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

VYZULTA (latanoprostene bunod ophthalmic solution) 0.024%, for topical ophthalmic use
Initial U.S. Approval: 2017

INDICATIONS AND USAGE
VYZULTA is a prostaglandin analog indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

DOSE AND ADMINISTRATION
1. Topical ophthalmic solution: 0.24 mg/mL latanoprostene bunod (0.024%) (3)
2. Use with Contact Lens

DOSAGE FORMS AND STRENGTHS
Topical ophthalmic solution: 0.24 mg/mL latanoprostene bunod (0.024%)

FULL PRESCRIBING INFORMATION: CONTENTS*
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18 ADVERSE REACTIONS

- None.

NOTICE: (HIGHLIGHTS OF PRESCRIBING INFORMATION) Contains important safety information. See full Prescribing Information for details.

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS

• Pigmentation: Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent. (5.1)
• Eyelash changes: Gradual changes to eyelashes including increased length, increased thickness and number of eyelashes. Usually reversible upon discontinuation of treatment. (5.2)

Most common ocular adverse reactions with incidence > 2% are conjunctival hyperemia, eye irritation (4%), eye pain (5%), and instillation site pain (1%).

See 17 PATIENT COUNSELING INFORMATION

Revised: 06/2018

FULL PRESCRIBING INFORMATION
1 INDICATIONS AND USAGE
VYZULTA (latanoprostene bunod ophthalmic solution) 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dosage is one drop in the conjunctival sac of the affected eye(s) once daily in the evening. (2)

DOSAGE FORMS AND STRENGTHS

The recommended dosage is one drop in the conjunctival sac of the affected eye(s) once daily in the evening. Do not administer more than one drop (0.24 mg/mL) of VYZULTA to any one eye in 24 hours. (2)

VYZULTA should be used with caution in patients with a history of irritable eye syndrome (iritis/syndrome) and should generally not be used in patients with active intraocular inflammation as it may exacerbate this condition. (2)

5.2 Eyelash Changes

Eyelash changes are usually reversible upon discontinuation of treatment. (5.2)

5.3 Intraocular Inflammation

VYZULTA should be used with caution in patients with a history of iritis/syndrome (iritis/syndrome) and should generally not be used in patients with active intraocular inflammation as it may exacerbate this condition. (2)

5.4 Macular Edema

Macular edema, including cystoid macular edema, has been reported in patients administered long-term (≥ 12 months) treatment with a prostaglandin analog, including VYZULTA, should be evaluated by the possibility of increased pigmentation, including permanent changes. The long-term effects of increased pigmentation are not known.

Iris color change 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 may not fleckles of the iris appear to be affected by treatment. While treatment with prostaglandin analogs may produce increased pigmentation of the iris, these patients should be examined regularly for the occurrence of pigmentary changes to the iris. (5.1)

5.6 Use with Contact Lens

- Usually reversible upon discontinuation of treatment. (5.2)

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling.

- Pigmentation [see Warnings and Precautions (5.1)]
- Eyelash Changes [see Warnings and Precautions (5.2)]
- Intraocular Inflammation [see Warnings and Precautions (5.3)]
- Macular Edema [see Warnings and Precautions (5.4)]
- Bacterial Keratitis [see Warnings and Precautions (5.5)]
- Use with Contact Lens [see Warnings and Precautions (5.6)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under relatively 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.

VYZULTA was evaluated in 811 patients in 2 controlled clinical trials of up to 2 years duration. The most common ocular adverse reactions observed in patients treated with latanoprostene bunod were increased pigmentation of the iris (8%), eye irritation (4%), eye pain (3%), and instillation site pain (2%). Approximately 0.8% of patients discontinued treatment due to one or more of the above adverse reactions including increased pigmentation, conjunctival irritation, eye irritation, eye pain, conjunctival edema, vision blurred, punctate keratitis and foreign body sensation.

6 USE IN SPECIFIC POPULATIONS

6.1 Pregnancy

Risk Summary

VYZULTA is not available human data for the use of VYZULTA during pregnancy to inform any drug associated risks.

Latanoprostene bunod has caused miscarriages, abortion, and fetal harm in animals. Latanoprostene bunod administered by intravenous injection at doses ≥ 300 mcg/kg/day (23 times the clinical dose) produced 100% embryofetal lethality. (8.1)

Latanoprostene bunod produced structural abnormalities at doses ≥ 0.24 mcg/kg/day (23 times the clinical dose) produced 100% embryofetal lethality. (8.1)

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VYZULTA (latanoprostene bunod ophthalmic solution) 0.024%, for topical ophthalmic use

6.2 Nursing Mothers

It is not known whether VYZULTA is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VYZULTA is administered to a nursing woman. (8.2)

6.3 Pediatric Use

VYZULTA has not been studied in children or adolescents less than 18 years of age. (8.3)

6.4 Geriatric Use

VYZULTA has not been studied in patients aged ≥ 65 years. (8.4)

9 SAFETY INFORMATION

9.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

9.2 Pharmacodynamics

9.3 Pharmacokinetics

9.4 Pharmacology

10 PATIENT COUNSELING INFORMATION

11 DESCRIPTION

VYZULTA contains a combination of two active ingredients: latanoprostene bunod (0.024%) and benzalkonium chloride. VYZULTA is indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

12 CLINICAL PHARMACOLOGY

12.1 Mechanisms of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL TRIALS

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

- None.

NOTICE: (HIGHLIGHTS OF PRESCRIBING INFORMATION) Contains important safety information. See full Prescribing Information for details.

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS

- Pigmentation: Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent. (5.1)
- Eyelash changes: Gradual changes to eyelashes including increased length, increased thickness and number of eyelashes. Usually reversible upon discontinuation of treatment. (5.2)

Most common ocular adverse reactions with incidence > 2% are conjunctival hyperemia, eye irritation (4%), eye pain (5%), and instillation site pain (1%).

See 17 PATIENT COUNSELING INFORMATION

Revised: 06/2018
Its chemical structure is:

was not observed at the 0.024% dose.

chronic fibrosis/inflammation in the 0.04% dose male groups, with drops of 0.04% per dose, bid. The systemic exposures are equivalent latanoprostene bunod to one eye of cynomolgus monkeys: control bunod. The potential to impact fertility can be partially characterized acid, resulting from oral dosing with latanoprost in lifetime rodent in long-term animal studies. Latanoprost acid is a main metabolite Latanoprostene bunod has not been tested for carcinogenic activity microneutral assay. Chromosomal aberrations were observed rat bone marrow.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Latanoprostene bunod is not a prodrugs and does not induce microsome mutagenicity in the in vivo rat bone marrow micronucleus assay. Chromosomal aberrations were observed in vitro with human lymphocytes in the absence of metabolic activation. Latanoprostene bunod has not been tested for carcinogenic activity in long-term animal studies. Latanoprost acid is a major metabolite of latanoprostene bunod. Exposure of rats and mice to latanoprost, resulting from oral dosing with latanoprost in lifetime robust bioassays, was not carcinogenic.

Fertility studies have not been conducted with latanoprostene bunod. No information is available regarding the potential for fertility changes that may be characterized by exposure to latanoprost, a common metabolite of both latanoprost and latanoprostene bunod. Latanoprostene bunod has not been found to have any effect on male or female fertility in animal studies.

13.2 Animal Toxicology and/or Pharmacology

A 9 month toxicity study administered topical ocular doses of latanoprostene bunod to one eye of cynomolgus monkeys: control one eye, one drop of 0.024%, bid, one drop of 0.04%, bid and two drops of 0.04% g/sid, bid. The systemic exposures are equivalent to 4.2, 8.5, and 13.5 fold the clinical dose, respectively, on body surface area basis (assuming 100% absorption). Microscopic evaluation of the lungs after 8 months observed pleural/subpleural fibrosis. Ocular inflammation in the 0.04% dose group was observed with increasing incidence and severity compared to controls. Lung toxicity was not observed at the 0.04% dose.