

# New Nitric Oxide Medication to Reduce Intraocular Pressure Takes on Glaucoma from a New Angle



Nitric oxide has become a popular dietary supplement—usually in the form of beetroot juice—because it can help improve blood flow and lower blood pressure. As it turns out, nitric oxide also works as a glaucoma treatment. And no, it's not eating beets and green leafy vegetables. This novel eye drop could be the first glaucoma treatment to lower intraocular pressure by using nitric oxide to target the trabecular meshwork.<sup>1</sup>

## How Nitric Oxide Works in the Body

Nitric oxide is a gas that's naturally produced inside the body. It only survives for a few seconds, but that's all the time it needs to make quite an impact on your health. One of its jobs is to relax blood vessels, which improves blood flow and lowers blood pressure.<sup>2</sup> Nitric oxide regulates blood flow in the brain, prevents atherosclerosis, and helps heal wounds, repair muscles and fight bacteria.<sup>3</sup>

## Nitric Oxide Regulates Intraocular Pressure

Inside the eye, fluid called the aqueous or vitreous humor (depending on whether it's in front of or behind the lens) provides the pressure needed to hold the eye's shape. The amount of aqueous fluid and its flow in the front of the eye determine whether intraocular pressure goes up or down, so several mechanisms regulate the fluid's volume by making sure that the amount of fluid released in the front of the eye is offset by allowing drainage. One of these mechanisms is the trabecular meshwork.<sup>4</sup>

The trabecular meshwork is like a one-way valve that opens to let aqueous humor circulate and drain in the front of the eye. When the meshwork fails—which can be due to normal aging of cells, DNA damage or other causes—fluid can't circulate properly, intraocular pressure builds and glaucoma develops.<sup>5</sup>

So how does all of this relate to nitric oxide? It turns out that the trabecular meshwork is regulated by cells that depend in part on nitric oxide. Glaucoma treatments work by lowering intraocular pressure, but none of the current medications affect the trabecular meshwork directly. That may be about to change. After many years of trial-and-error, researchers have finally developed a medication that uses nitric oxide to target the trabecular meshwork.

## Novel Nitric Oxide Treatment Currently in the Pipeline

The first glaucoma treatment to ever use nitric oxide has already succeeded in large clinical trials that demonstrated its ability to lower intraocular pressure in early- and late-stage glaucoma. If it gains FDA approval, it won't just be the first of its type, it will be the first new glaucoma treatment of any kind in decades—a fact that highlights the extreme challenge of glaucoma research. Scientists have been diligently working all that time, but progress comes in small steps at a slow pace, especially when sources of funding are constantly in flux.

The new medication, called Vesneo, will eventually be available as an ophthalmic solution and approved to treat open angle glaucoma and ocular hypertension (which is elevated pressure without overt vision loss)<sup>6</sup>. When it is metabolized, it forms two active ingredients—latanoprost acid and nitric oxide. The nitric oxide works by boosting fluid outflow through the trabecular meshwork, while latanoprost acid affects outflow through another mechanism called the uveoscleral pathway.

Patients with glaucoma have good reason to hope that Vesneo will reach the market soon, but it has hit a roadblock: While it was on target for FDA approval in July 2016—and the FDA was satisfied with its safety and efficacy

—approval was delayed due to manufacturing issues.<sup>7</sup> While the medication will not need to go through further clinical trials, the pharmaceutical manufacturer will have to solve its problems before the FDA will issue final approval, and no one has offered a timeline for when that might happen.

## Challenges Aboard for New Treatments

The time and patience required by glaucoma researchers to get this far is almost unfathomable. First, they had to determine that nitric oxide was a viable target—a concept that only emerged in 2014 after years of studying the eye. After that, researchers devoted more years to developing and testing a medication that could deliver a short-lived gas like nitric oxide. Then they had to fund clinical trials and complete all the FDA requirements, which are incredibly costly. Now, on the brink of FDA approval, manufacturing delays arise that add to the challenge of getting novel glaucoma treatments on the market. While Glaucoma Research Foundation can't help manufacturing shortages, we can keep researchers moving forward to the next new breakthrough. But we need your financial support to make it happen.

*Glaucoma Research Foundation depends on your donation to support research leading to new treatments and patient education. [Donate today](#) and join our cause.*

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<sup>1</sup>“Association of Dietary Nitrate Intake With Primary Open-Angle Glaucoma: A Prospective Analysis From the Nurses' Health Study and Health Professionals Follow-up Study,” March 2016, <http://archophth.jamanetwork.com/article.aspx?articleid=2480455>

<sup>2</sup>“Nitric Oxide,” 2009, <http://www.dermnetnz.org/topics/nitric-oxide/>

<sup>3</sup>“Nitric Oxide Regulates the Repair of Injured Skeletal Muscle,” January 2011, <http://www.sciencedirect.com/science/article/pii/S1089860310004428>

<sup>4</sup>“Autonomic Control of the Eye,” January 2015, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4919817/>

<sup>5</sup> “Damage Within Trabecular Meshwork in Glaucoma Better Understood,” February 2012, <http://ophthalmologytimes.modernmedicine.com/ophthalmologytimes/news/modernmedicine/modern-medicine-feature-articles/damage-within-trabecular-mes>

<sup>6</sup> “New Glaucoma Treatment on Track for FDA Approval,” September 2015, <http://www.pharmacytimes.com/product-news/new-glaucoma-treatment-on-track-for-fda-approval>

<sup>7</sup>“Manufacturing Issues Thwart FDA Approval for Valeant Eye Drug,” July 2016, <http://www.fiercebiotech.com/biotech/manufacturing-issues-thwart-fda-approval-for-valeant-eye-drug>

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### Glaucoma Research Foundation

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