Safety and Efficacy of Dexamethasone Ophthalmic Insert (Dextenza®) in the Management of Clinically Significant Dry Eye

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If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Safety and Efficacy of Dexamethasone Ophthalmic Insert (Dextenza®) in the Management of Clinically Significant Dry Eye

Application No.: IRB00246348

Funded By: Ocular Therapeutix, Inc.

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You are being asked to join a research study. Participation in this study is voluntary. Even if you decide to join now, you can change your mind later.

1. Research Summary (Key Information):

The information in this section is intended to be an introduction to the study only. Complete details of the study are listed in the sections below. If you are considering participation in the study, the entire document should be discussed with you before you make your final decision. You can ask questions about the study now and at any time in the future.

Dry eye is a common public health problem with an estimated 25 million Americans affected by this condition. It is a chronic, possibly progressive inflammatory condition that leads to symptoms of ocular (eye) discomfort as well as blurred vision. A number of topical eye-drop treatments have been effective in reducing inflammation, however, the requirement of frequent instillation of drops can cause discomfort and blurring of vision and requires remembering and dexterity for instillation and these drops usually have preservative that can be harmful to the eye surface.

Dextenza® is a dexamethasone insert approved by US-FDA in November 2018 for the treatment of post-surgical eye inflammation and pain. It is inserted into the lower tear duct. Dextenza® is resorbable (absorbs into the eye) and does not require removal. We hypothesize that Dextenza® could mimic short-term steroid eyedrop use in patients with clinically significant dry eye to improve symptoms and eye surface findings, as was previously shown with steroid drops. If successful, the benefits of this treatment

over traditional topical drops include the elimination of frequent drop instillation as well as reduced harm to the eye surface from physical irritation and preservatives present in those drops.

Participants must be over 18 and have a previous or current diagnosis of dry eye by an eye care specialist. Participants will have total of 4 visits over a 42-day period. Potential risks include increased intraocular pressure and worsening dry eye symptoms. If the patient is at harm due to adverse reactions, rescue medication will be used to alleviate symptoms. There is no cost to participate.

2. Why is this research being done?

This research is being done to study whether Dextenza® can safely and effectively improve symptoms and signs in the treatment of clinically significant dry eye.

This study seeks to establish a new "dropless" means of ocular surface disease management. Traditional anti-inflammatory treatments for ocular surface disease such as dexamethasone and loteprednol are administered as topical drops. However, the requirement of frequent instillation of drops by the patients is problematic causing discomfort and blurring of vision and requires remembering and dexterity for instillation; poor compliance is not uncommon. In addition, we believe that instillation of drops disturbs the homeostasis of the natural tear film due to physical and chemical trauma due to large drop volume hammering on the eye surface. In addition, almost all of the steroid drops have harmful preservatives that can bother the tear film and the eye surface. Therefore, a "dropless" treatment of dry eye is desirable. Dextenza® could mimic short-term topical steroid use in a tapering manner in patients with clinically significant dry eye and show efficacy in improving its symptoms and signs.

Are there any investigational drugs/procedures?

Dextenza® has been approved by the Food and Drug Administration (FDA) for the treatment of post-surgical ocular inflammation and pain. It is not approved for use in dry eye. The FDA is allowing the use of Dextenza® in this study.

Who can join this study?

Adults with dry eye (DES) syndrome or keratoconjunctivitis sicca (KCS) who require topical steroid treatment may join.

How many people will be in this study?

About 85 people will be enrolled in this study.

3. What will happen if you join this study?

If you agree to be in this study, an initial screening and eye exam will be performed prior to study drug application. Thereafter, the following information on the next page corresponding to each visit will be collected over the course of 42 days:

Procedure	Run In* (Day -14 to -7)	Visit 1* (Day 1)	Visit 2 (Day 14)	Visit 3 (Day 28)	Visit 4 (Day 42)	Early Termination
Informed Consent	X	X**				
Inclusion/Exclusion/Demographics	X	X**				
Medical history and concurrent illnesses	X	X**				
Concomitant medications	X	X	X	X	X	X
Pregnancy Test		X			X	X
Log/Dispense Rescue Meds	X	X	X	X	X	
Insert Study Drug/Control		X				
Best Spectacle-corrected Vision Acuity (BSCVA)		X			X	X
Visual Analog Scale Questionnaires	X	X		X	X	X
Schirmer Tear Test (W/O anesthesia)	X	X			X	X
Ocular Surface Staining (corneal and conjunctival)	X	X	X	X	X	X
Intraocular Pressure Recording	X	X	X	X	X	X
Slit Lamp Exam	X	X	X	X	X	X
Dilated Fundus Exam	X	X**			X	X
Rescue medication recording	X		X	X	X	X
Adverse Event recording		X	X	X	X	X

*If no run-in required, patient will start at baseline visit/ Day 1
**Required in absence of run-in visit

Insertion of Dextenza®:

- Your eye will be randomized to receive Dextenza®..
- Randomization will be a 50/50 chance, like flipping a coin.
- The other eye will automatically receive the control treatment. For example, if the right eye of the patient gets randomized to receive the study drug, left eye will automatically be the control eye. If the right eye gets randomized to receive the control drug, the left eye will receive the study drug.
- The control used is a tear duct plug (Vera90TM) that is about the same size as the study drug but without the study drug (dexamethasone).
- The study Physician will place both the study drug and control tear duct plug at Day 1.

Double-Blind Study Protocol:

- The study is double-blind (double-masked), meaning the physician enrolling the patient and inserting the drug will be different than the examining physician throughout the course of the 42-day period who does not know which eye the study drug was administered in.
- In the case of an adverse event, the examining physician can break masking to identify which eye was assigned the study drug to decide future course of action.

Descriptions of the above table items are listed below:

1. Informed consent

   Informed consent will be given to you to review at the time of approach in the clinical setting or sent to your home. You will be given ample time review the consent form and will return on the day of the study visit with any questions. All questions will be answered, and a discussion will be had with the person obtaining consent prior to the consent form being signed.

2. Inclusion/Exclusion Criteria
   You will be screened for inclusion and exclusion criteria to determine eligibility for the study.

3. Medical History and Review of Systems
   We will conduct a full review of your medical and ocular history.

4. Concomitant Medication
   We will review any medication you are being given at the same time as the study.

5. Pregnancy test
   A standard urine pregnancy test provided by Ocular Therapeutix will be performed on females who are able to become pregnant at Baseline and Exit visit. A positive test will exclude you from enrollment into the study as well as will be considered a serious adverse event if occurred during the study period. It is essential for female participants who are able to become pregnant to use an acceptable birth control method.

   The biospecimens (urine) you provide for this research study will be processed and then immediately discarded. Your samples will be used as part of this research study only and will not be used or distributed for future research.

6. Log/Dispense Rescue Medication
   If necessary, the physician will administer rescue medications if you have worsening dry eye symptoms or increased intraocular pressure.

7. Visual Analog Scale (VAS).

   You will complete VAS questionnaires for each eye in regard to eye dryness, eye discomfort, and eye fatigue. The most bothersome symptoms will be determined (of the three symptoms) at baseline and used throughout the study as the main symptom.

   You will be given the questionnaire and expected to complete on your own. Help may be given if you have difficulty reading or understanding of the definition of the questions.

8. Visual acuity (VA)/ Best Spectacle Corrected Visual Acuity (BSCVA)
   Distance visual acuity will be measured using your usual correction for distance (if wearing).

9. Schirmer's test without anesthesia.
   This test involves placing a small piece of filter paper against the conjunctiva for 5 minutes to observe how much tear volume is being produced. The filter paper is removed after 5 minutes, and the length of the paper wetted is measured to estimate tear production. The testing will be performed as minimally disturbing to the ocular surface as possible.

10. Ocular surface staining (OSS).
    The application of non-toxic stains to the ocular surface (in the form of yellow and green eye drops) facilitates the evaluation of the tear film and demonstrate areas of damage on the ocular surface

11. Intraocular Pressure (IOP) Recording
    Measure the fluid pressure inside the eye. IOP is an important aspect in the evaluation of patients at risk of glaucoma, as well as those on steroids as sometimes patients have elevated pressure with use of topical steroids.

12. Slit Lamp Exam
    The slit-lamp examination provides a magnified view of the eye structures.

13. Dilated Fundus Examination (DFE)
    A procedure that uses eye drops to dilate or enlarge the pupil in order to obtain a better view of the interior surface of the eye.

14. Rescue Medication Recording (see item 6)

15. Adverse Event Recording
    In the case of adverse events (increased IOP, cataract formation or worsening cataract, redness, pain, or stinging, etc.), the study physician will record all events and determine course of action.

How long will you be in the study?
You will be in this study for an expected duration of 42 days, plus an additional 14 day run in period if an eyedrop wash out is needed.

4. What happens to data that are collected in the study?

Johns Hopkins and our research partners work to advance science and public health. The data we collect about you are important to this effort.

If you join this study, you should understand that you will not own your research data. If researchers use your data to create a new product or idea, including those that may have commercial value, you will not benefit financially from those efforts.

How will your data be shared now and in the future?
Sharing data is part of research and may increase what we can learn from each study.

Often, data sharing is required as a condition of funding or for publishing study results. It also is needed to allow other researchers to validate study findings and to come up with new ideas.

Your aggregated data may be shared:
- directly with research collaborators, other researchers, sponsors, government agencies, publishers of papers and other research partners
- through government or other databases/repositories

Data sharing could change over time, and may continue after the study ends.

We will do our best to protect and maintain your data in a safe way. Generally, if we share your data without identifiers (such as your name, address, date of birth) no further review and approval by an Institutional Review Board (IRB) is needed. If data are shared with identifiers, further IRB review and approval may be needed. The IRB will determine whether additional consent is required.

5. What are the risks or discomforts of the study?

Dextenza®

CONTRAINDICATIONS

- DEXTENZA is contraindicated (should not be used) in patients with active corneal, conjunctival or canalicular infections, including herpes simplex keratitis/cold sore of the cornea, and infections of the tear ducts.

WARNINGS AND PRECAUTIONS

- Increase in eye pressure
  - Prolonged use of corticosteroids 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. Intraocular pressure should be monitored during the course of the treatment.
- Bacterial Infection
  - Corticosteroids may suppress the host response and thus increase the chance of secondary ocular infections. Sometimes, steroids may mask infection and enhance existing infection.
- Viral Infections
  - Use of ocular steroids may prolong the course and may worsen the severity of many viral infections of the eye (including herpes simplex or cold sore).
- Fungal Infections
  - Mold or yeast invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Appropriate cultures should be taken.

Rescue Medication

- In patients with worsening of dry eye signs but not necessarily the symptoms, topical loteprednol 0.5% (**Lotemax**) drops up to 4 times a day can be used at the discretion of the physician.
- In patients with increased intraocular pressure (more than 5 points any either eye) topical beta blocker/betaxolol 0.5% (**Betoptic**) drops can be used 2 times a day to bring down the pressure at the discretion of the physician.

Dilation Drops

- Dilation drops should be used carefully in patients with narrow angle glaucoma, or those with zonular instability
- The dilation drops may burn upon instillation.
- Your pupils will be dilated, making your vision blurry and sensitive to light for a few hours after instillation.
- In rare, but severe cases, patients can have a vasovagal response to the drops and become light-headed or pass out.

Flourescein (yellow dye) and Lissamine Green (green dye) Stain

- Some of the staining might stay on the eye or eyelid for up to an hour after instillation. It can be removed by natural tears, or by using an eyewash, lid scrub and/or artificial tear.

Placebo-Control

- As one eye receives the study drug and the other eye receives a control tear duct plug, the control eye may experience exacerbated dry eye symptoms during the duration of the study.

Topical Steroid Medication Wash Out

- Patients who are on steroid drops will be placed in a 14-day wash-out period, in both eyes. A possible risk of discontinuing medication is increased dryness.

Interviews or questionnaires

You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Identifiable private information

There is the risk that information about you may become known to people outside this study.

Unknown risk

There may be side effects and discomforts in this study that are not yet known.

6. Are there benefits to being in the study?

You may or may not benefit from being in this study. Using Dextenza® to treat dry eye may eliminate the discomfort and constant need for applying traditional topical drops while also preventing damage to the ocular surface.

If you take part in this study, you may help others in the future.

7. What are your options if you do not want to be in the study?

You do not have to join this study. Should you choose to decline to participate in the study, you should continue following the medication regimen prescribed for your dry eye diagnosis. Alternative options should be discussed in detail with your provider or other health care professionals. If you do not join, your care at Johns Hopkins will not be affected.

Other options include:
A steroid drop, which has presumably the same benefit of medically treating the ocular surface inflammation. However, having to repetitively instill the drop could possibly bother the tear film homeostasis not only chemically but also physically. In addition, steroid drops have a preservative (BAK), which are known to be harmful to ocular surface.

A regular tear duct plug has the benefit of increasing the natural tear lake. However, if not combined to an anti-inflammatory therapy such as steroid drop, there is a risk of trapping inflamed tears on the ocular surface, which can worsen the condition.

There are no other approved ophthalmic treatments for dry eye as you are already on (or have been) a prescription eyedrop and over the counter artificial tears.

8. Will it cost you anything to be in this study?

No, participating in the study will not cost anything.

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet). This Sheet will give you the following information:

- The procedures, tests, or drugs that are part of this research and that will be paid for by the study (no cost to you).

- The procedures, tests, or drugs that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

No, you will not be paid to be in this study. However, parking vouchers will be provided for every study visit.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or share your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be maintained and how will the confidentiality of your data be protected?

HIPAA Authorization for Disclosure of Protected Health Information

What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Johns Hopkins Medicine and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?

The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Johns Hopkins, for example if needed for your clinical care or study oversight. To improve coordination of your research and clinical care, some information about the study you join will be included in your electronic medical record.

By signing this form, you give permission to the research team to share your information with others outside of Johns Hopkins. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team.

We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Reports or articles may be written about the study. You will not be identified by name in these reports or articles.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your *information* may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

How will your information be protected?
Only the certified research personnel will collect and see the clinical information regarding the patients as well as the study related information. The study data will be stored in the Hopkins SAFE desktop which requires special permission and password to access. Data without patient identifiers including but not limited to name, date of birth, address, or medical record number will be saved separately via SAFE desktop and analyzed in an anonymous manner, by a professional statistician. Only the pooled data from the study subjects will be shared with anyone, including the sponsor, in the forms of tables.
However, in the case of an audit both Johns Hopkins IRB as well as United States Food and Drug Administration might request to examine individual case forms with your specific information with identifiers.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. You might be asked to give us a list of other health care providers that you use.

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form, you will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the study results. You can search this Web site at any time. If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study doctor and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

What is the Institutional Review Board (IRB) and how does it protect you?
This study has been reviewed by Johns Hopkins University Institutional Review Board (IRB), a group of people that reviews human research studies. The IRB can help you if you have questions about your rights as a research participant or if you have other questions, concerns or complaints about this research study. You may contact the IRB at 410-502-2092 or jhmeirb@jhmi.edu.

What should you do if you have questions about the study, or are injured or ill as a result of being in this study?
Call the principal investigator, **Dr. Esen Akpek** at **410-955-5214.** If you wish, you may contact the principal investigator by letter. The address is on page 1 of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-502-2092.

If you have an urgent medical problem or think you are injured or ill because of this study, call 911 or go to your local emergency department. You should also call **Dr. Esen Akpek** at **410-955-5214** during regular office hours and at **443-824-3393** after hours and on weekends. If this doctor is not available, the operator will page the "on call physician."

16. What does your signature on this consent form mean?

Your signature on this form means that you have reviewed the information in this form, you have had a chance to ask questions, and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT PROCESS

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time

Signature of Participant	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).