PDL DRUG REVIEW

Proprietary Name: Vyzulta®
Common Name: latanoprostene bunod
PDL Category: Ophthalmics- Prostaglandins

Comparable Products	Preferred Drug List Status
latanoprost	Preferred
Travatan Z	Preferred

Summary

Pharmacology/Usage: Latanoprostene bunod, the active ingredient of Vyzulta®, is a prostaglandin analog. It is thought to lower intraocular pressure by increasing outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes. Reduction of intraocular pressure reduces the risk of glaucomatous visual field loss. Reduction of intraocular pressure starts about 1 to 3 hours after the first administration.

Indications: For the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

There is no pregnancy category for this product; however, the risk summary indicates that there are no available human data for use during pregnancy to inform any drug associated risks. Use in the pediatric population 16 years and younger is not recommended due to potential safety concerns.

Dosage Forms: Topical ophthalmic solution: 0.24mg/ml (0.024%). Also contains the preservative benzalkonium chloride. Store unopened bottle in the refrigerator; once opened, may store at room temperature for 8 weeks.

Recommended Dosage: Instill 1 drop into the conjunctival sac of the affected eye(s) once daily in the evening. Do not administer more than once daily as it has been shown that more frequent use of prostaglandin analogs may lessen the intraocular pressure lowering effect. Contact lenses should be removed prior to use, and the lenses may be reinserted 15 minutes after administration.

If Vyzulta® is to be used concomitantly with other topical ophthalmic products to lower IOP, administer each product at least 5 minutes apart.

Drug Interactions: There are no drug interactions listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Vyzulta®). There was no placebo data found in the prescribing information to compare with.* The most frequently reported adverse events included conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%). There were about 0.6% of patients who discontinued therapy due to ocular adverse reactions, including ocular hyperemia, conjunctival irritation, eye irritation, eye pain, conjunctival edema, vision blurred, punctate keratitis, and foreign body sensation.

Vyzulta® may cause changes to pigmented tissue, with the most commonly reported changes with prostaglandin analogs being increased pigmentation of the iris and periorbital tissue (eyelid). Pigmentation is expected to increase as long as treatment is used. After discontinuing treatment, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes are likely to be reversible. Iris color change may be noticeable for several months to years.

Vyzulta® may gradually change eyelashes and vellus hair in the treated eye. The changes included increased length, thickness, and number of lashes or hair. Furthermore, the changes are generally reversible with discontinuation of treatment.

Use Vyzulta® with caution in those with a history of intraocular inflammation (iritis/uveitis) and Vyzulta® should generally not be used in patients with active intraocular inflammation as it may exacerbate this condition.

Macular edema has been reported during treatment with prostaglandin analogs. Use Vyzulta® with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Bausch & Lomb Inc.

Analysis: The metabolites of latanoprostene bunod are latanoprost acid and butanediol mononitrate. In clinical studies up to 12 months, patients with open-angle glaucoma or ocular hypertension who had an average baseline IOP of 26.7mmHg resulted in up to 7 to 9mmHg IOP lowering with Vyzulta®. This limited information was found in the prescribing information but there was no comparator data provided.

Place in Therapy: Vyzulta® is a topical prostaglandin analog indicated for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension.

In the 2016 randomized, phase 3, multicenter, double-masked APOLLO study by Weinreb et al[2], 420 subjects were randomized to a 3-month regimen of latanoprostene bunod (QPM) or timolol 0.5% (1 drop BID) to assess the primary endpoint of IOP measured at each of the 9 assessment time points. At all 9 time points, non-inferiority between treatments was shown, and the mean IOP in the study eye was significantly lower in the latanoprostene bunod group than the timolol group ($p \leq 0.002$). In addition, at all 9 time points, the percentage of subjects with mean IOP ≤18mmHg and the percentage with IOP reduction ≥25% were significantly higher in the latanoprostene group vs the timolol group (mean IOP ≤18mmHg: 22.9% vs 11.3%, $p=0.005$; IOP reduction ≥25%: 34.9% vs 19.5%, $p=0.001$). The percentage of treated eyes experiencing at least 1 ocular treatment emergent adverse event was comparable between treatment groups. Two discontinued treatment in the latanoprostene group due to ocular adverse events as compared with 5 in the timolol group. The authors concluded that latanoprostene bunod demonstrated significantly greater IOP lowering than timolol throughout the day over 3 months of treatment.

In the 2016 randomized, double-masked, non-inferiority LUNAR study by Medeiros et al[3], 387 subjects were randomized to latanoprostene bunod or timolol 0.5% (1 drop BID) for 3 months to assess the primary outcome of IOP measured at the specified time points. Results suggested that non-inferiority of latanoprostene bunod to timolol 0.5% was demonstrated in regard to IOP lowering, and it also met criteria for statistical superiority over timolol at all time points except the 8AM time point at week 2. The authors concluded that latanoprostene bunod was non-inferior to timolol and resulted in significantly greater IOP lowering over 3 months.

A 2015 randomized, investigator-masked, dose-ranging study compared latanoprost 0.005% with latanoprostene bunod of various doses, including 0.024% and 0.040%. All treatments led to significant reductions in mean diurnal IOP from baseline at all follow-up visits; however, the latanoprostene bunod 0.024% and 0.040% treatments demonstrated a significantly greater reduction from baseline in diurnal IOP compared with the latanoprost group ($p=0.005$ and $p=0.009$, respectively) at day 28.[4]

There is some evidence at this time that may suggest that Vyzulta® is more effective than timolol and latanoprost in a clinical trial; however, there is no evidence that it is safer or more effective than all other available, more cost-effective medications. It is therefore recommended that Vyzulta® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Vyzulta [package insert]. Bridgewater, NJ: Bausch & Lomb, a division of Valeant Pharmaceuticals; 2017.

[2] Weinreb RN, Scassellati Sforzolini B, Vittitow J, et al. Latanoprostene bunod 0.024% versus timolol maleate 0.5% in subjects with open-angle glaucoma or ocular hypertension: The APOLLO Study. *Ophthalmology*. 2016; 123(5): 965-73.

[3] Medeiros FA, Martin KR, Peace J, et al. Comparison of latanoprostene bunod 0.024% and timolol maleate 0.5% in open-angle glaucoma or ocular hypertension: The LUNAR study. *Am J Ophthalmol*. 2016; 168:250-259.

[4] Weinreb RN, Ong T, Scassellati Sforzoline B, et al. A randomized, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: the VOYAGER study. *Br J Ophthalmol*. 2015; 99(6): 738-45.