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# Today's Strategies for Managing Allergic Conjunctivitis:

Meeting Patient Demand for

**RAPID ITCH RELIEF**



# Today's Strategies for Managing Allergic Conjunctivitis: Meeting Patient Demand for Rapid Itch Relief

## PARTICIPANTS



**Terrence P. O'Brien, MD, Moderator,** is Professor of Ophthalmology, Cornea and External Diseases at Bascom Palmer Eye Institute of the University of Miami in Palm Beach Gardens, Fla.



**Douglas Katsev, MD,** is a cornea and external disease specialist in private practice at the Sansum Clinic in Santa Barbara, Calif.



**Michael Ehrenhaus, MD,** is Director of Cornea and External Disease at the State University of New York (SUNY) Downstate Medical Center. He is also Director of New York Cornea Consultants in Queens, NY.



**Barry A. Schechter, MD,** is Director of the Department of Cornea and External Disease at the Florida Eye Microsurgical Institute in Boynton Beach and Boca Raton, Fla.

*The participants are paid consultants of ISTA Pharmaceuticals, Inc.*

### PREVALENCE, SYMPTOMS AND DIAGNOSIS OF ALLERGIC CONJUNCTIVITIS

**Terrence P. O'Brien, MD:** An estimated 40 million Americans suffer from seasonal and

perennial allergies to common allergens such as pollen, mold, dust and pet dander.<sup>1</sup> About half of these allergy sufferers have allergic conjunctivitis.<sup>2</sup> So while allergy may not be the most sight-threatening condition we deal with, it certainly is one of the most common chronic diseases patients suffer with that we are called

upon to treat. How prevalent is allergic conjunctivitis in your patient population?

**Douglas Katsev, MD:** During the devastating fires we had a couple years ago in Santa Barbara, the burning vegetation and smoke exacerbated allergic conjunctivitis for many patients. Then we had a quiet period, but now it is worse again, as the vegetation is rapidly re-growing and producing a heavy allergen load. During fall 2010, nearly one-quarter of our patient visits were for allergic conjunctivitis, which is unusually high.

**Barry A. Schechter, MD:** As Dr. O'Brien and I both know, South Florida's warm climate and long blooming season contribute to a very high rate of allergic conjunctivitis. I myself suffer from some seasonal allergic conjunctivitis (SAC) and I have several staff members with perennial pet allergies, so I'm very attentive to my patients' concerns about allergy.

Not only are we seeing an overall increase in the rate of allergy, but the impact of ocular allergy is greater in today's technology-based economy. Looking at a computer for an extended period of time is much more challenging when your eyes are itchy, and uncomfortable.

**Dr. O'Brien:** We know that itching is the hallmark clinic symptom, but let's talk about the differential diagnosis of allergic conjunctivitis. Clearly there's an overlap of inflammatory conditions that affect the ocular surface that can create a diagnostic challenge.

**Dr. Katsev:** Allergic conjunctivitis can certainly be misdiagnosed. The patient may actually have dry eye (which is compounded by taking an oral antihistamine), blepharitis or meibomitis, or some combination of various conditions.

**Michael Ehrenhaus, MD:** I have seen a lot of patients who are being treated for dry eye and blepharitis but are still uncomfortable because the allergic conjunctivitis component hasn't been treated. The reality is that when there are multiple underlying conditions, that hallmark itching of allergic conjunctivitis can be harder to sort out, and that is something we need to be looking for and treating.

**Dr. Schechter:** It is important to perform a complete evaluation of the ocular surface. We stain with fluorescein and lissamine green dye to identify any pathology of the cornea or conjunctiva. It is important to distinguish dry eye or blepharitis from allergic conjunctivitis and then treat those conditions appropriately. Once we've confirmed a diagnosis of allergic conjunctivitis, it is useful, whenever possible, to identify the allergen because it helps patients to practice avoidance, which is the best way of treating any allergic condition.

**Dr. O'Brien:** We can't underestimate the importance of differentiating these common clinical diagnoses and guiding the patient to specific therapy. Even though there are many over-the-counter (OTC) options, patients may be completely mistreating their disease when they don't seek clinical expertise for specific diagnosis. And when they do come to us, we shouldn't be cavalier and suggest they try whatever



**"During fall 2010, nearly one-quarter of our patient visits were for allergic conjunctivitis ..."**

***Douglas Katsev, MD***

works for them. That is disappointing to the patient who is suffering and seeking expert recommendations for the management of their condition.

## THERAPEUTIC OPTIONS

**Dr. O'Brien:** We have quite a few options for the management of itching associated with allergic conjunctivitis, including systemic anti-allergy medications, topical corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs), and topical antihistamines and mast cell stabilizers. First, let's discuss the advantages and disadvantages of oral antihistamines.



**"It is important to distinguish dry eye or blepharitis from allergic conjunctivitis and then treat those conditions appropriately."**

**Barry A. Schechter, MD**

**Dr. Schechter:** Many of our allergic conjunctivitis patients take systemic anti-allergy medications for their general allergy symptoms. However, oral medications may have a negative impact on mucous membrane and ocular surface hydration. And of course, we can also see rebound hyperemia from misuse of topical vasoconstrictors.

**Dr. O'Brien:** With all the direct-to-consumer promotions of OTC products, many patients don't even think of them as medications, so we have to be careful to specifically inquire about OTC oral antihistamine and vasoconstrictor use in the patient history.

**Dr. Katsev:** Helping patients understand how these agents may actually worsen their ocular symptoms is a major role for us in dealing with itching associated with allergic conjunctivitis. My preference is to stop the oral medication and move to a topical agent for the itching.

**Dr. O'Brien:** I certainly agree. I particularly dislike oral agents for children because of the potential for central nervous system side effects, such as sedation or drowsiness.

How about NSAIDs and corticosteroids? What are the pros and cons of their use in the acute management of itching associated with allergic conjunctivitis?

**Dr. Katsev:** Although some NSAIDs are approved for allergic conjunctivitis, I follow current practice and do not use them first line. I do use topical steroids, but I tend to reserve them for more severe forms of ocular allergy.

**Dr. Schechter:** NSAIDs can be beneficial in controlling itching associated with allergic conjunctivitis. I have my patients utilize them for brief periods when symptoms are particularly irksome. Steroids work very quickly but may have potential side effects such as elevated intraocular pressure, lowered immunity, vulnerability to fungal pathogens, recurrence of latent herpetic keratitis, and cataract formation.

**Dr. Ehrenhaus:** A large proportion of my patient population is already at high risk for glaucoma due to hereditary and lifestyle factors, so they are vulnerable to steroid-induced glaucoma. Steroids will make them feel more comfortable very quickly but if overused can lead to problems in a relatively short period of time, so I prefer to

stay away from this drug class when I have other options that are safe and effective.

**Dr. O'Brien:** Corticosteroids can play an important role in addressing inflammation when they are pulsed for those patients with more severe or breakthrough symptoms. For most patients, however, we can manage ocular itch associated with allergic conjunctivitis with an agent that has a significant antihistaminic effect combined with mast cell stabilization. Fortunately, over the last few years we have seen the development of newer topical antihistaminic compounds.

## **FAST, EFFECTIVE RELIEF OF OCULAR ITCHING WITH BEPOTASTINE BESILATE 1.5%**

**Dr. Schechter:** One of those is BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% [ISTA Pharmaceuticals]. Although primarily a highly selective antihistamine, BEPREVE also stabilizes mast cells to prevent histamine release, contributing to its effectiveness throughout the allergic cascade.<sup>3</sup> Animal and clinical studies have provided additional support for the activity of bepotastine in both the early and late phases of the allergic reaction that produces the itching associated with allergic conjunctivitis.<sup>4</sup>

### **BEPREVE LABEL SUMMARY**

#### **INDICATIONS AND USAGE**

BEPREVE is a histamine H1 receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

#### **DOSAGE AND ADMINISTRATION**

Instill one drop of BEPREVE into the affected eye(s) twice a day (BID).

#### **WARNINGS AND PRECAUTIONS**

To minimize contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

Patients should be advised not to wear a contact lens if their eye is red. BEPREVE should not be used to treat contact lens-related irritation. BEPREVE should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

BEPREVE is for topical ophthalmic use only.

#### **ADVERSE REACTIONS**

The most common reported adverse reaction occurring in approximately 25% of subjects was a mild taste following instillation. Other adverse reactions occurring in 2-5% of subjects were eye irritation, headache, and nasopharyngitis.

Please see full prescribing information for BEPREVE on the last page.

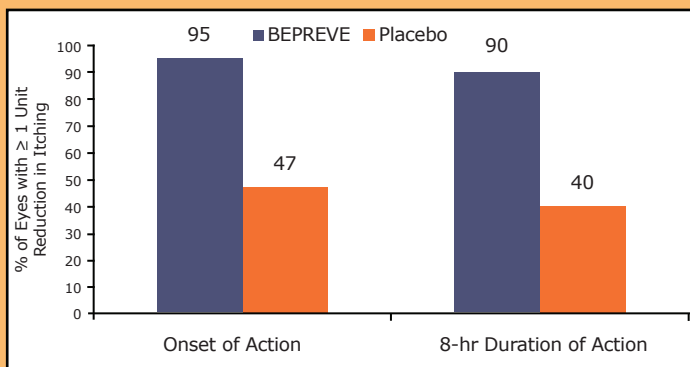


Figure 1. Rapid, long-lasting clinical relief with bepotastine besilate 1.5%. Clinical significance is at least a 1-unit reduction in itching score.<sup>5</sup>

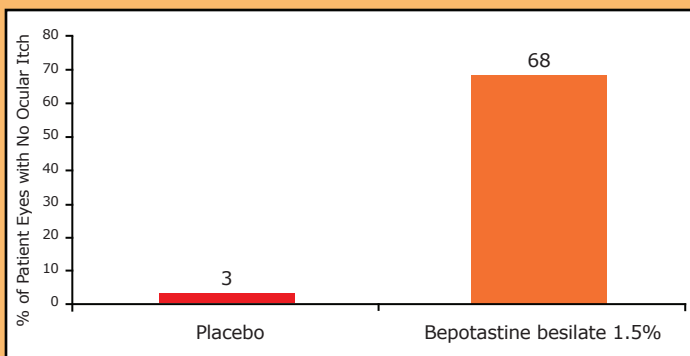


Figure 2. Percentage of "severe" patient eyes with no ocular itch at 3 minutes.<sup>7</sup>

**Dr. O'Brien:** I agree that the bi-phasic action of bepotastine is really important. The rapid onset of action provides significant relief of ocular itch. What has the clinical trial experience been with this agent in the treatment of ocular itch associated with allergic conjunctivitis?

**Dr. Katsev:** The BEPREVE clinical trial data showed that within three minutes, 95 percent of subjects experienced a clinically significant reduction in itching.<sup>5</sup> That quick relief is absolutely key. And the effect doesn't go away for hours—the data also show that 90 percent of patients have sustained relief over at least 8 hours<sup>5</sup> (see *Figure 1*). The best part is that this efficacy is achieved with minimal

drying and no drowsiness. The most common adverse event with bepotastine is mild taste in about 25 percent of patients.<sup>6</sup> My experience is similar to the clinical trials in that I am not aware of any of my patients discontinuing use of BEPREVE because of this effect. BEPREVE has become my first-line treatment for ocular itching associated with allergic conjunctivitis. In my hands, the rapid onset and long action of this drop have been a very effective combination.

**Dr. Ehrenhaus:** BEPREVE is also very effective against severe itching associated with allergic conjunctivitis. In the BEPREVE clinical trials, 68 percent of patients with more severe symptoms (rated at least 3.0 on a 0 to 4 scale) experienced total elimination of itching within 3 minutes, compared to just 3 percent of patients on placebo<sup>7</sup> (see *Figure 2*).

**Dr. O'Brien:** How do you feel about the twice-daily dosing of BEPREVE, given that we also have once-daily allergy medications available?

**Dr. Katsev:** Sorting out the ideal dosing for allergy therapy



**"... the bi-phasic action of bepotastine is really important."**

**Terrence P. O'Brien, MD**

has been a little bit challenging. Initially, I thought less frequent dosing would be my preference, but I've actually moved away from once-daily dosing to twice-daily dosing because I think it's more helpful to tell patients to use the eyedrop in the morning and then again at night if they need it. Dealing with breakthrough symptoms is challenging if the medication says "once daily." Telling patients they can use a once-daily product a second time creates confusion. It sets a bad precedent when we want patients to adhere closely to our instructions and to the labeling for so many other drugs.

**Dr. O'Brien:** In other therapeutic categories, there are very good reasons to limit the number of drops. With pre- or post-surgical NSAIDs and glaucoma drops we want to maximize compliance and minimize inconvenience, but with a symptomatic, often seasonal complaint such as itching associated with allergic conjunctivitis, I am much less concerned about these issues. I agree that twice-a-day dosing for a symptomatic condition is really beneficial for allowing that additional dosing as the symptoms break through.

**Dr. Ehrenhaus:** What's also important to me is that the vehicle be very comfortable. That's particularly important with kids. I

thought q.d. dosing was really the answer for pediatric patients, but in fact these young patients often have breakthrough symptoms so I find that once daily just isn't enough. It is nice to have something like BEPREVE that gives them quick relief and doesn't sting so they aren't fighting their parents on instilling drops.



**" In the BEPREVE clinical trials, 68 percent of patients with more severe symptoms experienced total elimination of itching within 3 minutes ... "**

**Michael Ehrenhaus, MD**

**Dr. Katsev:** The other thing I've found is that patients like the size of the BEPREVE bottle. At 10 mL, it is bigger than other allergy drops, so most patients can get two months of therapy with one co-

pay. And for those who waste a lot of drops because of difficulty with instillation, it's also helpful not to run out before they are eligible for a re-fill. Bottle size may seem like a minor factor, but it's one of the things I consider in making a treatment decision because it is a tangible benefit to patients.

#### References:

1. Asthma & Allergy Foundation for America. [www.aafa.org](http://www.aafa.org), accessed November 2010.
2. Bassett C. Ocular Allergies. *Asthma & Allergy Advocate*. Summer 2007. American Academy of Allergy Asthma & Immunology Web site. [www.aaaai.org/patients/advocate/](http://www.aaaai.org/patients/advocate/). Accessed November 3, 2008.
3. Yato N, Murata T, Saito N, et al. Anti-allergic activity of bepotastine besilate (TAU-284), a new anti-allergic drug. *Nippon Yakurigaku Zasshi* 1997;110(1):19-29.
4. Abelson MB, Trokildsen GL, Williams JJ, et al. Time to onset and duration of action of the antihistamine bepotastine besilate ophthalmic solutions 1.0% and 1.5% in allergic conjunctivitis: A Phase III, single-center, prospective, randomized, double-masked, placebo-controlled, conjunctival allergen challenge assessment in adults and children. *Clin Ther* 2009;31:1908-1921.
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# BEPREVE®

(bepotastine besilate  
ophthalmic solution) 1.5%

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BEPREVE (bepotastine besilate ophthalmic solution) 1.5% safely and effectively.

See full prescribing information for BEPREVE.

## BEPREVE (bepotastine besilate ophthalmic solution) 1.5%

Initial U.S. Approval: 2009

### INDICATIONS AND USAGE

BEPREVE is a histamine H<sub>1</sub> receptor antagonist indicated for the treatment of itching associated with allergic conjunctivitis. (1)

### DOSAGE AND ADMINISTRATION

Instill one drop into the affected eye(s) twice a day (BID). (2)

### DOSAGE FORMS AND STRENGTHS

Solution containing bepotastine besilate, 1.5%. (3)

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is a histamine H<sub>1</sub> receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

### 2 DOSAGE AND ADMINISTRATION

Instill one drop of BEPREVE into the affected eye(s) twice a day (BID).

### 3 DOSAGE FORMS AND STRENGTHS

Topical ophthalmic solution containing bepotastine besilate 1.5%.

### 4 CONTRAINDICATIONS

None.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Contamination of Tip and Solution

To minimize contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

#### 5.2 Contact Lens Use

Patients should be advised not to wear a contact lens if their eye is red. BEPREVE should not be used to treat contact lens-related irritation.

BEPREVE should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

#### 5.3 Topical Ophthalmic Use Only

BEPREVE is for topical ophthalmic use only.

### 6 ADVERSE REACTIONS

The most common reported adverse reaction occurring in approximately 25% of subjects was a mild taste following instillation. Other adverse reactions occurring in 2-5% of subjects were eye irritation, headache, and nasopharyngitis.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

Pregnancy Category C. Teratogenicity studies have been performed in animals. Bepotastine besilate was not found to be teratogenic in rats during organogenesis and fetal development

## WARNINGS AND PRECAUTIONS

- To minimize the risk of contamination, do not touch dropper tip to any surface. Keep bottle tightly closed when not in use. (5.1)
- BEPREVE should not be used to treat contact lens-related irritation. (5.2)
- Remove contact lenses prior to instillation of BEPREVE. (5.2)

## ADVERSE REACTIONS

The most common adverse reaction occurring in approximately 25% of patients was a mild taste following instillation. Other adverse reactions which occurred in 2-5% of subjects were eye irritation, headache, and nasopharyngitis. (6)

To report SUSPECTED ADVERSE REACTIONS, contact ISTA Pharmaceuticals, Inc. at 1-877-788-2020, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 01/2010

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

at oral doses up to 200 mg/kg/day (representing a systemic concentration approximately 3,300 times that anticipated for topical ocular use in humans), but did show some potential for causing skeletal abnormalities at 1,000 mg/kg/day. There were no teratogenic effects seen in rabbits at oral doses up to 500 mg/kg/day given during organogenesis and fetal development (>13,000 times the dose in humans on a mg/kg basis). Evidence of infertility was seen in rats given oral bepotastine besilate 1,000 mg/kg/day; however, no evidence of infertility was observed in rats given 200 mg/kg/day (approximately 3,300 times the topical ocular use in humans). The concentration of radiolabeled bepotastine besilate was similar in fetal liver and maternal blood plasma following a single 3 mg/kg oral dose. The concentration in other fetal tissues was one-third to one-tenth the concentration in maternal blood plasma.

An increase in stillborns and decreased growth and development were observed in pups born from rats given oral doses of 1,000 mg/kg/day during perinatal and lactation periods. There were no observed effects in rats treated with 100 mg/kg/day.

There are no adequate and well-controlled studies of bepotastine besilate in pregnant women. Because animal reproduction studies are not always predictive of human response, BEPREVE (bepotastine besilate ophthalmic solution) 1.5% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

#### 8.3 Nursing Mothers

Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 µg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection limits. The milk concentration was higher than the maternal blood plasma concentration at each time of measurement.

It is not known if bepotastine besilate is excreted in human milk. Caution should be exercised when BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is administered to a nursing woman.

#### 8.4 Pediatric Use

Safety and efficacy of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% have not been established in pediatric patients under 2 years of age. Efficacy in pediatric patients under 10 years of age was extrapolated from clinical trials conducted in pediatric patients greater than 10 years of age and from adults.

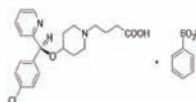
### 8.5 Geriatric Use

No overall difference in safety or effectiveness has been observed between elderly and younger patients.

### 11 DESCRIPTION

BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is a sterile, topically administered drug for ophthalmic use. Each mL of BEPREVE contains 15 mg bepotastine besilate.

Bepotastine besilate is designated chemically as (+)-4-[[[S]-p-chloro-α-2-pyridylbenzyl]oxy]-1-piperidine butyric acid monobenzenesulfonate. The chemical structure for bepotastine besilate is:



Bepotastine besilate is a white or pale yellowish crystalline powder. The molecular weight of bepotastine besilate is 547.06 daltons. BEPREVE ophthalmic solution is supplied as a sterile, aqueous 1.5% solution, with a pH of 6.8.

The osmolality of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is approximately 290 mOsm/kg.

Each mL of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% contains:

**Active:** Bepotastine besilate 15 mg (equivalent to 10.7 mg bepotastine)

**Preservative:** benzalkonium chloride 0.005%  
**Inactives:** monobasic sodium phosphate dihydrate, sodium chloride, sodium hydroxide to adjust pH, and water for injection, USP.

### 12 CLINICAL PHARMACOLOGY

#### 12.1 Mechanism of Action

Bepotastine is a topically active, direct H<sub>1</sub>-receptor antagonist and an inhibitor of the release of histamine from mast cells.

#### 12.3 Pharmacokinetics

**Absorption:** The extent of systemic exposure to bepotastine following topical ophthalmic administration of bepotastine besilate 1% and 1.5% ophthalmic solutions was evaluated in 12 healthy adults. Following one drop of 1% or 1.5% bepotastine besilate ophthalmic solution to both eyes four times daily (QID) for seven days, bepotastine plasma concentrations peaked at approximately one to two hours post-instillation. Maximum plasma concentration for the 1% and 1.5% strengths were 5.1 ± 2.5 ng/mL and 7.3 ± 1.9 ng/mL, respectively. Plasma concentration at 24 hours post-instillation were below the quantifiable limit (2 ng/mL) in 11/12 subjects in the two dose groups.

**Distribution:** The extent of protein binding of bepotastine is approximately 55% and independent of bepotastine concentration.

**Metabolism:** *In vitro* metabolism studies with human liver microsomes demonstrated that bepotastine is minimally metabolized by CYP450 isozymes.

*In vitro* studies demonstrated that bepotastine besilate does not inhibit the metabolism of various cytochrome P450 substrate via inhibition of CYP3A4, CYP2C9, and CYP2C19. The effect of bepotastine besilate on the metabolism of substrates of CYP1A2, CYP2C8, CYP2D6 was not studied. Bepotastine besilate has a low potential for drug interaction via inhibition of CYP3A4, CYP2C9, and CYP2C19.

**Excretion:** The main route of elimination of bepotastine besilate is urinary excretion (with approximately 75-90% excreted unchanged in urine).

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term dietary studies in mice and rats were conducted to evaluate the carcinogenic potential of bepotastine besilate. Bepotastine besilate did not significantly induce neoplasms in mice receiving a nominal dose of up to 200 mg/kg/day for 21 months or rats receiving a nominal dose of up to 97 mg/kg/day for 24 months. These dose levels represent systemic exposures approximating 350 and 200 times that achieved with human topical ocular use.

The no observable adverse effect levels for bepotastine besilate based on nominal dose levels in carcinogenicity tests were 18.7 to 19.9 mg/kg/day in mice and 9.6 to 9.8 mg/kg/day in rats (representing exposure margins of approximately 60 and 20 times the systemic exposure anticipated for topical ocular use in humans).

There was no evidence of genotoxicity in the Ames test, in CHO cells (chromosome aberrations), in mouse hepatocytes (unscheduled DNA synthesis), or in the mouse micronucleus test.

When oral bepotastine was administered to male and female rats at doses up to 1,000 mg/kg/day, there was a slight reduction in fertility index and surviving fetuses. Infertility was not seen in rats given 200 mg/kg/day oral bepotastine besilate (approximately 3,300 times the systemic concentration anticipated for topical ocular use in humans).

### 14 CLINICAL STUDIES

Clinical efficacy was evaluated in 2 conjunctival allergen challenge (CAC) studies (237 patients). BEPREVE (bepotastine besilate ophthalmic solution) 1.5% was more effective than its vehicle for relieving ocular itching induced by an ocular allergen challenge, both at a CAC 15 minutes post-dosing and a CAC 8 hours post dosing of BEPREVE.

The safety of BEPREVE was evaluated in a randomized clinical study of 861 subjects over a period of 6 weeks.

### 16 HOW SUPPLIED/STORAGE AND HANDLING

BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is supplied in a white low density polyethylene plastic squeeze bottle with a white controlled dropper tip and a white polypropylene cap in the following size:

5 mL (NDC 67425-007-50)  
10 mL (NDC 67425-007-75)

### STORAGE

Store at 15°–25°C (59°–77°F).

### 17 PATIENT COUNSELING INFORMATION

#### 17.1 Topical Ophthalmic Use Only

For topical ophthalmic administration only.

#### 17.2 Sterility of Dropper Tip

Patients should be advised to not touch dropper tip to any surface, as this may contaminate the contents.

#### 17.3 Concomitant Use of Contact Lenses

Patients should be advised not to wear a contact lens if their eye is red. Patients should be advised that BEPREVE should not be used to treat contact lens-related irritation.

Patients should also be advised to remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

### Rx only

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Irvine, CA 92618

By: Bausch & Lomb Incorporated  
Tampa, FL 33637

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