24 Hour Summary of the Ophthalmic Devices Panel Meeting

March 21, 2024

Introduction:

The Ophthalmic Devices Panel of the Medical Devices Advisory Committee for the Food and Drug Administration met on March 21, 2024, to discuss, make recommendations, on information related to the De Novo request by Balance Ophthalmics, Inc. for the safety and effectiveness of the FSYX Ocular Pressure Adjusting Pump (FSYX OPAP) System. The FSYX OPAP System is indicated as adjunctive therapy for the reduction of intraocular pressure (IOP) during use in adult patients with open-angle glaucoma and IOP ≤ 21 mmHg.

Panel Deliberations/ FDA Questions:

Question 1:

The sponsor proposes the following Indications for Use (IFU):

> **The FSYX™ Ocular Pressure Adjusting Pump (FSYX OPAP) is indicated as adjunctive therapy for the reduction of intraocular pressure during nightly use in adult patients with open-angle glaucoma and intraocular pressure ≤ 21 mmHg.**

The conventional IOP measurement is defined by the pressure difference between the inside of the anterior segment of the eye and the environment immediately outside, as measured by applanating the cornea. Conventionally, this immediate outside environment is atmospheric pressure. However, when applying negative pressure using the FSYX OPAP device, this environment is below atmospheric pressure. An alternative IOP parameter was devised by Balance Ophthalmics to measure IOP while the device is in use (i.e., with negative pressure [NP] on), as the Goldmann applanator cannot be used while a patient is wearing the goggles. This parameter was found to be lowered only while the device is in use (i.e., with NP on) and the reduction ended once the device was turned off. However, Balance Ophthalmics defines this alternative parameter as TCPD relative to atmospheric pressure without accounting for the NP microenvironment. Although the data demonstrated that this alternative IOP is lowered temporarily when the device is in use, Balance Ophthalmics acknowledges that conventional IOP actually increases by 21.7% - 26.9% with device use. Hence, IOP defined in one way increases, while IOP defined in another way decreases.

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?

The panel agreed that the device lowers intraocular pressure (IOP). Although some panelists believed there was clinical benefit to lowering IOP for several hours a day, other panelists expressed uncertainty of this benefit in the treatment of glaucoma. The panel noted that additional data regarding the dose-response relationship and treatment duration are needed to understand the clinical benefit. The panel recommended future evaluation of retinal nerve fiber layer (RNFL) and visual fields (VF) to monitor for glaucoma progression in postmarket studies.

Question 2:

In support of the demonstration of effectiveness, the sponsor has submitted data from the CP-X19 pivotal study and 21 additional studies (see Section 8 - Report of Prior Investigations in FDAs executive summary).

In the CP-X19 pivotal study, the pre-specified primary and secondary effectiveness endpoints were met:

- **58.1% (54/93) of study eyes and 1.1% (1/93) of control eyes demonstrated a ≥20% reduction of IOP (by excursion tonometry) at the Week-52 clinic visit.**
- **63.4% (59/93) of study eyes and 3.2% (3/93) of control eyes demonstrated a ≥20% reduction of IOP (by excursion tonometry) at the Week-52 sleep lab visit.**

Measurements by Goldmann applanation tonometry show that after cessation of device use, the IOP reverts closely to the IOP measured before device use.

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 ≤ 21 mmHg? If not, what additional assessments do you recommend?

The panel agreed that the data demonstrated a reasonable assurance of effectiveness as an adjunctive therapy for the indicated patient population. However, all panelists re-emphasized the need for postmarket studies to evaluate glaucoma progression and recommended monitoring of VFs, optical coherence tomography (OCT), and patient-reported outcomes (PROs) to evaluate health-related quality of life (HRQOL) and visual changes.

Question 3:

In the CP-X19 pivotal trial, the following were the key safety findings at one year:

- **Ocular adverse events (most frequently reported):**
  - **eyelid edema (11.8%),**
  - **signs and symptoms of dry eye (5.4%),**
  - **conjunctival hyperemia (4.3%),**
  - **eye pain (3.2%), eyelid erythema (2.2%),**

  - **loss of best-corrected distance visual acuity ≥10 letters from baseline (2.2%), and**
  - **posterior vitreous detachment (2.2%).**
- **Periorbital adverse events:**
  - **periorbital edema (12.9%),**
  - **periorbital contact dermatitis (4.3%), and**
  - **periorbital pain (2.2%)**

The post hoc analysis of visual field conducted by a third-party reading center revealed mean deviation worsening ≥2.5 dB in four study eyes (6.5%) at Weeks 26 and three study eyes (4.8%) at Week 52.

Optical coherence tomography (OCT) examinations were collected from 62 participants at the Week 26 and Week 52 visit and evaluated post hoc by a third party reading center. No formal quantitative analysis of OCT data had been planned or was conducted.

a) **Do you believe the available data demonstrates reasonable assurance of safety at 1 year?**

b) **Do you believe the available data demonstrates reasonable assurance of long-term safety?**
c) **If not, what additional data do you recommend?**

The panel believed that the available data does demonstrate a reasonable assurance of safety at 1 year. The panelists noted that a larger sample size and additional OCT and VF data would have provided greater assurance of safety of the device.

The panel generally believed that the data did not demonstrate a reasonable assurance of long-term safety. The panelists believed that long-term safety should be evaluated in a postmarket study and recommended collection of VF, OCT, corneal topography and pachymetry data. The panel also recommended that data include patients ages 65 years and older due to the prevalence of low-tension glaucoma in this age range. Panelists also recommended that data be collected on injuries caused by use of the device at home and on a sufficient number of patients that are able to demonstrate 6-8 hours of device use per night and longevity of use in a larger population. The majority of the panelists recommended a 3-year study to fully demonstrate a reasonable assurance of long-term safety.

Question 4:

The currently proposed device labeling recommends: 1) Range of programmable negative pressure (NP) between -5 to -20 mmHg; and 2) Range of wear time between 1 to 8 hours

The following data is available for range of programmable NP:

- **CP-X19 trial:**
  - **93 participants with a range of mean NP between -10.0 mmHg to -12.1 mmHg.**

  - **8 participants who used the device with NP between -17 mmHg to -20 mmHg for at least 26 weeks during the trial. Of these eight, three (37.5%) experienced ocular and/or periorbital AEs.**
  - **53 participants used devices programmed >-12 mmHg at some point during the trial. 38 of these 53 completed the trial while 15 discontinued early. Of these 38, 18 were reported with a device-related AE.**

- **CP-X10 trial:**
  - **64 participants with a range of mean NP between -10.59 mmHg to -11.46 mmHg.**

The following data is available for range of wear time:

- **CP-X19 trial**
  - **93 participants with average daily wear time ranging from 5.44 to 5.63 hours**
  - **61 participants with average wear time at the Week-52 sleep lab visit of 2.9±0.3 hours 11:00 pm – 2:00 am and 2.6±0.5 hours 2:00 am – 5:00 am.**
- **CP-X10 trial**
  - **64 participants with average daily wear time ranging from 3.74 to 4.38 hours (average 4.4)**

a) Do you believe the available data supports the proposed range of programmable NP;
b) Do you believe the available data supports the proposed range of wear time?
c) If not, what do you recommend?

The panel had mixed opinions on whether the available data supports the proposed range of programmable NP. The panelists who believed that there was not enough available data to support the programmable NP range suggested that a more appropriate maximum applied NP would be 15-17 mmHg.

A majority of the panelists did not believe the available data supported the proposed range of wear time. The panel largely agreed that based on the data provided by the sponsor, the maximum daily wear time should be limited to 6 hours.

Question 5:

The sponsor proposed the following IFU:

> **The FSYX™ Ocular Pressure Adjusting Pump (FSYX OPAP) is indicated as adjunctive therapy for the reduction of intraocular pressure during nightly use in adult patients with open-angle glaucoma and IOP ≤ 21 mmHg.**

In the CP-X19 pivotal trial, IOP was measured via pneumotonometry with the excursion goggles, before and during NP application, during in-clinic visits. The proportion of study eyes with at least 20% IOP reduction (relative to atmospheric pressure) was 58.1% (at

Week 52) and the mean IOP changed from 18.0 mmHg to 11.4 mmHg. The mean transcorneal pressure difference (TCPD) increase (i.e., relative to the microenvironment surrounding the eye that is created by the goggles) in the study eye was 23.4 mmHg.

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?

The panel discussed the inclusion of the term "adjunctive therapy" in the IFU. For those who believed that it is important to include the term "adjunctive therapy", they noted that it was important to emphasize that the device should not serve as the primary treatment modality for patients with open-angle glaucoma and IOP $\leq$ 21 mmHg. Other panelists stated that "adjunctive therapy" should be removed given that patients may not actively be on other adjunctive treatments but may benefit from use of the device. Additionally, the panel discussed the phrase "during nightly use" given that many patients have alternative sleep schedules (i.e., sleep during the day). The panel overwhelmingly agreed with this sentiment and proposed that the term "during nightly use" in the IFU be replaced with "during sleep".

The panelists also recommended that the IFU include the term "temporary" to more clearly describe that the effect of IOP reduction only applies during device use. After the device is removed, the patient's IOP will return to the IOP prior to NP application.

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?

All panelists agreed that 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.

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Transcripts may be downloaded from:

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