Supplement to

July 2020

CRST
Cataract & Refractive Surgery Today

MILLENNIALEYE

Sponsored by

EyePoint PHARMACEUTICALS

Utilizing the First Intracameral Steroid for Cataract Surgery

At MillennialEYE Live, four pioneering surgeons discussed how DEXYCU (dexamethasone intraocular suspension) 9% is incorporated into cataract surgery.

Robert J. Weinstock, MD, Moderator | Mitchell A. Jackson, MD
Cathleen M. McCabe, MD | Jonathan D. Solomon, MD

MODERATOR

ROBERT J. WEINSTOCK, MD
- Director of Cataract and Refractive Surgery, Eye Institute of West Florida, Tampa Bay, and The Weinstock Laser Eye Center, Largo, Florida
- rjweinstock@yahoo.com
- Financial disclosure: Consultant (Alcon, Bausch + Lomb, Beyeonics, EyePoint Pharmaceuticals, Eyevance, Johnson & Johnson Vision, Kala Pharmaceuticals, Lensar, Omeros, Participants)

PANEL

MITCHELL A. JACKSON, MD
- Founder and CEO, Jacksoneye, Lake Villa, Illinois
- mjlaserdoc@msn.com; Twitter @djmjspin
- Financial disclosure: Consultant (EyePoint Pharmaceuticals)

CATHLEEN M. MCCABE, MD
- Medical Director and Cataract and Refractive Surgery Specialist, The Eye Associates in Bradenton and Sarasota, Florida
- Chief Medical Officer, Eye Health America, Roswell, Georgia
- cmccabe13@hotmail.com; Twitter @cathyeye
- Financial disclosure: Consultant and Speaker (Alcon, Allergan, Bausch + Lomb, EyePoint Pharmaceuticals, Johnson & Johnson Vision); Research support (Alcon, Johnson & Johnson Vision)

JONATHAN D. SOLOMON, MD
- Refractive/Cataract Director, Solomon Eye Physicians & Surgeons, Bowie, Maryland
- Director of Research, Bowie Vision Institute, Bowie Health Campus, Bowie, Maryland
- Adjunct-Assistant Professor, Cornea, Cataract, and Refractive Surgery, University of Maryland School of Medicine, Department of Ophthalmology & Visual Sciences
- jonathansolomonmd@gmail.com
- Financial disclosure: Speaker (EyePoint Pharmaceuticals)

Utilizing the First Intracameral Steroid for Cataract Surgery

At MillennialEYE Live, four pioneering surgeons discussed how DEXYCU (dexamethasone intraocular suspension) 9% is incorporated into cataract surgery.

Once cataract surgery is complete, patients are prescribed various eye drops to manage postoperative pain and inflammation. This fall at MillennialEYE Live, four surgeons talked about how to integrate DEXYCU, the first intracameral steroid approved for the treatment of postoperative inflammation, into cataract surgery protocols.

Robert J. Weinstock, MD: I'm excited to be with three very innovative and successful ophthalmologists to discuss new modalities for delivering medications to the eye during cataract surgery. There is now available an intracameral steroid suspension that is FDA approved to treat postoperative inflammation. This medication, DEXYCU (EyePoint Pharmaceuticals), is a 9% dexamethasone suspension that can be injected at the end of a cataract surgery case.

All four of us have had some early experience with this technology. I'd like us to share the things we've learned, including how it's impacted our practices, how our peers can be successful with DEXYCU, and how it's now becoming our steroid of choice after cataract surgery. What do you think is the standard of care for most cataract surgeons? How many different medications are we typically prescribing to our cataract patients?

Jonathan D. Solomon, MD: I think everybody has their own protocol, but the vast majority of surgeons prescribe three different medications–a nonsteroidal anti-inflammatory drug

(NSAID), a steroid, and an antibiotic. Some might prescribe two drops where one is a combination.

Dr. Weinstock: Now with DEXYCU, we have a well-known medication, dexamethasone, in an FDA-approved intracameral form. It has a manufacturing process whose safety and reliability we can hang our hat on. Does this change things? Does it help your comfort level for doing injections at the end of surgery?

Mitchell A. Jackson, MD: Having an FDA-approved product is a no-brainer. Because it's FDA-approved, we know the clinical trial data behind it. We can bring it in easily. It's really the first option for intracameral injection that we've had in our facility. Our facility only allows FDA-approved—and no compounded—products to be used intracamerally.

Cathleen M. McCabe, MD: Similarly, we've had a longstanding commitment to using only FDA-approved products. DEXYCU gives us an alternative to steroid drops for the eye to get the medication it needs after surgery.

Dr. Weinstock: With DEXYCU, we're delivering a 9% dexamethasone suspension into the eye, behind the iris, at the end of cataract surgery. What do you think about that concept? How will it affect patients long term? Do we need to choose the right candidates?

> I like this product for my cataract patients. There will always be postoperative inflammation—more so when patients have very dense cataracts and I have a limited view of the retina. By adding a steroid in the eye for sustained release, I know they're getting the right amount of medicine for the right duration.
>
> – Mitchell A. Jackson, MD

Dr. Jackson: I like this product for my cataract patients. There will always be postoperative inflammation—more so when patients have very dense cataracts and I have a limited view of the retina. By adding a steroid in the eye for sustained release, I know they're getting the right amount of medicine for the right duration.

Dr. Weinstock: We are all trained to automate what we do. I follow the same protocol and use DEXYCU for all cataract patients. When all patients get the same thing, the staff gets continuity and there's less opportunity for error. Things run more smoothly.

> I follow the same protocol and use DEXYCU for all cataract patients. When all patients get the same thing, the staff gets continuity and there's less opportunity for error. Things run more smoothly.
>
> – Robert J. Weinstock, MD

Dr. Weinstock: I think we all agree that in most cases, steroids are still the standard of care in cataract surgery, but we don't want some of the side effects. Are you worried about any issues with pressure and corneal edema from putting this small dose of dexamethasone suspension inside the eye at the end of surgery?

Dr. Weinstock: We notice that this medication tends to diffuse into the eye and disappear. That little sphere of dexamethasone gets smaller and smaller over the first week to 10 days, dissolving away slowly.

Dr. McCabe: It's just like we would taper our steroid drops. It naturally tapers the dose.

HOW DEXYCU IS DELIVERED

Dr. Weinstock: Let's discuss the delivery of DEXYCU in terms of what we do in the operating room and how we integrate this into the flow of surgery. DEXYCU comes in a prepackaged kit. Either the surgeon or a scrub technician can get it ready for surgery. It allows us to consistently deliver the right amount of product behind the iris at the end of surgery.

I'm sure everybody's technique is a little bit different. What has your experience been so far? Does using DEXYCU require more time or pose any challenges for your staff?

Dr. Solomon: There was a bit of a learning curve. You can go through either your paracentesis or your main incision, or even make a separate paracentesis. I go through the main incision. If there happens to be a little bit of shallowing of the anterior chamber, I'm not bothered by that because I like to move relatively quickly. Using the 25-gauge cannula, I place DEXYCU right behind the iris, pushing the plunger very rapidly, and then removing the cannula from the eye. Next, I reinflate the anterior chamber with my antibiotic as a means to bring it back up to what I'd consider to be a normal physiologic state.

> I have the scrub technician start to prepare the DEXYCU while I'm doing irrigation and aspiration of the viscoelastic after IOL implantation. I like to hydrate the main incision and go through my paracentesis site, placing the DEXYCU posterior to the iris and under the edge of the anterior capsule-IOL optic junction. Then I completely hydrate and seal the anterior chamber paracentesis side incision, and we're done.
>
> – Mitchell A. Jackson, MD

> We want a steroid to control anterior chamber inflammation in our patients, and in the FDA trial, three times more patients were clear at day 8: 60% (n = 94/156) versus 20% (n = 16/80) with placebo. So we know that it's effective. We can reduce the need for rescue medication such as ocular steroids or NSAIDs and have confidence that DEXYCU is going to do the job it needs to do.
>
> – Cathleen M. McCabe, MD

Dr. Weinstock: That's a perfect technique. It's exactly how I started doing it as well. For me, there was a little bit of a learning curve because DEXYCU sometimes wants to stick to the end of the 25-gauge cannula. I need to brush it against the bottom of the iris, the capsule, or the lens to grab it off the tip of the cannula.

Dr. McCabe: Sometimes there is a little bit of the DEXYCU coating the end of the cannula that can cause the spherule to cling to the cannula. I wipe that off on the conjunctiva at the entrance to the paracentesis when I'm about to enter the eye. This technique has been helpful in more easily disengaging DEXYCU from the cannula.

Another pearl: Before I'm ready to put DEXYCU in the anterior chamber, I like to hydrate my incision. I don't want to hydrate after I put it in because I'm trying to minimize how much fluid I put in the eye. I leave the eye a little firmer than I want it to be because I know I'm going to have some egress of balanced salt solution as I go in. I use a paracentesis, which also helps to minimize fluid loss. I place DEXYCU inferior in the capsular bag, just distal to the optic. I use the edge of the optic to scrape off the little spherule, which helps it stay put without moving into the inferior angle. This approach has been very reliable for me.

Dr. Jackson: I have the scrub technician start to prepare the DEXYCU while I'm doing irrigation and aspiration of the viscoelastic after IOL implantation. I like to hydrate the main incision and go through my paracentesis site, placing the DEXYCU posterior to the iris and under the edge of the anterior capsule-IOL optic junction. Then I completely hydrate and seal the anterior chamber paracentesis side incision, and we're done.

Dr. Weinstock: I think it's important to know that it's a very forgiving delivery. Like anything else, delivery is not going to be perfect every single time, but the medication is still going to work just fine. If you go in through the main wound and put DEXYCU under the iris and the eye collapses, the little spherule can come up into the anterior chamber like an air bubble, but we've found from early experience that the eye will do fine if that happens. If it drops down into the angle or sticks to the optic of the IOL close to the cornea, it goes away. If you see the DEXYCU break into multiple smaller spheres, that does not affect the outcomes. Even if we see a bit of localized corneal edema for a day or 2, like we would see after a dense cataract removal, the endothelial pump will clear the edema. So, I've noticed the same things, and like Dr. McCabe, I tend to go through the paracentesis. I make sure that the eye is well sealed, and I gently go in and put it right in the bag, right at the junction of the haptic and the optic, and it does kind of stick to it there. So, even if the chamber does collapse, the stickiness wants to keep it there.

Dr. McCabe: You might be concerned when you first see that there's a little residual medication remaining on the optic, but it has not been a concern for us.

Dr. Weinstock: That's a good point, because we want to educate our referring doctors and any others who might see the patient in the postoperative period. To the uninitiated, it might look like a foreign body or an infection. We tell them that if they see this, it is likely just residual medication that will disappear over time.

Dr. McCabe: Absolutely. It can be reassuring to referring doctors and, ultimately, the patient, if we offer a few different pictures that show what it looks like and where it's typically located.

Dr. Jackson: Right, because patients might see it. I always tell patients that if they see the medication, that's a good thing. They know that the medicine is in the eye, so it kind of reassures them. On the other hand, for the referring doctors, we really need to educate them, so they don't think it's an adverse event.

'REAL-WORLD' RESULTS

Dr. Weinstock: Let's talk about the results you've seen using DEXYCU in cataract surgery. In the FDA phase 3 pivotal trial, the cumulative percentage of subjects receiving rescue medication of ocular steroid or NSAID by day 30 was significantly lower in the DEXYCU treatment group (20%; n = 31/156) compared to placebo (54%; n = 43/80). Not only was that significant, but it also raised the confidence of surgeons.

Dr. McCabe: This is the critical thing, right? We want a steroid to control anterior chamber inflammation in our patients, and in the FDA trial, three times more patients were clear at day 8: 60% (n = 94/156) versus 20% (n = 16/80) with placebo. So, we know that it's effective. We can reduce the need for rescue medication such as ocular steroids or NSAIDs and have confidence that DEXYCU is going to do the job it needs to do.

Dr. Jackson: And the A/C clearing numbers you mention were achieved without an NSAID onboard, so they show the efficacy of DEXYCU alone. That's huge for just a steroid. A lot of us use an NSAID as well, which should further reduce inflammation.

> We tailor medication to everyone's individual needs, which may mean we add medications later in the treatment profile or extend the profile if the patient needs it. For example, if I know a patient has a history of chronic uveitis, I use DEXYCU, but because it likely will not still have an anti-inflammatory effect after 30 days, I might use a topical steroid at that point. I can use DEXYCU with other medications as a 'belt and suspenders' approach.
>
> – Cathleen M. McCabe, MD

Dr. Weinstock: What do you think about how long DEXYCU remains in the eye? Are patients coming back a few weeks later with a red eye? Do they need any additional medications or more NSAIDS than you think they normally would?

Dr. McCabe: We haven't seen patients return with a red eye. That said, using this medication alone is not a cookie-cutter approach for every patient. We tailor medication to everyone's individual needs, which may mean we add medications later in the treatment profile or extend the profile if the patient needs it. For example, if I know a patient has a history of chronic uveitis, I use DEXYCU, but because it likely will not still have an anti-inflammatory effect after 30 days, I might use a topical steroid at that point. I can use DEXYCU with other medications as a 'belt and suspenders' approach.

Dr. Weinstock: That's a good point. We're putting a steroid in the eye, but a high-risk patient like someone with diabetes or a history of macular edema may do best, if we prescribe a topical steroid as well, as long as we check the pressure and watch for complications. I would say it is visibly still present at one week, minimally. I like the way it slowly dissolves because we get verification and peace of mind that it's hanging around, getting the patient through that postoperative period.

Dr. Jackson: I've seen it remain visible all the way to 30 days in a few patients. It's slow release, and it's still working.

Dr. McCabe: I don't necessarily dilate patients at every visit, so if I put it far enough in the bag peripherally, I don't see it. Nevertheless, I know it's still there because the proof is in how the patients are doing. They have no anterior segment flare, so I know that they're controlled and I don't have to worry.

Dr. Weinstock: I still prefer to use a topical NSAID with DEXYCU because I think it offers some added comfort for postoperative pain and reduces foreign body sensation. I also think it's important to control inflammation in both pathways. Until we have an intracameral NSAID, do you think that surgeons will continue to use an NSAID along with DEXYCU?

Dr. Solomon: I do. That certainly is going to be my means of management at this point. I don't think we've seen inflammation disappear with any single medication, so we will continue to pair it with an NSAID postoperatively.

Dr. McCabe: I do the same. I think the nice thing about NSAIDs is that they usually require fewer drops per day, so they're a little bit easier for patients to take. There's no complicated tapering schedule like we have with topical steroids.

Dr. Weinstock: This has been really helpful. I appreciate your candid comments and your educational communication about DEXYCU, how to use it, and how to integrate it into your practice. I'm sure we're going to learn a lot more about this product, and it helps to hear from innovative surgeons who are willing to break new ground. ■

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DEXYCU™ safely and effectively. See full prescribing information for DEXYCU.

DEXYCU (dexamethasone intraocular suspension) 9%, for intraocular administration

Initial U.S. Approval: 1958

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

DEXYCU is a corticosteroid indicated for the treatment of postoperative inflammation (1).

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

- For intraocular administration (2).
- Administer 0.005 mL of DEXYCU into the posterior chamber inferiorly behind the iris at the end of ocular surgery (2).

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

Intraocular suspension: 9% equivalent to dexamethasone 103.4 mg/mL in a single-dose vial provided in a kit (3).

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

None (4).

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

- Increase in intraocular pressure (IOP): Monitor for increases in IOP (5.1).
- Delayed Healing: Monitor for delayed healing (5.2).
- Infection Exacerbation: Monitor and treat for any exacerbations of bacterial, viral or fungal infections (5.3).
- Cataract Progression: Cataracts may develop or progress in phakic patients (5.4).

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

In controlled studies, the most common adverse reactions reported by 5-15% of patients were intraocular pressure increased, corneal edema and iritis (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact EyePoint Pharmaceuticals US at 1-833-EYEPOINT (1-833-393-7646) or FDA at 1 800-FDA-1088 or www.fda.gov/medwatch.

Revised: 12/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

DEXYCU (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

2 DOSAGE AND ADMINISTRATION

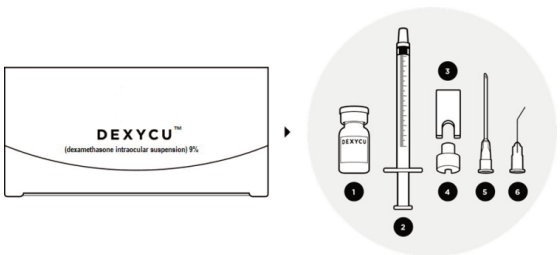
2.1 Dosing Information

DEXYCU should be administered as a single dose, intraocularly in the posterior chamber at the end of surgery. The dose is 0.005 mL of dexamethasone 9% (equivalent to 517 micrograms).

2.2 Preparation and Administration

Each kit of DEXYCU is for a single administration. After preparation, 0.005 mL will be administered.

The DEXYCU administration kit contains the following items:



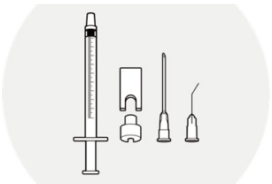
1. One glass vial: 0.5 mL of DEXYCU
2. One sterile 1-mL syringe
3. One sterile syringe guide
4. One sterile syringe ring
5. One sterile 18-gauge needle (1½ inches long), plastic cap attached
6. One sterile 25-gauge bent cannula (8 mm long), plastic cap attached

Step 1.

Prepare a sterile field. Remove the components of the administration kit from their respective pouches:

- syringe
- syringe guide
- syringe ring
- needle
- cannula

Place onto the sterile field.

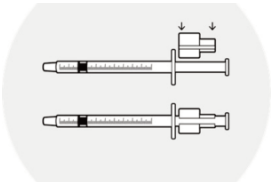


Step 2.

Withdraw the syringe plunger approximately 1 inch.

Place the syringe ring on the plunger (slit facing the plunger).

Apply slight downward pressure until the syringe ring "snaps" into place.

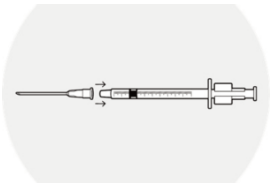


Step 3.

Place the 18-gauge needle firmly on the syringe.

Remove the cap from the needle.

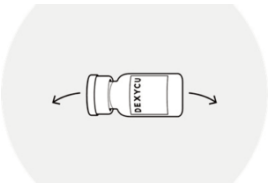
Depress the plunger completely and then withdraw the plunger to fill the syringe with air.



Step 4.

Vigorously shake the vial of DEXYCU sideways for a minimum of 30 seconds.

The suspended drug material must be used immediately after shaking.



Step 5.

Remove the blue plastic flip-cap from the vial and wipe the top of rubber stopper with an alcohol pad.

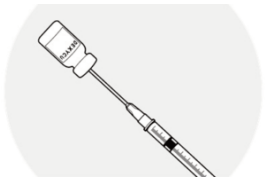
Invert the vial.

Step 6.

Insert the needle into the vial and inject the air into the vial.

Making sure the needle tip is immersed in the drug material pooled in the neck of the inverted vial, fill the syringe by slowly withdrawing the plunger approximately 0.2 mL.

Remove the needle from the vial and discard the unused portion in the vial.



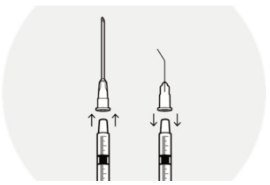
Step 7.

Remove the needle from the syringe.

Firmly place the cannula on the syringe and remove the plastic cap.

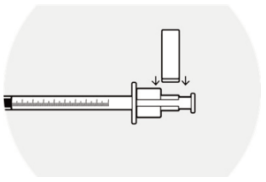
Hold the syringe vertically with the cannula pointing up.

Depress the plunger to expel air bubbles from syringe.



Step 8.

Affix the syringe guide over the syringe ring on the plunger.

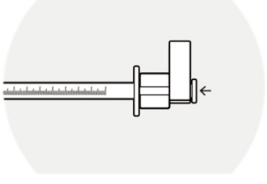


Step 9.

Depress the plunger until the syringe guide/ring mechanism comes gently into contact with the flange of the syringe.

Lightly tap/flick the barrel of the syringe to remove any excess drug from the tip of the cannula.

Do not wipe or touch the tip of the cannula to remove excess drug.

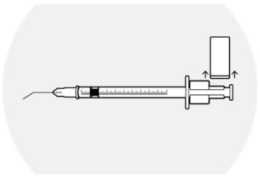


Step 10.

Remove the syringe guide, leaving the syringe ring in place.

Caution to not move the plunger. The space between the syringe ring and the top of the plunger is the medication injection volume that will be applied to the patient's eye.

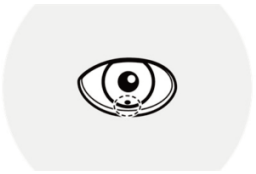
The syringe is now ready for injection.



Step 11.

In a single slow motion, inject 0.005 mL of the drug material behind the iris in the inferior portion of the posterior chamber. If the sphere of administered drug after intraocular injection appears to be larger than 2 mm in diameter, excess drug material may be removed by irrigation and aspiration in the sterile surgical setting.

PLEASE NOTE: Some drug material will remain in the syringe after the injection—this is necessary for accurate dosing. Discard unused portion remaining in the syringe after administration.



3 DOSAGE FORMS AND STRENGTHS

DEXYCU contains dexamethasone 9% w/w (103.4 mg/mL) as a sterile suspension for intraocular ophthalmic administration. DEXYCU is provided as a kit for administration of a single dose of 0.005 mL of 9% dexamethasone (equivalent to 517 micrograms of dexamethasone).

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Increase in Intraocular Pressure

Prolonged use of corticosteroids including DEXYCU may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma.

5.2 Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of corticosteroids.

5.3 Exacerbation of Infection

The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures.

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

5.4 Cataract Progression

The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Increase in Intraocular Pressure *[see Warning and Precautions (5.1)]*
- Delayed Healing *[see Warnings and Precautions (5.2)]*
- Infection Exacerbation *[see Warnings and Precautions (5.3)]*
- Cataract Progression *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials 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.

The following adverse events rates are derived from three clinical trials in which 339 patients received the 517 microgram dose of DEXYCU. The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis. Other ocular adverse reactions occurring in 1-5% of subjects included, corneal endothelial cell loss, blepharitis, eye pain, cystoid macular edema, dry eye, ocular inflammation, posterior capsule opacification, blurred vision, reduced visual acuity, vitreous floaters, foreign body sensation, photophobia, and vitreous detachment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of DEXYCU (dexamethasone intraocular suspension) 9% 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 abdominal wall/intestines and kidneys in rabbits at doses 7 and 5 times higher than the injected recommended human ophthalmic dose (RHOD) of DEXYCU (517 micrograms dexamethasone), respectively *[see Data]*.

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 7-times the injected RHOD of DEXYCU, on a mg/m^2 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 5-times the injected RHOD of DEXYCU, on a mg/m^2 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, interfere with endogenous corticosteroid production, or cause other unwanted effects. There is no information regarding the presence of injected DEXYCU in human milk, the effects on breastfed infants, or the effects on milk production to inform risk of DEXYCU to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for DEXYCU and any potential adverse effects on the breastfed child from DEXYCU.

8.4 Pediatric Use

Safety and effectiveness of DEXYCU in pediatric patients have not been established.

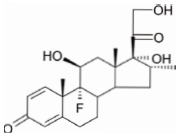
8.5 Geriatric Use

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

11 DESCRIPTION

DEXYCU (dexamethasone intraocular suspension) 9% is a corticosteroid, sterile, white to off-white opaque suspension for intraocular administration. Each vial of DEXYCU contains 0.5 mL of 9% w/w dexamethasone suspension equivalent to 51.7 mg of dexamethasone. The inactive ingredient is acetyl triethyl citrate. DEXYCU does not contain an antimicrobial preservative.

The chemical name of dexamethasone is pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16α)-. It has a molecular formula of $C_{22}H_{29}FO_5$ and a molecular weight of 392.46 grams per mole. Its structural formula is:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dexamethasone is a corticosteroid. Corticosteroids have 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

Systemic exposure to dexamethasone was evaluated in a subgroup of patients enrolled in two studies (n=25 for the first study and n=13 for the second study). The patients received a single intraocular injection of DEXYCU containing 342 mcg or 517 mcg of dexamethasone at the end of cataract surgery and blood samples were collected prior to surgery and at several time points post-surgery between Day 1 and up to Day 30. In the first study, the dexamethasone plasma concentrations on post-surgery Day 1 ranged from 0.09 to 0.86 ng/mL and from 0.07 to 1.16 ng/mL following administration of DEXYCU 342 mcg and 517 mcg, respectively. In the second study, dexamethasone plasma concentrations on post-surgery Day 1 ranged from 0.349 to 2.79 ng/mL following administration of DEXYCU 517 mcg. In both the studies, dexamethasone plasma concentrations declined over time and very few patients had quantifiable dexamethasone plasma concentrations at the final time point of sampling (Day 15 or Day 30).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to determine whether DEXYCU has the potential for carcinogenesis or mutagenesis. Fertility studies have not been conducted in animals

14 CLINICAL STUDIES

Clinical efficacy was evaluated in a randomized, double-masked, placebo-controlled trial (NCT02006888) in which subjects received either DEXYCU or placebo (vehicle). A dose of 5 microliters of DEXYCU (equivalent to 517 micrograms of dexamethasone), a dose equivalent to 342 micrograms of dexamethasone or vehicle was administered by the physician at the end of the surgical procedure. The primary efficacy endpoint for the study was the proportion of patients with anterior chamber cell clearing (i.e., cell score=0) on postoperative day (POD) 8. The presence of anterior cells was assessed using a slit lamp binocular microscope up to 30 days post treatment. The percentage of patients with anterior chamber clearing at Day 8 was 20% in the placebo group, and 57%, and 60% in the 342 and 517 microgram treatment groups, respectively (Table 1). The percentage of subjects receiving rescue medication of ocular steroid or NSAID was significantly lower at Day 3, 8, 15 and 30 in the 342 and 517 microgram treatment groups compared to placebo (Table 2).

Table 1: Proportion of subjects with clearing of the anterior chamber cells by visit

Visits	Treatments			Difference and 97.5% CI	
	Placebo N=80	DEX342 N=158	DEX517 N=156	DEX342 vs Placebo	DEX517 vs Placebo
Day 1	7 (9%)	17 (11%)	24 (15%)	2% (-7%, 11%)	7% (-3%, 16%)
Day 3	13 (16%)	60 (38%)	44 (28%)	22% (9%, 34%)	12% (0%, 24%)
Day 8	16 (20%)	90 (57%)	94 (60%)	37% (24%, 50%)	40% (27%, 54%)
Day 15	21 (26%)	83 (52%)	91 (58%)	26% (12%, 40%)	32% (18%, 46%)
Day 30	28 (35%)	113 (72%)	103 (66%)	36% (22%, 51%)	31% (16%, 46%)

Subjects who received rescue medication were treated as failure.

Table 2: Proportion of subjects receiving rescue medications

Visits	Number (Percent) of Patients Receiving Rescue Medication, and 95% CI		
	Placebo N=80	DEX342 N=158	DEX517 N=156
Day 1	10 (13%); 6%, 22%	9 (6%); 3%, 10%	10 (6%); 3%, 12%
Day 3	30 (38%); 27%, 49%	9 (6%); 3%, 10%	16 (10%); 6%,16%
Day 8	40 (50%); 39%, 61%	12 (8%); 4%, 13%	16 (10%); 6%,16%
Day 15	43 (54%); 42%, 65%	22 (14%); 9%, 20%	26 (17%); 11%, 24%
Day 30	43 (54%); 42%, 65%	25 (16%); 10%, 22%	31 (20%); 14%, 27%

Subjects who received an ocular corticosteroid or NSAID in study eye.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each kit of DEXYCU contains a single dose for a single patient. The 2-mL glass vial is filled with 0.5 mL of 9% dexamethasone intraocular suspension and has a blue cap (NDC # 71879-001-01).

Each kit also contains one sterile 18-gauge, 1.5-inch needle with a plastic cap attached, one sterile plastic 1-mL syringe for withdrawal of the vial contents, one sterile 25-gauge 8-mm cannula with a plastic cap attached for the intraocular administration, and one syringe assembly pouch containing a sterile ring and a sterile syringe guide used for measuring and injection of the 0.005 mL dose.

Store at 20°C to 25°C (68°F to 77°F).

Manufactured for: EyePoint Pharmaceuticals US, Inc. Watertown, MA 02472

DEXYCU®
(dexamethasone intraocular suspension) 9%