

# Qué necesita saber el paciente

## Usos aprobados

OZURDEX® (implante intravítreo de dexametasona) es un medicamento recetado que consiste en un implante que se inyecta en el ojo (vítreo) y se utiliza:

- Para tratar a adultos con edema macular diabético
- Para tratar a adultos con inflamación de la mácula (edema macular) después de una oclusión de la rama venosa retiniana (ORVR) u oclusión venosa retiniana central (OVR)
- Para tratar a adultos con inflamación no infecciosa de la úvea (uveítis) que afecta al segmento posterior del ojo

## INFORMACIÓN IMPORTANTE DE SEGURIDAD

### Cuándo no debe usarse OZURDEX®

No use OZURDEX® si tiene una infección de cualquier tipo en el ojo o alrededor de él, entre las que se incluyen la mayoría de las enfermedades virales de la córnea y conjuntiva, incluidas las infecciones virales en caso de herpes activo, vaccinia, varicela, infecciones micobacterianas y micosis.

No use OZURDEX® si tiene glaucoma que ha avanzado hasta una relación copa-disco superior a 0.8.

No use OZURDEX® si se ha roto la parte posterior de la cápsula del cristalino.

No use OZURDEX® si es alérgico a cualquiera de sus componentes.

### Advertencias y precauciones

Las inyecciones en el vítreo del ojo, incluidas las de OZURDEX®, se asocian con infección ocular grave (endoftalmitis), inflamación intraocular, aumento de la presión intraocular y desprendimiento de retina. Su oftalmólogo deberá realizar un seguimiento periódico después de la inyección.

**Consulte más Información importante de seguridad en las páginas siguientes.**

# Información clave acerca de OZURDEX®

- La inflamación de la retina puede estar provocada por diferentes factores
- OZURDEX® es un corticosteroide y actúa ayudando a reducir la inflamación de la retina. OZURDEX® ayuda mejorando la agudeza visual
- OZURDEX® es un implante diminuto que libera medicamento lentamente a lo largo del tiempo, sin necesidad de administrar inyecciones mensuales. Se disolverá en unos meses y no será necesario extraerlo
- OZURDEX® se inyecta directamente en la parte posterior del ojo, con absorción sistémica mínima
- Existe la posibilidad de que se produzca un incremento en la presión intraocular que por lo general regresa a su nivel inicial. Si esto le sucediera, será observado por su médico para determinar la necesidad de tratamiento mediante gotas oculares y, en raras ocasiones, mediante intervención quirúrgica
- Tras la administración reiterada de OZURDEX®, puede producirse una catarata. Si esto sucediera, será necesario realizar una cirugía de catarata y restaurar la visión
- En estudios clínicos, OZURDEX® mejoró la visión de los pacientes sin necesidad de administrar inyecciones mensuales

## INFORMACIÓN IMPORTANTE DE SEGURIDAD (continuación)

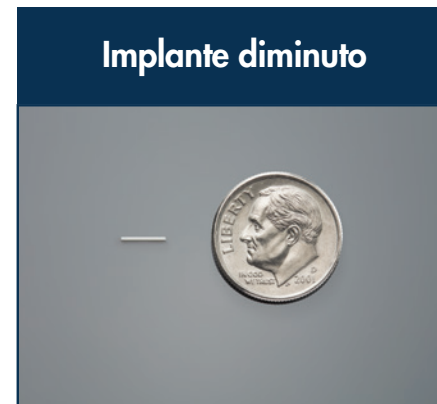
### Advertencias y precauciones (continuación)

El uso de corticosteroides, incluido OZURDEX®, puede producir cataratas subcapsulares, incremento de la presión intraocular, glaucoma, así como aumentar el establecimiento de infecciones oculares secundarias, bacterianas, fúngicas o víricas. Informe a su médico si tiene antecedentes de herpes ocular simplex dado que no se recomienda el uso de corticosteroides en estos pacientes.

Consulte más Información importante de seguridad en las páginas siguientes.

# El implante OZURDEX®

**Ozurdex®**  
(dexamethasone intravitreal  
implant) 0.7 mg



## INFORMACIÓN IMPORTANTE DE SEGURIDAD (continuación)

### Efectos secundarios habituales en el edema macular diabético

Entre los efectos secundarios más habituales informados para pacientes con edema macular se incluyen los siguientes: cataratas, incremento de la presión intraocular, hemorragia subconjuntival, reducción de la agudeza visual, inflamación de la conjuntiva, moscas volantes, edema conjuntival, desprendimiento vítreo, opacidades vítreas, aneurisma en la retina, sensación de presencia de un cuerpo extraño, erosión corneal, inflamación de la córnea, inflamación de la cámara anterior, desgarro de la retina, párpado caído, hipertensión arterial y bronquitis.

### Efectos secundarios habituales en la oclusión venosa retiniana y uveítis

Entre los efectos secundarios más habituales informados para pacientes con oclusión venosa retiniana y uveítis se incluyen los siguientes: aumento de la presión intraocular, hemorragia subconjuntival, dolor ocular, enrojecimiento ocular, hipertensión ocular, catarata, desprendimiento vítreo y dolor de cabeza.

### Información de asesoramiento para el paciente

Tras inyecciones repetidas de OZURDEX®, puede producirse una catarata. Si fuera así, su visión disminuirá y tendrá que ser operado para quitar la catarata y recuperar la visión. Es posible que se produzca un incremento de la presión intraocular con OZURDEX® que tendrá que ser tratada con gotas oculares y, raramente, con una intervención quirúrgica.

En los días posteriores a una inyección con OZURDEX®, corre el riesgo de padecer posibles complicaciones, en particular, entre otras, el desarrollo de infección ocular grave o incremento de la presión intraocular.

Consulte más Información importante de seguridad en la página siguiente.

# Preguntas frecuentes

**Ozurdex**<sup>®</sup>  
(dexamethasone intravitreal  
implant) 0.7 mg

**P:** ¿Cómo funciona OZURDEX<sup>®</sup>?

**R:** OZURDEX<sup>®</sup> es un implante que se disuelve lentamente con el tiempo y libera un corticosteroide llamado dexametasona. Este medicamento ayuda a reducir la inflamación en la retina. OZURDEX<sup>®</sup> ayuda mejorando la agudeza visual.

**P:** ¿Cómo administrará OZURDEX<sup>®</sup> mi médico?

**R:** La inyección del implante OZURDEX<sup>®</sup> solo tardará unos instantes. El implante se inyectará en la parte posterior del ojo llamada el humor vítreo.

**P:** ¿Cuán comunes son las inyecciones intravítreas?

**R:** Las inyecciones intravítreas se utilizan con frecuencia para tratar diferentes enfermedades oftálmicas. Su médico ha recibido una formación específica para administrar inyecciones intravítreas.

**P:** ¿Qué puedo esperar durante el procedimiento de inyección?

**R:** Durante el procedimiento estará despierto. Su médico seguirá los pasos necesarios para limpiar la superficie del ojo y, a continuación, adormecerá el área para mayor comodidad.

**P:** ¿Sentiré algo durante la inyección del implante OZURDEX<sup>®</sup>?

**R:** Es posible que durante la inyección sienta algo de presión. A continuación oírás un clic cuando el médico oprima el botón que libera el implante OZURDEX<sup>®</sup> en el ojo.

**P:** ¿Qué más tengo que saber sobre el tratamiento con OZURDEX<sup>®</sup>?

**R:** Es posible que se forme una catarata si recibe tratamientos reiterados con OZURDEX<sup>®</sup>. Si esto ocurriera, su visión podría disminuir y tendrá que ser sometido a una intervención para quitar la catarata y recuperar la visión. Además, podría desarrollar el aumento de presión en el interior del ojo con OZURDEX<sup>®</sup>. Su médico le observará para determinar la necesidad de tratamiento ya sea con gotas oculares o, en raras ocasiones, mediante intervención quirúrgica.

**P:** ¿Qué sucede después de la intervención?

**R:** Después de la intervención, su médico revisará el ojo y, a continuación, estará listo para marcharse a casa. No olvide seguir las instrucciones del médico.

## INFORMACIÓN IMPORTANTE DE SEGURIDAD (continuación)

### Información de asesoramiento para el paciente (continuación)

Si se produce enrojecimiento en el ojo, se vuelve sensible a la luz, le duele o se produce un cambio en la visión, deberá acudir inmediatamente a su oftalmólogo para que le atienda. Podría tener la visión borrosa provisionalmente después de recibir una inyección y no deberá conducir ni utilizar maquinaria hasta que la visión se haya restablecido.

**Consulte la Información de prescripción que se incluye.**



# OZURDEX<sup>®</sup>

(dexamethasone intravitreal implant) 0.7 mg

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OZURDEX<sup>®</sup> safely and effectively. See full prescribing information for OZURDEX<sup>®</sup>.

**OZURDEX<sup>®</sup> (dexamethasone intravitreal implant), for intravitreal injection**

Initial U.S. Approval: 1958

## INDICATIONS AND USAGE

OZURDEX<sup>®</sup> is a corticosteroid indicated for:

- The treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) (1.1)
- The treatment of non-infectious uveitis affecting the posterior segment of the eye (1.2)
- The treatment of diabetic macular edema (1.3)

## DOSAGE AND ADMINISTRATION

- For ophthalmic intravitreal injection. (2.1)
- The intravitreal injection procedure should be carried out under controlled aseptic conditions. (2.2)
- 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<sup>®</sup> solid polymer drug delivery system. (3)

## CONTRAINDICATIONS

- Ocular or periocular infections (4.1)
- Glaucoma (4.2)
- Torn or ruptured posterior lens capsule (4.3)
- Hypersensitivity (4.4)

## 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)
- 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. (5.2)

## ADVERSE REACTIONS

In controlled studies, the most common adverse reactions reported by 20–70% of patients were cataract, increased intraocular pressure and conjunctival hemorrhage. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Allergan at 1-800-678-1605 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2020

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

#### 1.1 Retinal Vein Occlusion

**OZURDEX**<sup>®</sup> (dexamethasone intravitreal implant) is indicated for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

#### 1.2 Posterior Segment Uveitis

**OZURDEX**<sup>®</sup> is indicated for the treatment of non-infectious uveitis affecting the posterior segment of the eye.

#### 1.3 Diabetic Macular Edema

**OZURDEX**<sup>®</sup> is indicated for the treatment of diabetic macular edema.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 General Dosing Information

For ophthalmic intravitreal injection.

#### 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). Adequate anesthesia and a broad-spectrum microbicide applied to the periocular skin, eyelid and ocular surface are recommended to be given prior to the injection.

Remove the foil pouch from the carton and examine for damage. Then, open the foil pouch over a sterile field and gently drop 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.

Slowly depress the actuator button until an audible click is noted. Before withdrawing the applicator from the eye, make sure that the actuator button is fully depressed and has locked flush with the applicator surface. 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 **OZURDEX**<sup>®</sup> is administered to the other eye.

### 3 DOSAGE FORMS AND STRENGTHS

Intravitreal implant containing dexamethasone 0.7 mg in the **NOVADUR**<sup>®</sup> solid polymer drug delivery system.

### 4 CONTRAINDICATIONS

#### 4.1 Ocular or Periocular Infections

**OZURDEX**<sup>®</sup> (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 Glaucoma

**OZURDEX**<sup>®</sup> is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8.

#### 4.3 Torn or Ruptured Posterior Lens Capsule

**OZURDEX**<sup>®</sup> is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber. Laser posterior capsulotomy in pseudophakic patients is not a contraindication for **OZURDEX**<sup>®</sup> use.

#### 4.4 Hypersensitivity

**OZURDEX**<sup>®</sup> is contraindicated in patients with known hypersensitivity to any components of this product [see *Adverse Reactions* (6)].

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Intravitreal Injection-related Effects

Intravitreal injections, including those with **OZURDEX**<sup>®</sup>, have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments.

Patients should be monitored regularly following the injection [see *Patient Counseling Information* (17)].

#### 5.2 Steroid-related Effects

Use of corticosteroids including **OZURDEX**<sup>®</sup> may produce posterior subcapsular cataracts, increased intraocular pressure, and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses [see *Adverse Reactions* (6.1)].

Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trials Experience

Because clinical trials 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.

Adverse reactions associated with ophthalmic steroids including **OZURDEX**<sup>®</sup> include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

#### *Retinal Vein Occlusion and Posterior Segment Uveitis*

The following information is based on the combined clinical trial results from 3 initial, randomized, 6-month, sham-controlled studies (2 for retinal vein occlusion and 1 for posterior segment uveitis):

**Table 1: Adverse Reactions Reported by Greater than 2% of Patients**

| MedDRA Term                    | OZURDEX <sup>®</sup><br>N=497 (%) | Sham<br>N=498 (%) |
|--------------------------------|-----------------------------------|-------------------|
| Intraocular pressure increased | 125 (25%)                         | 10 (2%)           |
| Conjunctival hemorrhage        | 108 (22%)                         | 79 (16%)          |
| Eye pain                       | 40 (8%)                           | 26 (5%)           |
| Conjunctival hyperemia         | 33 (7%)                           | 27 (5%)           |
| Ocular hypertension            | 23 (5%)                           | 3 (1%)            |
| Cataract                       | 24 (5%)                           | 10 (2%)           |
| Vitreous detachment            | 12 (2%)                           | 8 (2%)            |
| Headache                       | 19 (4%)                           | 12 (2%)           |

Increased IOP with **OZURDEX**<sup>®</sup> peaked at approximately week 8. During the initial treatment period, 1% (3/421) of the patients who received **OZURDEX**<sup>®</sup> required surgical procedures for management of elevated IOP.

Following a second injection of **OZURDEX**<sup>®</sup> in cases where a second injection was indicated, the overall incidence of cataracts was higher after 1 year.

In a 2-year observational study, among patients who received >2 injections, the most frequent adverse reaction was cataract 54% (n= 96 out of 178 phakic eyes at baseline). Other frequent adverse reactions from the 283 treated eyes, regardless of lens status at baseline, were increased IOP 24% (n=68) and vitreous hemorrhage 6.0% (n=17).

#### *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 2 were 3% in the **OZURDEX**<sup>®</sup> group and 1% in the Sham group. The most common ocular (study eye) and non-ocular adverse reactions are shown in Tables 2 and 3:

**Table 2: Ocular Adverse Reactions Reported by ≥ 1% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients**

| MedDRA Term                   | OZURDEX <sup>®</sup><br>N=324 (%) | Sham<br>N=328 (%) |
|-------------------------------|-----------------------------------|-------------------|
| <b>Ocular</b>                 |                                   |                   |
| Cataract <sup>1</sup>         | 166/243 <sup>2</sup> (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%)            |

**Table 2: Ocular Adverse Reactions Reported by ≥ 1% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients (continued)**

| MedDRA Term       | OZURDEX®<br>N=324 (%) | Sham<br>N=328 (%) |
|-------------------|-----------------------|-------------------|
| <b>Non-ocular</b> |                       |                   |
| Hypertension      | 41 (13%)              | 21 (6%)           |
| Bronchitis        | 15 (5%)               | 8 (2%)            |

<sup>1</sup> Includes cataract, cataract nuclear, cataract subcapsular, lenticular opacities in patients who were phakic at baseline. Among these patients, 61% of **OZURDEX®** subjects vs. 8% of sham-controlled subjects underwent cataract surgery.

<sup>2</sup> 243 of the 324 **OZURDEX®** subjects were phakic at baseline; 230 of 328 sham-controlled subjects were phakic at baseline.

Increased Intraocular Pressure

**Table 3: Summary of Elevated Intraocular Pressure (IOP) Related Adverse Reactions**

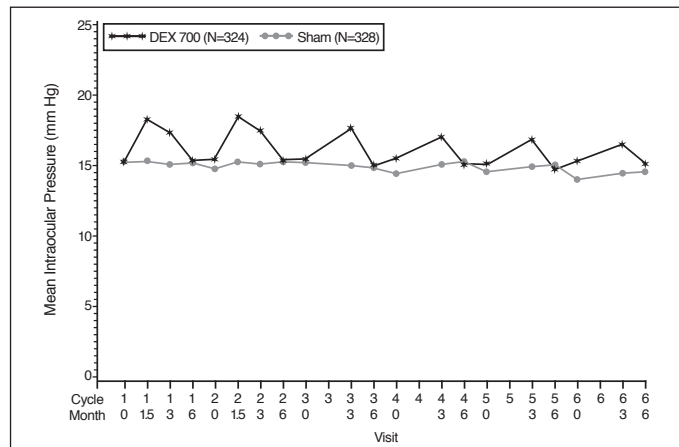
| IOP  | Treatment: N (%)  |               |
|--|-------------------|---------------|
|  | OZURDEX®<br>N=324 | Sham<br>N=328 |
| IOP elevation ≥10 mm Hg from Baseline at any visit | 91 (28%)          | 13 (4%)       |
| ≥30 mm Hg IOP at any visit                         | 50 (15%)          | 5 (2%) 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

\* **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 **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 **OZURDEX®** group (68%) compared with Sham (21%). The median time of cataract being reported as an adverse event was approximately 15 months in the **OZURDEX®** group and 12 months in the Sham group. Among these patients, 61% of **OZURDEX®** subjects vs. 8% of sham-controlled subjects underwent cataract surgery, generally between Month 18 and Month 39 (Median Month 21 for **OZURDEX®** group and 20 for Sham) of the studies.

**6.2 Postmarketing Experience**

The following reactions have been identified during post-marketing use of **OZURDEX®** in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to **OZURDEX®**, or a combination of these factors, include: complication of device insertion resulting in ocular tissue injury including sclera, subconjunctiva, lens and retina (implant misplacement), device dislocation with or without corneal edema, endophthalmitis, hypotony of the eye (associated with vitreous leakage due to injection), and retinal detachment.

**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**

Risk Summary

There are no adequate and well-controlled studies with **OZURDEX®** in pregnant women. Topical ocular administration of dexamethasone in mice and rabbits during the period of organogenesis produced cleft palate and embryofetal death in mice, and malformations of the

abdominal wall/intestines and kidneys in rabbits at doses 5 and 4 times higher than the recommended human ophthalmic dose (RHOD) of **OZURDEX**<sup>®</sup> (0.7 milligrams dexamethasone), respectively.

In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

#### Data

##### Animal Data

Topical ocular administration of 0.15% dexamethasone (0.75 mg/kg/day) on gestational days 10 to 13 produced embryofetal lethality and a high incidence of cleft palate in mice. A dose of 0.75 mg/kg/day in the mouse is approximately 5 times an **OZURDEX**<sup>®</sup> injection in humans (0.7 mg dexamethasone) on a mg/m<sup>2</sup> basis. In rabbits, topical ocular administration of 0.1% dexamethasone throughout organogenesis (0.20 mg/kg/day, on gestational day 6 followed by 0.13 mg/kg/day on gestational days 7-18) produced intestinal anomalies, intestinal aplasia, gastroschisis and hypoplastic kidneys. A dose of 0.13 mg/kg/day in the rabbit is approximately 4 times an **OZURDEX**<sup>®</sup> injection in humans (0.7 mg dexamethasone) on a mg/m<sup>2</sup> basis. A no-observed-adverse-effect-level (NOAEL) was not identified in the mouse or rabbit studies.

## 8.2 Lactation

### Risk Summary

Systemically administered corticosteroids are present in human milk and can suppress growth and interfere with endogenous corticosteroid production or cause other unwanted effects. There is no information regarding the presence of dexamethasone in human milk, the effects on the breastfed infants, or the effects on milk production to inform risk of **OZURDEX**<sup>®</sup> to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for **OZURDEX**<sup>®</sup> and any potential adverse effects on the breastfed child from **OZURDEX**<sup>®</sup>.

## 8.4 Pediatric Use

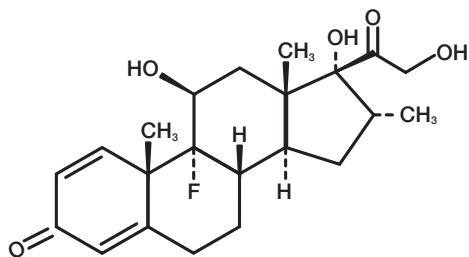
Safety and effectiveness of **OZURDEX**<sup>®</sup> in pediatric patients have not been established.

## 8.5 Geriatric Use

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

## 11 DESCRIPTION

**OZURDEX**<sup>®</sup> is an intravitreal implant containing 0.7 mg (700 mcg) dexamethasone in the **NOVADUR**<sup>®</sup> solid polymer sustained-release drug delivery system. **OZURDEX**<sup>®</sup> is preloaded into a single-use, **DDS**<sup>®</sup> applicator to facilitate injection of the rod-shaped implant directly into the vitreous. The **NOVADUR**<sup>®</sup> system contains poly (D,L-lactide-co-glycolide) PLGA intravitreal polymer matrix without a preservative. The chemical name for dexamethasone is Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11 $\beta$ ,16 $\alpha$ )-. Its structural formula is:



MW 392.47; molecular formula: C<sub>22</sub>H<sub>29</sub>FO<sub>5</sub>

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.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Dexamethasone, a 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.

### 12.3 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 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 [<sup>14</sup>C]-dexamethasone with human cornea, iris-ciliary body, choroid, retina, vitreous humor, and sclera tissues for 18 hours, no metabolites were observed.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to determine whether **OZURDEX**<sup>®</sup> (dexamethasone intravitreal implant) has the potential for carcinogenesis or mutagenesis. Fertility studies have not been conducted in animals.



## 14 CLINICAL STUDIES

### Retinal Vein Occlusion

The efficacy of **OZURDEX**<sup>®</sup> for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) was assessed in two, multicenter, double-masked, randomized, parallel studies.

Following a single injection, **OZURDEX**<sup>®</sup> demonstrated the following clinical results for the percent of patients with  $\geq 15$  letters of improvement from baseline in best-corrected visual acuity (BCVA):

**Table 4: Number (Percent) of Patients with  $\geq 15$  Letters Improvement from Baseline in BCVA**

| Study Day | Study 1                       |               |          | Study 2                       |               |          |
|-----------|-------------------------------|---------------|----------|-------------------------------|---------------|----------|
|           | OZURDEX <sup>®</sup><br>N=201 | Sham<br>N=202 | p-value* | OZURDEX <sup>®</sup><br>N=226 | Sham<br>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  $\geq 15$  letters (3-line) improvement in BCVA cumulative response rate curves were significantly faster with **OZURDEX**<sup>®</sup> compared to sham ( $p < 0.01$ ), with **OZURDEX**<sup>®</sup> treated patients achieving a 3-line improvement in BCVA earlier than sham-treated patients.

The onset of a  $\geq 15$  letter (3-line) improvement in BCVA with **OZURDEX**<sup>®</sup> 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 **OZURDEX**<sup>®</sup> 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 **OZURDEX**<sup>®</sup> versus sham at week 8 (primary time point) (47% versus 12%). The percent of patients achieving a 3-line improvement from baseline BCVA was 43% for patients receiving **OZURDEX**<sup>®</sup> versus 7% for sham at week 8.

### Diabetic Macular Edema

The efficacy of **OZURDEX**<sup>®</sup> 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 **OZURDEX**<sup>®</sup> 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 **OZURDEX**<sup>®</sup> and 12.2% from Sham).

**Table 5: Visual Acuity outcomes at Month 39 (All randomized subjects with LOCF<sup>a</sup>)**

| Study          | Outcomes                                 | OZURDEX <sup>®</sup> | Sham       | Estimated Difference (95% CI) |
|----------------|--|----------------------|------------|-------------------------------|
| 1 <sup>a</sup> | Mean (SD) Baseline BCVA (Letters)        | 56 (10)              | 57 (9)     |                               |
|                | Median (range) Baseline BCVA (Letters)   | 59 (34-95)           | 58 (34-74) |                               |
|                | Gain of $\geq 15$ letters in BCVA (n(%)) | 34 (21%)             | 19 (12%)   | 9.3% (1.4%, 17.3%)            |
|                | Loss of $\geq 15$ 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 <sup>b</sup> | Mean (SD) Baseline BCVA (Letters)        | 55 (10)              | 56 (9)     |                               |
|                | Median (range) Baseline BCVA (Letters)   | 58 (34-72)           | 58 (36-82) |                               |
|                | Gain of $\geq 15$ letters in BCVA (n(%)) | 30 (18%)             | 16 (10%)   | 8.4% (0.9%, 15.8%)            |
|                | Loss of $\geq 15$ 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)              |

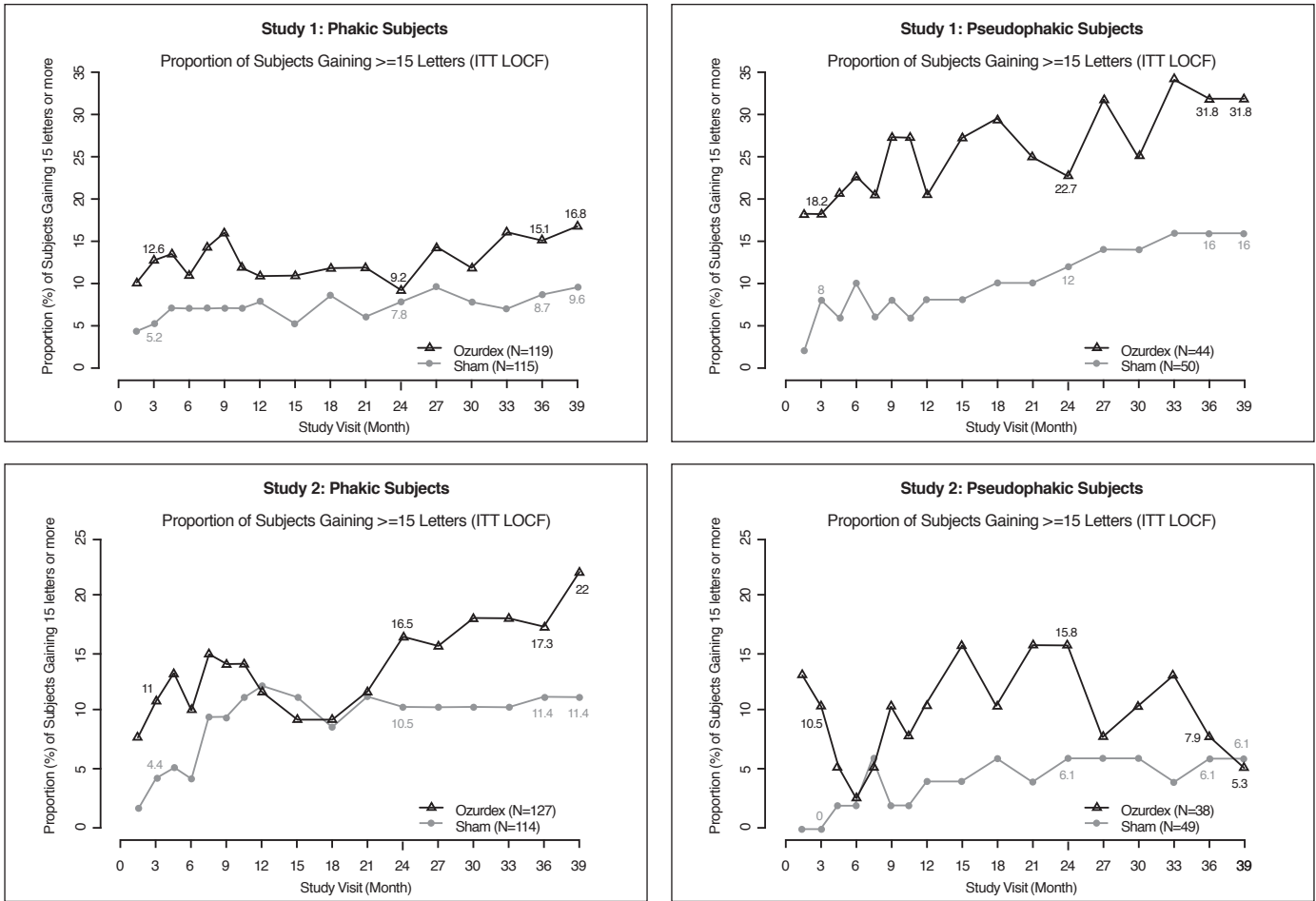
<sup>a</sup>Study 1: **OZURDEX**<sup>®</sup> N=163; Sham, N=165

<sup>b</sup>Study 2: **OZURDEX**<sup>®</sup> N=165; Sham, N=163

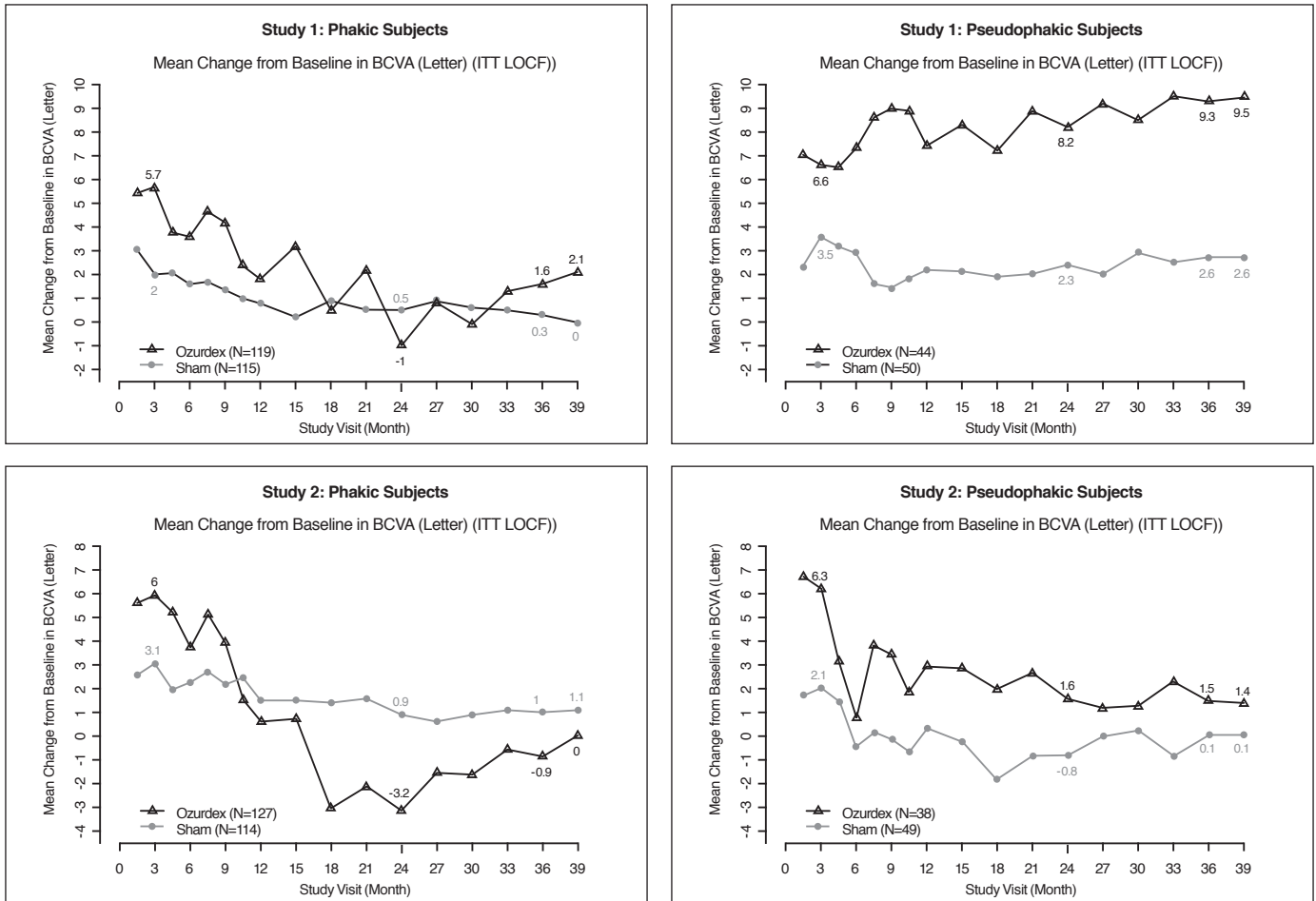
<sup>c</sup>14% (16.8% from **OZURDEX**<sup>®</sup> and 12.2% from Sham) of patients had BCVA outcome at Month 39, for the remaining patients, the data at Month 36 or earlier was carried forward.

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  $\geq 15$  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 6.

**Table 6: Visual Acuity outcomes at Month 39 (Subgroup for pooled data with LOCF<sup>a</sup>)**

| Subgroup (Pooled)         | Outcomes                           | OZURDEX <sup>®</sup> | Sham       | Estimated Difference (95% CI) |
|---------------------------|------------------------------------|----------------------|------------|-------------------------------|
| <sup>a</sup> 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)                |
| <sup>b</sup> 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)               |

<sup>a</sup>Pseudophakic: OZURDEX<sup>®</sup>, N=82; Sham, N=99

<sup>b</sup>Phakic: OZURDEX<sup>®</sup>, N=246; Sham, N=229

<sup>c</sup>14% (16.8% from OZURDEX<sup>®</sup> 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.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

OZURDEX<sup>®</sup> (dexamethasone intravitreal implant) 0.7 mg is supplied in a foil pouch with 1 single-use plastic applicator, NDC 0023-3348-07.

**Storage:** Store at 15°C to 30°C (59°F to 86°F).

## 17 PATIENT COUNSELING INFORMATION

### Steroid-related Effects

Advise patients that a cataract may occur after repeated treatment with OZURDEX<sup>®</sup>. If this occurs, advise patients that their vision will decrease, and they will need an operation to remove the cataract and restore their vision.

Advise patients that they may develop increased intraocular pressure with OZURDEX<sup>®</sup> treatment, and the increased IOP will need to be managed with eye drops, and, rarely, with surgery.

### Intravitreal Injection-related Effects

Advise patients that in the days following intravitreal injection of OZURDEX<sup>®</sup>, patients are at risk for potential complications including in particular, but not limited to, the development of endophthalmitis or elevated intraocular pressure.

### When to Seek Physician Advice

Advise patients that if the eye becomes red, sensitive to light, painful, or develops a change in vision, they should seek immediate care from an ophthalmologist.

### Driving and Using Machines

Inform patients that they may experience temporary visual blurring after receiving an intravitreal injection. Advise patients not to drive or use machines until this has been resolved.

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