IMPORTANT SAFETY INFORMATION

OZURDEX® should not be used if you have any infections or diseases in the eye, or surrounding eye area, including most viral diseases of the cornea and conjunctiva, including active herpes viral infection of the eye, vaccinia, varicella, mycobacterial infections, and fungal diseases.

Please see additional Important Safety Information on page 7.
Your eyes

What makes up the eye?

- **Uveal tract**
  - Iris
  - Ciliary body
  - Choroid

- Vitreous gel
- Retina
- Macula
- Fovea
- Optic nerve

How does the eye work?

Light enters through the cornea, passes through the opening in the iris, called the pupil, and then to the lens, which focuses light on the retina—the inner lining of the back of the eye. The retina is lined with light-sensitive cells, or photoreceptors, called rods and cones. The macula is the center of the retina, and it is responsible for sharp central vision. The fovea is a small depression in the macula that provides the sharpest vision of all. When light reaches the retina, the photoreceptors send impulses along the optic nerve to the brain, which interprets them as vision.

What role does the uvea play in the eye?

The uvea, or uveal tract, is the middle layer of the eye. The 3 parts of the uvea—the iris, ciliary body, and choroid—have important functions.

The iris, which is the colored part of the eye, contracts and dilates to control how much light enters the eye. By adjusting, it allows you to see under a variety of lighting conditions.

The ciliary body releases aqueous humor, which nourishes the front part of the eye. It also contains the ciliary muscle, which changes the shape of the lens to help you focus.

The choroid is a layer of connective tissue and blood vessels, located between the sclera (white of the eye) and the retina. The choroid nourishes the inner parts of the eye.

Why is a healthy uvea important?

A healthy uvea is essential for normal vision. When a disease such as uveitis occurs, it may lead to impaired vision or loss of vision. In the next section of this booklet, you will learn more about uveitis.
What is noninfectious uveitis affecting the back segment of the eye?

Uveitis (pronounced you-vee-eye-tis) is inflammation of the uvea. Inflammation is caused by retinal cells, your immune system’s white blood cells, and the chemicals these cells release.

Noninfectious uveitis means that although the uvea is inflamed, no bacteria or viruses are found in the eye. The inflammation may be caused indirectly by a disease affecting one of your body’s other systems, but often no cause can be found. When that is the case, you may be having an autoimmune reaction, which means, for an unknown reason, the body is reacting to some of its own cells as if they were foreign invaders, creating vitreous haze.

Noninfectious uveitis affecting the back segment of the eye may include the middle section of the eye around the ciliary body (reaching the edge of the retina). It also may affect the choroid and other parts of the back of the eye, including the entire retina and the blood vessels of the retina.

What are the symptoms?

Noninfectious uveitis affecting the back segment of the eye is usually painless. Your vision may be decreased and you may see irregular floating black spots (floaters). More severe posterior uveitis affecting the retina can lead to significant loss of vision.

How the condition affects the eye

The inflammation associated with noninfectious uveitis affecting the back segment of the eye can cause immune cells to enter the vitreous gel that fills the back of your eye, creating what is known as vitreous haze. The haze can contribute to decreased vision.

Uveitis can damage the eye and cause long-term complications that reduce vision. While many people have only a single episode of uveitis, others may have recurrences over months to years. It is very important to receive medical treatment for the inflammation of noninfectious uveitis affecting the back segment of the eye.
Why did my doctor choose OZURDEX® (dexamethasone intravitreal implant)?

OZURDEX® has been approved by the U.S. Food and Drug Administration (FDA) to treat noninfectious inflammation of the uvea (uveitis) affecting the back segment of the eye. Your doctor will discuss with you the reasons why OZURDEX® was selected, as well as the benefits and risks of treatment.

You can learn more about OZURDEX® in the following pages, including pages dedicated to Important Safety Information—facts you should be familiar with as an OZURDEX® patient.

How does the OZURDEX® intravitreal implant work?

OZURDEX® is a biodegradable implant that provides sustained release of the corticosteroid dexamethasone. Corticosteroids, such as dexamethasone, block chemical pathways that lead to inflammation, leakage from the retinal blood vessels, and swelling (edema) of the retina.

Are intravitreal injections common?

Yes. Intravitreal injections are now used to deliver medication to treat many types of eye conditions. Your Retina Specialist is specially trained in giving eye injections.

APPROVED USE

OZURDEX® (dexamethasone intravitreal implant) is a prescription medicine that is an implant injected into the eye (vitreous) and used:

— To treat adults with noninfectious inflammation of the uvea (uveitis) affecting the back segment of the eye

IMPORTANT SAFETY INFORMATION

OZURDEX® should not be used if you have any infections or diseases in the eye, or surrounding eye area, including most viral diseases of the cornea and conjunctiva, including active herpes viral infection of the eye, vaccinia, varicella, mycobacterial infections, and fungal diseases.

OZURDEX® should not be used if you have glaucoma.

Please see additional Important Safety Information on page 9.
What is a biodegradable implant?
A biodegradable implant is one that doesn’t need to be removed after it releases medication. OZURDEX® (dexamethasone intravitreal implant) uses advanced NOVADUR® drug delivery technology, in which biodegradable material is combined with the active drug dexamethasone to form a tiny rod-shaped implant. Inside the eye, the implant is slowly dissolved by the vitreous gel that fills the eye, releasing dexamethasone.

How is OZURDEX® administered?
The OZURDEX® implant is so tiny that it can be injected into the eye (vitreous) with a procedure in your doctor’s office. Each implant is already inside a special applicator device that is needed to perform the insertion. The implant will be injected into the vitreous humor inside your eye. This is known as an intravitreal injection.

Will I receive OZURDEX® more than once?
The OZURDEX® implant slowly dissolves, releasing medication. As the level of medication decreases over time, swelling or inflammation may affect your vision again. If this occurs, your doctor may recommend another OZURDEX® injection.

IMPORTANT SAFETY INFORMATION (continued)
OZURDEX® should not be used if you have a posterior lens capsule that is torn or ruptured. You should not use OZURDEX® if you are allergic to any of its ingredients.

Injections into the vitreous in the eye, including those with OZURDEX®, are associated with serious eye infection (endophthalmitis), eye inflammation, increased eye pressure, and retinal detachments. Your eye doctor may monitor you regularly after the injection.

Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased eye pressure, glaucoma, and may increase the establishment of secondary eye infections due to bacteria, fungi, or viruses. Let your doctor know if you have a history of ocular herpes simplex.

Please see additional Important Safety Information on page 11.
What results can I expect with an OZURDEX® intravitreal implant?

In a clinical study, 77 patients were treated with OZURDEX® (dexamethasone intravitreal implant) and 76 patients received sham (simulated) injections. Forty-seven percent of those who received OZURDEX® (36 patients) achieved a vitreous haze score of zero (where a score of zero means no inflammation) at week 8—compared with 12% of those who received sham injections (9 patients). Also, at week 8, 43% of OZURDEX® patients (33 patients) gained 3 or more lines of vision on the eye chart, compared with 7% of sham-treated patients (5 patients).

It’s important to remember that each case of noninfectious uveitis affecting the back segment of the eye is unique. Your own results may vary.

Is there anyone who should not be given OZURDEX®?

You should not receive OZURDEX® if:

— You have any infections or diseases in the eye, or surrounding eye area, including most viral diseases of the cornea and conjunctiva, including active herpes viral infection of the eye, vaccinia, varicella, mycobacterial infections, and fungal diseases

— You have glaucoma

— You have a posterior lens capsule that is torn or ruptured

— You are allergic to any of its ingredients

IMPORTANT SAFETY INFORMATION (continued)

The most common side effects reported include: increased eye pressure, conjunctival blood spot, eye pain, eye redness, ocular hypertension, cataract, vitreous detachment, and headache.

After repeated injections with OZURDEX®, a cataract may occur. If this occurs, your vision will decrease and you will need an operation to remove the cataract and restore your vision.

Please see additional Important Safety Information on page 13.
What happens during the injection procedure?

You will be awake during the procedure. Your doctor will follow steps that include ensuring the surface of the eye is clean and numbing the surface of the eye to help keep you comfortable. OZURDEX® (dexamethasone intravitreal implant) is injected using a special applicator device that's about the size of a pen. The applicator is designed to help your doctor deliver OZURDEX® to the vitreous where the medication is needed. As the injection occurs, you may feel some pressure. You may then hear a click when your doctor presses the button that releases the OZURDEX® implant in your eye.

Are there any risks associated with intravitreal injections?

Injections into the vitreous in the eye, including those with OZURDEX®, are associated with serious eye infection (endophthalmitis), eye inflammation, increased eye pressure, and retinal detachments. Your eye doctor may monitor you regularly after the injection.

Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased eye pressure, glaucoma, and may increase the establishment of secondary eye infections due to bacteria, fungi, or viruses. Let your doctor know if you have a history of ocular herpes simplex.

The most common side effects reported include: increased eye pressure, conjunctival blood spot, eye pain, eye redness, ocular hypertension, cataract, vitreous detachment, and headache.

After repeated injections with OZURDEX®, a cataract may occur. If this occurs, your vision will decrease and you will need an operation to remove the cataract and restore your vision. You may develop increased eye pressure with OZURDEX® that will need to be managed with eye drops and, rarely, with surgery.

In the days following injection with OZURDEX®, you may be at risk for potential complications including in particular, but not limited to, the development of serious eye infection or increased eye pressure. If your eye becomes red, sensitive to light, painful, or develops a change in vision, you should seek immediate care from your eye doctor. You may experience temporary visual blurring after receiving an injection and should not drive or use machinery until your vision has resolved.

These are not the only risks associated with intravitreal injections. If you experience other side effects, you should immediately contact your eye doctor. Your Retina Specialist will discuss the possible risks with you before performing the injection.

IMPORTANT SAFETY INFORMATION (continued)

You may develop increased eye pressure with OZURDEX® that will need to be managed with eye drops, and rarely, with surgery.

Please see the full Prescribing Information in the pocket of this booklet.
APPROVED USE

OZURDEX® (dexamethasone intravitreal implant) is a prescription medicine that is an implant injected into the eye (vitreous) and used:

— To treat adults with noninfectious inflammation of the uvea (uveitis) affecting the back segment of the eye.

IMPORTANT SAFETY INFORMATION

OZURDEX® should not be used if you have any infections or diseases in the eye, or surrounding eye area, including most viral diseases of the cornea and conjunctiva, including active herpes viral infection of the eye, vaccinia, varicella, mycobacterial infections, and fungal diseases.

OZURDEX® should not be used if you have glaucoma.

OZURDEX® should not be used if you have a posterior lens capsule that is torn or ruptured.

You should not use OZURDEX® if you are allergic to any of its ingredients.

Injections into the vitreous in the eye, including those with OZURDEX®, are associated with serious eye infection (endophthalmitis), eye inflammation, increased eye pressure, and retinal detachments. Your eye doctor may monitor you regularly after the injection.

Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased eye pressure, glaucoma, and may increase the establishment of secondary eye infections due to bacteria, fungi, or viruses. Let your doctor know if you have a history of ocular herpes simplex.

The most common side effects reported include: increased eye pressure, conjunctival blood spot, eye pain, eye redness, ocular hypertension, cataract, vitreous detachment, and headache.

After repeated injections with OZURDEX®, a cataract may occur. If this occurs, your vision will decrease and you will need an operation to remove the cataract and restore your vision. You may develop increased eye pressure with OZURDEX® that will need to be managed with eye drops, and rarely, with surgery.

In the days following injection with OZURDEX®, you may be at risk for potential complications including in particular, but not limited to, the development of serious eye infection or increased eye pressure. If your eye becomes red, sensitive to light, painful, or develops a change in vision, you should seek immediate care from your eye doctor. You may experience temporary visual blurring after receiving an injection and should not drive or use machinery until your vision has resolved.

OZURDEX® is for prescription use only.

Please see the full Prescribing Information in the pocket of this booklet.
Be aware and follow up

How may OZURDEX® (dexamethasone intravitreal implant) affect eye pressure?

Corticosteroids, such as OZURDEX® can cause the fluid pressure inside the eye to increase. This is not something you can feel. So, following the injection, your doctor should regularly monitor your eye pressure. If you experience this side effect, treatment such as medicated eye drops or surgery may be required to lower the pressure.

Can OZURDEX® cause cataracts?

Some patients who receive OZURDEX® intravitreal implants may develop cataracts, or their existing cataracts may worsen. It’s important to remember that not treating noninfectious uveitis affecting the back segment of the eye may lead to irreversible vision loss. You should discuss this issue with your doctor.

Doctor’s instructions

You should return to the office as follows:

______________________________

______________________________

______________________________

To help assess the effectiveness and safety of your treatment, please note any of the following:

— Vision improvement
— Eye becomes red, sensitive to light, painful, or develops a change in vision—please contact your eye doctor immediately

<table>
<thead>
<tr>
<th>Change</th>
<th>Date &amp; Time</th>
</tr>
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<tbody>
<tr>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

Your “to do” list

Before injection ______________________
______________________________

Day of injection ______________________
______________________________

After injection ______________________
______________________________

IMPORTANT SAFETY INFORMATION

The most common side effects reported include: increased eye pressure, conjunctival blood spot, eye pain, eye redness, ocular hypertension, cataract, vitreous detachment, and headache.

Please see additional Important Safety Information on back cover.
IMPORTANT SAFETY INFORMATION (continued)

After repeated injections with OZURDEX®, a cataract may occur. If this occurs, your vision will decrease and you will need an operation to remove the cataract and restore your vision. You may develop increased eye pressure with OZURDEX® that will need to be managed with eye drops, and rarely, with surgery.

Please see the full Prescribing Information in the pocket of this booklet.

Visit www.Ozurdex.com for more information about uveitis.
**INDICATIONS AND USAGE**

OZURDEX® 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)

**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 1-800-433-8871 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.
FULL PRESCRIBING INFORMATION

1  INDICATIONS AND USAGE

1.1  Retinal Vein Occlusion
OZURDEX® (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® is indicated for the treatment of non-infectious uveitis affecting the posterior segment of the eye.

1.3  Diabetic Macular Edema
OZURDEX® 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 periorcular 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® 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
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  Glaucoma
OZURDEX® 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® 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® use.

4.4  Hypersensitivity
OZURDEX® 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®, 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® may produce posterior subcapsular cataracts, increased intraocular pressure,
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 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.

Adverse reactions associated with ophthalmic steroids including OZURDEX® 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

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

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

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

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® 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

<table>
<thead>
<tr>
<th>MedDRA Term</th>
<th>OZURDEX® N=324 (%)</th>
<th>Sham N=328 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cataract¹</td>
<td>166/243² (68%)</td>
<td>49/230 (21%)</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>73 (23%)</td>
<td>44 (13%)</td>
</tr>
<tr>
<td>Visual acuity reduced</td>
<td>28 (9%)</td>
<td>13 (4%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>19 (6%)</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>Vitreous floaters</td>
<td>16 (5%)</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>Conjunctival edema</td>
<td>15 (5%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Dry eye</td>
<td>15 (5%)</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>14 (4%)</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>Vitreous opacities</td>
<td>11 (3%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Retinal aneurysm</td>
<td>10 (3%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>7 (2%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Corneal erosion</td>
<td>7 (2%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>6 (2%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Anterior Chamber Inflammation</td>
<td>6 (2%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Table 2: Ocular Adverse Reactions Reported by ≥ 1% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients (continued)

<table>
<thead>
<tr>
<th>MedDRA Term</th>
<th>OZURDEX® N=324 (%)</th>
<th>Sham N=328 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal tear</td>
<td>5 (2%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Eyelid ptosis</td>
<td>5 (2%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td><strong>Non-ocular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>41 (13%)</td>
<td>21 (6%)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>15 (5%)</td>
<td>8 (2%)</td>
</tr>
</tbody>
</table>

1 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.

2 243 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

<table>
<thead>
<tr>
<th>IOP</th>
<th>Treatment: N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OZURDEX® N=324</td>
</tr>
<tr>
<td>IOP elevation ≥10 mm Hg from Baseline at any visit</td>
<td>91 (28%)</td>
</tr>
<tr>
<td>≥30 mm Hg IOP at any visit</td>
<td>50 (15%)</td>
</tr>
<tr>
<td>Any IOP lowering medication</td>
<td>136 (42%)</td>
</tr>
<tr>
<td>Any surgical intervention for elevated IOP*</td>
<td>4 (1.2%)</td>
</tr>
</tbody>
</table>

* 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 (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
Pregnancy Category C

Risk Summary
There are no adequate and well-controlled studies with OZURDEX® in pregnant women. Animal reproduction studies using topical ocular administration of dexamethasone were conducted in mice and rabbits. Cleft palate and embryofetal death in mice and malformations of the intestines and kidneys in rabbits were observed. OZURDEX® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data
Topical ocular administration of 0.15% dexamethasone (0.375 mg/kg/day) on gestational days 10 to 13 produced embryofetal lethality and a high incidence of cleft palate in mice. A dose of 0.375 mg/kg/day in the mouse is approximately 3 times an OZURDEX® injection in humans (0.7 mg dexamethasone) on a mg/m2 basis. In rabbits, topical ocular administration of 0.1% dexamethasone throughout organogenesis (0.13 mg/kg/day, on gestational day 6 followed by 0.20 mg/kg/day on gestational days 7-18) produced intestinal anomalies, intestinal aplasia, gastrochisis and hypoplastic kidneys. A dose of 0.13 mg/kg/day in the rabbit is approximately 4 times an OZURDEX® injection in humans (0.7 mg dexamethasone) on a mg/m2 basis.

8.3 Nursing Mothers
Systemically administered corticosteroids are present in human milk and can suppress growth and interfere with endogenous corticosteroid production. The systemic concentration of dexamethasone following intravitreal treatment with OZURDEX® is low [see Clinical Pharmacology (12.3)]. It is not known whether intravitreal treatment with OZURDEX® could result in sufficient systemic absorption to produce detectable quantities in human milk. Exercise caution when OZURDEX® is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness of OZURDEX® 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® is an intravitreal implant containing 0.7 mg (700 mcg) dexamethasone in the NOVADUR® solid polymer sustained-release drug delivery system. OZURDEX® is preloaded into a single-use, 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 without a preservative. The chemical name for dexamethasone is Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16α)-. Its structural formula is:

![Structural formula of dexamethasone]

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 [14C]-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
No adequate studies in animals have been conducted to determine whether OZURDEX® (dexamethasone intravitreal implant) has the potential for carcinogenesis.

Although no adequate studies have been conducted to determine the mutagenic potential of 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.
Retinal Vein Occlusion

The efficacy of OZURDEX® 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® demonstrated the following clinical results for the percent of patients with ≥ 15 letters of improvement from baseline in best-corrected visual acuity (BCVA):

<table>
<thead>
<tr>
<th>Study Day</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OZURDEX®</td>
<td>Sham</td>
</tr>
<tr>
<td>Day 30</td>
<td>40 (20%)</td>
<td>15 (7%)</td>
</tr>
<tr>
<td>Day 60</td>
<td>58 (29%)</td>
<td>21 (10%)</td>
</tr>
<tr>
<td>Day 90</td>
<td>45 (22%)</td>
<td>25 (12%)</td>
</tr>
<tr>
<td>Day 180</td>
<td>39 (19%)</td>
<td>37 (18%)</td>
</tr>
</tbody>
</table>

*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 OZURDEX® compared to sham (p < 0.01), with 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 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 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 OZURDEX® 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® versus 7% for sham at week 8.

Diabetic Macular Edema

The efficacy of 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 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 OZURDEX® and 12.2% from Sham).

Table 5: Visual Acuity outcomes at Month 39 (All randomized subjects with LOCF*)

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

*Study 1: OZURDEX® N=163; Sham, N=165
*Study 2: OZURDEX® N=165; Sham, N=163
*14% (16.8% from 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

Study 1: Phakic Subjects
Proportion of Subjects Gaining ≥15 Letters (ITT LOCF)

Study 2: Phakic Subjects
Proportion of Subjects Gaining ≥15 Letters (ITT LOCF)

Study 1: Pseudophakic Subjects
Proportion of Subjects Gaining ≥15 Letters (ITT LOCF)

Study 2: Pseudophakic Subjects
Proportion of Subjects Gaining ≥15 Letters (ITT LOCF)

Figure 3: Mean BCVA Change from Baseline

Study 1: Phakic Subjects
Mean Change from Baseline in BCVA (Letter) (ITT LOCF)

Study 2: Phakic Subjects
Mean Change from Baseline in BCVA (Letter) (ITT LOCF)

Study 1: Pseudophakic Subjects
Mean Change from Baseline in BCVA (Letter) (ITT LOCF)

Study 2: Pseudophakic Subjects
Mean Change from Baseline in BCVA (Letter) (ITT LOCF)
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>c</sup>)

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

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

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

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

### 16 HOW SUPPLIED/STORAGE AND HANDLING

OZURDEX® (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 15º-30ºC (59º-86ºF).

### 17 PATIENT COUNSELING INFORMATION

#### Steroid-related Effects

Advise patients that a cataract may occur after repeated treatment with OZURDEX®. 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® 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®, 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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