Virginia Department of Health Professions
Board of Optometry

Perimeter Center
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September 14, 2020
Virtual Meeting
1:00 p.m.

Agenda

Virginia Board of Optometry
TPA-Formulary Committee Meeting

VIRTUAL MEETING

******Refer to Page 2 of the Agenda for Meeting Access Information******

Call to Order – Fred E. Goldberg, O.D., Chair
- Welcome and Roll Call
- Introductions

Ordering of Agenda – Dr. Goldberg

Public Comment – Dr. Dr. Goldberg
The Board will receive all public comment related to agenda items at this time. The Board will not receive comment on any regulatory process for which a public comment period has closed or any pending or closed complaint or disciplinary matter. **(See instructions on page 2 for providing public comment during virtual meeting.)**

Discussion Items – Leslie Knachel/Elaine Yeatts **Pages 1-34**
- Review of 18VAC105-20-47(2) Therapeutic Pharmaceutical Agents, Topically Administered Schedule VI Agents

Next Steps – Dr. Goldberg

Meeting Adjournment – Dr. Goldberg

This information is in **DRAFT** form and is subject to change.

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Instructions for Accessing September 14, 2020 Virtual Full Board Meeting and Providing Public Comment

- **Access:** Perimeter Center building access remains restricted to the public due to the COVID-19 pandemic. To observe this virtual meeting, use one of the joining options below. Participation capacity is limited and is on a first come, first serve basis due to the capacity of CISCO WebEx technology.
- **Written Public Comment**: Written comments are **strongly preferred** due to the limits of the electronic meeting platform and should be submitted by email to leslie.knachel@dhp.virginia.gov no later than 12:00 noon on Friday, September 11, 2020. The written comments will be made available to the committee members for review prior to the meeting.
- **Oral Public Comment**: Oral comments will be received during the committee meeting from persons who have submitted an email to leslie.knachel@dhp.virginia.gov no later than 12:00 noon on Friday, September 11, 2020, indicating they wish to offer oral comment at the committee meeting. Comment may be offered by these individuals when their names are announced by the meeting chair.
- Public participation connections will be muted following the public comment periods.
- Should the Board enter into a closed session, public participants will be blocked from seeing and hearing the discussion. When the Committee re-enters into open session, public participation connections to see and hear the board meeting will be restored.
- Please call from a location without background noise.
- Dial (804) 597-4129 to report an interruption during the broadcast.
- FOIA Council *Electronic Meetings Public Comment* form for submitting feedback on this electronic meeting may be accessed at http://foiacouncil.dls.virginia.gov/sample%20letters/welcome.htm.

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BOARD OF OPTOMETRY
VIRTUAL FULL BOARD MEETING
JULY 17, 2020

TIME AND PLACE:	The Virginia Board of Optometry (Board) meeting was called to order at 9:01 a.m.
PRESIDING OFFICER:	Fred E. Goldberg, O.D. President (On-Site)
MEMBERS PARTICIPATING ON-SITE:	Steven A. Linas, O.D.
MEMBERS PARTICIPATING VIRTUALLY:	Lisa Wallace-Davis, O.D. Vice-President Devon Cabot, Citizen Member Helene Clayton-Jeter, O.D. Clifford A. Roffis, O.D.
MEMBERS NOT PRESENT:	All Members were present.
STAFF PRESENT ON-SITE:	Leslie L. Knachel, Executive Director Kelli Moss, Deputy Executive Director Celia Wilson, Administrative Assistant Matt Treacy, Media Production Specialist
STAFF PARTICIPATING VIRTUALLY:	David Brown, D.C., Agency Director Charis Mitchell, Assistant Attorney General, Board Counsel Elaine Yeatts, Senior Policy Analyst Barbara Allison-Bryan, M.D., Agency Deputy Director Anthony C. Morales, Operations Manager Tamara Farmer, Administrative Assistant Yetty Shobo, Deputy Executive Director, Healthcare Workforce Data Center Me-Lien Chung, Discipline Case Specialist
OTHERS PRESENT:	Bo Keeney, Virginia Optometric Association Christine Markus, King and Spalding, LLC Robert Bohannon
CALL TO ORDER QUORUM	Dr. Goldberg welcomed attendees and requested that Ms. Knachel take a roll call of the board members present. With six members of the Board present, a quorum was established. Ms. Knachel introduced new staff member, Me-Lien Chung, Disciplinary Case Specialist. Dr. Goldberg read the Board's mission statement.
ORDERING OF AGENDA:	There were no changes to the agenda
PUBLIC COMMENT:	There was no public comment.
APPROVAL OF MINUTES:	Dr. Linas moved to approve the meeting minutes for the February 7, 2020 - Full Board Meeting.

The motion was properly seconded. A roll call vote was taken. The motion carried with an unanimous aye vote.

DIRECTOR'S REPORT:

Dr. Brown reported on agency measures to ensure the safety of agency staff and other individuals in the building during the COVID-19 pandemic and to keep the boards functioning in a telework environment.

LEGISLATIVE/REGULATORY UPATE:

2020 Legislative/Regulatory Update

Ms. Yeatts presented the following information to the Board:

- 2020 legislative session overview
- Consideration of Board recommendation for resubmission of clean-up bill for Chapter 32, Optometry Law.

  The Board discussed the need for the proposed legislation.

  Ms. Cabot moved to resubmit the proposed legislation as presented for the 2021 legislative session..

  The motion was properly seconded. A roll call vote was taken.

  The motion carried with an unanimous aye vote.

- HB 967 – Consideration of any waiver of experience requirements for the spouse of an active duty military or veteran

  The Board discussed the options for addressing the waiver.

  Dr. Linas moved to delegate decisions related to waiver requests to be handled on a case-by case basis by the Executive Director in consultation with the Board's President.

  The motion was properly seconded. A roll call vote was taken.

  The motion carried with an unanimous aye vote.

  Dr. Linas requested that legislation related to sending an email to notify patients of transfer or medical records when closing or relocating. Ms. Yeatts indicated that this applied to all boards within DHP and consideration would be given for resubmission.

- Regulations for E-prescribing waiver is under view by the administration.
- Repeal of regulations for Professional Designation is under review by administration.
- Regulations for handling fees became effective on 03/05/2020
- Regulations for inactive licenses became effective on 03/04/2020
- Petition for Rulemaking – Consideration of Haine petition to restrict number of contact lenses per prescription.

  The Board discussed the petition.

Ms. Cabot moved to reject the petition for rulemaking because the Board concurred with the comment from the National Association of Optometrists and Opticians that it is contrary to the spirit of Federal Trade Commission law and rules and the regulation would be very difficult to monitor or enforce.

The motion was properly seconded. A roll call vote was taken.

The motion carried with an unanimous aye vote.

- Federal Contact Lens Rule amendments are in process of being finalized, but are not yet effective. Once effective the Board may need to take regulatory action to include the changes. This topic will be included on the agenda for the next board meeting.

DISCUSSION ITEMS:

Healthcare Workforce Data Center (HWDC) Presentation
Dr. Shobo presented the results of the HWDC's 2020 survey of Virginia's optometrists.

Dr. Clayton-Jeter moved to accept the HWDC data as presented by Dr. Shobo.

The motion was properly seconded. A roll call vote was taken.

The motion carried with an unanimous aye vote.

Continuing Education (CE)
Ms. Knachel requested that the Board consider not conducting a CE audit of licensees for the licensure period of January 1, 2019 – March 31, 2020, so that staff resources could be focused on the current discipline caseload.

Dr. Linas moved to not conduct a CE audit of licensees for the licensure period of January 1, 2019 – March 31, 2020.

The motion was properly seconded. A roll call vote was taken.

The motion carried with an unanimous aye vote.

Ms. Knachel stated that she has received numerous inquiries about whether the Board will change any of its current CE requirements because of the COVID-19 pandemic. The consensus of the Board is that it is too early in the licensure period to make changes and there are opportunities for licensees to attend online courses where the licensee and the lecturer may communicate with one another as required by the regulations.

No action was initiated at this time, but the Board asked for this issue to be placed on the next agenda for further consideration.

Ms. Knachel presented a draft Telepractice Guidance Document for the Board's consideration.

The Board discussed the guidance document.

Dr. Wallace-Davis moved to accept the guidance document as submitted.

The motion was properly seconded. A roll call vote was taken.

The motion carried with an unanimous aye vote.

BOARD COUNSEL REPORT: Ms. Mitchell provided a general update of the Attorney General's office and the effects of the pandemic.

PRESIDENT'S REPORT: Dr. Goldberg reported provided a report on the effects of the pandemic on optometry practice. Additionally, he provided comments on attending the Association of Regulatory Boards of Optometry's virtual meeting.

BOARD OF HEALTH PROFESSION'S REPORT: Dr. Clayton-Jeter reported the activities of the Board of Health Professions.

ASSOCIATION OF REGULATORY BOARDS ANNUAL MEETING REPORT: Dr. Goldberg included his comments during the President's Report.

STAFF REPORTS:

Executive Director's Report

Ms. Knachel reported on the following:

- Licensee Statistics
- E-Prescribing Waiver Requests
- Outreach activities
- Updated licensing forms
- Board calendar for 2021

Discipline Report

Ms. Moss provided an overview of the discipline caseload.

NEW BUSINESS:

Elections

Dr. Goldberg asked for nominations for President of the Board.

Dr. Linas moved to nominate Dr. Goldberg for President.

The motion was properly seconded. No other nominations were received. A roll call vote was taken.

The motion carried with an unanimous aye vote.

Dr. Goldberg asked for nominations for Vice-President of the Board.

Dr. Wallace-Davis moved to nominate Ms. Cabot for Vice-President.

The motion was properly seconded. No other nominations were received. A roll call vote was taken.

The motion carried with an unanimous aye vote.

Dr. Goldberg asked if there was any other new business. Ms. Knachel requested the Board consider an inquiry that was received the day before the meeting regarding a newly approved drug named UPneeq. The Board discussed whether this drug could be prescribe under current regulations. Ms. Mitchell indicated that there is a statutory process to determine what is included in the TPA-Formulary and following this process will allow for adequate research and public comment. Ms. Knachel asked the Board to consider convening the TPA-Formulary Committee to review the drug and make recommendations to the Board.

The Board discussed the issue.

Dr. Clayton-Jeter moved to convene the TPA-Formulary Committee to review the existing structure of the formulary. The motion was not seconded. After further discussion, Dr. Clayton-Jeter withdrew her previous motion.

Dr. Clayton-Jeter moved to convene the TPA-Formulary Committee to review 18VAC105-20-47(A)(2), Topically Administered Schedule VI Agents, of the regulations and make recommendations to the Board at its next meeting.

The motion was properly seconded. A roll call vote was taken. The motion carried with an unanimous aye vote.

NEXT MEETING: Dr. Goldberg stated that the next board meeting is scheduled for October 16, 2020.

ADJOURNMENT: The meeting adjourned at 12:08 p.m.

_____
Fred Goldberg, O.D.
Chair

_____
Leslie L. Knachel, M.P.H.
Executive Director

Regulations of the Virginia Board of Optometry

18VAC105-20-46. Treatment guidelines for TPA certified optometrists.

A. TPA-certified optometrists may treat diseases and abnormal conditions of the human eye and its adnexa which may be treated with medically appropriate pharmaceutical agents as referenced in 18VAC105-20-47. The adnexa is defined as conjoined, subordinate or immediately associated anatomic parts of the human eye, including eyelids and eyebrows.

B. In addition, the following may be treated:

1. Glaucoma (excluding the treatment of congenital and infantile glaucoma). Treatment of angle closure shall follow the definition and protocol prescribed in subsection C of this section.

2. Ocular-related post-operative care in cooperation with patient's surgeon.

3. Ocular trauma to the above tissues as in subsection A of this section.

4. Uveitis.

5. Anaphylactic shock (limited to the administration of intramuscular epinephrine).

C. The definition and protocol for treatment of angle closure glaucoma shall be as follows:

1. As used in this chapter, angle closure glaucoma shall mean a closed angle in the involved eye with significantly increased intraocular pressure, and corneal microcystic edema.

2. Treatment shall be limited to the initiation of immediate emergency care with appropriate pharmaceutical agents as prescribed by this chapter;

3. Once the diagnosis of angle closure glaucoma has been established by the optometrist, the ophthalmologist to whom the patient is to be referred should be contacted immediately;

4. If there are no medical contraindications, an oral osmotic agent may be administered as well as an oral carbonic anhydrase inhibitor and any other medically accepted, Schedule III, IV or VI, oral antiglaucomic agent as may become available; and

5. Proper topical medications as appropriate may also be administered by the optometrist.

D. An oral Schedule VI immunosuppressive agent shall only be used when 1) the condition fails to appropriately respond to any other treatment regimen; 2) such agent is prescribed in consultation with a physician; and 3) treatment with such agent includes monitoring of systemic effects.

18VAC105-20-47. Therapeutic pharmaceutical agents.

A. A TPA-certified optometrist, acting within the scope of his practice, may procure, administer and prescribe medically appropriate therapeutic pharmaceutical agents (or any therapeutically appropriate combination thereof) to treat diseases and abnormal conditions of the human eye and its adnexa within the following categories:

1. Oral analgesics - Schedule II controlled substances consisting of hydrocodone in combination with acetaminophen and Schedule III, IV and VI narcotic and nonnarcotic agents.

2. Topically administered Schedule VI agents:

a. Alpha-adrenergic blocking agents;

b. Anesthetic (including esters and amides);

c. Anti-allergy (including antihistamines and mast cell stabilizers);

d. Anti-fungal;

e. Anti-glaucoma (including carbonic anhydrase inhibitors and hyperosmotics);

f. Anti-infective (including antibiotics and antivirals);

g. Anti-inflammatory;

h. Cycloplegics and mydriatics;

i. Decongestants; and

j. Immunosuppressive agents.

3. Orally administered Schedule VI agents:

a. Aminocaproic acids (including antifibrinolytic agents);

b. Anti-allergy (including antihistamines and leukotriene inhibitors);

c. Anti-fungal;

d. Anti-glaucoma (including carbonic anhydrase inhibitors and hyperosmotics);

e. Anti-infective (including antibiotics and antivirals);

f. Anti-inflammatory (including steroidal and nonsteroidal);

g. Decongestants; and

h. Immunosuppressive agents.

B. Schedule I, II and V drugs are excluded from the list of therapeutic pharmaceutical agents.

C. Over-the-counter topical and oral medications for the treatment of the eye and its adnexa may be procured for administration, administered, prescribed or dispensed.

Optometry Specific Statutes

§ 54.1-3222. TPA certification; certification for treatment of diseases or abnormal conditions with therapeutic pharmaceutical agents.

A. The Board shall certify an optometrist to prescribe for and treat diseases or abnormal conditions of the human eye and its adnexa with therapeutic pharmaceutical agents (TPAs), if the optometrist files a written application, accompanied by the fee required by the Board and satisfactory proof that the applicant:

1. Is licensed by the Board as an optometrist and certified to administer diagnostic pharmaceutical agents pursuant to Article 4 (§ 54.1-3220 et seq.);

2. Has satisfactorily completed such didactic and clinical training programs for the treatment of diseases and abnormal conditions of the eye and its adnexa as are determined, after consultation with a school or college of optometry and a school of medicine, to be reasonable and necessary by the Board to ensure an appropriate standard of medical care for patients; and

3. Passes such examinations as are determined to be reasonable and necessary by the Board to ensure an appropriate standard of medical care for patients.

B. TPA certification shall enable an optometrist to prescribe and administer, within his scope of practice, Schedule II controlled substances consisting of hydrocodone in combination with acetaminophen and Schedules III through VI controlled substances and devices as set forth in the Drug Control Act (§ 54.1-3400 et seq.) to treat diseases and abnormal conditions of the human eye and its adnexa as determined by the Board, within the following conditions:

1. Treatment with oral therapeutic pharmaceutical agents shall be limited to (i) analgesics included on Schedule II controlled substances as defined in § 54.1-3448 of the Drug Control Act (§ 54.1-3400 et seq.) consisting of hydrocodone in combination with acetaminophen, and analgesics included on Schedules III through VI, as defined in §§ 54.1-3450 and 54.1-3455 of the Drug Control Act, which are appropriate to alleviate ocular pain and (ii) other Schedule VI controlled substances as defined in § 54.1-3455 of the Drug Control Act appropriate to treat diseases and abnormal conditions of the human eye and its adnexa.

2. Therapeutic pharmaceutical agents shall include topically applied Schedule VI drugs as defined in § 54.1-3455 of the Drug Control Act (§ 54.1-3400 et seq.).

3. Administration of therapeutic pharmaceutical agents by injection shall be limited to the treatment of chalazia by means of injection of a steroid included in Schedule VI controlled substances as set forth in § 54.1-3455 of the Drug Control Act (§ 54.1-3400 et seq.). A TPA-certified optometrist shall provide written evidence to the Board that he has completed a didactic and clinical training course provided by an accredited school or college of optometry that includes training in administration of TPAs by injection prior to administering TPAs by injection pursuant to this subdivision.

4. Treatment of angle closure glaucoma shall be limited to initiation of immediate emergency care.

5. Treatment of infantile or congenital glaucoma shall be prohibited.

6. Treatment through surgery or other invasive modalities shall not be permitted, except as provided in subdivision 3 or for treatment of emergency cases of anaphylactic shock with intramuscular epinephrine.

7. Entities permitted or licensed by the Board of Pharmacy to distribute or dispense drugs, including, but not limited to, wholesale distributors and pharmacists, shall be authorized to supply TPA-certified optometrists with those therapeutic pharmaceutical agents specified by the Board on the TPA-Formulary.

1996, cc. 152, 158; 2004, c. 744; 2015, c. 355; 2018, c. 280.

§ 54.1-3223. Regulations relating to instruction and training, examination, and therapeutic pharmaceutical agents.

A. The Board shall promulgate such regulations governing the treatment of diseases and abnormal conditions of the human eye and its adnexa with therapeutic pharmaceutical agents by TPA-certified optometrists as are reasonable and necessary to ensure an appropriate standard of medical care for patients, including, but not limited to, determinations of the diseases and abnormal conditions of the human eye and its adnexa that may be treated by TPA-certified optometrists, treatment guidelines, and the drugs specified on the TPA-Formulary.

In establishing standards of instruction and training, the Board shall consult with a school or college of optometry and a school or college of medicine and shall set a minimum number of hours of clinical training to be supervised by an ophthalmologist. The didactic and clinical training programs may include, but need not be limited to, programs offered or designed either by schools of medicine or schools or colleges of optometry or both or some combination thereof.

The Board may prepare, administer, and grade appropriate examinations for the certification of optometrists to administer therapeutic pharmaceutical agents or may contract with a school of medicine, school or college of optometry, or other institution or entity to develop, administer, and grade the examinations.

In order to maintain a current and appropriate list of therapeutic pharmaceuticals on the TPA-Formulary, current and appropriate treatment guidelines, and current and appropriate determinations of diseases and abnormal conditions of the eye and its adnexa that may be treated by TPA-certified optometrists, the Board may, from time to time, amend such regulations. Such regulations shall be exempt from the requirements of the Administrative Process Act (§ 2.2-4000 et seq.), except to any extent that they may be specifically made subject to §§ 2.2-4024, 2.2-4030, and 2.2-4031; the Board's regulations shall, however, comply with § 2.2-4103 of the Virginia Register Act (§ 2.2-4100 et seq.). The Board shall, however, conduct a public hearing prior to making amendments to the TPA-Formulary, the treatment guidelines or the

determinations of diseases and abnormal conditions of the eye and its adnexa that may be treated by TPA-certified optometrists. Thirty days prior to conducting such hearing, the Board shall give written notice by mail of the date, time, and place of the hearing to all currently TPA-certified optometrists and any other persons requesting to be notified of the hearings and publish notice of its intention to amend the list in the Virginia Register of Regulations. During the public hearing, interested parties shall be given reasonable opportunity to be heard and present information prior to final adoption of any TPA-Formulary amendments. Proposed and final amendments of the list shall also be published, pursuant to § 2.2-4031, in the Virginia Register of Regulations. Final amendments to the TPA-Formulary shall become effective upon filing with the Registrar of Regulations. The TPA-Formulary shall be the inclusive list of the therapeutic pharmaceutical agents that a TPA-certified optometrist may prescribe.

B. To assist in the specification of the TPA-Formulary, there shall be a seven-member TPA-Formulary Committee, as follows: three Virginia TPA-certified optometrists to be appointed by the Board of Optometry, one pharmacist appointed by the Board of Pharmacy from among its licensees, two ophthalmologists appointed by the Board of Medicine from among its licensees, and the chairman who shall be appointed by the Board of Optometry from among its members. The ophthalmologists appointed by the Board of Medicine shall have demonstrated, through professional experience, knowledge of the optometric profession. In the event the Board of Pharmacy or the Board of Medicine fails to make appointments to the TPA-Formulary Committee within 30 days following the Board of Optometry's requesting such appointments, or within 30 days following any subsequent vacancy, the Board of Optometry shall appoint such members.

The TPA-Formulary Committee shall recommend to the Board those therapeutic pharmaceutical agents to be included on the TPA-Formulary for the treatment of diseases and abnormal conditions of the eye and its adnexa by TPA-certified optometrists.

(1996, cc. 152, 158; 2004, c. 744.)

§ 54.1-3224. Denial, etc., of TPA certification; disciplinary actions; summary suspension under certain circumstances.

A. The Board of Optometry may deny, refuse to renew, revoke, or suspend any TPA-certificate issued to a TPA-certified optometrist, or applied for by a licensed optometrist in accordance with the provisions of this article, or may discipline or reprimand any certificate holder for violations of this chapter or the Board's regulations.

B. The Board may take action summarily to suspend a TPA-certified optometrist's certification under this section by means of a telephone conference call if, in the opinion of a majority of the Board, (i) a good faith effort to convene a regular meeting of the Board has failed and (ii) there is an imminent danger to the public health or safety which warrants this action.

(1996, cc. 152, 158.)

Drug Laws as of July 1, 2020

§ 54.1-3301. Exceptions.

This chapter shall not be construed to:

2. Prevent any legally qualified practitioner of dentistry, or veterinary medicine or any prescriber, as defined in § 54.1-3401, acting on behalf of the Virginia Department of Health or local health departments, from administering or supplying to his patients the medicines that he deems proper under the conditions of § 54.1-3303 or from causing drugs to be administered or dispensed pursuant to §§ 32.1-42.1 and 54.1-3408, except that a veterinarian shall only be authorized to dispense a compounded drug, distributed from a pharmacy, when (i) the animal is his own patient, (ii) the animal is a companion animal as defined in regulations promulgated by the Board of Veterinary Medicine, (iii) the quantity dispensed is no more than a seven-day supply, (iv) the compounded drug is for the treatment of an emergency condition, and (v) timely access to a compounding pharmacy is not available, as determined by the prescribing veterinarian;

7. Interfere with any legally qualified practitioner of optometry, certified or licensed to use diagnostic pharmaceutical agents, from purchasing, possessing or administering those controlled substances as specified in § 54.1-3221 or interfere with any legally qualified practitioner of optometry certified to prescribe therapeutic pharmaceutical agents from purchasing, possessing, or administering to his own patients those controlled substances as specified in § 54.1-3222 and the TPA formulary, providing manufacturers' samples of these drugs to his own patients, or dispensing, administering, or selling ophthalmic devices as authorized in § 54.1-3204;

This section shall not be construed as exempting any person from the licensure, registration, permitting and record keeping requirements of this chapter or Chapter 34 of this title.

§ 54.1-3303. Prescriptions to be issued and drugs to be dispensed for medical or therapeutic purposes only.

A. A prescription for a controlled substance may be issued only by a practitioner of medicine, osteopathy, podiatry, dentistry or veterinary medicine who is authorized to prescribe controlled substances, or by a licensed nurse practitioner pursuant to § 54.1-2957.01, a licensed physician assistant pursuant to § 54.1-2952.1, or a TPA-certified optometrist pursuant to Article 5 (§ 54.1-3222 et seq.) of Chapter 32.

B. A prescription shall be issued only to persons or animals with whom the practitioner has a bona fide practitioner-patient relationship or veterinarian-client-patient relationship. If a practitioner is providing expedited partner therapy consistent with the recommendations of the Centers for Disease Control and Prevention, then a bona fide practitioner-patient relationship shall not be required.

A bona fide practitioner-patient relationship shall exist if the practitioner has (i) obtained or caused to be obtained a medical or drug history of the patient; (ii) provided information to the patient about the benefits and risks of the drug being prescribed; (iii) performed or caused to be performed an appropriate examination of the patient, either physically or by the use of

instrumentation and diagnostic equipment through which images and medical records may be transmitted electronically; and (iv) initiated additional interventions and follow-up care, if necessary, especially if a prescribed drug may have serious side effects. Except in cases involving a medical emergency, the examination required pursuant to clause (iii) shall be performed by the practitioner prescribing the controlled substance, a practitioner who practices in the same group as the practitioner prescribing the controlled substance, or a consulting practitioner.

A practitioner who has established a bona fide practitioner-patient relationship with a patient in accordance with the provisions of this subsection may prescribe Schedule II through VI controlled substances to that patient, provided that, in cases in which the practitioner has performed the examination required pursuant to clause (iii) by use of instrumentation and diagnostic equipment through which images and medical records may be transmitted electronically, the prescribing of such Schedule II through V controlled substance is in compliance with federal requirements for the practice of telemedicine.

For the purpose of prescribing a Schedule VI controlled substance to a patient via telemedicine services as defined in § 38.2-3418.16, a prescriber may establish a bona fide practitioner-patient relationship by an examination through face-to-face interactive, two-way, real-time communications services or store-and-forward technologies when all of the following conditions are met: (a) the patient has provided a medical history that is available for review by the prescriber; (b) the prescriber obtains an updated medical history at the time of prescribing; (c) the prescriber makes a diagnosis at the time of prescribing; (d) the prescriber conforms to the standard of care expected of in-person care as appropriate to the patient's age and presenting condition, including when the standard of care requires the use of diagnostic testing and performance of a physical examination, which may be carried out through the use of peripheral devices appropriate to the patient's condition; (e) the prescriber is actively licensed in the Commonwealth and authorized to prescribe; (f) if the patient is a member or enrollee of a health plan or carrier, the prescriber has been credentialed by the health plan or carrier as a participating provider and the diagnosing and prescribing meets the qualifications for reimbursement by the health plan or carrier pursuant to § 38.2-3418.16; and (g) upon request, the prescriber provides patient records in a timely manner in accordance with the provisions of § 32.1-127.1:03 and all other state and federal laws and regulations. Nothing in this paragraph shall permit a prescriber to establish a bona fide practitioner-patient relationship for the purpose of prescribing a Schedule VI controlled substance when the standard of care dictates that an in-person physical examination is necessary for diagnosis. Nothing in this paragraph shall apply to: (1) a prescriber providing on-call coverage per an agreement with another prescriber or his prescriber's professional entity or employer; (2) a prescriber consulting with another prescriber regarding a patient's care; or (3) orders of prescribers for hospital out-patients or in-patients.

For purposes of this section, a bona fide veterinarian-client-patient relationship is one in which a veterinarian, another veterinarian within the group in which he practices, or a veterinarian with whom he is consulting has assumed the responsibility for making medical judgments regarding the health of and providing medical treatment to an animal as defined in § 3.2-6500, other than an equine as defined in § 3.2-6200, a group of agricultural animals as defined in § 3.2-6500, or bees as defined in § 3.2-4400, and a client who is the owner or other caretaker of the animal, group of agricultural animals, or bees has consented to such treatment and agreed to follow the

instructions of the veterinarian. Evidence that a veterinarian has assumed responsibility for making medical judgments regarding the health of and providing medical treatment to an animal, group of agricultural animals, or bees shall include evidence that the veterinarian (A) has sufficient knowledge of the animal, group of agricultural animals, or bees to provide a general or preliminary diagnosis of the medical condition of the animal, group of agricultural animals, or bees; (B) has made an examination of the animal, group of agricultural animals, or bees, either physically or by the use of instrumentation and diagnostic equipment through which images and medical records may be transmitted electronically or has become familiar with the care and keeping of that species of animal or bee on the premises of the client, including other premises within the same operation or production system of the client, through medically appropriate and timely visits to the premises at which the animal, group of agricultural animals, or bees are kept; and (C) is available to provide follow-up care.

C. A prescription shall only be issued for a medicinal or therapeutic purpose in the usual course of treatment or for authorized research. A prescription not issued in the usual course of treatment or for authorized research is not a valid prescription. A practitioner who prescribes any controlled substance with the knowledge that the controlled substance will be used otherwise than for medicinal or therapeutic purposes shall be subject to the criminal penalties provided in § 18.2-248 for violations of the provisions of law relating to the distribution or possession of controlled substances.

D. No prescription shall be filled unless a bona fide practitioner-patient-pharmacist relationship exists. A bona fide practitioner-patient-pharmacist relationship shall exist in cases in which a practitioner prescribes, and a pharmacist dispenses, controlled substances in good faith to a patient for a medicinal or therapeutic purpose within the course of his professional practice.

In cases in which it is not clear to a pharmacist that a bona fide practitioner-patient relationship exists between a prescriber and a patient, a pharmacist shall contact the prescribing practitioner or his agent and verify the identity of the patient and name and quantity of the drug prescribed.

Any person knowingly filling an invalid prescription shall be subject to the criminal penalties provided in § 18.2-248 for violations of the provisions of law relating to the sale, distribution or possession of controlled substances.

E. Notwithstanding any provision of law to the contrary and consistent with recommendations of the Centers for Disease Control and Prevention or the Department of Health, a practitioner may prescribe Schedule VI antibiotics and antiviral agents to other persons in close contact with a diagnosed patient when (i) the practitioner meets all requirements of a bona fide practitioner-patient relationship, as defined in subsection B, with the diagnosed patient and (ii) in the practitioner's professional judgment, the practitioner deems there is urgency to begin treatment to prevent the transmission of a communicable disease. In cases in which the practitioner is an employee of or contracted by the Department of Health or a local health department, the bona fide practitioner-patient relationship with the diagnosed patient, as required by clause (i), shall not be required.

F. A pharmacist may dispense a controlled substance pursuant to a prescription of an out-of-state practitioner of medicine, osteopathy, podiatry, dentistry, optometry, or veterinary medicine, a

nurse practitioner, or a physician assistant authorized to issue such prescription if the prescription complies with the requirements of this chapter and the Drug Control Act (§ 54.1-3400 et seq.).

I. A TPA-certified optometrist who is authorized to prescribe controlled substances pursuant to Article 5 (§ 54.1-3222 et seq.) of Chapter 32 may issue prescriptions in good faith or provide manufacturers' professional samples to his patients for medicinal or therapeutic purposes within the scope of his professional practice for the drugs specified on the TPA-Formulary, established pursuant to § 54.1-3223, which shall be limited to (i) analgesics included on Schedule II controlled substances as defined in § 54.1-3448 of the Drug Control Act (§ 54.1-3400 et seq.) consisting of hydrocodone in combination with acetaminophen; (ii) oral analgesics included in Schedules III through VI, as defined in §§ 54.1-3450 and 54.1-3455 of the Drug Control Act (§ 54.1-3400 et seq.), which are appropriate to relieve ocular pain; (iii) other oral Schedule VI controlled substances, as defined in § 54.1-3455 of the Drug Control Act, appropriate to treat diseases and abnormal conditions of the human eye and its adnexa; (iv) topically applied Schedule VI drugs, as defined in § 54.1-3455 of the Drug Control Act; and (v) intramuscular administration of epinephrine for treatment of emergency cases of anaphylactic shock.

§ 54.1-3401. Definitions.

As used in this chapter, unless the context requires a different meaning:

"Practitioner" means a physician, dentist, licensed nurse practitioner pursuant to § 54.1-2957.01, licensed physician assistant pursuant to § 54.1-2952.1, pharmacist pursuant to § 54.1-3300, TPA-certified optometrist pursuant to Article 5 (§ 54.1-3222 et seq.) of Chapter 32, veterinarian, scientific investigator, or other person licensed, registered, or otherwise permitted to distribute, dispense, prescribe and administer, or conduct research with respect to a controlled substance in the course of professional practice or research in the Commonwealth.

§ 54.1-3408. Professional use by practitioners.

A. A practitioner of medicine, osteopathy, podiatry, dentistry, or veterinary medicine or a licensed nurse practitioner pursuant to § 54.1-2957.01, a licensed physician assistant pursuant to § 54.1-2952.1, or a TPA-certified optometrist pursuant to Article 5 (§ 54.1-3222 et seq.) of Chapter 32 shall only prescribe, dispense, or administer controlled substances in good faith for medicinal or therapeutic purposes within the course of his professional practice.

R. This section shall not interfere with any prescriber issuing prescriptions in compliance with his authority and scope of practice and the provisions of this section to a Board agent for use pursuant to subsection G of § 18.2-258.1. Such prescriptions issued by such prescriber shall be deemed to be valid prescriptions.

§ 54.1-3455. Schedule VI.

The following classes of drugs and devices shall be controlled by Schedule VI:

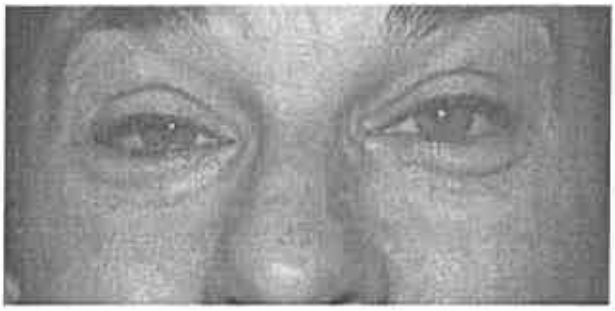
1. Any compound, mixture, or preparation containing any stimulant or depressant drug exempted from Schedules III, IV or V and designated by the Board as subject to this section.

2. Every drug, not included in Schedules I, II, III, IV or V, or device, which because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not generally recognized among experts qualified by scientific training and experience to evaluate its safety and efficacy as safe for use except by or under the supervision of a practitioner licensed to prescribe or administer such drug or device.

3. Any drug, not included in Schedules I, II, III, IV or V, required by federal law to bear on its label prior to dispensing, at a minimum, the symbol "Rx only," or which bears the legend "Caution: Federal Law Prohibits Dispensing Without Prescription" or "Caution: Federal Law Restricts This Drug To Use By Or On The Order Of A Veterinarian" or any device which bears the legend "Caution: Federal Law Restricts This Device To Sales By Or On The Order Of A _____." (The blank should be completed with the word "Physician," "Dentist," "Veterinarian," or with the professional designation of any other practitioner licensed to use or order such device.)

Eye Health / Eye Health A-Z

What Is Ptosis?



Leer en Español: ¿Qué Es la Ptosis?

Written By: Stephen N Lipsky MD
Reviewed By: Kierstan Boyd
Oct. 29, 2019

Ptosis is when the upper eyelid droops over the eye. The eyelid may droop just a little, or so much that it covers the pupil (the black dot at the center of your eye that lets light in). Ptosis can limit or even completely block normal vision.

Children and adults can have ptosis. Fortunately, this condition can be treated to improve vision as well as appearance.

Ptosis in children

Children born with ptosis have what is called congenital ptosis. This can be caused by problems with the muscle that lifts the eyelid (called the levator muscle).

The most obvious sign of ptosis is a drooping eyelid. Another sign is when the upper eyelid creases do not line up evenly with each other. A child with ptosis may tip their head back, lift up their chin, or raise their eyebrows to try to see better. Over time, these movements can cause head and neck problems.

Sometimes, a child born with ptosis can also have other eye-related problems. They can include eye movement issues, eye muscle disease, tumors (on the eyelid or elsewhere) and other problems.

Having ptosis puts a child at risk for vision problems. If the child's eyelid droops so much that it blocks vision, amblyopia (also called "lazy eye") can develop. One eye will have better vision than the other. A child with ptosis can also have astigmatism, where they see blurry images. The child may also develop misaligned (crossed) eyes.

Ptosis in adults

Adults get ptosis (called involutional ptosis) when the levator muscle stretches or separates away from their eyelid. This can be caused by aging or an eye injury. Sometimes ptosis happens as a side effect after certain eye surgery. Rarely, diseases or tumors can affect the eyelid muscle, causing ptosis.

Your ophthalmologist will find the cause of your ptosis in order to recommend treatment. They will do a complete eye exam, and may also want you to have blood tests and imaging tests. The ophthalmologist will likely recommend surgery to help the eyelid muscle work better.

Ptosis treatment for children

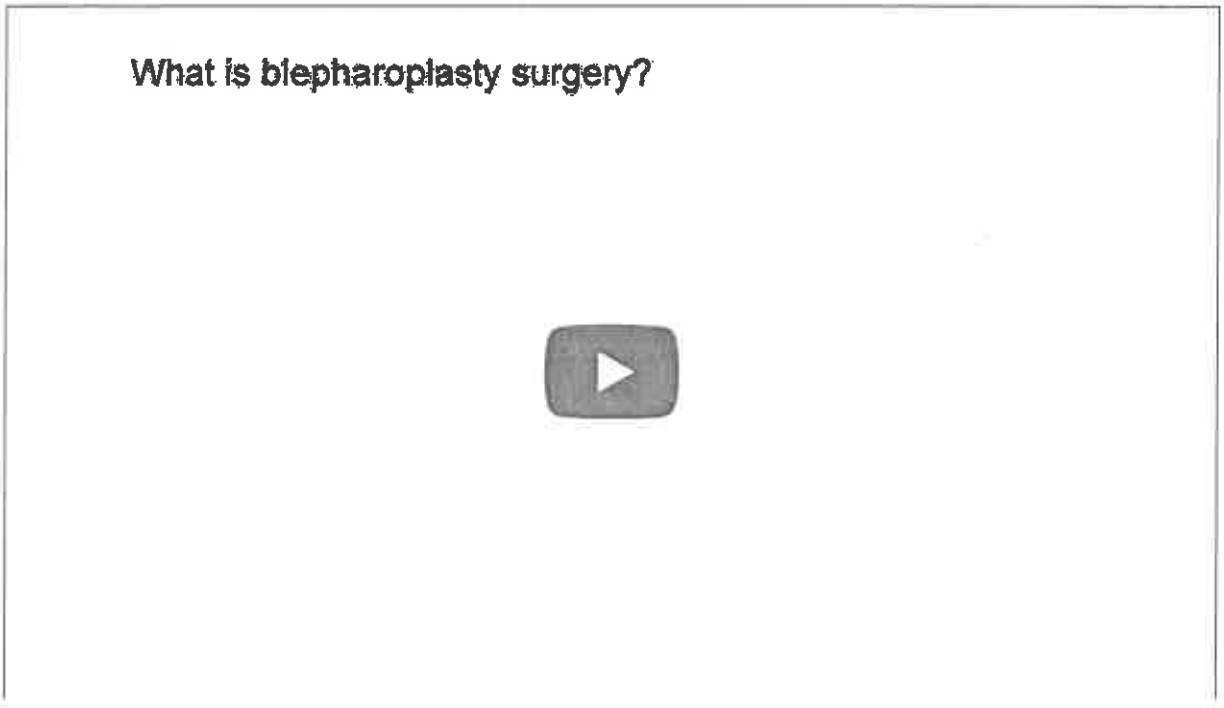
Ophthalmologists consider the following factors when deciding the best way to treat ptosis in children:

- The child's age
- Whether one or both eyelids are involved
- The eyelid height
- The strength of the eyelid's muscle
- The eye's movements

In most cases, ophthalmologists recommend surgery to treat ptosis in children. This is to either tighten the levator muscle or attach the eyelid to other muscles that can help lift the eyelid. The goal is to improve vision.

If the child also has amblyopia, that condition must be treated as well. Amblyopia may be treated by wearing an eye patch or special eyeglasses, or using certain eye drops, to strengthen the weaker eye.

All children with ptosis—whether or not they have surgery—should see their ophthalmologist regularly for eye exams. Ask your child's ophthalmologist how often exams are needed. Because kids' eyes grow and change shape, they need to be checked for amblyopia, refractive disorders, and other eye problems.



U.S. FOOD & DRUG ADMINISTRATION

NDA 212520

NDA APPROVAL

RVL Pharmaceuticals, Inc
Attention: Joann Stavole, MS, RAC
Senior Director, Regulatory Affairs
400 Crossing Boulevard
Bridgewater, NJ 08807

Dear Ms. Stavole:

Please refer to your new drug application (NDA) dated September 16, 2019, received September 16, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for UPNEEQ (oxymetazoline hydrochloride ophthalmic solution), 0.1%. This new drug application provides for the use of UPNEEQ (oxymetazoline hydrochloride ophthalmic solution), 0.1% for acquired blepharoptosis.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Instructions for Use) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 212520**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable. We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable due to the small number of patients with acquired blepharoptosis in the pediatric population.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, call Ms. Jacquelyn Smith, Senior Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Acting Director
Division of Ophthalmology
Office of Specialty Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Instructions for Use
- Carton and Container Labeling

022

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

WILEY A CHAMBERS
07/08/2020 02:59:06 PM

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use UPNEEQ safely and effectively. See full prescribing information for UPNEEQ.

UPNEEQ (oxymetazoline hydrochloride ophthalmic solution), 0.1%, for topical ophthalmic use
Initial U.S. Approval: 1964

----------INDICATIONS AND USAGE----------
UPNEEQ is indicated for the treatment of acquired blepharoptosis in adults. (1)

----------DOSAGE AND ADMINISTRATION----------
Instill one drop into one or both ptotic eye(s) once daily. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Ophthalmic solution, 0.1% oxymetazoline as salt, equivalent to 0.09% oxymetazoline as base.

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Alpha-adrenergic agonists as a class may impact blood pressure. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens. (5.1)
- Use with caution in patients with cerebral or coronary insufficiency or Sjögren's syndrome and advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop. (5.2)
- Advise patients to seek immediate medical care if pain, redness, blurred vision and photophobia occur (signs and symptoms of acute angle closure). (5.3)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence 1-5%) are: punctate keratitis, conjunctival hyperemia, dry eye, vision blurred, instillation site pain, eye irritation and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact RVL Pharmaceuticals, Inc. at 1-877-482-3788 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 7/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
UPNEEQ is indicated for the treatment of acquired blepharoptosis in adults.

2 DOSAGE AND ADMINISTRATION
Instill one drop of UPNEEQ into one or both ptotic eye(s) once daily. Discard the single patient-use container immediately after dosing.

Contact lenses should be removed prior to instillation of UPNEEQ and may be reinserted 15 minutes following its administration.

If more than one topical ophthalmic drug is being used, the drugs should be administered at least 15 minutes between applications.

3 DOSAGE FORMS AND STRENGTHS
UPNEEQ (oxymetazoline hydrochloride ophthalmic solution), 0.1%, equivalent to 0.09% as oxymetazoline base, is formulated for topical ocular delivery as a sterile, non-preserved, clear, colorless to slightly yellow ophthalmic solution.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Potential Impacts on Cardiovascular Disease
Alpha-adrenergic agonists may impact blood pressure. UPNEEQ should be used with caution in patients with severe or unstable cardiovascular disease, orthostatic hypotension, and uncontrolled hypertension or hypotension. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension/hypotension to seek immediate medical care if their condition worsens.

5.2 Potentiation of Vascular Insufficiency
UPNEEQ should be used with caution in patients with cerebral or coronary insufficiency, or Sjogren's syndrome. Advise patients to seek immediate medical care if signs and symptoms of potentiation of vascular insufficiency develop.

5.3 Risk of Angle Closure Glaucoma
UPNEEQ may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute angle closure glaucoma develop.

5.4 Risk of Contamination
Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 360 subjects with acquired blepharoptosis were treated with UPNEEQ once daily in each eye for at least 6 weeks in three controlled Phase 3 clinical trials, including 203 subjects treated with UPNEEQ for 6 weeks and 157 subjects treated with UPNEEQ for 12 weeks. Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation and headache.

7 DRUG INTERACTIONS

7.1 Anti-hypertensives/Cardiac Glycosides
Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta-blockers, anti-hypertensives, and/or cardiac glycosides is advised.

Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.

7.2 Monoamine Oxidase Inhibitors
Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary

There are no available data on UPNEEQ use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, there were no adverse developmental effects observed after oral administration of oxymetazoline hydrochloride in pregnant rats and rabbits at systemic exposures up to 7 and 278 times the maximum recommended human ophthalmic dose (MRHOD), respectively, based on dose comparison. *[see Data]*. The estimated background risks of major birth defects and miscarriage for the indicated population are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Animal Data

Effects on embryo-fetal development were evaluated in rats and rabbits following oral administration of oxymetazoline hydrochloride during the period of organogenesis. Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 0.2 mg/kg/day in pregnant rats during the period of organogenesis (28 times the MRHOD, on a dose comparison basis). Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 1 mg/kg/day in pregnant rabbits during the period of organogenesis (278 times the MRHOD, on a dose comparison basis).

Maternal toxicity, including decreased maternal body weight, was produced at the high dose of 1 mg/kg/day in pregnant rabbits and was associated with findings of delayed skeletal ossification.

In a rat prenatal and postnatal development study, oxymetazoline hydrochloride was orally administered to pregnant rats once daily from gestation day 6 through lactation day 20. Maternal toxicity was produced at the high dose of 0.2 mg/kg/day (28 times the MRHOD, on a dose comparison basis) in pregnant rats and was associated with an increase in pup mortality and reduced pup body weights. Delayed sexual maturation was noted at 0.1 mg/kg/day (14 times the MRHOD on a dose comparison basis). Oxymetazoline hydrochloride did not have any adverse effects on fetal development at a dose of 0.05 mg/kg/day (7 times the MRHOD, on a dose comparison basis).

8.2 Lactation

Risk Summary

No clinical data are available to assess the effects of oxymetazoline on the quantity or rate of breastmilk production, or to establish the level of oxymetazoline present in human breastmilk post-dose. Oxymetazoline was detected in the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for UPNEEQ and any potential adverse effects on the breastfed child from UPNEEQ.

8.4 Pediatric Use

Safety and effectiveness of UPNEEQ have not been established in pediatric patients under 13 years of age.

8.5 Geriatric Use

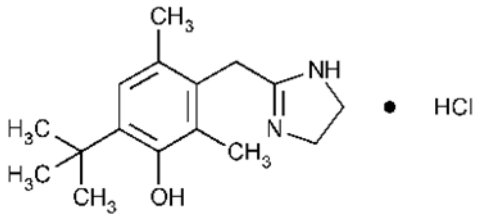
Three hundred and fifteen subjects aged 65 years and older received treatment with UPNEEQ (n = 216) or vehicle (n = 99) in clinical trials. No overall differences in safety or effectiveness were observed between subjects 65 years of age and older and younger subjects.

10 OVERDOSAGE

Accidental oral ingestion of topical intended solutions (including ophthalmic solutions and nasal sprays) containing imidazoline derivatives (e.g., oxymetazoline) in children has resulted in serious adverse events requiring hospitalization, including nausea, vomiting, lethargy, tachycardia, decreased respiration, bradycardia, hypotension, hypertension, sedation, somnolence, mydriasis, stupor, hypothermia, drooling, and coma. Keep UPNEEQ out of reach of children.

11 DESCRIPTION

UPNEEQ (oxymetazoline hydrochloride ophthalmic solution), 0.1% contains oxymetazoline hydrochloride, an alpha adrenoceptor agonist. UPNEEQ is an aseptically prepared, sterile, non-preserved ophthalmic solution. The chemical name is 6-tert-Butyl-3-(2-imidazolin-2-ylmethyl)-2,4-dimethylphenol monohydrochloride, and the molecular mass is 296.84. Oxymetazoline HCl is freely soluble in water and ethanol and has a partition coefficient of 0.1 in 1-octanol/water. The molecular formula of oxymetazoline HCl is $C_{16}H_{24}N_2O \cdot HCl$, and its structural formula is:



Each mL of UPNEEQ (oxymetazoline hydrochloride ophthalmic solution) 0.1% contains 1 mg of oxymetazoline hydrochloride, equivalent to 0.09 mg (0.09%) of oxymetazoline free base. The ophthalmic solution contains the following inactive ingredients: calcium chloride, hydrochloric acid (used to adjust pH to 5.8 to 6.8), hypromellose, magnesium chloride, potassium chloride, sodium acetate, sodium chloride, sodium citrate, and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Oxymetazoline is an alpha adrenoceptor agonist targeting a subset of adrenoreceptors in Mueller's muscle of the eyelid.

12.2 Pharmacodynamics

In safety and efficacy studies, Study RVL-1201-201 and Study RVL-1201-202, the pharmacodynamics of UPNEEQ was assessed using an objective photographic measure, marginal reflex distance 1 (MRD1). MRD1 is the distance from the central pupillary light reflex to the central margin of the upper lid. The maximum increase in MRD1 was observed approximately 2 hours post dose in both studies. The MRD1 increase continued through 8 hours post dose.

12.3 Pharmacokinetics

Absorption

The pharmacokinetics of oxymetazoline was evaluated in 24 healthy adult subjects following single-drop administration of UPNEEQ to each eye. The total dose of oxymetazoline HCl was 0.07 mg. Following ocular administration of UPNEEQ, the time to reach peak oxymetazoline concentration (T_{max}) values ranged from 0.5 to 12 hours with a median T_{max} of 2 hours. The oxymetazoline mean ± standard deviation (SD) peak concentration (C_{max}) and area under the concentration-time curve (AUC_{inf}) were 30.5 ± 12.7 pg/mL and 468 ±214 pg*hr/mL, respectively.

Distribution

An *in vitro* study demonstrated that oxymetazoline is 56.7% to 57.5% bound to human plasma proteins.

Elimination

The oxymetazoline mean terminal half-life ($t_{½}$) following administration of UPNEEQ in healthy adult subjects is 8.3 hours and ranged from 5.6 to 13.9 hours.

Metabolism

In vitro studies using human liver microsomes showed that oxymetazoline was minimally metabolized, generating mono-oxygenated and dehydrogenated products of oxymetazoline. The percentage of

parent drug oxymetazoline remaining was 95.9% after a 120-minute incubation with human liver microsomes.

Excretion
The excretion of oxymetazoline following administration of UPNEEQ has not been characterized in humans.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
Oxymetazoline hydrochloride was not associated with an increased incidence of neoplastic or proliferative changes in transgenic mice given oral doses of 0.5, 1.0, or 2.5 mg/kg/day oxymetazoline hydrochloride for 6 months.

Mutagenesis
Oxymetazoline hydrochloride revealed no evidence of mutagenic or clastogenic potential based on the results of two *in vitro* genotoxicity tests (Ames assay and human lymphocyte chromosomal aberration assay) and one *in vivo* gentoxicity test (mouse micronucleus assay).

Impairment of Fertility
Effects on fertility and early embryonic development were evaluated in rats following oral administration of 0.05, 0.1, or 0.2 mg/kg/day oxymetazoline hydrochloride prior to and during mating and through early pregnancy. Decreased number of corpora lutea and increased post-implantation losses were noted at 0.2 mg/kg/day oxymetazoline hydrochloride (28 times the MRHOD, on a dose comparison basis). However, no treatment related effects on mating parameters were noted at 0.2 mg/kg/day oxymetazoline hydrochloride.

14 CLINICAL STUDIES

UPNEEQ was evaluated for the treatment of acquired blepharoptosis in two randomized, double-masked, vehicle-controlled, parallel-group clinical efficacy trials. Both studies were randomized in an approximate 2:1 ratio of active versus vehicle. Efficacy was assessed with the Leicester Peripheral Field Test (LPFT) (primary) and photographic measurement of Marginal reflex distance 1 (MRD1). The primary efficacy endpoints were ordered in a hierarchy to compare UPNEEQ to vehicle on the mean increase from baseline (Day 1 Hour 0) in number of points seen on the top 4 rows of the LPFT in the study eye at Hour 6 on Day 1 and Hour 2 on Day 14.

In Trial 1, a total of 140 subjects were randomized 94 patients to the UPNEEQ group and 46 patients to the vehicle group. Treatments were administered once daily to each eye for 42 days (6 weeks). The mean age of the subjects was 64 years. In Trial 2, a total of 164 subjects were randomized 109 patients to the UPNEEQ group and 55 patients to the vehicle group. Treatments were administered once daily to each eye for 42 days (6 weeks). The mean age of the subjects was 63 years.

In both trials, each patient had a designated study eye. The increases in the number of points seen in the superior visual field in the study eye of the UPNEEQ group compared to the vehicle group were statistically significant at both time points, showing that the improvement in superior visual field was evident at the 2-hour time point and maintained at the 6-hour time point. The results from both trials

on the primary endpoint are presented below.

Observed and Change from Baseline in Mean Points Seen in Superior Visual Field on LPFT in the Study Eye at Primary Efficacy Time Points (ITT Population)

	Trial 1			Trial 2		
	Points Seen (SD) in Superior Visual Field		Mean Difference, [95% CL] [a] p-value[a]	Points Seen (SD) in Superior Visual Field		Mean Difference, [95% CL] [a] p-value[a]
	UPNEEQ N = 94	Vehicle N = 46	UPNEEQ vs Vehicle	UPNEEQ N = 109	Vehicle N = 55	UPNEEQ vs Vehicle
Baseline	17.0 (4.4)	16.9 (5.2)		17.6 (4.3)	17.6 (5.5)	
Day 1, Hour 6, Observed mean	22.2 (6.2)	18.4 (6.0)		23.9 (6.7)	19.7 (6.2)	
Mean change from baseline	5.2 (6.0)	1.5 (3.9)	3.7 [1.8, 5.6] **p< 0.01**	6.3 (6.7)	2.1 (4.3)	4.2 [2.4, 6.1] p<**0.01**
Day 14, Hour 2, Observed mean	23.4 (5.6)	19.1 (6.1)		25.3 (6.4)	20.0 (5.8)	
Mean change from baseline	6.4 (5.0)	2.2 (5.8)	4.2 [2.0, 6.0] **p< 0.01**	7.7 (6.4)	2.4 (5.3)	5.3 [3.7, 7.1] **p<0.01**

CL = confidence limit; LPFT = Leicester Peripheral Field Test; ITT (intent-to-treat) – included all randomized subjects who received at least one dose of study medication; SD = standard deviation

[a] p-value and 95% CI were based on ANCOVA model adjusted for baseline LFPT points.

Marginal reflex distance 1 (MRD1), showed a positive effect with UPNEEQ treatment. Greater MRD1 increases were observed for the UPNEEQ group than the vehicle group on day 1 at 6 hours post dose and on day 14 at 2 hours post dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

UPNEEQ (oxymetazoline hydrochloride ophthalmic solution), 0.1% is an aseptically prepared, sterile, non-preserved, clear, colorless to slightly yellow ophthalmic solution; 0.3 mL fill in a clear, low-density polyethylene, single patient-use container in a foil pouch.

NDC 73687-062-15	Carton of 15 single patient-use containers individually foil-pouched provided within a child-resistant zipper bag.
NDC 73687-062-32	Carton of 30 single patient-use containers individually foil-pouched provided within a child-resistant zipper bag.

Storage: Store at 20°C to 25°C (68°F to 77°F). Protect from excessive heat. Keep out of reach of children.

Store foil-pouched single patient-use containers in the original child-resistant zipper bag. Opened containers should be discarded immediately after use.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Instructions for Use).

When to Seek Medical Care

- Alpha-adrenergic agonists as a class may impact blood pressure. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens *[see Warnings and Precautions (5.1)]*.
- Use with caution in patients with cerebral or coronary insufficiency or Sjögren's syndrome and advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop *[see Warnings and Precautions (5.2)]*.
- Advise patients to seek immediate medical care if signs and symptoms of acute narrow-angle glaucoma develop *[see Warnings and Precautions (5.3)]*.

Administration Instructions

Use with Contact Lenses

Advise patients that contact lenses should be removed prior to administration of UPNEEQ and can be re-inserted 15 minutes following administration *[see Dosage and Administration (2)]*.

Use with Other Ophthalmic Drugs

If more than one topical ophthalmic drug is being used, the drugs should be administered at least 15 minutes between applications.

Administration

Advise patients that the solution from one single patient-use container is to be used immediately after opening to dose one or both eye(s). The single patient-use container, including any remaining contents, should be discarded immediately after administration *[see Dosage and Administration (2)]*.

Storage and Handling Instructions

Handling the Single Patient-Use Container

Advise patients not to touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

Storage Information

Instruct patients to keep the foil-pouched, single patient-use containers sealed within the child-resistant zipper bag until ready to use. Keep out of reach of children.

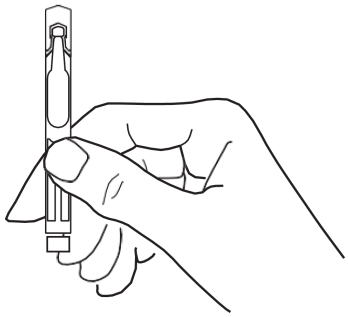
To report SUSPECTED ADVERSE REACTIONS, contact RVL Pharmaceuticals, Inc. at 1-877-482-3788 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

Bridgewater, New Jersey 08807
Patents 9,867,808 and 8,357,714
Made in the U.S.A.
Manufactured for RVL Pharmaceuticals, Inc.

INSTRUCTIONS FOR USE
UPNEEQ (up-NEEK)
(oxymetazoline hydrochloride ophthalmic solution), 0.1%
for topical ophthalmic use

Read this Instructions for Use before you start using UPNEEQ and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment.

UPNEEQ single patient-use container after removal from its individual foil pouch.



Important Information You Need to Know Before Using UPNEEQ

- **UPNEEQ is for use in the eye.**
- UPNEEQ can be harmful if swallowed.
- UPNEEQ is supplied as single patient-use containers individually packaged in a foil pouch. The single patient-use containers come in a child-resistant zipper bag. Do not remove a single patient-use container from the child-resistant zipper bag until you are ready to use UPNEEQ.
- Wash your hands before each use to make sure you do not infect your eyes while using UPNEEQ.
- If you are using UPNEEQ with other eye (ophthalmic) medicines, you should wait at least 15 minutes between using UPNEEQ and the other medicines.
- If you wear contact lenses, remove them before using UPNEEQ. You should wait at least 15 minutes before placing them back into your eyes.

Using UPNEEQ

- Do not let the tip of the UPNEEQ single patient-use container touch your eye or any other surfaces to avoid contamination or injury to your eye.
- Use 1 drop of UPNEEQ in the affected eye 1 time each day.
- Each single patient-use container of UPNEEQ will give you enough medicine to treat both eyes 1 time each day if needed.
- There is some extra UPNEEQ in each single patient-use container in case you miss getting the drop into your eye.

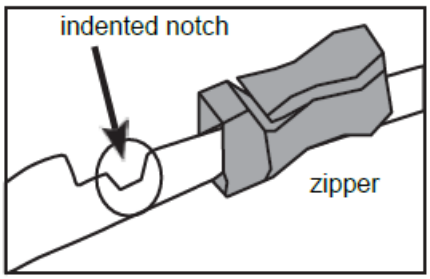
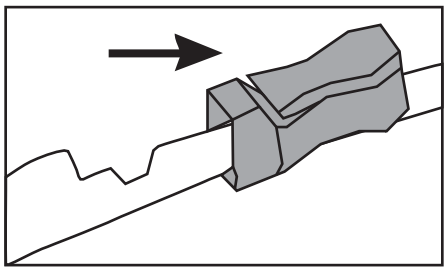
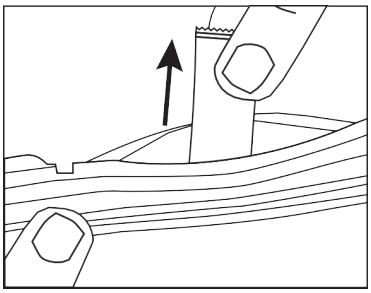
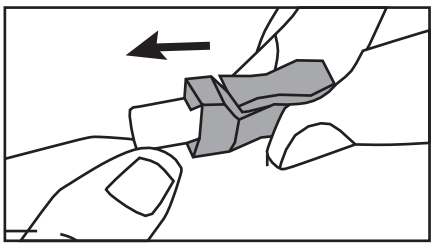
Storing UPNEEQ

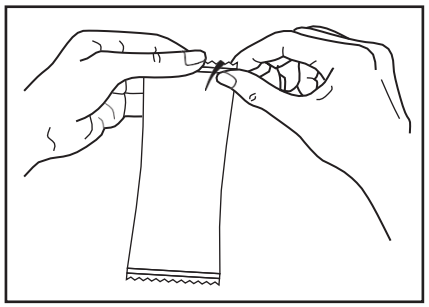
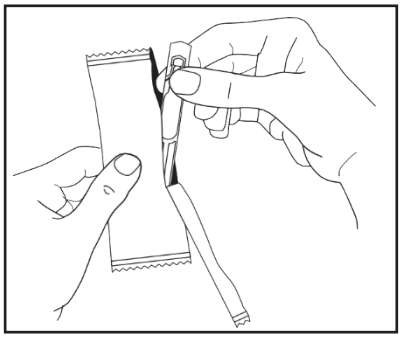
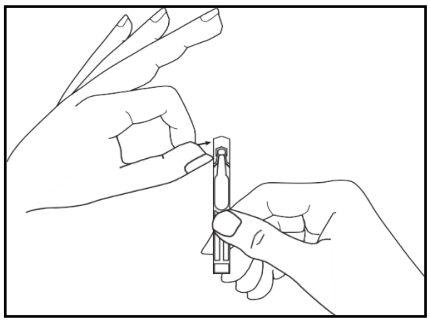
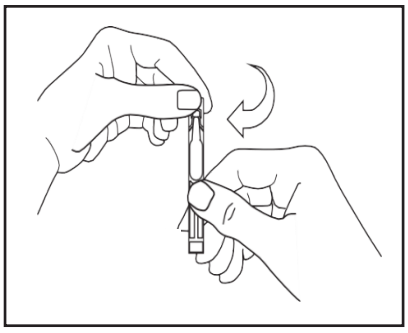
- Store UPNEEQ at room temperature between 68°F to 77°F (20°C to 25°C).
- Store UPNEEQ single patient-use containers in the child-resistant zipper bag they come in.
- Protect UPNEEQ from excessive heat.
- **Keep UPNEEQ and all medicines out of the reach of children.**

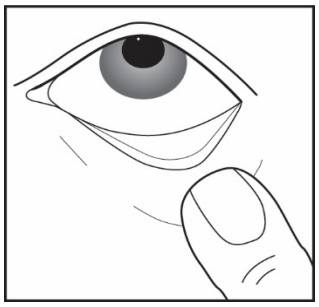
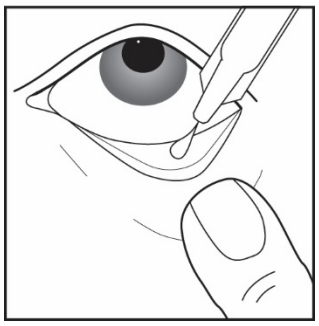
Disposing of UPNEEQ

- After you have applied the daily dose of medicine, throw away (dispose of) the single patient-use container and any unused UPNEEQ.
- Do not save any unused UPNEEQ.

Follow Step 1 to Step 11 each time you use UPNEEQ:

Step 1. Line up the zipper with the indented notch along the top edge of the child-resistant zipper bag (see **Figure A**) then press down and slide the zipper to open (see **Figure B**).	**Figure A**  **Figure B** 
Step 2. Remove 1 UPNEEQ foil pouch from the child-resistant zipper bag (see **Figure C**) and reseal the bag right away (see **Figure D**).	**Figure C**  **Figure D** 

Step 3. Hold the foil pouch upright and tear the foil at the serrated edge (see **Figure E)**.	**Figure E** 
Step 4. Remove the single patient-use container from the foil pouch and then hold it by the long flat end (see **Figure F**).	**Figure F** 
Step 5. Hold the single patient-use container upright and tap the top of the container gently to make sure that the medicine is in the bottom part of the container (see **Figure G**).	**Figure G** 
Step 6. Open the single patient-use container by twisting off the tab (see **Figure H**). **Do not** let the tip of the container touch your eye or any other surfaces.	**Figure H** 

Step 7. Tilt your head backwards. If you are not able to tilt your head, lie down. **Step 8.** Gently pull your lower eyelid downwards and look up (see **Figure I**).	**Figure I** 
Step 9. Place the tip of the single patient-use container close to your eye, but be careful not to touch your eye with it (see **Figure J)**. **Step 10.** Gently squeeze the single patient-use container and let 1 drop of UPNEEQ fall into the space between your lower eyelid and your eye (see **Figure J**). If a drop misses your eye, try again.	**Figure J** 
Step 11. Repeat **Step 7 to Step 10** for your other eye if instructed to do so by your healthcare provider. There is enough UPNEEQ in one container for both eyes if needed. • After you have applied the daily dose of UPNEEQ, throw away the opened single patient-use container with any remaining medicine. • Be sure to keep this medicine away from children. • If you use contact lenses, wait at least 15 minutes before placing them back into your eyes.	

Manufactured for RVL Pharmaceuticals, Inc.
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This Instruction for Use has been approved by the U.S. Food and Drug Administration.
Approved: July 2020