Appendix A
Protocol

Investigator-Initiated Study Protocol

In Clinic O**p**tometrist Inse**r**tion of D**e**xtenza **P**rior to C**a**taract Su**r**g**e**ry

The PREPARE Study

Compound:	DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg, for intracanalicular use
Study Name:	In Clinic O**p**tometrist Inse**r**tion of D**e**xtenza **P**rior to C**a**taract Su**r**g**e**ry **The Prepare Study**
Clinical Phase:	Investigator-Initiated Clinical Trial
Date of Issue:	9/24/2020
Primary Investigator:	Mitch Ibach, OD
Sub Investigator:	Justin Schweitzer, OD John Berdahl, MD Doug Wallin, OD Keith Rasmussen, OD Vance Thompson, MD Larae Zimprich, OD Jason Schmit, OD Daniel Terveen, MD
Site Name & Location:	Vance Thompson Vision Center 3101 West 57th Street Sioux Falls, South Dakota 57108

CLINICAL STUDY PROTOCOL SYNOPSIS

TITLE	The PREPARE Study
SITE LOCATION(S)	Vance Thompson Vision Center 3101 West 57th Street Sioux Falls, South Dakota 57108
PRINCIPAL INVESTIGATOR	Mitch Ibach, OD
OBJECTIVE(S)	To evaluate the clinical outcomes with optometrist pre-surgical insertion of DEXTENZA in the clinical office setting in patients undergoing same-day cataract surgery compared to standard of care steroid therapy.
STUDY DESIGN	Prospective Open-label Interventional Study
STUDY DURATION	2-3 months from start-up
ESTIMATED STUDY COMPLETION DATE	Insert date of study completion
POPULATION Sample Size: Target Population:	 N=60 (30 patients, 60 eyes) Patients planning to undergo sequential bilateral cataract surgery.
TREATMENT(S) Study Drug Dose/Route/Schedule:	 DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg, for intracanalicular use All patients will be enrolled for cataract surgery. Each study subject will have their first eye randomized to either the Control Group or the Experimental Group. The second eye will be selected for the opposite group. All eyes will receive intracameral dexamethasone+moxifloxacin+ketorolac (DMK) at the time of surgery. All eyes will be placed on topical antibiotic (Vigamox 0.5%) QID for one week and topical NSAID ((Prolensa (Bromfenac 0.07%)) QD for one month. **Experimental Group (Treatment A):** 30 eyes will receive DEXTENZA insertion, placed in the office by the optometrist prior to their same-day cataract surgery. **Control Group (Treatment B):** 30 eyes will receive

	topical prednisolone acetate 1% QID for one week, TID for one week, BID for one week, QD for one week.
ENDPOINT(S)	
Primary:	To determine the effect of dexamethasone intracanalicular insert through Week 4 as measured by: • Mean anterior chamber cell/flare score as measured by Slit Lamp Biomicroscopy evaluation using grading scale of 0 to 4 + (SUN Working Group Grading Scheme) at post-op Day 1, Day 7, and Week 4. • Mean pain score as measured by Visual Analog Score numerical grading scale 0-10 at post-op Day 1, Day 7, and Week 4. To determine patient preference through Week 4 as measured by: • Adapted COMTOL Questionnaire at Week 4.
Secondary:	To determine the effect of dexamethasone intracanalicular insert through Week 4 or 12: • Incidence of increased intraocular pressure (IOP) >10mmHg above baseline as measured by Goldmann Applanation Tonometer at post-op Day 1, Day 7, and Week 4. • Incidence of Cystoid Macular Edema (CME) as measured by optical coherence tomography (OCT) at post-op Week 4. To determine physician ease of insertion following dexamethasone intracanalicular insert placement prior to same-day surgery as measured by: • Physician Ease of Use Survey following dexamethasone intracanalicular placement on Surgical Visit Day 0. To determine eye drop therapy burden on the patient through Week 4 as measured by: • Eye Drop Burden Questionnaire at post-op Day 7 and Week 4.

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Introduction and Rationale

Introduction

Dextenza (dexamethasone 0.4mg ophthalmic insert) is a steroid eluting intracanalicular plug approved on-label for the treatment of pain and postoperative inflammation in patients who've undergone ocular surgery. Utilizing Dextenza, in place of ophthalmic steroid drops, will provide patients with a lessened number of post-operative drops which decreases both contamination possibilities and improper drug installation. Dextenza's hydrogel technology is proposed to offer patients a gradual sustained delivery of steroid to the ocular surface which may decrease subjective post-operative pain.

Post-operative drop regimens frequently induce both concerns and questions for patients undergoing ocular surgery. Poor compliance with postoperative medications can lead to unexpected and or unsatisfactory outcomes. In post-operative cataract surgery patients, un-treated or non-resolving inflammation can lead to pain, anterior chamber inflammation, and potentially cystoid macular edema (CME). Lessening the risk of these adverse events due to drop complications is a key benefit of Dextenza. There may be future possibilities to combine intracameral medication combinations (antibiotic, steroid, NSAID) plus Dextenza to further reduce the patient post-operative drop burden.

On introduction to the market, Dextenza was most commonly inserted in the operating room (OR) pre-cataract surgery, but other instillation protocols will increase practitioner adoption and patient access. Increasing optometrist administration in clinic allows for another route for insurance reimbursement while freeing up ophthalmologists in the OR.

Rationale

DEXTENZA (dexamethasone 0.4mg ophthalmic insert) has increasing research and evidence for post-cataract surgery patients, but a gap remains in best practices for instillation timing and protocols. In clinic insertion provides another route for device administration which can help foster additional reimbursement codes.

Dextenza's ability to treat post-operative inflammation while also increasing remaining tear volume by punctal occlusion has potential to improve visual outcomes for patients while also decreasing post-operative drop inconvenience. The studied patient population is having their initial cataract evaluation and surgery on the same day, decreasing patient inconvenience, adding Dextenza is another arrow in the quiver.

Rationale for Study Design

This prospective contralateral eye study will compare the outcomes of 30 patients undergoing cataract surgery. All eyes will receive intracameral DMK at the conclusion of surgery. All eyes will be treated with Vigamox 0.5% QID for 1 week and Prolensa

(bromfenac 0.07%) QD for 1 month. After randomization, one eye per patient will receive Dextenza in place of topical steroid while the other eye has topical prednisolone acetate 1% QID 1 week, TID 1 week, BID 1 week, and QD 1 week. The primary endpoints of anterior chamber cell and mean pain score correlate to the initial FDA approval trial for Dextenza. The study inclusion and exclusion criteria were chosen based on patients who normally would be successful with cataract surgery, including the absence of pre-existing intraocular inflammation or macular edema. The study follow-up visits were based on the Vance Thompson Vision standard postoperative follow-up protocols.

Study Objectives

Primary Objective

To determine the effect of dexamethasone intracanalicular insert through Week 4 as measured by:

- Mean anterior chamber cell score as measured by Slit Lamp Biomicroscopy evaluation using grading scale of 0 to 4 + (SUN Working Group Grading Scheme) at post-op Day 1, Day 7, and Week 4.
- Mean pain score as measured by Visual Analog Score numerical grading scale 0-10 at post-op Day 1, Day 7, and Week 4.

To determine patient preference through Week 4 as measured by:

- Adapted COMTOL Questionnaire at Week 4.

Secondary Objectives

To determine the effect of dexamethasone intracanalicular insert through Week 4 or 12:

- Mean anterior chamber flare score as measured by Slit Lamp Biomicroscopy evaluation using grading scale of 0 to 4 + (SUN Working Group Grading Scheme) at post-op Day 1, Day 7, and Week 4.
- Incidence of increased intraocular pressure (IOP) >10mmHg above baseline as measured by Goldmann Applanation Tonometer at post-op Day 1, Day 7, and Week 4.
- Incidence of Cystoid Macular Edema (CME) as measured by optical coherence tomography (OCT) at post-op Week 4.

To determine physician ease of insertion following dexamethasone intracanalicular insert placement prior to same-day surgery as measured by:

- Physician Ease of Use Survey following dexamethasone intracanalicular placement on Surgical Visit Day 0.

To determine eye drop therapy burden on the patient through Week 4 as measured by:

- Eye Drop Burden Questionnaire at post-op Day 7 and Week 4.

Study Design

Study Description and Duration

This prospective, open-label, randomized, investigator-sponsored clinical study seeks to investigate a new protocol for in-clinic Dextenza insertion by optometrists at the day of surgery. This three month study will study the clearance of intraocular pain and inflammation comparing topical steroids versus Dextenza.

Selection, Withdrawal, and Replacement of Patients

Study Population

The study aims to enroll 30 patients undergoing routine sequential bilateral cataract surgery.

Inclusion Criteria

A patient's study eye must meet the following criteria to be eligible for inclusion in the study:

- Patients 18 years of age or older, undergoing routine, uncomplicated, sequential bilateral cataract surgery.
- Willing and able to comply with clinic visits and study related procedures
- Willing and able to sign the informed consent form

Exclusion Criteria

A patient who meets any of the following criteria will be excluded from the study:

- Patients under the age of 18.
- Patients who are pregnant (must be ruled out in women of child-bearing age with pregnancy test).
- Active infectious ocular or systemic disease.
- Patients with active infectious ocular or extraocular disease.
- Patients actively treated with local or systemic immunosuppression including systemic corticosteroids.
- Patients with known hypersensitivity to Dexamethasone.
- Patients with severe disease that warrants critical attention, deemed unsafe for the study by the investigator.
- Patients with proliferative diabetic retinopathy or uncontrolled diabetes as deemed by an A1C > 10.0.
- Patients with a history of ocular inflammation or macular edema.
- Patients with a pre-existing epiretinal membrane (ERM)
- Patients with allergy or inability to receive intracameral antibiotic.
- Patients on systemic non-steroidal anti-inflammatory drugs (NSAID) greater than 1,200 mg/day

- Patients with a corticosteroid implant (i.e. Ozurdex).

Treatment Logistics and Accountability

Packaging, Labeling, and Storage

Intracanalicular dexamethasone insert must be stored in a secure area accessible only to the Investigator and their designee(s) and refrigerated and stored between 2^{o} C and 8^{0} C. Intracanalicular dexamethasone insert contains 0.4 mg dexamethasone and is designed to provide a sustained and tapered release of therapeutic levels of dexamethasone to the ocular surface for up to 30 days for the reduction of post-surgical inflammation and pain associated with ocular surgery. Dexamethasone is an anti-inflammatory 9-fluoro-glucocorticoid (also termed a glucocorticoid agonist) and is the active ingredient found in MAXIDEX® 0.1% (dexamethasone ophthalmic suspension), which contains approximately 50 µg of dexamethasone per drop.

Study inserts will be supplied by Ocular Therapeutix in a sealed foil pouch containing one intracanalicular dexamethasone insert in a foam carrier.

Study inserts will be shipped to the site via overnight shipping using cold packs to maintain a temperature of 2° to 8° C. The Investigator, or an approved representative (e.g. pharmacist), will ensure that all study drug inserts are stored in a secured area, under recommended storage conditions and in accordance with applicable regulatory requirements. The shipping box is to be opened and stored immediately at the site in a refrigerator intended for investigational products at a temperature of 2° to 8°C.

When the insert is removed from the refrigerator, it should be visually inspected. Exposure of the insert to temperatures outside these limits it not recommended. Records of actual storage conditions (i.e. temperature log) at the study site must be maintained; and must include a record of the dates, when the refrigerator was checked, the initials of person checking, and the temperature.

Supply and Disposition of Treatments

Study insert will be shipped at a temperature of 2° to 8°C to the investigator as needed during the study.

Treatment Accountability

All study insert accountability records will be kept current.

The investigator will account for all opened and unopened packaging of study inserts. These records will contain the dates, quantity, and study medication

- Inserted in each patient,
- disposed of at the site or returned to Ocular Therapeutix

All accountability records will be made available for inspection by regulatory agency inspectors.

Concomitant Medications and Procedures

At the discretion of their physician, patients may continue to receive all medications and standard treatments administered for other conditions.

Study Schedule of Events and Visit Descriptions

Schedule of Events

Study assessments and procedures are presented by visit in Table 1 below.

Table 1 Schedule of Events

Study Procedure	Screening/ Baseline	First Eye Surgical Visit Day 0	First Eye Day 1	Second Eye Surgical Visit Day 0	Second Eye Day 1	Day 7 Both Eyes	Day 30 Both Eyes	Day 90 post-op Both Eyes	Early Termination
Visit	**VISIT 1**	**VISIT 2**	**VISIT 3**	**VISIT 4**	**VISIT 5**	**VISIT 6**	**VISIT 7**	**VISIT 8**	
Windows for Visits	**(Day -30 to 0)**					**+/- 2 day from first eye sx**	**+/- 5 days from first eye sx**	**+/- 7 days from first eye sx**	
Inclusion/Exclusion	X								
Informed Consent	X								
Demographics	X								
Medical History and Concurrent Illnesses	X	X	X	X	X	X	X	X	
Concomitant Medications	X	X	X	X	X	X	X	X	
Uncorrected Distance VA	X		X		X	X	X	X	
MRX	X					X	X	X	
BCVA (ETDRS at 4m)	X					X	X	X	
Ophthalmic Examination (dilated fundus exam)	X						X		
Slit lamp exam	X		X		X	X	X	X	
Grade cataract density (scale 1 to 4)		X		X					
OCT	X						X		
Intraocular Pressure	X		X		X	X	X	X	
Indicate the incision type, location, and size (mm)		X		X					
Type of IOL (e.g. monofocal, toric, multifocal, etc.) and lens power		X		X					
Record any surgical complications		X		X					
Subject reported AEs prior to or after surgery		X	X	X	X	X	X	X	
Intracanalicular dexamethasone insert (*if randomized to Dextenza arm)		X		X					
Intracameral injection of NSAID+antibiotic+steroid combo		X		X					
Physician Ease of Use Survey		X		X					
Eye Drop Burden Questionnaire						X	X		
Adapted COMTOL Questionnaire							X		
Ocular Pain Assessment	X		X		X	X	X	X	
Anterior chamber cell count	X		X		X	X	X	X	
Anterior chamber cell flare	X		X		X	X	X	X	
Insert Visualization		X	X	X	X	X	X	X	
Prescribe post-operative topical therapy regimen (*specific to each study group)		X		X					

5.2 Study Visit Descriptions

5.2.1 Study Procedures

Screening/Baseline

After the patient has provided informed consent, the following information will be collected (if the data was collected within 30 days of the screening exam it may be pulled forward from the subject previous exam):

- Inclusion/exclusion
- Demographics
- Medical history and concurrent illnesses
- Concomitant medications
- Distance VA
- MRX
- BCVA
- Ophthalmic Examination (dilated fundus exam)
- Slit lamp Exam
- OCT
- IOP
- Ocular Pain Assessment
- Anterior Chamber Cell Count
- Anterior Chamber Cell Flare

Surgical Visit Day 0 First Eye

- Medical history and concurrent illnesses
- Concomitant medications
- Grade Cataract Density (scale 1 to 4)
- Indicate incision type, location, and size
- Type of IOL and lens power
- Record any surgical complications
- Subject reported AEs prior to or after surgery
- Insert intracanalicular dexamethasone insert (*if randomized to Dextenza arm)
- Physician Ease of Use Survey
- Intracameral injection of NSAID+abx+steroid combo
- Insert visualization
- Prescribe post-operative regimen (*specific to each eye)

Day 1 First Eye (To be completed prior to 2nd eye sx)

- Medical history and concurrent illnesses
- Concomitant medications
- Distance VA
- Slit lamp Exam
- IOP
- Subject reported AEs prior to or after surgery
- Ocular Pain Assessment

- Anterior Chamber Cell Count
- Anterior Chamber Cell Flare
- Insert visualization

Surgical Visit Day 0 Second Eye (To be completed one day after first eye sx)

- Medical history and concurrent illnesses
- Concomitant medications
- Grade Cataract Density (scale 1 to 4)
- Indicate incision type, location, and size
- Type of IOL and lens power
- Record any surgical complications
- Subject reported AEs prior to or after surgery
- Insert intracanalicular dexamethasone insert (*if randomized to Dextenza arm)
- Physician Ease of Use Survey
- Intracameral injection of NSAID+abx+steroid combo
- Insert visualization
- Prescribe post-operative regimen (*specific to each eye)

Day 1 Second Eye

- Medical history and concurrent illnesses
- Concomitant medications
- Distance VA
- Slit lamp Exam
- IOP
- Subject reported AEs prior to or after surgery
- Ocular Pain Assessment
- Anterior Chamber Cell Count
- Anterior Chamber Cell Flare
- Insert visualization

Day 7 (+/- 2 days from first eye sx)

- Medical history and concurrent illnesses
- Concomitant medications
- Distance VA
- MRX
- BCVA
- Slit lamp Exam
- IOP
- Subject reported AEs prior to or after surgery
- Eye Drop Burden Questionnaire
- Ocular Pain Assessment
- Anterior Chamber Cell Count

- Anterior Chamber Cell Flare
- Insert visualization

Day 28-35 (+/- 5 days from first eye sx)

- Medical history and concurrent illnesses
- Concomitant medications
- Distance VA
- MRX
- BCVA
- Ophthalmic examination (dilated fundus exam)
- Slit lamp Exam
- OCT
- IOP
- Subject reported AEs prior to or after surgery
- Eye Drop Burden Questionnaire
- Adapted COMTOL Questionnaire
- Ocular Pain Assessment
- Anterior Chamber Cell Count
- Anterior Chamber Cell Flare
- Insert visualization

Month 3 (+/- 7 days from first eye sx)

- Medical history and concurrent illnesses
- Concomitant medications
- Distance VA
- BCVA
- Slit lamp Exam
- IOP
- Subject reported AEs prior to or after surgery
- Ocular Pain Assessment
- Anterior Chamber Cell Count
- Anterior Chamber Cell Flare
- Insert visualization

Unscheduled Visits

All attempts should be made to keep patients on the study schedule. Unscheduled visits may be necessary to repeat testing following abnormal laboratory results, for follow-up of AEs, or for any other reason, as warranted.

Adverse Event Information Collection

The investigator (or designee) will record all AEs that occur during the study The definition of an AE and SAE, and information on the determination of

severity and relationship to treatment are provided in Section 6.

Rescue Criteria

- Patients should be rescued at any time at the discretion of the investigator.
- The following rescue criteria are to be applied by the investigator:
    - ≥ Grade 3 anterior chamber cells
    - Ocular pain score of > 5 due to ocular inflammation
- Patients requiring rescue therapy will be prescribed: topical steroid and topical NSAID per the discretion of the investigator.

If a patient requires rescue therapy in the eye containing the dexamethasone insert, the insert will not be removed, and subjects will be followed for safety.

Safety Definitions, Reporting, and Monitoring

Definitions

Adverse Event

An AE is any untoward medical occurrence in a patient administered a study drug which may or may not have a causal relationship with the study drug. Therefore, an AE is any unfavorable and unintended sign (including abnormal laboratory finding), symptom, or disease which is temporally associated with the use of a study drug, whether or not considered related to the study drug.

An AE also includes any worsening (i.e. any clinically significant change in frequency and/or intensity) of a pre-existing condition that is temporally associated with the use of the study drug.

Serious Adverse Event

A SAE is any untoward medical occurrence that at any dose:

- Results in **death** – includes all deaths, even those that appear to be completely unrelated to study drug (e.g. a car accident in which a patient is a passenger).
- Is **life-threatening** – in the view of the investigator, the patient is at immediate risk of death at the time of the event. This does not include an AE that had it occurred in a more severe form, might have caused death.
- Requires in-patient **hospitalization** or prolongation of existing hospitalization. In-patient hospitalization is defined as admission to a hospital or an emergency room for longer than 24 hours. Prolongation of existing hospitalization is defined as a hospital stay that is longer than

was originally anticipated for the event, or is prolonged due to the development of a new AE as determined by the investigator or treating physician.

- Results in persistent or significant **disability/incapacity** (substantial disruption of one's ability to conduct normal life functions).
- Is a **congenital anomaly/birth defect**
- Is an **important medical event** – Important medical events may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the patient or may require intervention to prevent 1 of the other serious outcomes listed above (e.g., intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse). Any malignancy (other than basal cell skin cancers) would be considered a medically important event.

Recording and Reporting Adverse Events

All AEs and SAEs will be recorded only if they are medically relevant.

All SAEs, regardless of assessment of causal relationship to study insert will be reported to Ocular Therapeutix.

To report an SAE, Ocular Therapeutix will be contacted at the following:

ocutx.pharmacovigilance@propharmagroup.com
SAE hotline: 844-668-3948

The investigator will promptly report to the IRB all unanticipated problems involving risks to patients. This includes death from any cause and all SAEs related to the use of the study insert. All SAEs will be reported to the IRB, regardless of assessed causality.

Study Variables

Demographic and Baseline Characteristics

Baseline characteristics will include standard demography (e.g. age, race, weight, height, etc.), disease characteristics including medical history, and medication history for each patient.

Ethical and Regulatory Considerations

Good Clinical Practice Statement

It is the responsibility of the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Informed Consent

The principles of informed consent are described in ICH Guidelines for GCP.

Ocular Therapeutix will have the right to review and comment on the informed consent form.

It is the responsibility of the investigator or designee (if acceptable by local regulations) to obtain written informed consent from each patient prior to his/her participation in the study and after the aims, methods, objectives, and potential hazards of the study have been explained to the patient in language that he/she can understand. The ICF will be signed and dated by the patient and by the investigator or authorized designee who reviewed the ICF with the patient.

Patients who can write but cannot read will have the ICF read to them before signing and dating the ICF.
Patients who can understand but who can neither write nor read will have the ICF read to them in presence of an impartial witness, who will sign and date the ICF to confirm that informed consent was given.

The original ICF will be retained by the investigator as part of the patient's study record, and a copy of the signed ICF will be given to the patient.

If new safety information results in significant changes in the risk/benefit assessment, the ICF will be reviewed and updated appropriately. All study patients will be informed of the new information and provide their written consent if they wish to continue in the study. The original signed revised ICF will be maintained in the patient's study record and a copy will be given to the patient.

Patient Confidentiality and Data Protection

The investigator will take all appropriate measures to ensure that the anonymity of each study patient will be maintained.

The patient's and investigator's personal data will be treated in compliance with all applicable laws and regulations.

Institutional Review Board

An appropriately constituted IRB, as described in ICH Guidelines for GCP, will review and approve:

- The protocol, ICF, and any other materials to be provided to the patients (e.g. advertising) before any patient may be enrolled in the study
- Any amendment or modification to the study protocol or ICF before implementation, unless the change is necessary to eliminate an

immediate hazard to the patients, in which case the IRB will be informed as soon as possible

Ongoing studies will be reviewed by the IRB/EC on an annual basis or at intervals appropriate to the degree of risk.

In addition, the IRB will be informed of any event likely to affect the safety of patients or the continued conduct of the clinical study.

A copy of the IRB approval letter will be sent to Ocular Therapeutix prior to shipment of drug insert supplies to the investigator. The approval letter will include the study title, the documents reviewed, and the date of the review.

Records of the IRB review and approval of all study documents (including approval of ongoing studies) will be kept on file by the investigator.

APPENDICES

Protocol Appendix A: Ease of use Survey
Protocol Appendix B: Eye Drop Burden Questionnaire
Protocol Appendix C: Adapted COMTOL

REFERENCES

1. DEXTENZA [PACKAGE INSERT]. BEDFORD, MA: OCULAR THERAPEUTIX, INC; 2019.

2. Walters TR, Bafna S, Vold S, et al. Efficacy and Safety of Sustained Release Dexamethasone for the Treatment of Ocular Pain and Inflammation after Cataract Surgery: Results from Two Phase 3 Studies. *J Clin Exp Ophthalmol*. 2016;7(4):1-11.

3. Tyson SL, Bafna S, Gira JP, et al. Multicenter randomized phase 3 study of a sustained-release intracanalicular dexamethasone insert for treatment of ocular inflammation and pain after cataract surgery. [published correction appears *in J Cataract Refract Surg*. 2019;45(6):895]. *J Cataract Refract Surg*. 2019;45(2):204-212.

Protocol Appendix A: Ease of Use Survey

The investigator will grade the level of ease of insertion of the intracanalicular insert on a 0 to 10-point scale.

The Investigator will record ease of insertion procedure on the appropriate Case Report Form.

0	1	2	3	4	5	6	7	8	9	10

Very Easy

Very Hard

Protocol Appendix B: **Eye Drop Burden Questionnaire**

		Never 1	Rarely 2	Sometimes 3	Usually 4	Always 5
1.	I forget to administer my eye drops.					
2.	It is difficult and/or frustrating to administer my eye drops.					
3.	My eye drops burn and/or sting when I administer them.					
4.	My eye drop treatment interferes with the daily activities of my life.					
5.	I forget to wash my hands prior to administering my eye drops.					
6.	I accidentally administer more and/or less than one eye drop to the eye.					
7.	The drops miss my eye when I administer them.					
8.	The bottle tip touches my eye when using my eye drops.					
	Add up the numbers for each statement to calculate the total Eye Drop Burden Score. Total Eye Drop Burden Score = ___ Low Eye Drop Burden: 8-18 Moderate Eye Drop Burden: 19-29 High Eye Drop Burden: 30-40					

Protocol Appendix C: Adapted COMTOL

Comparison of Ophthalmic Medications for Tolerability (COMTOL) Questionnaire (adapted to compare physician & patient administered 'fewer-drops' regimen ((Treatment A- Experimental Group)) to patient-only administered total topical therapy ((Treatment B- Control Group)).

Interviewer: Please read the following verbatim!

Thank you for participating in our study. Your evaluation of the test "fewer-drops" treatment (Treatment A- Experimental Group) that the surgeon and you administered following your surgery compared to the total eyedrops (Treatment B- Control Group) you administered following surgery is most valuable to us. We would greatly appreciate your assistance by answering the following questions as best as possible. All answers are confidential.

Every patient received both treatment regimens. Every patient received Treatment A in one eye and Treatment B in the opposite eye. For clarification, here are the definitions of each treatment group:

Treatment A (Experimental Group- fewer-drops, physician & patient administered):

- Dextenza (steroid punctal plug/insert) + Vigamox drops 4x/day for 1st week + Prolensa drops 1x/day for one month

Treatment B (Control Group- total topical eyedrop therapy, patient-only administered):

- Prednisolone drops 4x/day for 1st week, 3x/day for 2nd week, 2x/day for 3rd week, 1x/day for 4th week + Vigamox drops 4x/day for 1st week + Prolensa drops 1x/day for one month

1. ***(Interviewer: Questions 1 and 2 are to be asked only at the Month 1 Visit).***

Now that you tried both test regimens, did you prefer the Treatment A (fewer-drops, physician & patient administered) regimen or the Treatment B (total eyedrop therapy, patient-only administered) regimen?

(Interviewer: Please check the appropriate response below).
_____ Treatment A regimen (Experimental Group-fewer drops)
_____ Treatment B regimen (Control Group-all drops)
_____ Neither (Do not read)

2. Why did you prefer your selected treatment? ***(Interviewer: Read response from Question 1)***

‘Fewer-Drops’ Physician/Patient-Administered Therapy (Treatment A): Patient Reported Outcomes

3. ***(Interviewer: Read the following).*** I am going to read to you a list of various side effects that may occur in some patients who receive Treatment A regimen (‘fewer-drops’ physician & patient administered regimen) following ophthalmic surgery. You may have experienced none, some, or all these side effects during the past month. As I read the list, please tell me if you experienced that side effect. ***(Interviewer: Check affirmative responses on the far left column of the list below Question #4. Place a check under the column marked “I did not have the symptom” below Question #4 for those symptoms not experienced by the patient. If patient experienced none of these side effects, please check "None of these symptoms" below and go to Question #6).***

4. ***(Interviewer: Refer to Question #3 and read the following).*** I am now going to read to you the side-effects you said you experienced in the last question. For each side effect I mention, please tell me how frequently you experienced each side effect during the past month. ***(interviewer- hand respondent Card "A" with frequency scales.)*** That is, did you experience the side effect rarely, a few times, often, use ally, almost always, or always? ***(Interviewer: Place check under appropriate column below for each checked side effect mentioned by respondent).***

	I Did Not Have the Symptom	Rarely	A Few Times	Fairly Often	Usually	Almost Always	Always
__ Burning/stinging in eyes	( )	( )	( )	( )	( )	( )	( )
__ Redness in eyes	( )	( )	( )	( )	( )	( )	( )
__ Blurred vision	( )	( )	( )	( )	( )	( )	( )
__ Bitter taste	( )	( )	( )	( )	( )	( )	( )
__ Unusual taste	( )	( )	( )	( )	( )	( )	( )
__ Itchy eyes	( )	( )	( )	( )	( )	( )	( )
__ Discharge from eyes	( )	( )	( )	( )	( )	( )	( )
__ Swelling of eyelids	( )	( )	( )	( )	( )	( )	( )
__ Brow ache	( )	( )	( )	( )	( )	( )	( )
__ Dimming of vision	( )	( )	( )	( )	( )	( )	( )
__ Difficulty in focusing from near to far	( )	( )	( )	( )	( )	( )	( )
__ Dry eyes	( )	( )	( )	( )	( )	( )	( )
__ Trouble reading	( )	( )	( )	( )	( )	( )	( )
__ Trouble seeing at night	( )	( )	( )	( )	( )	( )	( )
__ Tearing	( )	( )	( )	( )	( )	( )	( )
__ None of these symptoms	( )	( )	( )	( )	( )	( )	( )

5. ***(Interviewer: Refer to Question #4 and read the following).*** I am again going to repeat the side-effects you just mentioned. For each side effect I mention, please tell me if you have been bothered by it: not at all, a little, some, quite a bit, very much so, or extremely so? ***(Interviewer: Place check under appropriate columns below)***

	Not at all	A little	Some	Quite a bit	Very much so	Extremely so
__ Burning/stinging in eyes	( )	( )	( )	( )	( )	( )
__ Redness in eyes	( )	( )	( )	( )	( )	( )
__ Blurred vision	( )	( )	( )	( )	( )	( )
__ Bitter taste	( )	( )	( )	( )	( )	( )
__ Unusual taste	( )	( )	( )	( )	( )	( )
__ Itchy eyes	( )	( )	( )	( )	( )	( )
__ Discharge from eyes	( )	( )	( )	( )	( )	( )
__ Swelling of eyelids	( )	( )	( )	( )	( )	( )
__ Brow ache	( )	( )	( )	( )	( )	( )
__ Dimming of vision	( )	( )	( )	( )	( )	( )
__ Difficulty in focusing from near to far	( )	( )	( )	( )	( )	( )
__ Dry eyes	( )	( )	( )	( )	( )	( )
__ Trouble reading	( )	( )	( )	( )	( )	( )
__ Trouble seeing at night	( )	( )	( )	( )	( )	( )
__ Tearing	( )	( )	( )	( )	( )	( )

6. During the past month has your quality of life been interfered with by these side effects: not at all, a little, some, quite a bit, very much so, or extremely so?

__ Not at all
__ A little
__ Some
__ Quite a bit
__ Very much so
__ Extremely so

7. ***(Interviewer*)**. I am now going to show you a list of activities you might do during a typical day. You may perform none, some, or all of these activities. For each one on the list, please tell me whether you perform it on a routine basis. ***(Interviewer: Hand***

respondent Card B with activities and check each activity below that is mentioned by respondent. Then circle those activities for each patient on Card B)

__ Driving during the day
__ Driving at night
__ Lifting or carrying groceries
__ Climbing 1 flight of stairs
__ Walking several blocks
__ Reading the newspaper
__ Reading other than the newspaper

8. ***(Interviewer:)*** I am now going to repeat each of the activities you just said you do routinely. For each one, please tell me if you were limited at all in performing each activity in the past month because of the **Treatment A regimen** (**fewer-drops regimen administered by the physician & patient).** That is, were you limited: not at all, a little, some, quite a bit, very much so, or extremely so? ***(Interviewer: Please check off under appropriate column below)***

		Not at all	A little	Some	Quite a bit	Very much so	Extremely so
__	Driving during day	( )	( )	( )	( )	( )	( )
__	Driving at night	( )	( )	( )	( )	( )	( )
__	Lifting or carrying groceries	( )	( )	( )	( )	( )	( )
__	Climbing 1 flight of stairs	( )	( )	( )	( )	( )	( )
__	Walking several blocks	( )	( )	( )	( )	( )	( )
__	Reading the newspaper	( )	( )	( )	( )	( )	( )
__	Reading other than the newspaper	( )	( )	( )	( )	( )	( )

9. If you were limited in performing any activities due to the **Treatment A regimen** (**fewer-drops physician & patient administered regimen)**, during the past month, has your quality of life been interfered with by these activity limitations: not at all, a little, some, quite a bit, very much so, or extremely so?

__ Not at all
__ A little
__ Some
__ Quite a bit
__ Very much so
__ Extremely so

Total Topical Eyedrop therapy patient-administered: Patient Reported Outcomes

10. ***(Interviewer: Read the following).*** I am going to read to you a list of various side effects that may occur in some patients who receive **Treatment B (self-administered total eyedrop therapy following ophthalmic surgery)**. You may have experienced none, some, or all these side effects during the past month. As I read the list, please tell me if you experienced that side effect. ***(Interviewer: Circle affirmative responses on the list below. Place a check under the column marked "I did not have the symptom" below for those symptoms not experienced by the patient. If patient experienced none of these side effects, please check "None of these symptoms" below and go to Question # 10).***

11. ***(Interviewer: Refer to Question #7 and read the following).*** I am now going to read to you the side-effects you said you experienced in the last question. For each side effect I mention, please tell me how frequently you experienced each side effect during the past month. ***(interviewer- hand respondent Card "A" with frequency scales.)*** That is, did you experience the side effect rarely, a few times, often, usually, almost always, or always? ***(Interviewer: Place check under appropriate column below for each circled side effect mentioned by respondent).***

	I Did Not Have the Symptom	Rarely	A Few Times	Fairly Often	Usually	Almost Always	Always
__ Burning/stinging in eyes	( )	( )	( )	( )	( )	( )	( )
__ Redness in eyes	( )	( )	( )	( )	( )	( )	( )
__ Blurred vision	( )	( )	( )	( )	( )	( )	( )
__ Bitter taste	( )	( )	( )	( )	( )	( )	( )
__ Unusual taste	( )	( )	( )	( )	( )	( )	( )
__ Itchy eyes	( )	( )	( )	( )	( )	( )	( )
__ Discharge from eyes	( )	( )	( )	( )	( )	( )	( )
__ Swelling of eyelids	( )	( )	( )	( )	( )	( )	( )
__ Brow ache	( )	( )	( )	( )	( )	( )	( )
__ Dimming of vision	( )	( )	( )	( )	( )	( )	( )
__ Difficulty in focusing from near to far	( )	( )	( )	( )	( )	( )	( )
__ Dry eyes	( )	( )	( )	( )	( )	( )	( )
__ Trouble reading	( )	( )	( )	( )	( )	( )	( )
__ Trouble seeing at night	( )	( )	( )	( )	( )	( )	( )
__ Tearing	( )	( )	( )	( )	( )	( )	( )
__ None of these symptoms	( )	( )	( )	( )	( )	( )	( )

12. ***(Interviewer: Refer to Question #7 and read the following).*** I am again going to repeat the side-effects you just mentioned. For each side effect I mention, please tell me if you have been bothered by it: not at all, a little, some, quite a bit, very much so, or extremely so? ***(Interviewer: Place check under appropriate columns below)***

	Not at all	A little	Some	Quite a bit	Very much so	Extremely so
__ Burning/stinging in eyes	( )	( )	( )	( )	( )	( )
__ Redness in eyes	( )	( )	( )	( )	( )	( )
__ Blurred vision	( )	( )	( )	( )	( )	( )
__ Bitter taste	( )	( )	( )	( )	( )	( )
__ Unusual taste	( )	( )	( )	( )	( )	( )
__ Itchy eyes	( )	( )	( )	( )	( )	( )
__ Discharge from eyes	( )	( )	( )	( )	( )	( )
__ Swelling of eyelids	( )	( )	( )	( )	( )	( )
__ Brow ache	( )	( )	( )	( )	( )	( )
__ Dimming of vision	( )	( )	( )	( )	( )	( )
__ Difficulty in focusing from near to far	( )	( )	( )	( )	( )	( )
__ Dry eyes	( )	( )	( )	( )	( )	( )
__ Trouble reading	( )	( )	( )	( )	( )	( )
__ Trouble seeing at night	( )	( )	( )	( )	( )	( )
__ Tearing	( )	( )	( )	( )	( )	( )

13. During the past month has your quality of life been interfered with by these side effects: not at all, a little, some, quite a bit, very much so, or extremely so?

__ Not at all
__ A little
__ Some
__ Quite a bit
__ Very much so
__ Extremely so

14. (Interviewer*).** I am now going to show you a list of activities you might do during a typical day. You may perform none, some, or all of these activities. For each one on the list, please tell me whether you perform it on a routine basis. ***(Interviewer: Hand respondent Card B with activities and check each activity below that is mentioned by respondent. Then circle those activities for each patient on Card B)

__ Driving during the day
__ Driving at night
__ Lifting or carrying groceries
__ Climbing 1 flight of stairs
__ Walking several blocks
__ Reading the newspaper
__ Reading other than the newspaper

15. (Interviewer:) I am now going to repeat each of the activities you just said you do routinely. For each one, please tell me if you were limited at all in performing each activity in the past month because of **Treatment B (total topical eyedrops you administered).** That is, were you limited: not at all, a little, some, quite a bit, very much so, or extremely so? ***(Interviewer: Please check off under appropriate column below)***

		Not at all	A little	Some	Quite a bit	Very much so	Extremely so
__	Driving during day	( )	( )	( )	( )	( )	( )
__	Driving at night	( )	( )	( )	( )	( )	( )
__	Lifting or carrying groceries	( )	( )	( )	( )	( )	( )
__	Climbing 1 flight of stairs	( )	( )	( )	( )	( )	( )
__	Walking several blocks	( )	( )	( )	( )	( )	( )
__	Reading the newspaper	( )	( )	( )	( )	( )	( )
__	Reading other than the newspaper	( )	( )	( )	( )	( )	( )

16. If you were limited in performing any activities due to **Treatment B (total topical eyedrops you administered),** during the past month, has your quality of life been interfered with by these activity limitations: not at all, a little, some, quite a bit, very much so, or extremely so?

__ Not at all

__ A little
__ Some
__ Quite a bit
__ Very much so
__ Extremely so

17. During the past month, how often did you miss **one or more doses of the eyedrop medication**?

__ I did not miss any doses
__ Rarely
__ A few times
__ Fairly often
__ Usually
__ Almost always
__ Always

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18. Overall, how satisfied, if at all, have you been **with the regimen you stated you preferred**? ***(Interviewer: Hand respondent Card C with satisfaction scales)*** Would you say you were totally satisfied, very satisfied, somewhat satisfied, somewhat dissatisfied, very dissatisfied or totally dissatisfied***? (Interviewer: Record only one response below)***

__ Totally satisfied
__ Very satisfied
__ Somewhat satisfied
__ Somewhat dissatisfied
__ Very dissatisfied
__ Totally dissatisfied

Thank respondent and terminate interview.

Signature of Interviewer Date

Card A

I did not have the symptom

Rarely

A few times

Fairly often

Usually

Almost always

Always

Card B

Driving during the day

Driving at night

Lifting or carrying groceries

Climbing 1 flight of stairs

Walking several blocks

Reading the newspaper

Reading other than the newspaper

Card C

Totally satisfied

Very satisfied

Somewhat satisfied

Somewhat dissatisfied

Very dissatisfied

Totally dissatisfied