HIGHLIGHTS OF PRESCRIBING INFORMATION

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

LATISSE™ (bimatoprost ophthalmic solution) 0.03%
Initial U.S. Approval: 2001

————INDICATIONS AND USAGE————

LATISSE™ is a prostaglandin analog, indicated to treat hypotrichosis of the eyelashes by increasing their growth including length, thickness and darkness. (1)

————DOSAGE AND ADMINISTRATION————

Apply nightly directly to the skin of the upper eyelid margin at the base of the eyelashes using the accompanying applicators. Blot any excess solution beyond the eyelid margin. Dispose of the applicator after one use. Repeat for the opposite eyelid margin using a new sterile applicator. (2)

————DOSAGE FORMS AND STRENGTHS————

Bimatoprost ophthalmic solution 0.3 mg/mL. (3)

————CONTRAINDICATIONS————

Hypersensitivity. (4.1)

————WARNINGS AND PRECAUTIONS————

Concurrent administration of **LATISSE™** and IOP-lowering prostaglandin analogs in ocular hypertensive patients may decrease the IOP-lowering effect. Patients using these products concomitantly should be closely monitored for changes to their intraocular pressure. (5.1)
Pigmentation of the eyelids and iris may occur. Iris pigmentation is likely to be permanent. (5.2, 5.3)

————ADVERSE REACTIONS————

Most common adverse events (incidence approximately 3% - 4%) are eye pruritus, conjunctival hyperemia, and skin hyperpigmentation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Allergan at 1-800-433-8871 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for Patient Counseling Information and FDA-approved Patient Package Insert.

Revised 12/2008

FULL PRESCRIBING INFORMATION: Contents*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LATISSE™ (bimatoprost ophthalmic solution) 0.03% is indicated to treat hypotrichosis of the eyelashes by increasing their growth including length, thickness and darkness.

2 DOSAGE AND ADMINISTRATION

Ensure the face is clean, makeup and contact lenses are removed. Once nightly, place one drop of **LATISSE™** (bimatoprost ophthalmic solution) 0.03% on the disposable sterile applicator supplied with the package and apply evenly along the skin of the upper eyelid margin at the base of the eyelashes. The upper lid margin in the area of lash growth should feel lightly moist without runoff. Blot any excess solution runoff outside the upper eyelid margin with a tissue or other absorbent cloth. Dispose of the applicator after one use. Repeat for the opposite eyelid margin using a new sterile applicator.

Do not reuse applicators and do not use any other brush/applicator to apply **LATISSE™.**

Do not apply to the lower eyelash line (see **WARNINGS AND PRECAUTIONS**, **5.3** and **PATIENT COUNSELING INFORMATION, 17**).

Additional applications of **LATISSE™** will not increase the growth of eyelashes.

Upon discontinuation of treatment, eyelash growth is expected to return to its pre-treatment level.

3 DOSAGE FORMS AND STRENGTHS

Bimatoprost ophthalmic solution 0.3 mg/mL.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

LATISSE™ is contraindicated in patients with hypersensitivity to bimatoprost or any other ingredient in this product.

5 WARNINGS AND PRECAUTIONS

5.1 Effects on Intraocular Pressure

Bimatoprost ophthalmic solution **(LUMIGAN®)** lowers intraocular pressure (IOP) when instilled directly to the eye in patients with elevated IOP. In clinical trials, in patients with or without elevated IOP, **LATISSE™** lowered IOP, however, the magnitude of the reduction was not cause for clinical concern.

In ocular hypertension studies with **LUMIGAN®,** it has been shown that exposure of the eye to more than one dose of bimatoprost daily may decrease the intraocular pressure lowering effect. In patients using **LUMIGAN®** or other prostaglandin analogs for the treatment of elevated intraocular pressure, the concomitant use of **LATISSE™** may interfere with the desired reduction in IOP. Patients using prostaglandin analogs including **LUMIGAN®** for IOP reduction should only use **LATISSE™** after consulting with their physician and should be monitored for changes to their intraocular pressure (see **PATIENT COUNSELING INFORMATION, 17**).

5.2 Iris Pigmentation

Increased iris pigmentation has occurred when the same formulation of bimatoprost ophthalmic solution (**LUMIGAN®**) was instilled directly onto the eye. Although iridal pigmentation was not reported in clinical studies with **LATISSE™**, patients should be advised about the potential for increased brown iris pigmentation which is likely to be permanent.

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long term effects of increased pigmentation are not known. Iris color changes seen with administration of bimatoprost ophthalmic solution may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. Treatment with **LATISSE™** solution can be continued in patients who develop noticeably increased iris pigmentation.

Patients who receive treatment with **LATISSE™** should be informed of the possibility of increased pigmentation (see **PATIENT COUNSELING INFORMATION, 17**).

5.3 Lid Pigmentation

Bimatoprost has been reported to cause pigment changes (darkening) to periorbital pigmented tissues and eyelashes. The pigmentation is expected to increase as long as bimatoprost is administered, but has been reported to be reversible upon discontinuation of bimatoprost in most patients.

5.4 Hair Growth Outside the Treatment Area

There is the potential for hair growth to occur in areas where **LATISSE™** solution comes in repeated contact with the skin surface. It is important to apply **LATISSE™** only to the skin of the upper eyelid margin at the base of the eyelashes using the accompanying sterile applicators, and to carefully blot any excess **LATISSE™** from the eyelid margin to avoid it running onto the cheek or other skin areas (see **PATIENT COUNSELING INFORMATION, 17**).

5.5 Intraocular Inflammation

LATISSE™ solution should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

5.6 Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost

ophthalmic solution (**LUMIGAN®**) for elevated IOP. **LATISSE™** should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

5.7 Contamination of LATISSE™ or Applicators

The **LATISSE™** bottle must be kept intact during use. It is important to use **LATISSE™** solution as instructed, by placing one drop on the single-use-per eye applicator. The bottle tip should not be allowed to contact any other surface since it could become contaminated. The accompanying sterile applicators should only be used on one eye and then discarded since reuse of applicators increases the potential for contamination and infections. There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products (see **PATIENT COUNSELING INFORMATION, 17**).

5.8 Use with Contact Lenses

LATISSE™ contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to application of solution and may be reinserted 15 minutes following its administration (see **PATIENT COUNSELING INFORMATION, 17**).

6 ADVERSE REACTIONS

The following information is based on clinical trial results from a multicenter, double-masked, randomized, vehicle-controlled, parallel study including 278 adult patients for four months of treatment.

The most frequently reported adverse events were eye pruritis, conjunctival hyperemia, skin hyperpigmentation, ocular irritation, dry eye symptoms, and erythema of the eyelid. These events occurred in less than 4% of patients.

Adverse reactions reported with bimatoprost ophthalmic solution (**LUMIGAN®**) for the reduction of intraocular pressure include, ocular dryness, visual disturbance, ocular burning, foreign body sensation, eye pain, blepharitis, cataract, superficial punctuate keratitis, eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, conjunctival edema, abnormal hair growth, iritis, infections (primarily colds and upper respiratory tract infections), headaches, and asthenia.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Teratogenic effects: In embryo/fetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 33 or 97 times, respectively, the maximum intended human exposure (based on blood AUC levels after topical ophthalmic administration to the cornea or conjunctival sac).

At doses at least 41 times the maximum intended human exposure, the gestation length was reduced in the dams, the incidence of dead fetuses, late resorptions, peri- and postnatal pup mortality was increased, and pup body weights were reduced.

There are no adequate and well-controlled studies of bimatoprost ophthalmic solution 0.03% administration in pregnant women. Because animal reproductive studies are not always predictive of human response, **LATISSE™** should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

It is not known whether **LATISSE™** solution is excreted in human milk, although in animal studies, bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when **LATISSE™** is administered to a nursing woman.

8.4 Pediatric Use

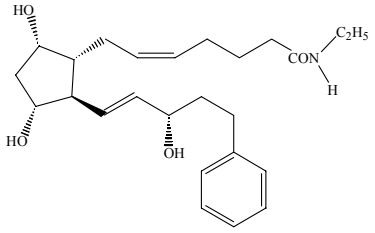
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients.

11 DESCRIPTION

LATISSE™ (bimatoprost ophthalmic solution) 0.03% is a synthetic prostaglandin analog. Its chemical name is (Z)-7-[(1R,2R,3R,5S)-3,5-Dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-5-N-ethylheptenamide, and its molecular weight is 415.58. Its molecular formula is $C_{25}H_{37}NO_4$. Its chemical structure is:



Bimatoprost is a powder, which is very soluble in ethyl alcohol and methyl alcohol and slightly soluble in water. **LATISSE™** is a clear, isotonic, colorless, sterile ophthalmic solution with an osmolality of approximately 290 mOsmol/kg.

Contains: Active: bimatoprost 0.3 mg/mL; **Preservative:** benzalkonium chloride 0.05 mg/mL; **Inactives:** sodium chloride; sodium phosphate, dibasic; citric acid; and purified water. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH. The pH during its shelf life ranges from 6.8 - 7.8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Bimatoprost is a structural prostaglandin analog. Although the precise mechanism of action is unknown the growth of eyelashes is believed to occur by increasing the percent of hairs in, and the duration of the anagen or growth phase.

12.3 Pharmacokinetics

Absorption

After one drop of bimatoprost ophthalmic solution 0.03% was administered once daily into both eyes (cornea and/or conjunctival sac) of 15 healthy subjects for two weeks, blood concentrations peaked within 10 minutes after dosing and were below the lower limit of detection (0.025 ng/mL) in most subjects within 1.5 hours after dosing. Mean C_{max} and $AUC_{0\text{-}24hr}$ values were similar on days 7 and 14 at approximately 0.08 ng/mL and 0.09 ng•hr/mL, respectively, indicating that steady state was reached during the first week of ocular dosing. There was no significant systemic drug accumulation over time.

Distribution

Bimatoprost is moderately distributed into body tissues with a steady-state volume of distribution of 0.67 L/kg. In human blood, bimatoprost resides mainly in the plasma. Approximately 12% of bimatoprost remains unbound in human plasma.

Metabolism

Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation. Bimatoprost then undergoes oxidation, N-deethylation, and glucuronidation to form a diverse variety of metabolites.

Elimination

Following an intravenous dose of radiolabeled bimatoprost (3.12 µg/kg) to six healthy subjects, the maximum blood concentration of unchanged drug was 12.2 ng/mL and decreased rapidly with an elimination half-life of approximately 45 minutes. The total blood clearance of bimatoprost was 1.5 L/hr/kg. Up to 67% of the administered dose was excreted in the urine while 25% of the dose was recovered in the feces.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses of up to 2 mg/kg/day and 1 mg/kg/day respectively (approximately 192 and 291 times the recommended human exposure based on blood AUC levels after topical corneal and/or conjunctival sac administration respectively) for 104 weeks.

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* mouse micronucleus tests.

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day.

14 CLINICAL STUDIES

LATISSE™ solution was evaluated for its effect on overall eyelash prominence in a multicenter, double-masked, randomized, vehicle-controlled, parallel study including 278 adult patients for four months of treatment. The primary efficacy endpoint in this study was an increase in overall eyelash prominence as measured by at least a 1-grade increase on the 4-point Global Eyelash Assessment (GEA) scale, from baseline to the end of the treatment period (week 16). **LATISSE™** was more effective than vehicle as measured by the GEA score, with statistically significant differences seen at 8-week, 12-week, and 16-week (**primary endpoint**) treatment durations.

Table 1

Number (%) of subjects with at least a 1-grade increase from baseline in Global Eyelash Assessment (Primary Efficacy Endpoint – Week 16)

Week	**LATISSE™** N=137 N (%)	Vehicle N=141 N (%)
1	7 (5%)	3 (2%)
4	20 (15%)	11 (8%)
8	69 (50%)	21 (15%)
12	95 (69%)	28 (20%)
16	**107 (78%)**	**26 (18%)**
20	103 (79%)	27 (21%)

In this study, patients were also evaluated for the effect of **LATISSE™** solution on the length, thickness and darkness of their eyelashes. Improvements from baseline in eyelash growth as measured by digital image analysis assessing eyelash length, fullness/thickness, and darkness were statistically significantly more pronounced in the bimatoprost group at weeks 8, 12, and 16.

Table 2

Efficacy endpoint at Week 16 (Mean Change from Baseline)	**LATISSE™**	Vehicle
Eyelash growth (length) (mm; % increase)	N=137 1.4; 25%	N=141 0.1; 2%
Fullness/thickness (mm^2; % increase)	N=136 0.7; 106%	N=140 0.1; 12%
Eyelash darkness (intensity*; % increase in darkness)	N=135 -20.2; -18%	N=138 -3.6; -3%

* a negative value is representative of eyelash darkening

After the 16-week treatment period, a 4-week post-treatment period followed during which the effects of bimatoprost started to return toward baseline. The effect on eyelash growth is expected to abate following longer term discontinuation.

16 HOW SUPPLIED/STORAGE AND HANDLING

LATISSE™ (bimatoprost ophthalmic solution) 0.03% is supplied sterile in opaque white low density polyethylene dispenser bottles and tips with turquoise polystyrene caps accompanied by 60 sterile, disposable applicators:

3 mL in a 5 mL bottle NDC 0023-3616-03

Storage: LATISSE™ should be stored at 2° to 25°C (36° to 77°F).

17 PATIENT COUNSELING INFORMATION

17.1 Nightly Application

Patients should be informed that **LATISSE™** (bimatoprost ophthalmic solution) should be applied every night using only the accompanying sterile applicators. They should start by ensuring their face is clean, all makeup is removed, and their contact lenses removed (if applicable). Then carefully place one drop of **LATISSE™** solution on the disposable sterile applicator and brush cautiously along the skin of the upper eyelid margin at the base of the eyelashes. If any **LATISSE™** solution gets into the eye proper, it will not cause harm. The eye should not be rinsed.

Additional applications of **LATISSE™** will not increase the growth of eyelashes.

Patients should be informed not to apply to the lower eyelash line. Any excess solution outside the upper eyelid margin should be blotted with a tissue or other absorbent material.

The onset of effect is gradual but is not significant in the majority of patients until 2 months. Patients should be counseled that the effect is not permanent and can be expected to gradually return to the original level upon discontinuation of treatment with **LATISSE™**.

17.2 Handling the Bottle and Applicator

Patients should be instructed that the **LATISSE™** bottle must be maintained intact and to avoid allowing the tip of the bottle or applicator to contact surrounding structures, fingers, or any other unintended surface in order to avoid contamination of the bottle or applicator by common bacteria known to cause ocular infections. Patients should also be instructed to only use the applicator supplied with the product once and then discard since reuse could result in using a contaminated applicator. Serious infections may result from using contaminated solutions or applicators.

17.3 Potential for Intraocular Pressure Effects

LATISSE™ may lower intraocular pressure although not to a level that will cause clinical harm.

In patients using **LUMIGAN®** or other prostaglandin analogs for the treatment of elevated intraocular pressure, the concomitant use of **LATISSE™** may interfere with the desired reduction in IOP. Patients using prostaglandin analogs for IOP reduction should only use **LATISSE™** after consulting with their physician.

17.4 Potential for Eyelid Skin Darkening

Patients should be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of **LATISSE™**.

17.5 Potential for Iris Darkening

Although iridal pigmentation was not reported in clinical studies with **LATISSE™**, patients should be advised about the potential for increased brown iris pigmentation which is likely to be permanent. Increased iris pigmentation has occurred when the same formulation of bimatoprost ophthalmic solution (**LUMIGAN®**) was instilled directly onto the eye.

17.6 Potential for Unexpected Hair Growth or Eyelash Changes

Patients should be informed of the possibility of hair growth occurring outside of the target treatment area if **LATISSE™** repeatedly touches the same area of skin outside the treatment area. They should also be informed of the possibility of disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are likely reversible upon discontinuation of treatment.

17.7 When to Seek Physician Advice

Patients should be advised that if they develop a new ocular condition (e.g., trauma or infection), experience a sudden decrease in visual acuity, have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should

immediately seek their physician's advice concerning the continued use of **LATISSE™**. Patients on IOP-lowering medications should not use **LATISSE™** without prior consultation with their physician.

17.8 Use with Contact Lenses

Patients should be advised that **LATISSE™** solution contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to application of **LATISSE™** and may be reinserted 15 minutes following its administration.

--------Cut Here-✂----------

17.9 FDA-Approved Patient Package Insert

PATIENT INFORMATION

LATISSE™ (la teece) (bimatoprost ophthalmic solution) 0.03%

Read the Patient Information that comes with **LATISSE™** before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your physician about your treatment.

What is hypotrichosis of the eyelashes?

Hypotrichosis is another name for having inadequate or not enough eyelashes.

What is LATISSE™ solution?

LATISSE™ solution is a prescription treatment for hypotrichosis used to grow eyelashes, making them longer, thicker and darker.

Who should NOT take LATISSE™?

Do not use **LATISSE™** solution if you are allergic to one of its ingredients.

Are there any special warnings associated with LATISSE™ use?

LATISSE™ solution is intended for **use on the skin of the upper eyelid margins at the base of the eyelashes**. Refer to Illustration 2 below. **DO NOT APPLY** to the lower eyelid. If you are using **LUMIGAN®** or other products in the same class for elevated intraocular pressure (IOP), or if you have a history of abnormal IOP, you should only use **LATISSE™** under the close supervision of your physician.

LATISSE™ use may cause darkening of the eyelid skin which may be reversible. **LATISSE™** use may also cause increased brown pigmentation of the colored part of the eye which is likely to be permanent.

It is possible for hair growth to occur in other areas of your skin that **LATISSE™** frequently touches. Any excess solution outside the upper eyelid margin should be blotted with a tissue or other absorbent material to reduce the chance of this from happening. It is also possible for a difference in eyelash length, thickness, fullness, pigmentation, number of eyelash hairs, and/or direction of eyelash growth to occur between eyes. These differences, should they occur, will usually go away if you stop using **LATISSE™**.

Who should I tell that I am using LATISSE™?

You should tell your physician you are using **LATISSE™** especially if you have a history of eye pressure problems.

You should also tell anyone conducting an eye pressure screening that you are using **LATISSE™**.

What should I do if I get LATISSE™ in my eye?

LATISSE™ solution is an ophthalmic drug product. **LATISSE™** is not expected to cause harm if it gets into the eye proper. Do not attempt to rinse your eye in this situation.

What are the possible side effects of LATISSE™?

The most common side effects after using **LATISSE™** solution are an itching sensation in the eyes and/or eye redness. This was reported in approximately 4% of patients. **LATISSE™** solution may cause other less common side effects which typically occur on the skin close to where **LATISSE™** is applied, or in the eyes. These include skin darkening, eye irritation, dryness of the eyes, and redness of the eyelids.

If you develop a new ocular condition (e.g., trauma or infection), experience a sudden decrease in visual acuity, have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, you should immediately seek your physician's advice concerning the continued use of **LATISSE™** solution**.**

What happens if I stop using LATISSE™?

If you stop using **LATISSE™**, your eyelashes are expected to return to their previous appearance over several weeks to months.

Any eyelid skin darkening is expected to reverse after several weeks to months.

Any darkening of the colored part of the eye known as the iris is NOT expected to reverse and is likely permanent.

How do I use LATISSE™?

LATISSE™ solution is packaged as a 3 mL bottle of solution with 60 accompanying sterile, disposable applicators. The recommended dosage is one application nightly to the skin of the upper eyelid margin at the base of the eyelashes only.

Once nightly, start by ensuring your face is clean, makeup and contact lenses are removed. Remove an applicator from its tray. Then, holding the sterile applicator horizontally, place one drop of **LATISSE™** on the area of the applicator closest to the tip but not on the tip (see Illustration 1). Then immediately draw the applicator carefully across the skin of the upper eyelid margin at the base of the eyelashes (where the eyelashes meet the skin) going from the inner part of your lash line to the outer part (see Illustration 2). Blot any excess solution beyond the eyelid margin. Dispose of the applicator after one use.

Repeat for the opposite upper eyelid margin using a new sterile applicator. This helps minimize any potential for contamination from one eyelid to another.

Illustration 1

Illustration 2

DO NOT APPLY in your eye or to the lower lid. **ONLY** use the sterile applicators supplied with **LATISSE™** to apply the product. If you miss a dose, don't try to "catch up." Just apply **LATISSE™** solution the next evening. Fifty percent of patients treated with **LATISSE™** in a clinical study saw significant improvement by 2 months after starting treatment.

If any **LATISSE™** solution gets into the eye proper, it is not expected to cause harm. The eye should not be rinsed.

Don’t allow the tip of the bottle or applicator to contact surrounding structures, fingers, or any other unintended surface in order to avoid contamination by common bacteria known to cause infections.

Contact lenses should be removed prior to application of **LATISSE™** and may be reinserted 15 minutes following its administration.

Use of **LATISSE™** more than once a day will not increase the growth of eyelashes more than use once a day.

Store **LATISSE™** solution at 36^{o} to 77^{o}F (2^{o} to 25^{o}C).

General Information about LATISSE™.
Prescription treatments are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use **LATISSE™** solution for a condition for which it was not prescribed. Do not give **LATISSE™** to other people. It may not be appropriate for them to use.

This leaflet summarizes the most important information about **LATISSE™** solution. If you would like more information, talk with your physician. You can also call Allergan’s product information department at 1-800-433-8871.

What are the ingredients in LATISSE™?

Active ingredient: bimatoprost
Inactive ingredients: benzalkonium chloride; sodium chloride; sodium phosphate, dibasic; citric acid; and purified water. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH. The pH during its shelf life ranges from 6.8 - 7.8.

72041US10X