VYZULTA VISIONARIES

DEFINING THE APPROPRIATE PATIENT TYPES FOR MONOTHERAPY WITH VYZULTA

This supplement captures highlights from a roundtable discussion that took place on April 5, 2024, at the American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting in Boston, Massachusetts.

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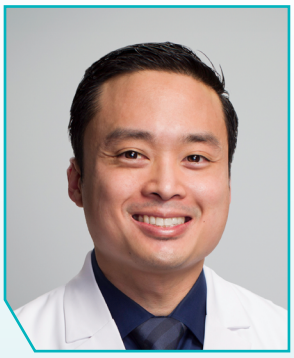

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Participants of this roundtable are paid consultants of Bausch + Lomb.

Introduction

The American Academy of Ophthalmology defines primary open-angle glaucoma as "a chronic, progressive optic neuropathy in adults in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This condition is associated with an open anterior chamber angle by gonioscopy. Primary open-angle glaucoma is a potentially blinding eye disease, but early diagnosis and treatment can generally prevent visual disability."[1] Elevated IOP (ocular hypertension) is an important modifiable risk factor in primary open-angle glaucoma, with numerous studies demonstrating that the prevalence of primary open-angle glaucoma increases with increasing IOP.[1]

The main goal in managing primary open-angle glaucoma or ocular hypertension is achievement of IOP control in the target range, which stabilizes the optic nerve, retinal nerve fiber layer, and visual field.[1] Options for IOP lowering include medications, laser therapy, and incisional surgery.[1] Results from numerous randomized controlled trials have demonstrated that IOP reduction decreases the rate and incidence of primary open-angle glaucoma progression.

Prostaglandin analog–containing eye drops are the most frequently prescribed initial medical therapy for IOP control in patients with open-angle glaucoma or ocular hypertension because they are efficacious and well tolerated, and only need to be instilled once per day.[1] VYZULTA® (latanoprostene bunod ophthalmic solution) 0.024% is a prostaglandin analog indicated for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension.[2] The efficacy and safety of VYZULTA have been evaluated in numerous clinical studies, inclusive of both prospective randomized controlled trials and real-world retrospective analyses.[3] Across studies, VYZULTA delivered powerful and sustained IOP reduction with excellent tolerability.[3]

In this roundtable discussion, 4 leaders in management of open-angle glaucoma and ocular hypertension shared their perspectives on the scientific data in support of VYZULTA. The faculty defined 4 distinct patient types appropriate for IOP lowering using VYZULTA and provided real-world examples of each of these patient types from their own clinical practices[1]:

- Those who **need a powerful first-line IOP-lowering treatment** when beginning their glaucoma journey
- Those who are **not adequately responding to their current PGA treatment**, including latanoprost 0.005%
- Those who **received a prior diagnosis of ocular hypertension** and may be at risk of developing open-angle glaucoma
- Those with **inadequately controlled IOP following SLT***

These patient cases provide real-world reinforcement of the VYZULTA clinical study findings, confirming why monotherapy with VYZULTA empowers both ophthalmologists and affected patients to **go for IOP control…*from the start***.

Why is VYZULTA an appropriate IOP-lowering monotherapy for diverse patient types?

Dr. Richens: In my view, VYZULTA is appropriate for patients with open-angle glaucoma or ocular hypertension who need their IOP reduced. This is particularly true in my practice in the Utah desert, where many of my patients with open-angle glaucoma or ocular hypertension are elderly and have numerous ocular comorbidities, particularly retinal comorbidities. When treating these patients, I don't hesitate to reach for VYZULTA first, given VYZULTA's efficacy and safety profile. Most of the patient types that I see are excellent candidates for VYZULTA.

> ***"I don't hesitate to reach for VYZULTA first, given VYZULTA's efficacy and safety profile."***
>
> ***—Dr. Sharon Richens***

Dr. Nguyen: There are many attributes of VYZULTA that make it an appealing option for my patients with open-angle glaucoma or ocular hypertension. VYZULTA is administered once daily,[2] which is a simple dosing regimen. I also like that VYZULTA delivers impressive IOP-lowering power in one drop. Specifically, in clinical studies of up to 12 months' duration evaluating patients with open-angle glaucoma or ocular hypertension and an average baseline IOP of 26.7 mmHg, the IOP-lowering effect of VYZULTA was up to 7 to 9 mmHg.[2]

Thinking beyond efficacy, it's important to note that VYZULTA is well tolerated. VYZULTA was evaluated in 811 patients in 2 controlled clinical trials of up to 12 months' duration, and the most common ocular adverse reactions were conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%).[2] Approximately 0.6% of patients 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.[2]

*In clinical trials, patients with a history of SLT in either eye >90 days prior to study entry could be enrolled.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation

Please see additional Important Safety Information throughout and full Prescribing Information for VYZULTA here.

VYZULTA®
(latanoprostene bunod ophthalmic solution), 0.024%

Why is VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% an appropriate IOP-lowering monotherapy for diverse patient types? (Continued)

Dr. Nguyen (cont'd): However, the main reason that I reach for VYZULTA before other prostaglandin analogs is the unique mechanism of action of VYZULTA. Latanoprostene bunod is thought to lower intraocular pressure by increasing outflow of aqueous humor through both the trabecular meshwork and the uveoscleral routes.[2] This dual mechanism of action, acting simultaneously on 2 different outflow pathways, is particularly important to me because all the physicians in my practice routinely perform minimally invasive glaucoma surgery (MIGS), and I believe that the success of our MIGS procedures depends on correct function of the eye's natural outflow system.

> *"The main reason that I reach for VYZULTA before other prostaglandin analogs is the unique mechanism of action of VYZULTA."*
>
> *—Dr. Bac Nguyen*

Dr. Richens: I anticipate that as our society continues to age, open-angle glaucoma and ocular hypertension will become more prevalent over time. Monotherapy with VYZULTA represents a good treatment strategy for my patients with these conditions. I don't want to place my patients on complex regimens of multiple treatments so they have to navigate multiple dosing regimens and are responsible for multiple copays. I tell my patients, "I want you on the right medication from the start. I just want you to be done searching for the appropriate treatment."

Dr. Parekh: I agree with both **Dr. Nguyen** and **Dr. Richens**. In the field of interventional glaucoma management, I have observed a push to substantially curb—or even eliminate—the use of IOP-lowering drops. However, I don't want to eliminate drops—I want to eliminate polypharmacy. What I want is an effective topical monotherapy that will provide reliable IOP control to my patients day in and day out. I believe VYZULTA represents such a therapy.

> *"What I want is an effective topical monotherapy that will provide reliable IOP control to my patients day in and day out. I believe VYZULTA represents such a therapy."*
>
> *—Dr. Jai Parekh*

The reason I emphasize the need for a reliable IOP-lowering drop is that as glaucoma treaters, we are interested in hitting our patients' IOP targets. The goal of treatment is to maintain the IOP within a range at which visual field loss is unlikely to substantially reduce a patient's health-related quality of life over their lifetime.[1] The target pressure is individualized for each patient and may need adjustment further down or even up in the course of the disease.[1]

When initiating IOP-lowering therapy, the physician assumes that the measured pretreatment IOP range contributed to optic nerve damage and is likely to cause further damage in the future.[1] Factors to consider when choosing a target pressure include the stage of overall glaucomatous damage (as determined by the degree of structural optic nerve injury and/or functional visual field loss), the baseline IOP at which damage occurred, the patient's age, and other ophthalmic and general medical considerations.[1] While such guidelines are valuable, the practical reality is that, in my real-world experience, my IOP goal is typically 13 to 15 mmHg for most patients. If a patient's IOP starts at 25 mmHg and then decreases to 20 mmHg, it is likely that their IOP hasn't decreased sufficiently and that their disease will progress. Through its IOP-lowering effect, VYZULTA gives us a way to modify the disease trajectory of open-angle glaucoma.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- Use with caution in patients with a history of intraocular inflammation (iritis/uveitis). VYZULTA should generally not be used in patients with active intraocular inflammation

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Why is VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% an appropriate IOP-lowering monotherapy for diverse patient types? (Continued)

Dr. Berdy: I echo all the points made by the others. In medicine, whenever we choose a therapy, we would like it to have a favorable efficacy and safety profile and a simple dosing regimen, and VYZULTA does have those attributes. However, what makes VYZULTA stand out to me is the science behind its molecular metabolism. After topical ocular administration, the latanoprostene bunod in VYZULTA is rapidly metabolized in the eye to latanoprost acid (active moiety), an F2α prostaglandin analog, and butanediol mononitrate; in turn, butanediol mononitrate is metabolized to 1,4-butanediol and nitric oxide **(Figure 1)**.[2] This represents advanced biochemical science and helps explain why VYZULTA increases outflow of aqueous humor through both the trabecular meshwork and the uveoscleral routes, rather than just via a single route.[2]

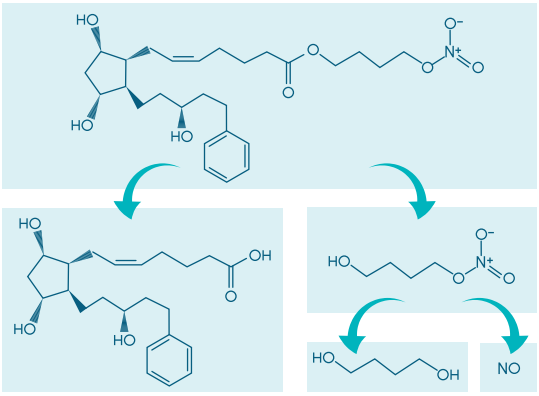

Figure 1. Chemical structure of latanoprostene bunod and its metabolites. Metabolites of latanoprostene bunod (top) include latanoprost acid (bottom left) and butanediol mononitrate, with subsequent release of nitric oxide (bottom right) and 1,4-butanediol (an inactive metabolite). Adapted from Hoy et al, 2018.[4]

It's important to point out that as a prostaglandin analog, VYZULTA does not exert its IOP-lowering effect by decreasing aqueous humor production.[1] I worry about the appropriateness of aqueous suppressants, including alpha-adrenergic agonists, beta-adrenergic agonists, and carbonic anhydrase inhibitors, for my patients—specifically, the safety risks that may be associated with long-term suppression of aqueous humor production.[1]

Dr. Richens: I find it instructive to think of VYZULTA as a drug that optimizes aqueous humor perfusion. Latanoprost helps improve aqueous humor perfusion through its singular mechanism of action, but VYZULTA's dual mechanism of action delivers an added layer of aqueous humor drainage that latanoprost cannot achieve on its own.

Dr. Parekh: Based on the features of VYZULTA, it is imperative that patients prescribed VYZULTA be able to fill their prescription as directed and not be subjected to product substitution at the pharmacy. My patients often specifically request that they not receive generic medications. This is largely attributable to my patients' perceptions that generic medications are less consistent than their brand-name counterparts. What's more important in my view, however, is that there is currently no generic formulation of latanoprostene bunod on the market, so a generic substitution will invariably result in the patient receiving generic latanoprost 0.005%—or a different prostaglandin analog entirely.

Dr. Berdy: We want what's best for our patients with open-angle glaucoma or ocular hypertension, and that's oftentimes monotherapy with VYZULTA. These are insidious conditions that develop slowly. I'm not thinking about how much my patient IOP's will stabilize over the coming weeks, but, rather, how IOP reduction can be sustained over years. Across a range of appropriate patient types, and inclusive of use as a first-line monotherapy option, VYZULTA is the appropriate place to begin a long-term IOP-lowering journey.

> ***"Across a range of appropriate patient types, and inclusive of use as a first-line monotherapy option, VYZULTA is the appropriate place to begin a long-term IOP-lowering journey."***
>
> ***—Dr. Gregg Berdy***

IMPORTANT SAFETY INFORMATION (CONTINUED)

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

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VYZULTA®
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VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%—for patients who need a **powerful first-line IOP-lowering treatment** when beginning their glaucoma journey

Dr. Berdy \\ Patient Case 1	

Background	**66-year-old white female**
	• Family history of risk factors for glaucoma
	  • Maternal aunt with open-angle glaucoma who required surgery
	  • Sister's physician reported she has "funny-looking" optic nerve heads

Medical history	• Hypertension and hypercholesterolemia, both controlled on medication
	• Complained of decreased vision and glare at night OU
	• Snellen visual acuity of 20/30 OU
	• Slit lamp examination:
	  • Pseudoexfoliation deposits on the iris surface and anterior lens capsule OU
	  • Grade 2+ nuclear sclerotic cataract OU
	• Cupping in both eyes based on cup-to-disc ratio
	  • Vertical 0.75, horizontal 0.65 OU
	  • Thin rim and superior notch OU
	• Gonioscopy shows 360° opening to the trabecular meshwork and Sampaolesi line OU

Prior IOP-lowering treatment	None
Baseline IOP	• 22 mmHg OU

Diagnostic workup	• Humphrey visual field
	  • Inferior nasal step OU
	  • Inferior Seidel's scotoma OU
	• Glaucoma diagnosis based on nerve fiber analysis showed superior thinning OU
	• Visual evoked potentials showed decreased amplitude and latency OU
	• Central corneal thickness of 510 µm OD and 505 µm OS

Patient Case #1, from **Dr. Berdy**'s practice, depicts a patient with multiple risk factors for glaucoma, including a family history and presence of pseudoexfoliation deposits. Family history is a well-established risk factor for glaucoma, with broad consensus that first-degree relatives of those with open-angle glaucoma are at greater risk of developing open-angle glaucoma themselves.[1] Moreover, the accumulation of pseudoexfoliation material on the pupil margin, anterior lens capsule, or corneal endothelium (ie, pseudoexfoliation syndrome) is a known secondary mechanism of IOP elevation.[1]

Dr. Berdy selected VYZULTA for this patient based on VYZULTA's mechanism of action, simple dosing regimen, and strong track record of IOP-lowering results in clinical studies. **Dr. Berdy** indicated that he desired this patient to achieve a target IOP of <14 mmHg. **Dr. Nguyen** agreed, noting, "This case represents an instance of buying this patient time before she requires SLT.* She may be a candidate for combined phacoemulsification/MIGS after a few years. She may not require additional medication with the intervention that she was given."

*In clinical trials, patients with a history of SLT in either eye >90 days prior to study entry could be enrolled.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products that were inadvertently contaminated by patients

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Dr. Berdy further elaborated on his decision-making process when administering VYZULTA: "We gave the patient a sample and brought her back after 3 or 4 weeks to see how well it worked. Her IOP dropped to 14 mmHg, and we were both satisfied. The patient was of Medicare age, so we had to perform a prior authorization. We gave her the sample while we were going through that process. Eventually, the approval was received." This case underscores the importance of examining each patient's individualized risk factors for glaucoma, rather than fixating on specific IOP values. **Dr. Berdy** noted, "The sooner we get the IOP lower, the better we're positioned for long-term treatment."

VYZULTA—for patients with **inadequate response to their current PGA treatment**, including latanoprost 0.005%

Dr. Richens \\ Patient Case 2	
Background	**77-year-old Pacific Islander female** • History of primary open-angle glaucoma
Prior IOP-lowering treatment	Latanoprost 0.005%
IOP prior to switch	16 mmHg OU
Diagnostic workup	• Referred to Dr. Richens' practice after evidence of retinal nerve fiber layer dropout, worsening superior arcuate scotoma, and nasal step • Disease progression worse OS than OD on visual field testing

Patient Case #2, from **Dr. Richens**' practice, depicts a patient who continued to show progression of primary open-angle glaucoma despite IOP lowering with latanoprost 0.005%. In general, if an IOP-lowering drug fails to reduce IOP sufficiently, then either switching to an alternative medication as monotherapy or adding medication is appropriate until the desired IOP level is attained.[1] In this case, upon switching to VYZULTA, this patient showed additional IOP lowering down to 13 mmHg in both eyes, which slowed further glaucoma progression. **Dr. Richens** emphasized the importance of initiating glaucoma treatment as promptly as possible: "Had this patient been placed on VYZULTA at the onset of symptoms, she might not have experienced the degree of visual field loss that we observed in this case. When someone with glaucoma is placed on IOP-lowering therapy too late, their vision doesn't come back."

IMPORTANT SAFETY INFORMATION (CONTINUED)

• Contact lenses should be removed prior to the administration of VYZULTA and may be reinserted 15 minutes after administration

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VYZULTA—for patients with a prior **diagnosis of ocular hypertension** who may be at risk of developing open-angle glaucoma

Dr. Parekh \\ Patient Case 3	
Background	**62-year-old female** • Some family members with ocular hypertension developed primary open-angle glaucoma years later
Medical history	• Primary medical history includes stage I breast cancer, osteoarthritis, and mild type 2 diabetes mellitus • Ocular medical history includes 2-year history of ocular hypertension
Prior IOP-lowering treatment	None
Baseline IOP	• 24-25 mmHg OU
Diagnostic workup	• Central corneal thickness of 505 µm/510 µm OU • Optical coherence tomography (OCT) was fully "green" but now shows some "yellow" • Humphrey visual field remained full (re-evaluated every 6 months)

Patient Case #3, from **Dr. Parekh**'s practice, underscores the fact that VYZULTA is an appropriate choice for patients with ocular hypertension who have not yet progressed to open-angle glaucoma. Upon initiation of VYZULTA treatment, this patient's IOP declined to 16-17 mmHg in both eyes, and it has remained stable for over 3 months. The patient signaled that normalization of her IOP has helped eliminate a source of stress in her life: "Doc, since my sisters have glaucoma, I have been worried about my own eye pressure. My pressure is better now. I'm so happy I'm on VYZULTA."

VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%—for patients with **inadequately controlled IOP following SLT***

Dr. Nguyen \\ Patient Case 4	
Background	**74-year-old African American female** • Family history of glaucoma • Father used IOP-lowering drops (now deceased) • Reported having "trouble using medications more than once a day"
Medical history	• Past medical history includes diabetes (managed with metformin) and hypertension (managed with losartan and metoprolol) • Diagnosed with glaucoma 20 years ago at age of 54 years • Underwent cataract extraction with intraocular lens implantation 9 years ago

*In clinical trials, patients with a history of SLT in either eye >90 days prior to study entry could be enrolled.

IMPORTANT SAFETY INFORMATION (CONTINUED)

• Most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%)

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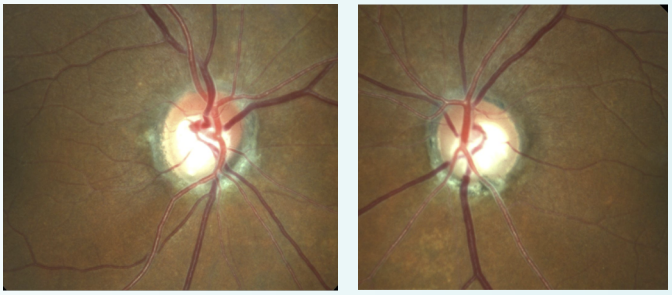
Prior IOP-lowering treatment	• IOP was 29 mmHg OD and 30 mmHg OS prior to treatment • Treated with latanoprost 0.005% for 11 years, resulting in IOP reduction to 15-16 mmHg OU • ~4 years ago, IOP began to slowly increase to 21 mmHg OD and 20 mmHg OS • Patient refused additional IOP-lowering drops • 3 years ago, SLT* was performed in both eyes with minimal response
IOP on latanoprost 0.005% OU	• 19 mmHg OU

Diagnostic workup with fundus images	• Snellen visual acuity 20/25 OU
	• Pachymetry of 491 µm OD and 495 µm OS
	• Gonioscopy
	  • D40R angle configuration OU
	  • Grade 2+ pigmented trabecular meshwork OU
	• Slit lamp examination within normal limits, except for the presence of a posterior chamber intraocular lens OU
	• Cup-to-disc ratio on fundus examination
	  • 0.7 with inferior notch and inferior retinal nerve fiber layer dropout OD
	  • 0.75 with inferior notch and inferior retinal nerve fiber layer dropout OS
	 
	• Humphrey visual field
	  • Superior arcuate defects OU match the patient's optic nerve findings

Patient Case #4, from **Dr. Nguyen**'s practice, recounts the story of a patient who experienced a substantial (>30%) IOP reduction with latanoprost 0.005%, but the patient's IOP still began to rise over time. Because the patient refused additional pharmacologic therapy, SLT was performed, but SLT failed to provide the desired IOP-lowering effect. By switching this patient from latanoprost 0.005% to VYZULTA, **Dr. Nguyen** was able to overcome the roadblock presented by the patient's minimal response to SLT while maintaining her on topical monotherapy. **Dr. Nguyen** observed, "Of the various interventions available to me, the decision to switch to VYZULTA was a straightforward one, with the added benefit of not compromising patient compliance through the introduction of additional bottles."

*In clinical trials, patients with a history of SLT in either eye >90 days prior to study entry could be enrolled.

IMPORTANT SAFETY INFORMATION

- Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent

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CHOOSE MONOTHERAPY WITH VYZULTA IN APPROPRIATE PATIENTS WHO[2]:

- Need a powerful first-line IOP-lowering treatment when beginning their glaucoma journey
- Are not adequately responding to their current PGA treatment, including latanoprost 0.005%
- Received a prior diagnosis of ocular hypertension and may be at risk of developing open-angle glaucoma
- Have inadequately controlled IOP following SLT*

GO FOR IOP **CONTROL** *FROM THE START*

*In clinical trials, patients with a history of SLT in either eye >90 days prior to study entry could be enrolled.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation
- Use with caution in patients with a history of intraocular inflammation (iritis/uveitis). VYZULTA should generally not be used in patients with active intraocular inflammation
- Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Use with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema
- There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products that were inadvertently contaminated by patients
- Contact lenses should be removed prior to the administration of VYZULTA and may be reinserted 15 minutes after administration
- Most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%)

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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References: 1. Gedde SJ, Vinod K, Wright MM, et al. Primary open-angle glaucoma Preferred Practice Pattern®. *Ophthalmology.* 2021;128(1):P71-P150. **2.** VYZULTA. Prescribing Information. Bausch & Lomb Inc. **3.** Lo TC, Chen YY, Hung MC, Chou P. Latanoprostene bunod 0.024% in the treatment of open-angle glaucoma and ocular hypertension: a meta-analysis. *J Clin Med.* 2022;11(15):4325. **4.** Hoy SM. Latanoprostene bunod ophthalmic solution 0.024%: a review in open-angle glaucoma and ocular hypertension. *Drugs.* 2018;78(7):773-780.

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