Brief Summary
Ophthalmic Devices Panel
of the
Medical Devices Advisory Committee
November 9, 2020

VisAbility Micro Insert System

Introduction:

The Ophthalmic Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on November 9, 2020, to discuss, make recommendations and vote on information regarding the Premarket Application (PMA) for the VisAbility Micro Insert System by Refocus Group, Inc. The meeting was held virtually and was open to the public via webstream.

The applicant has proposed the following Indication for Use for the VisAbility Micro Insert System:

The VisAbility Micro Insert is indicated for bilateral scleral implantation to improve unaided near vision in phakic, presbyopic patients between the ages of 45 and 60 years of age, who have a manifest spherical equivalent between -0.75D and +0.50 D with less than or equal to 1.00D of refractive cylinder in both eyes, and require a minimum near correction of at least +1.25 D reading add.

Panel Deliberations/FDA Questions:

Question 1

1. **The following is a summary of key safety information:**
   - **There were no prespecified safety endpoints; the study was designed to detect adverse events occurring at a rate of 1% or greater through the 24-month time period.**
   - **Out of 708 operated eyes of 360 subjects cumulatively, there were 365 ocular adverse events (AEs) that occurred in 260 (36.7%) eyes (primary and/or fellow) of 170 (47.2%) subjects through the 24-month follow-up period of the trial. Among these, there were:**
     - **Scleral perforations in 8 (1.1%) eyes of 8 (2.2%) subjects, 5 with vitreous prolapse, including one with inadvertent bleb creation unrecognized for 6 months.**
     - **Anterior segment ischemia in 5 (0.7%) eyes of 5 (1.4%) subjects.**
     - **Micro Insert segment removals in 13 (1.8%) eyes of 8 (2.2%) subjects.**
   - **After the 24-month follow-up period of the trial, the following removals were reported:**
     - **All segments in 18 eyes of 9 subjects**
     - **2 segments from 2 eyes of 1 subject**
     - **1 segment from 4 eyes of 4 subjects**

   Has the applicant provided reasonable assurance of safety of the device for the proposed indications for use?

The panelists noted that these safety issues may not be concerning in context of patients who need retinal detachment surgery, which is vision threatening. However, the panelists believed that the safety issues are concerning from the perspective of an elective procedure for someone who has healthy eyes and is looking for alternatives to contacts and spectacles for presbyopia. The panelists expressed concerns not knowing long term issues and the potential impact on any future procedures that patients may have to undergo. The panelists also raised concerns regarding the overall adverse event rate and minor adverse events as what may be perceived to be minor could have a broader impact on the patient.

Question 2

2. The following is a summary of key effectiveness information:

- **The pre-specified co-primary effectiveness endpoints were:**
  - **1st co-primary endpoint - Achievement of DCNVA 20/40 or better and gain ≥10 letters DCNVA in 75% of the primary eyes of implanted subjects at 12-months**
  - **2nd co-primary endpoint - Achievement of a statistically significant difference in the proportion of primary eyes with DCNVA 20/40 or better and gain of ≥10 letters in subjects randomized to treatment versus deferred surgery as part of the randomized controlled substudy at 6-months**
- **The study success criteria were not met. Study success was defined as achieving both endpoints.**
  - **To claim success on 1st co-primary effectiveness endpoint, the pre-specified target was:**

    Lower Confidence Interval (CI) ≥ 75%

    Analysis of this endpoint demonstrated that 79.1% (277/350) of subjects were responders where the lower bound of the CI was 74.5%, which was lower than the target value of 75%. Therefore, this endpoint was not met, and the study success criteria were not met.
  - **The second co-primary effectiveness endpoint was met.**
- **There was variability in effectiveness outcomes across sites, with only 3 out of 13 sites driving the 1st co-primary endpoint, and thus, the data may not be generalizable.**
- **The defocus curve exploratory analysis showed a 1-line difference in the mean change in visual acuity between the primary eyes of the control group and the treatment group at a near testing distance equivalent of 40 cm (2.50 D lens power). The exploratory analysis of the wavefront testing showed no clinically significant change per the applicant's assessment.**

Do the results provide reasonable assurance of the effectiveness of the device for the proposed indications for use?

Panelists did not have significant concerns with the lower bound of the 95% confidence interval missing the target for the first co-primary effectiveness endpoint. However, panelists had concerns about the trial design not controlling for bias (e.g., lack of masking), site variability, the subjective nature of the primary endpoint, the degree of effect, and indications of a learning effect biasing the effectiveness outcomes. Furthermore, even though panelists recognized that the patient reported outcomes (PRO) were not to be used to support a labeling claim, they had concerns regarding the quality of the PRO instrument and the results.

Question 3

3. **Based on the totality of evidence, do the benefits outweigh the risks for the proposed indications for use?**

Although one panelist thought that both the benefits and risks were small with the benefits slightly outweighing the risks, the panelist generally believed that the benefits do not outweigh the risks, based on questionable benefit and concerns about the risks. Besides the surgical risks, panelists were concerned about the overall number of adverse events, including the non-surgical adverse events of the anterior surface, such as dry eye. Panelists also discussed concerns about the uncertainty of the risks, including inadequate assessment of safety during the trial, longer-term cumulative rates of adverse events, and long-terms risks. The panelists raised concerns about longer term risk. There was also concern that there was lack of objective evidence of benefit, inconsistencies in the effectiveness results, and the degree of effect was not as great relative to alternatives. Other factors discussed by panelists when weighing the benefits to risks included that this is an elective procedure for a non-blinding condition and the mechanism of action is questionable.

Question 4

4. **Study 1: Extended Follow-up of Premarket Cohort**
   The applicant is currently following-up subjects from the IDE through 60-months post implantation (three additional years). This is an observational study designed to collect long-term safety and effectiveness data with study visits at 36, 48, and 60 months post-operatively.

   a. **Is this length of follow-up sufficient to address concerns related to the long-term safety and/or effectiveness of the device?**
   b. **If not, how long should the subjects continue to be followed post implantation for the purpose of this Post-Approval Study (PAS)?**

Some panelists proposed 10 years of follow-up or more due to concerns of potential late risks, such as extrusions and difficulty managing intraocular pressure in patients who develop glaucoma, but the panelists acknowledged that this may not be practical. They believed 5 years of follow-up total (either through a registry or an additional 3 years) would be adequate.

Question 5

5. **Study 2: New Enrollment PAS**
   The applicant proposes a new enrollment PAS to provide additional descriptive data on the intended patient population and to evaluate device performance stratified by surgeon experience. The applicant proposes a 1-year follow-up for all participants implanted with the device. The study did not propose any hypothesis testing, study success criteria, study goal, or a statistical test plan.
   The applicant proposes the following as the safety outcomes:
   Primary:
   - **Rate of occurrence of anterior segment ischemia (ASI; grades 2-4)**
   - **Rate of scleral perforations**

   Secondary:

- **Rate of secondary surgical interventions**
- **Conjunctival retraction**
- **Explant (full or partial)**

The applicant proposes a primary effectiveness outcome of change in distance-corrected near visual acuity (DCNVA) from baseline.

a. **Do you agree with the length of follow-up? If not, how long should subjects be followed after implantation?**
b. **Do you agree with the proposed safety endpoints?**
   i. **Primary Safety Endpoints**
   ii. **Secondary Safety Endpoints**

   If not, what safety endpoints do you recommend?
c. **Do you agree that this subjective assessment of DCNVA is appropriate for the primary effectiveness endpoint? If not, what effectiveness endpoint is more appropriate?**

The panelists generally did not believe that a 1-year study was sufficient. Panelists were less concerned about studying surgeon experience, because they did not think that the safety and effectiveness concerns were related to surgeon experience. Panelists recommended objective measures of effectiveness and to consider more sensitive and objective measures of safety. Panelists emphasized including outcomes measures to capture the patient perspective, including pain.

Panel Vote

The Panel voted on the safety, effectiveness, and benefit-risk profile of the VisAbility Micro Insert System.

On Question 1, the Panel voted 1-13-2 (yes, no, abstain) regarding whether there is reasonable assurance that the VisAbility Micro Insert System is safe for use in patients who meet the criteria specified in the proposed indication.

On Question 2, the Panel voted 3-13-0 (yes, no, abstain) regarding whether there is reasonable assurance that the VisAbility Micro Insert System is effective for use in patients who meet the criteria specified in the proposed indication.

On Question 3, the Panel voted 1-15-0 (yes, no, abstain) regarding whether the benefits of the VisAbility Micro Insert System outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

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