0 (0.0%)

The proportion of Dexamethasone (OZURDEX)-treated patients with increased intraocular pressure (≥ 25 mm Hg) peaked at week 3 and returned to baseline by week 26. During the treatment period, no patients required incisional surgery for glaucoma. Three patients required laser iridotomies in the study eye for the treatment of pupillary block, iris bombe, and raised intraocular pressure.

CONSTANCE 206207-025 (24-Month Post Approval Observational Study)

Refer to CONSTANCE Study Results under Treatment of Macular Edema

Treatment of Diabetic Macular Edema

The following information is based on the combined clinical trial results from 2 randomized, 3- year, sham-controlled studies in patients with diabetic macular edema. Discontinuation rates due to the adverse reactions listed in Table below were 3% in the Dexamethasone (OZURDEX)- group and 1% in the Sham group. The most common ocular (study eye) and non-ocular adverse reactions are shown in Tables below:

Table 3. Ocular Adverse Reactions Reported by ≥ 1% of Patients and Non-ocular Adverse ReactionsReported by ≥ 5%

MedDRA Term	**Dexamethasone (OZURDEX)-**N=324 (%)	**Sham** N=328 (%)
Ocular		
Cataract[1]	166/243[2] (68%)	49/230 (21%)
Conjunctival hemorrhage	73 (23%)	44 (13%)
Visual acuity reduced	28 (9%)	13 (4%)
Conjunctivitis	19 (6%)	8 (2%)
Vitreous floaters	16 (5%)	6 (2%)
Conjunctival edema	15 (5%)	4 (1%)
Dry eye	15 (5%)	7 (2%)
Vitreous detachment	14 (4%)	8 (2%)
Vitreous opacities	11 (3%)	3 (1%)
Retinal aneurysm	10 (3%)	5 (2%)
Foreign body sensation	7 (2%)	4 (1%)
Corneal erosion	7 (2%)	3 (1%)
Keratitis	6 (2%)	3 (1%)
Anterior Chamber Inflammation	6 (2%)	0 (0%)
Retinal tear	5 (2%)	2 (1%)
Eyelid ptosis	5 (2%)	2 (1%)
Non-Ocular		
Hypertension	41 (13%)	21 (6%)
Bronchitis	15 (5%)	8 (2%)

[1] Includes cataract, cataract nuclear, cataract subcapsular, lenticular opacities in patients who were phakic at baseline. Among these patients, 61% of Dexamethasone (OZURDEX)- subjects vs. 8% of sham-controlled subjects underwent cataract surgery.
[2] 243 of the 324 Dexamethasone (OZURDEX)- subjects were phakic at baseline; 230 of 328sham-controlled subjects were phakic at baseline.

Increased Intraocular Pressure

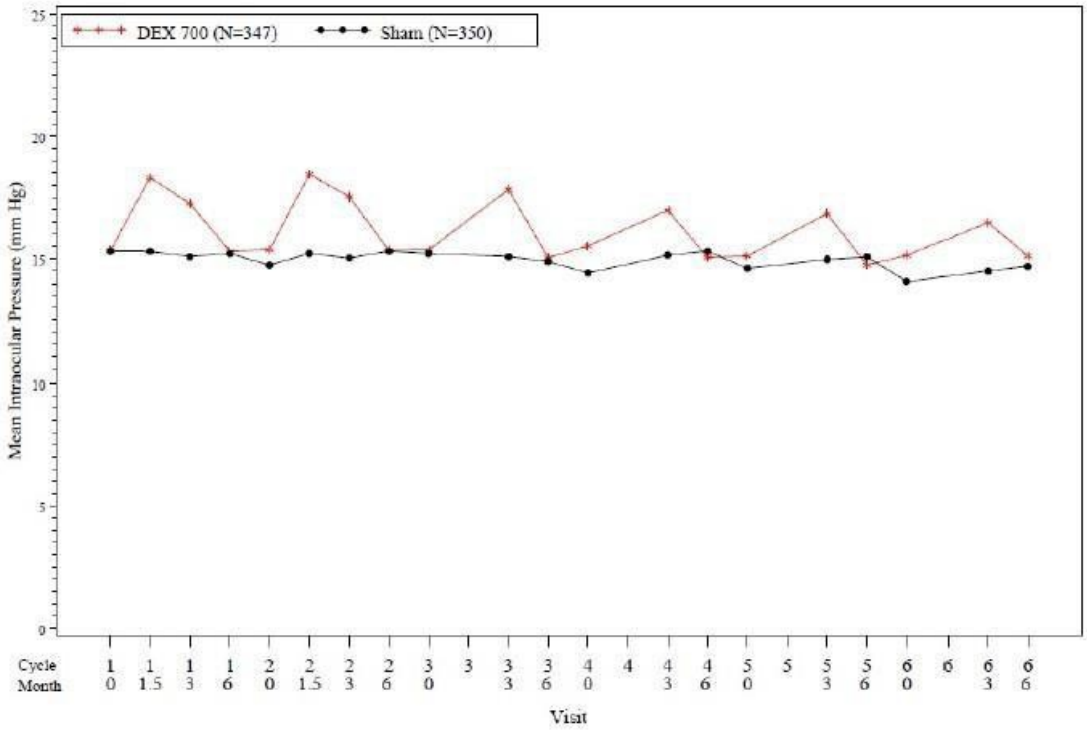
Table 4. Summary of Elevated Intraocular Pressure (IOP) Related Adverse Reactions

	Treatment: N (%)	
IOP	**Dexamethasone (OZURDEX) N=324**	**Sham N=328**
IOP elevation ≥10 mm Hg from Baseline at any visit	91 (28%)	13 (4%)
≥30 mm Hg IOP at any visit	50 (15%)	5 (2%)
Any IOP lowering medication	136 (42%)	32 (10%)
Any surgical intervention for elevated IOP*	4 (1.2%)	1 (0.3%)

* Dexamethasone (OZURDEX)-: 1 surgical trabeculectomy for steroid-induced IOP increase, 1 surgical trabeculectomy for iris neovascularization, 1 laser iridotomy, 1 surgical iridectomy
Sham: 1 laser iridotomy

The increase in mean IOP was seen with each treatment cycle, and the mean IOP generally returned to baseline between treatment cycles (at the end of the 6 month period) shown below:

Figure 1. Mean IOP during the study



Cataracts and Cataract Surgery

At baseline, 243 of the 324 Dexamethasone (OZURDEX)- subjects were phakic; 230 of 328 sham-controlled subjects were phakic. The incidence of cataract development in patients who had a phakic study eye was higher in the Dexamethasone (OZURDEX)- group (68%) compared with Sham (21%). The median time of cataract being reported as an adverse event was approximately15 months in the Dexamethasone (OZURDEX)- group and 12 months in the Sham group. Among these patients, 61% of Dexamethasone (OZURDEX)- subjects vs. 8% of sham-controlled subjects underwent cataract surgery, generally between Month 18 and Month 39 (Median Month 21 for Dexamethasone (OZURDEX)- group and 20 for Sham) of the studies.

7.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of Dexamethasone (OZURDEX) 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 Dexamethasone (OZURDEX).

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 resulting in ocular tissue injury (implant misplacement), Device dislocation with or without corneal edema.

8. OVERDOSE

Overdose with Dexamethasone (OZURDEX) has not been reported in clinical trials and would not be expected due to its method of administration.

9. USE IN SPECIFIC POPULATIONS

9.1 Pregnancy

Safety for use in pregnancy and lactation has not been established. There are no adequate data from the use of dexamethasone in pregnant women.

Topical dexamethasone has been shown to be teratogenic in mice, producing fetal resorptions and cleft palate. In the rabbit, dexamethasone produced fetal resorptions and multiple abnormalities involving the head, ears, limbs, palate, etc. Pregnant rhesus monkeys treated with dexamethasone sodium phosphate intramuscularly at 1 mg/kg/day every other day for 28 days or at 10 mg/kg/day once or every other day on 3 or 5 days between gestation days 23 and 49 had fetuses with minor cranial abnormalities. A 1 mg/kg/dose in pregnant rhesus monkeys would be approximately 85 times higher than a Dexamethasone (OZURDEX) injection in humans (assuming 60 kg body weight).

There are no adequate and well-controlled studies in pregnant women. Dexamethasone (OZURDEX) (dexamethasone intravitreal implant) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

9.2 Nursing Mothers

It is not known whether ocular administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Low level dexamethasone systemic exposure was detected following intraocular implantation of Dexamethasone (OZURDEX) in non- pregnant rabbits and monkeys. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Dexamethasone (OZURDEX) should not be used during pregnancy or lactation unless clearly necessary

9.3 Pediatric Use

Safety and effectiveness of Dexamethasone (OZURDEX) in pediatric patients has not been established.

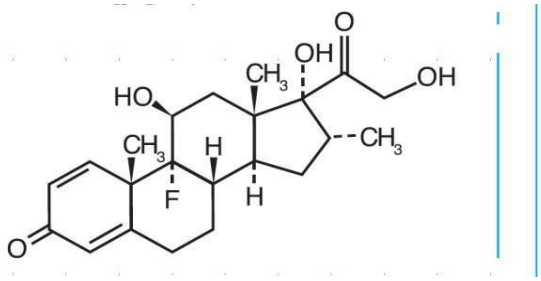
9.4 Geriatric Use

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

10. DESCRIPTION

Dexamethasone (OZURDEX) is an intravitreal implant containing 0.7 mg (700 μg) dexamethasone in the NOVADUR™ solid polymer drug delivery system. Dexamethasone (OZURDEX) is preloaded into a single-use, specially designed DDS® applicator to facilitate injection of the rod-shaped implant directly into the vitreous.

The NOVADUR™ system contains poly (D,L-lactide-co-glycolide) PLGA intravitreal polymer matrix. Dexamethasone (OZURDEX) is preservative-free. The chemical name for dexamethasone is pregna-1,4-diene-3,20-dione,9-fluoro-11,17,21-trihydoxy-16- methyl-,(11β,16α). Its structural formula is:



MW 392.47; molecular formula: $C_{22}H_{29}FO_5$.

Dexamethasone occurs as a white to cream-colored crystalline powder having not more than a slight odor, and is practically insoluble in water and very soluble in alcohol.

The PLGA matrix slowly degrades to lactic acid and glycolic acid.

11. CLINICAL PHARMACOLOGY

11.1 Mechanism of Action

Dexamethasone, a potent corticosteroid, has been shown to suppress inflammation by inhibiting multiple inflammatory cytokines resulting in decreased edema, fibrin deposition, capillary leakage and migration of inflammatory cells.

11.2 Pharmacokinetics

Plasma concentrations were obtained from 21 patients with macular edema due to branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO), and 21 patients with diabetic macular edema (DME) prior to dosing and at 4 to 5 additional post-dose timepoints on Days 1, 7, 21, 30, 45, 60, and 90 following the administration of the first intravitreal implant containing 0.7 mg dexamethasone. In RVO and DME patients, the majority of plasma dexamethasone concentrations were below the lower limit of quantitation (LLOQ= 50 pg/mL). Plasma dexamethasone concentrations from 12% of the samples were above the LLOQ, ranging from 52 pg/mL to 102 pg/mL. Plasma dexamethasone concentration did not appear to be related to age, body weight, or sex of patients.

In an *in vitro* metabolism study, following the incubation of [^{14}C]-dexamethasone with human cornea, iris-ciliary body, choroid, retina, vitreous humor, and sclera tissues for 18 hours, no metabolites were observed.

12. NONCLINICAL TOXICOLOGY

12.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No adequate studies in animals have been conducted to determine whether Dexamethasone (OZURDEX) (dexamethasone intravitreal implant) has the potential for carcinogenesis.

Although no adequate studies have been conducted to determine the mutagenic potential of Dexamethasone (OZURDEX), dexamethasone has been shown to have no mutagenic effects in bacterial and mammalian cells in vitro or in the in vivo mouse micronucleus test.

Adequate fertility studies have not been conducted in animals.

13. CLINICAL STUDIES

Retinal Vein Occlusion

The efficacy of Dexamethasone (OZURDEX) was assessed in two, multicenter, double- masked, randomized, parallel studies.

Following a single injection, Dexamethasone (OZURDEX) for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) demonstrated the following clinical results for the percent of patients with ≥ 15 letters of improvement from baseline in best-corrected visual acuity (BCVA):

Table 5. Number (Percent) of Patients with ≥ 15 Letters Improvement from Baseline in BCVA

	Study 1			**Study 2**		
Study Day	Dexamethasone (OZURDEX) N=201	Sham N=202	p-value	Dexamethasone (OZURDEX) N=226	Sham N=224	p-value
Day 30	40 (20%)	15 (7%)	< 0.01	51 (23%)	17 (8%)	< 0.01
Day 60	58 (29%)	21 (10%)	< 0.01	67 (30%)	27 (12%)	< 0.01
Day 90	45 (22%)	25 (12%)	< 0.01	48 (21%)	31 (14%)	0.039
Day 180	39 (19%)	37 (18%)	0.780	53 (24%)	38 (17%)	0.087

* P-values were based on the Pearson's Chi-square test.

In each individual study and in a pooled analysis, time to achieve ≥ 15 letters (3-line) improvement in BCVA cumulative response rate curves were significantly faster with Dexamethasone (OZURDEX) compared to sham ($p < 0.01$), with Dexamethasone (OZURDEX) -treated patients achieving a 3-line improvement in BCVA earlier than sham-treated patients.

The onset of a ≥15 letter (3 line) improvement in BCVA with Dexamethasone (OZURDEX) occurs within the first two months after implantation in approximately 20-30% of subjects. The duration of effect persists approximately one to three months after onset of this effect.

Posterior Segment Uveitis

The efficacy of Dexamethasone (OZURDEX) was assessed in a single, multicenter, masked, randomized study of 153 patients with non-infectious uveitis affecting the posterior segment of the eye.

After a single injection, the percent of patients reaching a vitreous haze score of 0 (where a score of 0 represents no inflammation) was statistically significantly greater for patients receiving Dexamethasone (OZURDEX) versus sham at week 8 (primary time point) (47% versus12%). The percent of patients achieving a 3-line improvement from baseline BCVA was 43% for patients receiving Dexamethasone (OZURDEX) versus 7% for sham at week 8.

Diabetic Macular Edema

The efficacy of Dexamethasone (OZURDEX) for the treatment of diabetic macular edema was assessed in two, multicenter, masked, randomized, sham-controlled studies. Subjects were to be evaluated for retreatment eligibility every three months starting from Month 6 but could only receive successive treatments at least 6 months apart. Retreatment was based on physician's discretion after examination

including Optical Coherence Tomography. Patients in the Dexamethasone (OZURDEX) arm received an average of 4 treatments during the 36 months.

The primary endpoint was the proportion of patients with 15 or more letters improvement in BCVA from baseline at Month 39 or final visit for subjects who exited the study at or prior to Month 36. The Month 39 extension was included to accommodate the evaluation of safety and efficacy outcomes for subjects who received re-treatment at Month 36. Only fourteen percent of the study patients completed the Month 39 visit (16.8% from Dexamethasone (OZURDEX) and 12.2% from Sham).

Table 6. Visual Acuity outcomes at Month 39 (All randomized subjects with LOCF[c])

Study	Outcomes	Dexamethasone (OZURDEX)	Sham	Estimated Difference (95% CI)
1[a]	Mean (SD) Baseline BCVA (Letters)	56 (10)	57 (9)	
	Median (range) Baseline BCVA (Letters)	59 (34-95)	58 (34-74)	
	Gain of ≥15 letters in BCVA (n(%))	34 (21%)	19 (12%)	9.3% (1.4%, 17.3%)
	Loss of ≥15 letters in BCVA (n(%))	15 (9%)	17 (10%)	-1.1% (-7.5%, 5.3%)
	Mean change in BCVA (SD)	4.1 (13.9)	0.9 (11.9)	3.2 (0.4%, 5.9%)
2[b]	Mean (SD) Baseline BCVA (Letters)	55 (10)	56 (9)	
	Median (range) Baseline BCVA (Letters)	58 (34-72)	58 (36-82)	
	Gain of ≥15 letters in BCVA (n(%))	30 (18%)	16 (10%)	8.4% (0.9%, 15.8%)
	Loss of ≥15 letters in BCVA (n(%))	30 (18%)	18 (11%)	7.1% (-0.5%, 14.7%)
	Mean change in BCVA (SD)	0.4 (17.5)	0.8 (13.6)	-0.7 (-4.1, 2.6)

[a] Study 1: Dexamethasone (OZURDEX), N=163; Sham, N=165

[b] Study 2: Dexamethasone (OZURDEX), N=165; Sham, N=163

[c] 14% (16.8% from Dexamethasone (OZURDEX) and 12.2% from Sham) of patients had BCVA outcome at Month 39, for the remaining patients, the data at Month 36 or earlier was carried forward.

Visual acuity outcomes by lens status (Phakic or Pseudophakic) at different visits are presented in Figure 2 and Figure 3. The occurrence of cataracts impacted visual acuity during the study. The visual acuity improvement from baseline increases during a treatment cycle, peaks at approximately 3

Months posttreatment and diminishes thereafter. Patients who were pseudophakic at baseline achieved greater mean BCVA change from baseline at the final study visit.

Figure 2. Proportion of Subjects with ≥ 15 Letters Improvement from Baseline BCVA in the Study Eye

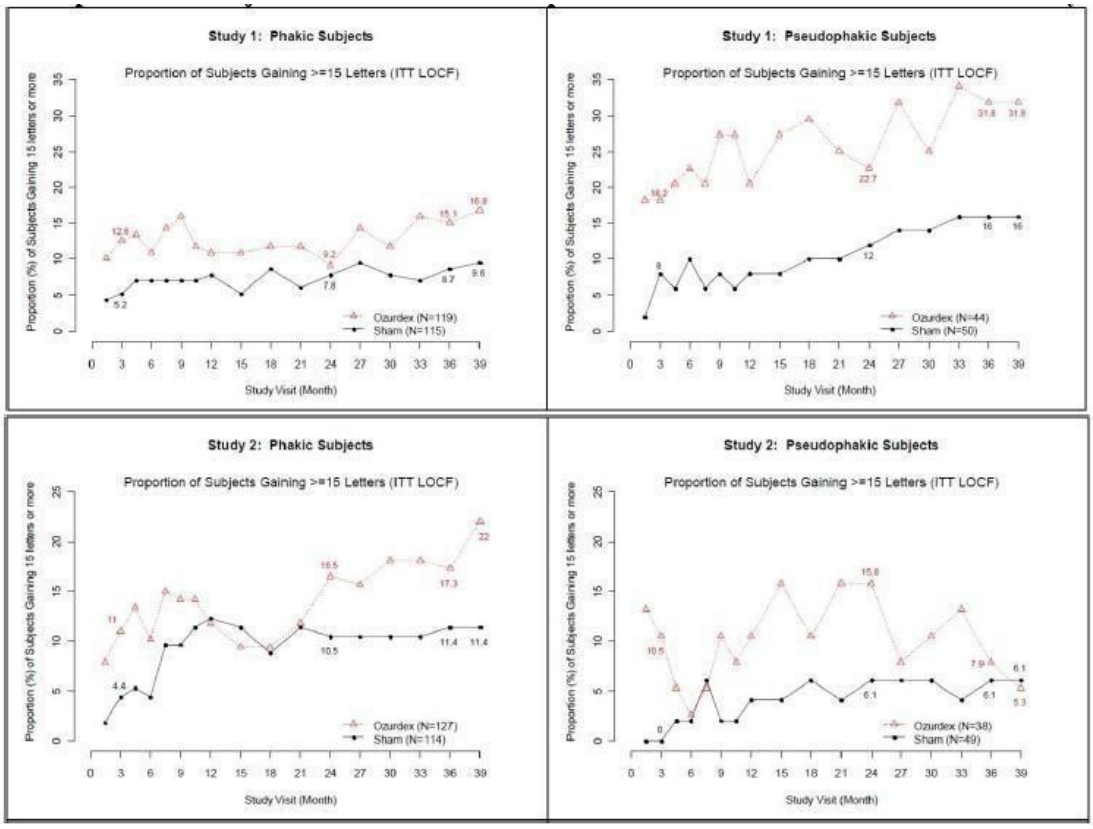
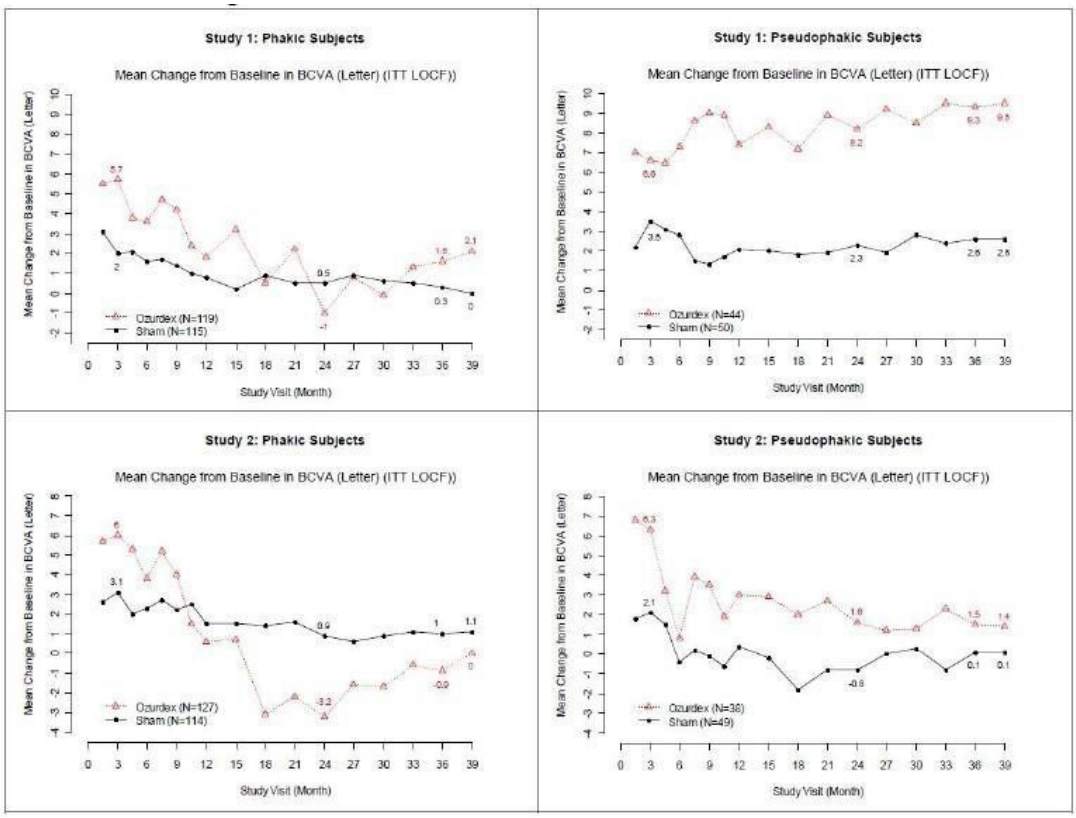


Figure 3. Mean BCVA Change from Baseline



The best corrected visual acuity outcomes for the Pseudophakic and Phakic subgroups from Studies 1 and 2 at Month 39 are presented in Table below.

Table 7. Visual Acuity outcomes at Month 39 (Subgroup for pooled data with LOCF[c])

Subgroup (Pooled)	**Outcomes**	**Dexamethasone (OZURDEX)**	**Sham**	**Estimated Difference (95% CI)**
[a] Pseudophakic	Gain of ≥15 letters in BCVA (n(%))	16 (20%)	11 (11%)	8.4% (-2.2%, 19.0%)
	Loss of ≥15 letters in BCVA (n(%))	4 (5%)	7 (7%)	-2.2% (-9.1%, 4.7%)
	Mean change in BCVA (SD)	5.8 (11.6)	1.4 (12.3)	4.2 (0.8%, 7.6%)
[b] Phakic	Gain of ≥15 letters in BCVA (n(%))	48 (20%)	24 (11%)	9.0% (2.7%, 15.4%)
	Loss of ≥15 letters in BCVA (n(%))	41 (17%)	28 (12%)	4.4% (-1.9%, 10.7%)
	Mean change in BCVA (SD)	1.0 (16.9)	0.6 (12.9)	0.3 (-2.4, 3.0)

[a] Pseudophakic: Dexamethasone (OZURDEX), N=82; Sham, N=99

[b] Phakic: Dexamethasone (OZURDEX), N=246; Sham, N=229

[c] 14% (16.8% from Dexamethasone (OZURDEX) and 12.2% from Sham,) of patients had BCVA outcome at Month 39, for the remaining patients the data at Month 36 or earlier was used in the analysis.

14. HOW SUPPLIED/STORAGE AND HANDLING

One (1) implant with single-use plastic applicator system in white laminated aluminum foil pouch, box of 1's.

Storage: Store at temperatures not exceeding 30°C.

15. PATIENT COUNSELING INFORMATION

In the days following intravitreal injection of Dexamethasone (OZURDEX) patients are at risk for potential complications including in particular, but not limited to, the development of endophthalmitis or elevated intraocular pressure. If the eye becomes red, sensitive to light, painful, or develops a change in vision, the patients should seek immediate care from an ophthalmologist.

Patients may experience temporary visual blurring after receiving an intravitreal injection. They should not drive or use machines until this has resolved.

CAUTION: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to FDA: www.fda.gov.ph.

Seek medical attention at the first sign of ADR.

Date of First Authorization: January 2014

Date of Revision: June 2020

CCDS Version: 9.0 (with editorial update)

DR-XY43123

Manufactured by:
Allergan Pharmaceuticals Ireland
Castlebar Road, Westport, Co. Mayo, Ireland

Imported and Distributed by:
ZUELLIG PHARMA CORP.
Km. 14 West Service Road
South Super Hi-way cor. Edison Ave.
Brgy. Sun Valley, Paranaque City