Food and Drug Administration
Medical Devices Advisory Committee

Ophthalmic Devices Panel
Intraocular Pressure Adjusting Pump
March 21, 2024

Introduction:

On, March 21, 2024, the panel heard presentations from Balance Ophthalmics and the FDA and discussed, made recommendations, and answered questions on the information related to the de novo application for the FSYX Ocular Pressure Adjusting Pump (FSYX OPAP) system developed by Balance Ophthalmics. The device is indicated as adjunctive therapy for the reduction of intraocular pressure (IOP) during use in adult patients with open angle glaucoma and intraocular pressure equal to or less than 21 mm of mercury.

Balance Ophthalmics Presentation

1. Clinical Benefit:
IOP reductions were observed in every patient and across all populations in the 12-month pivotal Artemis trial conducted by the sponsor.

2. Safety:
No device-related serious adverse effects were observed in the pivotal 12-month Artemis study, and all device-related AEs resolved without sequelae. There was no observed damage to the structure or function of the optic nerve, visual field, cornea, or anterior segment. This is a noninvasive removable device, removable by the patient themselves at any time they choose.

3. Effectiveness:
Manometrically-measured IOP readings show results that are consistent with the measurements from clinical studies, which confirm that the OPAP device is actually lowering IOP. The Artemis trial showed statistically significant, consistent, and clinically meaningful reductions of IOP during use of the OPAP device.

4. Labeling:
The IOP nomenclature and the proposed indication is both accurate and appropriate, and can easily be understood by both physicians and patients, and it clearly points out that OPAP is an adjunctive therapy.

5. Unmet Need:
Glaucoma is the leading cause of irreversible blindness, and lowering IOP is the only way to slow glaucoma's progression. Nocturnal IOP is a major predictor of disease progression, and lowering IOP is more difficult in patients with an IOP of 21 or less. Treatments exist for controlling IOP during the day, but patients continue to get worse, presumably due to a lack of control of nighttime IOP.

6. Benefit-risk:
Given the inherent safety of the device and lack of device-related SAEs or AEs that did not resolve, and given the fact that no other treatments exist as adjunctive care in this difficult-to-treat population, the benefit-risk profile of OPAP is favorable.

Questions to Balance Ophthalmics

Balance Ophthalmics founder Dr. John Berdahl responded to questions about the OPAP device including, but not limited to, the following:

- Logistics of patients' nighttime use of goggles during the clinical trial
- Decay of treatment effect wherein pressure returns to baseline when the machine is turned off
- Ages of patients in clinical trial as compared to the ages of typical glaucoma patients
- Usage of systemic medications such as beta blockers in the patient population
- Patient-reported outcomes (PROs) relating to adherence rates as compared to CPAP devices, for example
- Changes in study protocol and patient population from the Apollo to the Artemis study
- Physicians' discretion as to negative pressure settings used in the Artemis study
- Instance of prior IOP-lowering interventions of clinical trial patients
- Device compliance and duration per night as it relates to interruption of patients' sleep patterns
- The device's effect on translaminar pressure
- Suitability of clinical trial durations of one year
- Methodology of OCT measurements and visual field stability or progression
- Labeling of the device to state its beneficial effect of IOP lowering versus visual field progression or stopping the progression of glaucoma

FDA Presentation

The FDA review team for the FSYX OPAP presented its findings on the device, which is eligible for evaluation under de novo as the device, based on its intended use and technological characteristics. It does not fit under any existing class one, two, or three regulation, and there is currently no approved premarket applications for the same device. Components of the FSYX OPAP include: a set of eye goggles which come in three different sizes and a programmable pressure modulating pump. When negative pressure is applied via the pump, there is a decrease in pressure applied locally to the eye, which results in a corresponding change to the pressure inside the eye.

The FDA provided in-depth background information on the history of the pre-submission and introduction of the device through the de novo pathway and interactions with FDA since 2017. Ultimately the sponsor's first de novo request was declined in September 2021 due to concerns regarding device effectiveness and safety. The sponsor then submitted a pre-submission in 2022 requesting feedback on the evidence needed to address the concerns raised and whether the data collected from their 12-month study would be sufficient to support their de novo request. Input from external experts or SGEs was also attained at the sponsor's request.

The FDA presented key findings from the sponsor's 12-month pivotal Artemis study. AEs and exclusions were explained in detail. Results from the study were also discussed: The results from the confirmed study demonstrate a mean percent decrease in IOP from baseline of 33.1% during -10 millimeters of mercury of negative pressure application, and 51.2% during -20 mm of mercury of negative pressure application.

As to benefit-risk, FDA found that IOP defined by the parameter of applied NP in front of the eye increases with device use, whereas IOP defined by the parameter of TCPD relative to atmospheric pressure decreases with device use. Based on the sponsor's IOP parameters, at the week-52 sleep lab visit in the Artemis trial, 63.4% of study eyes and 3.2% of control eyes achieved a reduction of IOP of 20% or

more while the device was in use. However, the benefit of the observed outcomes is uncertain since lowering excursion IOP while raising transcranial pressure difference between the eye and outside environment is not known to have the same benefit of slowing glaucoma progression.

Questions to FDA

FDA's review team responded to questions about the OPAP device and its de novo application, including, but not limited to, the following:

- Clarifications on patient sample in Artemis trial
- Concerns surrounding ocular surface well-being from SGEevaluation
- Recommendation of formal safety endpoints from FDA in Artemis study
- Age-related issues due to the younger skew of patients in the clinical trials completed
- Approval of materials used in manufacturing the device
- Concerns related to ambulation of patients while device is in use
- Emphasis on PROs especially for older populations that will use the device
- Suitability of a one-year study to demonstrate safety in the long term
- Clarifications on the indication for use
- Additional information as to FDA's requirements for other devices or drugs to treat glaucoma
- Physiology concerns
- Interest in post-market studies or surveillance on the product
- Quality of life outcomes for patients included in the study

Open Public Hearing

Seven individuals presented statements during the open public hearing portion of the event.

1. Dr. Michael Chaglasian shared his positive experiences with using the goggles to treat patients who have glaucoma. He found it to be an important adjunctive treatment option that is safe and well tolerated for many patients with glaucoma.

2. Mr. Mitch Hill shared his interest in the approval of the OPAP goggles due to the lack of available options for patients experiencing vision loss like himself. He believes the goggles would allow for control of IOP during sleeping hours and hopes to preserve his ability to carry out the activities he is still able to do.

3. Dr. Nathan Radcliffe discussed his enthusiasm as to the potential of the OPAP goggles and their adjunctive role in lowering IOP for glaucoma patients at night since these patients need multifaceted approaches for their therapy. He feels it would be an extra step that is lower risk than surgery, for example.

4. Dr. Manjool Shah explained his view that outside-the-box, novel ways to control glaucoma are needed and the goggles in question may be a way to keep fluctuations in nighttime IOP at bay so as to prevent visual field progression.

5. Dr. Robert Kersten described his journey with glaucoma and incompatibility with certain other surgical treatments due to past history. He finds the OPAP device particularly appealing due to the fact that it is noninvasive and could preserve his vision if it is successful in lowering the nocturnal differential between IOP and blood pressure.

6. Dr. Wallace Alward shared research he conducted on patients whose glaucoma was well-controlled with patients whose pressures were excellent but whose glaucoma continued to worsen. Based on his conviction that glaucoma damage to the optic nerve occurs during sleep, Dr. Alward feels that this technology could be helpful to many patients with glaucoma.

7. Ms. Hilary Golden described her experience with glaucoma and disease progression in light of the tools available to control a disease that cannot be controlled. She feels that the OPAP goggles would be another tool available to patients who are facing vision loss due to glaucoma.

Panel Deliberation

Panel members asked questions of both the sponsor and FDA regarding the presentation of the OPAP device and its de novo application. Questions included, but were not limited to, the following topics:

- Parameters of the clinical trial and requirements of analogous studies or devices
- Temporal relationship of adverse event occurrence by negative pressure application
- Mechanism of special controls when a device is granted through the de novo pathway
- Biomechanics of the eye during OPAP wear
- Relevance of corneal thickness to device outcomes
- Patient age concerns
- Patient use of other systemic medications during goggle use
- Unmet need due to unsuitability of trabeculectomy for certain patients and availability of this device as a safer option for glaucoma treatment
- Demonstration of goggle use
- Exclusions from study due to facial anatomy or prior surgery scarring
- Lack of formal safety endpoints in the Apollo and Artemis studies
- Patients' reasons for withdrawal of consent from clinical trials
- Device's effect on optic nerve blood flow
- PROs and reporting via a post-market study to analyze the long-term effects of device use
- Long-term safety profile of the device given the 12-month trial period
- Suitability of class two standard for the device as a low-risk intervention
- Dose modification and availability of relevant information in patient environments
- Safety of ambulation during goggle wear
- Contraindications for patients with ongoing intraocular treatments
- Poolability of data and conclusions from visual field readings
- Monthly replacement of goggles and cleaning instructions
- Temporal relationship between goggle use and IOP measurement
- Actual duration of device wear compared to indicated use
- Exclusions from study due to history of certain other glaucoma treatments
- Instance of AEs for study patients who had higher negative pressure

Contraindications for patients with disease too advanced to recommend the use of an at-home unsupervised medical device

The panel members then discussed amongst themselves their perspectives on the indication for use, effectiveness measurements, methodology, labeling, sufficiency of the length of the 12-month study to demonstrate safety, nomenclature, and risk-benefit profile of the device.

FDA Questions

FDA asked six questions of panel members. The five questions are included below with the panel's corresponding summary responses:

Question 1: Do you believe there is clinical benefit to the lowering of this alternative IOP parameter and increasing of TCPD on a daily basis for several hours?

Response: The panel's opinions on this question were mixed. Approximately half of the panel feels there is clinical benefit, but a strong minority is unsure or thinks there is likely a clinical benefit.

Question 2: Do you believe the IOP lowering as measured by excursion tonometry during use of the device observed in CP-X19 pivotal trial, in combination with data from the other supportive additional studies demonstrates a reasonable assurance of effectiveness as an adjunctive therapy for the reduction of intraocular pressure during use in adult patients with open-angle glaucoma and IOP $\leq$ 21 mmHg? If not, what additional assessments do you recommend?

Response: The panel uniformly agrees with the statement but would recommend a post-market study to examine longer-term outcomes on ongoing visual fields and OCTs, as well as patient-reported outcomes such as quality of life.

Question 3: Do you believe the available data demonstrates reasonable assurance of safety at 1 year? Do you believe the available data demonstrates reasonable assurance of long-term safety? If not, what additional data do you do you recommend?

Response: The panel consensus was that the available data demonstrates reasonable assurance of safety at one year. However, the majority of the panel recommends a three-year study to examine long-term issues related to device outcomes.

Question 4: Do you believe the available data supports the proposed range of programmable NP? Do you believe the available data supports the proposed range of wear time? If not, what do you recommend?

Response: The panel is divided on whether the data supports the proposed range of programmable NP and the members who did not feel it was supported recommended a cap of either 15 or 17. In general, the panel does not feel that the available data supports the proposed range of wear time and recommends a maximum of six hours.

Question 5: Does the proposed IFU statement use the appropriate nomenclature and language to accurately describe the function of the device with regard to IOP? If not, how should the IFU statement describe the function of the device?

Response: The panel generally believes that the wording of the proposed indication for use should be changed. Concerns included removing the word "adjunctive," saying it was to be used "during sleep" instead of "at night," and indicating that it entails a temporary reduction of pressure.

Question 6: Do the probable benefits of the FSYX OPAP device outweigh the probable risks for use in patients who meet the criteria specified in the proposed IFU?

Response: The panel consensus was that the probable benefits of the OPAP device do outweigh the probable risk for use in patients who met the criteria proposed.

Adjournment

FDA, the sponsor, and the panel members expressed their mutual gratitude for all parties' contributions to this Ophthalmics Devices Panel meeting and were dismissed.

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I approve the minutes of the meeting as recorded in this summary.

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Jayne S. Weiss, MD
Temporary Chairperson

I certify that I attended this meeting on March 21, 2024
and that these minutes accurately
reflect what transpired.

Akinola A. Awojope -S Digitally signed by Akinola A. Awojope -S
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Akinola Awojope, DrPH, MPH.
Designated Federal Officer (DFO).