DE NOVO CLASSIFICATION REQUEST FOR LUMINOPIA ONE

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Digital therapy device for amblyopia. A digital therapy device for amblyopia is a device that incorporates dichoptic presentations on visual displays through therapeutic algorithms to treat amblyopia or to improve visual acuity of patients with amblyopia.

NEW REGULATION NUMBER: 21 CFR 886.5500

CLASSIFICATION: Class II

PRODUCT CODE: QQU

BACKGROUND

DEVICE NAME: Luminopia One

SUBMISSION NUMBER: DEN210005

DATE DE NOVO RECEIVED: March 1, 2021

SPONSOR INFORMATION:

Luminopia, Inc.
955 Massachusetts Ave #335
Cambridge, Massachusetts 02139

INDICATIONS FOR USE

Luminopia One is a software-only digital therapeutic designed to be used with commercially available Head-Mounted Displays (HMDs) which are compatible with the software application. Luminopia One is indicated for improvement in visual acuity in amblyopia patients, aged 4-7, associated with anisometropia and/or with mild strabismus, having received treatment instructions (frequency and duration) as prescribed by a trained eye-care professional. Luminopia One is intended for both previously treated and untreated patients; however, patients with more than 12 months of prior treatment (other than refractive correction) have not been studied. Luminopia One is intended to be used as an adjunct to full-time refractive correction, such as glasses, which should also be worn under the HMD during Luminopia One therapy. Luminopia One is intended for prescription use only, in an at-home environment.

LIMITATIONS

Luminopia One is intended to be used as an adjunct to fulltime refractive correction such as glasses, which should also be worn under the Head-Mounted Display (HMD) headset during Luminopia One therapy.

Federal law restricts this digital therapeutic to sale by or on the order of an ophthalmologist or optometrist.

As outlined in the Indications for Use, Luminopia One is a prescription device for children ages 4 to 7 to improve visual acuity for certain medical conditions and should be used under the direct supervision of a trained eye-care professional. The device is indicated for use with compatible, commercially available head-mounted displays (HMDs). Currently, the Samsung Gear HMD is the only compatible HMD. For all other uses of such HMD, users should follow the user manual and instructional information for the specific HMD used with Luminopia One, including the age range specified by the HMD manufacturer.

Patients should only use HMDs that are compatible with Luminopia One, as described in the "Directions for Use" labeling. The Luminopia One device is currently authorized to be used with the following commercially available HMDs that have been validated as compatible with the software application:

- Samsung Gear HMD

Patients with an interpupillary distance of less than 52 mm should not use the Luminopia One device. The Luminopia One device has not been studied on patients with interpupillary distances of less than 52 mm. Attempting to use the Luminopia One device on these patients may result in decreased effectiveness of treatment and increased risk of adverse symptoms.

Because the Luminopia One clinical study did not follow patients after 12 weeks of use, limitations include:

- Safety and effectiveness of Luminopia One therapy beyond 12 weeks is unknown and was not evaluated in the clinical study.
- The durability of benefit from the Luminopia One device after treatment cessation is unknown (i.e., unknown whether visual acuity improvement at 12 weeks will be maintained or regress over time).
- The long-term effects of Head-Mounted Display (HMD) use in patients 4-7 years of age are unknown.

In the 12-week clinical study, use of Luminopia One did not demonstrate a clinically meaningful improvement in stereoacuity (depth perception).

Please refer to Luminopia One "Directions for Use" for a complete list of WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS, as well as a description of CLINICAL STUDY OUTCOMES.

DEVICE DESCRIPTION

Luminopia One is a Software as a Medical Device (SaMD) intended to improve visual acuity in pediatric patients with amblyopia (also known as lazy eye). The device is indicated for improvement in visual acuity at 12 weeks of use in amblyopia patients aged 4-7. The software is designed to be used with commercially available head-mounted displays (HMDs) (Figure 1) and is intended for at-home use. In this submission, the Samsung Gear HMD has been validated to be compatible with Luminopia One. The Patient should wear their refractive correction, such as glasses, under the HMD during treatment.

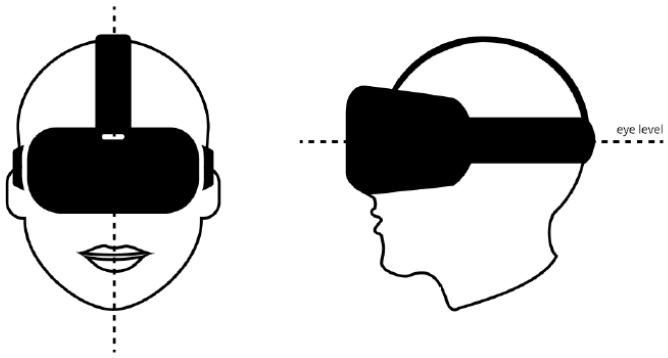

Figure 1. Luminopia One is used with compatible head-mounted displays.

The software allows patients to select videos to watch (Figure 2).

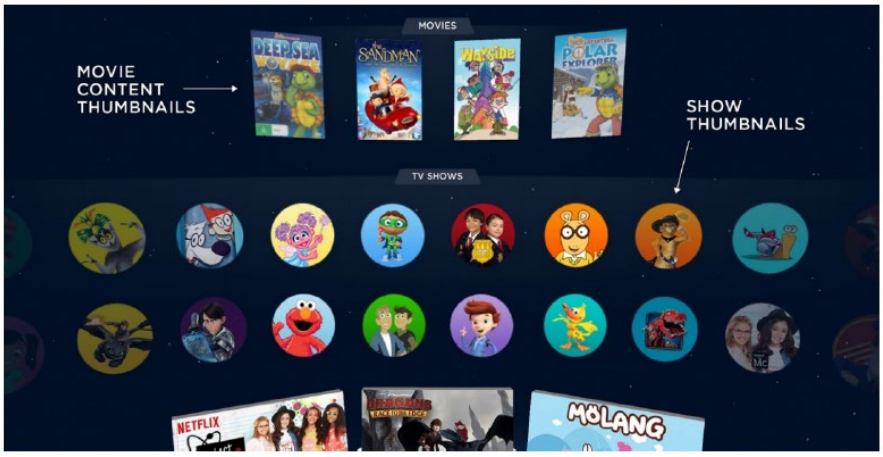

Figure 2. Selection menus for TV shows and movies

Treatment is provided through algorithms that apply modifications to the videos to encourage use of the amblyopic eye. The video presented to the fellow eye (the stronger eye) is different from the video presented to the amblyopic eye (weaker eye) (Figure 3). When a video begins in the software application, the patient will see a modified version of the original video through

each eye. This is intended to rebalance the visual input to the eyes and encourage weaker eye usage. The treatment regimen is the following: the patient watches the video 1 hour per day, 6 days per week for a total of 12 weeks.

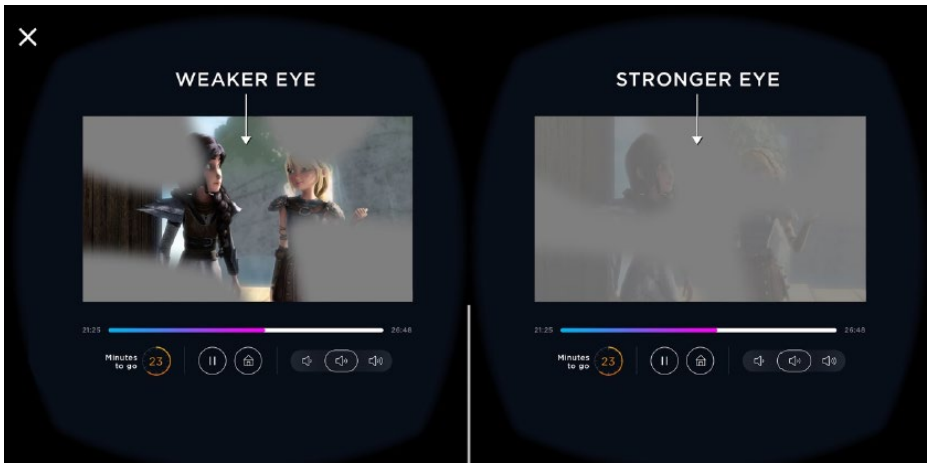

Figure 3. Left: Videos presented to the amblyopic eye (weaker eye); Right: video presented to the fellow eye (stronger eye).

Luminopia One also includes a Patient Portal. The Patient/Caregiver will also have access to an online Patient Portal where they can review the Patient's adherence and select their favorite videos to watch in the HMD. The Patient Portal enables the Caregiver to review the patient's progress and treatment plan
and curate content for the patient to watch. The Patient Portal is designed to be used by the Caregiver.

SUMMARY OF NONCLINICAL/BENCH STUDIES

PERFORMANCE TESTING - BENCH

Test	Purpose	Method	Acceptance Criteria	Results
HMD Temperature measurements	To prevent thermal injury and/or adverse events	Human subject wore the HMD with multiple temperature probes placed at different locations of HMD	IEC 60601-1; Temperature does not exceed 41°C on the human contacting parts of the HMD	Passed
Luminance and its uniformity	To ensure luminance is sufficiently high and uniform across the visual display	IEC63145-20-10: Eyewear display - Part 20-10: Fundamental measurement methods - Optical properties. Luminance measurements at 9 or more locations in the field of view (FOV) using a uniform white testing pattern to determine the luminance and uniformity across the FOV.	Minimum luminance should not be lower than 48 candela per square meter (Cd/m^2). The percent deviation from the average luminance at each location should not be higher than 50%	Passed
Contrast measurements	To ensure the visual display has sufficient	IEC63145-20-10: Eyewear display - Part 20-10: Fundamental	At least 90% at each location	Passed

	contrast to display quality video and video modifications implemented by software	measurement methods - Optical properties. Contrast measurements at 9 or more locations in the field of view using a test pattern, such as a grille pattern. Contrast can be calculated using the Michelson contrast equation		
HMD resolution	To ensure the quality of the video	Calculate the horizontal and vertical pixels per degree by measuring horizontal and vertical field of view and the number of pixels in the test image.	At least 14 pixels per degree	Passed
Crosstalk testing	To ensure that light from one eyepiece of the HMD cannot be seen by the other eye to prevent interference with the treatment	Measure luminance with the following combinations: (1) Both eyepieces have a uniform black test pattern (off); (2) Eyepiece 1 has a uniform white test pattern (on) and eyepiece 2 is off; (3) Eyepiece 1 is off and eyepiece 2 is on. See Information Display Measurements Standard 1.03 (IDMSv1.03) as reference.	Light entered from one eyepiece to another is not significantly higher than background levels.	Passed
Labeling comprehension testing	To ensure that the Direction of Use (DFU) conveys clear instructions to the parent/caregiver	DFU comprehension testing and device use testing: (1) caregiver and child pairs are tested through the knowledge tasks to demonstrate their understanding of the DFU; (2) caregiver and child pairs are tested through the performance tasks to demonstrate that they can use device successfully.	Testing demonstrated that caregivers and patients understood the directions of use and could use the device successfully. There were minimal use errors in the use of the device.	Passed

SOFTWARE

Luminopia One is a Software as a Medical Device (SaMD). It was reviewed according to the FDA Guidance document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005. The software was found to have a MODERATE level of concern because a failure of the device may result in a minor injury to a patient prior to risk mitigation. FDA reviewed the software documentation provided in support of Luminopia One and found it acceptable.

Software controls have been implemented in Luminopia One to minimize overuse of the device. The user will be presented a pop-up warning when the daily use of the device exceeds the prescribed length of time. A software control will implement a lock-out at the end of entire prescribed treatment regimen.

SUMMARY OF CLINICAL INFORMATION

A randomized controlled clinical study was conducted that evaluated 117 subjects age 4-7 years, treated for 12 weeks with Luminopia One (1 hour daily, 6 days a week, for 12 weeks) along with fulltime refractive correction, as compared to control treatment with refractive correction alone, with final assessment at the 12-week visit. Amblyopia is clinically defined as reduction of visual acuity (VA) that cannot be attributed to ocular or visual system abnormality or refractive error. The American Academy of Ophthalmology (AAO) considers amblyopia as an interocular difference of 2 lines or more or VA worse than or equal to 20/30 with best optical correction[1]. The Luminopia One clinical study inclusion criterion for VA met the AAO definition. Interim analysis was conducted per protocol after 75% of subjects completed the 12-week follow up visit. At that time there were 105 subjects (51 Luminopia One therapeutic group, 54 control group). The study was stopped early for success, per protocol, when 75% of subjects completed the 12-week visit, since primary effectiveness and safety endpoints were achieved at interim analysis. Final analysis included 117 subjects (58 Luminopia One therapeutic group, 59 control group), reported as descriptive outcome information in the device labeling.

The mean age of all study participants was 6.0 ± 1.0 years (n = 117). Among them, 56.4% (66/117) were male and 43.6% (51/117) were female. The mean age for the Luminopia One treatment group was 6.2 ± 0.9 (n = 58) years. In the treatment group, 60.3% (35/58) of the subjects were male and 39.7% (23/58) were female. The mean age for the control group (refractive correction only) was 5.9 ± 1.1 (n = 59). In the control group, 52.5% (31/59) of the subjects were male and 47.5% (28/59) were female.

In terms of ethnicity, 22.4% (13/58) of the subjects in the treatment group were Hispanic or Latino and 77.6% (45/58) were not Hispanic or Latino. In the control group, 10.2% (6/59) of the subjects were Hispanic or Latino and 89.8% (53/59) were not Hispanic or Latino.

The percentages of subjects whose right eye is amblyopic are 45.6% (26/57) for the treatment group and 47.5% (28/59) for the control group. The percentages of subjects whose left eye is amblyopic are 54.4% (31/57) for the treatment group and 52.5% (31/59) for the control group.

1. **Evidence of clinical benefit** for Luminopia One as used in the clinical study with refractive correction:

o Primary Effectiveness Endpoint: Mean improvements from baseline in amblyopic eye's best corrected visual acuity (BCVA) after 12-week treatment show statistically significant difference between the treatment and control groups; superiority of the treatment was demonstrated and the endpoint was met:

• Interim analysis (N=105, n=84): Mean change -0.180 (SD=0.15) logMAR in the therapeutic group, -0.080 (SD=0.14) logMAR in the control group (see Table 1 below). Average difference between groups -0.10 logMAR, greater improvement in the treatment group compared to control group (p=0.0012). Mean BCVA improvement in amblyopic eye was 1.8 lines in the treatment group vs. 0.8 lines

[1] https://www.aao.org/disease-review/amblyopia-types-diagnosis-treatment-new-perspectiv

in control group. Point estimate difference in improvement is 1.0 line (90% CI: 0.5-1.5 lines).

Table 1: Amblyopic Eye BCVA[1] – Intention-to-Treat (ITT) Population at Interim Analysis					Results	
	Treatment Group N=51	Control Group N=54	Difference in Change in BCVA[2] (90% CI)	P-value[3]	Stage 1 Alpha Level	Decision
Improvement from Baseline at 12 Weeks (lines)[4]	**1.8 ± 1.5 (41) 2.0 (-2.0, 6.0) [1.3, 2.3]**	**0.8 ± 1.4 (43) 1.0 (-2.0, 4.0) [0.4, 1.3]**	**1.0 (0.5, 1.5)**	**0.0012**	**0.0176**	**Reject H_0**
Change from Baseline at 12 Weeks (logMAR)	-0.18 ± 0.15 (41) -0.20 (-0.60, 0.20) [-0.23, -0.13]	-0.08 ± 0.14 (43) -0.10 (-0.40, 0.20) [-0.13, -0.04]				
Baseline (logMAR)	0.54 ± 0.21 (41) 0.50 (0.30, 1.00)	0.50 ± 0.19 (43) 0.40 (0.30, 1.00)				
12 Weeks (logMAR)	0.36 ± 0.23 (41) 0.30 (0.00, 1.10)	0.42 ± 0.21 (43) 0.40 (0.00, 1.00)				

[1]Based on participants with available data at baseline and in-window 12-week visits. Data presented as mean ± standard deviation (N) median (min, max). Change from baseline also includes [95% CI].
[2]Difference between groups (treatment - control) and 90% confidence interval are based on the coefficient associated treatment group from an ANOVA model. Positive difference between groups represents larger improvement in the treatment group.
[3]P-value is based on a one-sided F-test for the coefficient associated with treatment group from an ANOVA model.
[4]Original visual acuity measurements captured using logMAR. A 1-line improvement from baseline corresponds to a change of -0.10 logMAR.

The bar chart below (Figure 4) shows the mean BCVA improvements in the treatment group vs. the control group after 4, 8 and 12 weeks of treatment.

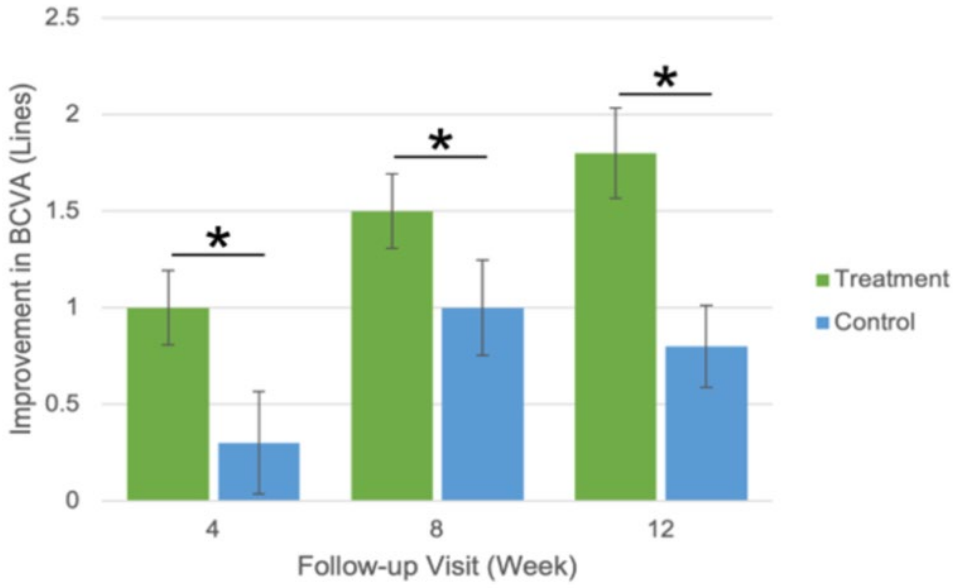

Figure 4. Improvement in amblyopic eye BCVA from baseline – ITT population at interim analysis at 4, 8, and 12 weeks (error bars denote ± SEM, * denotes p < 0.05)

• Final analysis (N=117, n=88): Mean change was -0.181 logMAR (SD=0.15) in the therapeutic group and -0.085 logMAR (SD=0.14) in the control group (see Table 2 below). The average difference between groups was -0.096 logMAR, larger improvement in Luminopia One group (p = 0.0011), consistent with interim analysis results. BCVA improved by 1.8 lines in the treatment group vs. 0.85 lines in the control group. Point estimate of difference between groups is 0.96 line (90% CI: 0.45-1.47 lines).

Table 2: Amblyopic Eye BCVA[1] – ITT Population at Final Analysis

	Treatment Group N=58	Control Group N=59	Difference in Change in BCVA[2] (90% CI)
Improvement from Baseline at 12 Weeks (lines)[4]	**1.81 ± 1.52 (42) 2.0 (-2.0, 6.0) [1.34, 2.28]**	**0.85 ± 1.35 (46) 1.0 (-2.0, 4.0) [0.45, 1.25]**	**0.96 (0.45, 1.47)**
Change from Baseline at 12 Weeks (logMAR)	-0.181 ± 0.152 (42) -0.200 (-0.600, 0.200) [-0.228, -0.134]	-0.085 ± 0.135 (46) -0.100 (-0.400, 0.200) [-0.125, -0.045]	
Baseline (logMAR)	0.536 ± 0.212 (42) 0.500 (0.300, 1.000)	0.507 ± 0.190 (46) 0.400 (0.300, 1.000)	
12 Weeks (logMAR)	0.355 ± 0.231 (42) 0.300 (0.000, 1.100)	0.422 ± 0.202 (46) 0.400 (0.000, 1.000)	

[1]Based on participants with available data at baseline and in-window 12-week visits. Data presented as mean ± standard deviation (N) median (min, max). Change from baseline also includes [95% CI].
[2]Difference between groups (treatment - control) and 90% confidence interval are based on the coefficient associated treatment group from an ANOVA model. Positive difference between groups represents larger improvement in the treatment group.
[3]P-value is based on a one-sided F-test for the coefficient associated with treatment group from an ANOVA model.
[4]Original visual acuity measurements captured using logMAR. A 1-line improvement from baseline corresponds to a change of -0.10 logMAR.
*Although the results from the interim analysis constitute the statistical conclusions from the study, the results from the final analysis are based on data from all enrolled participants.

o Secondary Effectiveness Endpoint: Amblyopic eye BCVA improvement 2 or more lines from baseline after 12 weeks, 62% of Luminopia subjects (95% CI: 46-76%) vs. 33% of control subjects (95% CI: 20-48%) (see the Table 3 below). This is part of the final analysis that was pre-specified as descriptive analysis only.

Table 3: Improvement in Amblyopic Eye BCVA ≥ 2 Lines[1] – ITT Population at Final Analysis

	Treatment Group N=58	Control Group N=59
Improvement ≥ 2 lines from Baseline to 4 weeks	34.0% (17/50) [21.2%, 48.8%]	24.5% (12/49) [13.3%, 38.9%]
Improvement ≥ 2 lines from Baseline to 8 weeks	50.0% (24/48) [35.2%, 64.8%]	31.8% (14/44) [18.6%, 47.6%]
Improvement ≥ 2 lines from Baseline to 12 weeks	61.9% (26/42) [45.6%, 76.4%]	32.6% (15/46) [19.5%, 48.0%]

[1]Based on participants with available data at baseline and in-window visits. Data presented as: % (n/N) [95% CI].
[2]P-value from post-hoc Chi-square test.
*Although the results from the interim analysis constitute the statistical conclusions from the study, the results from the final analysis are based on data from all enrolled participants.

o Supplemental analysis: Lines of improvement in BCVA**:** Luminopia One group demonstrates better visual acuity improvement outcome than control group at 4, 8 and 12 weeks (see the Table 4 below).

Table 4: Amblyopic Eye Change in BCVA by Visit[1] – ITT Population at Final Analysis

	4 Weeks		8 Weeks		12 Weeks	
Number of Lines Change (follow-up - baseline)[2]	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**
6-line improvement	0.0% (0/50)	0.0% (0/49)	0.0% (0/48)	0.0% (0/44)	2.4% (1/42)	0.0% (0/46)
4-line improvement	4.0% (2/50)	0.0% (0/49)	6.3% (3/48)	6.8% (3/44)	2.4% (1/42)	2.2% (1/46)
3-line improvement	10.0% (5/50)	8.2% (4/49)	12.5% (6/48)	13.6% (6/44)	31.0% (13/42)	10.9% (5/46)
2-line improvement	20.0% (10/50)	16.3% (8/49)	31.3% (15/48)	11.4% (5/44)	26.2% (11/42)	19.6% (9/46)
1-line improvement	32.0% (16/50)	22.4% (11/49)	29.2% (14/48)	31.8% (14/44)	23.8% (10/42)	19.6% (9/46)
No change	24.0% (12/50)	32.7% (16/49)	14.6% (7/48)	15.9% (7/44)	7.1% (3/42)	34.8% (16/46)
1-line decrease	8.0% (4/50)	10.2% (5/49)	6.3% (3/48)	13.6% (6/44)	2.4% (1/42)	10.9% (5/46)
2-line decrease	2.0% (1/50)	6.1% (3/49)	0.0% (0/48)	6.8% (3/44)	4.8% (2/42)	2.2% (1/46)
3-line decrease	0.0% (0/50)	2.0% (1/49)	0.0% (0/48)	0.0% (0/44)	0.0% (0/42)	0.0% (0/46)
7-line decrease	0.0% (0/50)	2.0% (1/49)	0.0% (0/48)	0.0% (0/44)	0.0% (0/42)	0.0% (0/46)

[1]Based on participants with available data and in-window visits. Categorical variables presented as n/N (%) where N is the number of participants with available data.

[2]Original visual acuity measurements captured using logMAR. A 1-line improvement from baseline corresponds to a change of -0.10 logMAR.

*Although the results from the interim analysis constitute the statistical conclusions from the study, the results from the final analysis are based on data from all enrolled participants.

o Exploratory Analyses:

- Stereoacuity (depth perception) did not show meaningful difference between groups.
- Mean Treatment Adherence with Luminopia One device was 75.7% from baseline to 12 weeks (note: 99% adherence with refractive correction was similar between groups).

2. **Evidence of clinical safety** for Luminopia One as used in clinical study with refractive correction:

Co-Primary Safety Endpoints:

o Adverse Events (AEs) demonstrate moderate probability of device-related adverse events. AE categories below demonstrate clinically meaningful higher rate in the Luminopia One group than in the control group (see Table 5 below):

• Overall AE rate: 25% of Luminopia One group (14 subjects, 25 events) vs. 13.6% of control group (all mild except one AE "worsening night terrors" severe)
• Headaches: 14.3% Luminopia One group (8 subjects, 9 events) vs. 1.7% control group (1 subject, 1 event) - All intermittent and mild, no Rx treatments, no OTC medication, all resolved without sequelae.
• Eye strain: 3.6% (2 subjects, 3 events) Luminopia One group vs. 0% control group
• "Other" includes "increased frequency of night terrors*, facial redness, eyelid-twitch, dizziness, parent-reported intermittent eye turning when tired": 7.1% (4 subjects, 5 events) Luminopia One group vs. 0% control group.

[*1 subject had prior history of night terrors, parent reported increase frequency of night terrors after beginning treatment, investigator graded as severe, parent withdrew child from the study.]

Table 5: Non-Serious Adverse Events[1] – As-Treated (AT) Population[2] at Final Analysis

	Treatment Group[2] (N=56)	Control Group[2] (N=59)
Diplopia	0 (0.0%) [0] [0.0%, 6.4%]	1 (1.7%) [1] [0.0%, 9.1%]
New heterotropia	4 (7.1%) [4] [2.0%, 17.3%]	4 (6.8%) [4] [1.9%, 16.5%]
Worsening heterotropia	0 (0.0%) [0] [0.0%, 6.4%]	1 (1.7%) [1] [0.0%, 9.1%]
Worsening BCVA	3 (5.4%) [4] [1.1%, 14.9%]	4 (6.8%) [4] [1.9%, 16.5%]
Headache	8 (14.3%) [9] [6.4%, 26.2%]	1 (1.7%) [1] [0.0%, 9.1%]
Nausea	0 (0.0%) [0] [0.0%, 6.4%]	0 (0.0%) [0] [0.0%, 6.1%]
Eye strain	2 (3.6%) [3] [0.4%, 12.3%]	0 (0.0%) [0] [0.0%, 6.1%]
Other[3]	4 (7.1%) [5] [2.0%, 17.3%]	0 (0.0%) [0] [0.0%, 6.1%]
Overall	14 (25.0%) [25] [14.4%, 38.4%]	8 (13.6%) [11] [6.0%, 25.0%]

[1]Includes events classified with Possible, Probable, or Definite relation to study treatment. Data presented as: n (%) [m] [95% CI], where n is number of participants with event and m is the number of events. Participants may experience more than one AE.

[2]AT is defined as subjects with > 0% adherence of device use are in the treatment arm, otherwise control; there are no control subjects treated with the device.

[3]Other AEs in treatment group include: Eye Twitch, Facial Redness, Increase in Frequency of Night Terrors, Dizziness, Parent-reported intermitted eye turning when tired

o Mean change non-amblyopic (fellow) eye BCVA from baseline, Luminopia One treatment group demonstrated non-inferiority to control group:

• Interim analysis (N=105, n=84): Mean change in fellow eye BCVA was -0.03 logMAR (SD=0.08) in therapeutic group and -0.02 logMAR (SD=0.06) in control group, indicating both groups had improvement in fellow eye vision. Difference

between groups was -0.02 logMAR with upper 95% confidence limit of 0.010 and p-value <0.0001 for non-inferiority test, outcome suggests no additional risk for fellow eye vision and reverse amblyopia associated with Luminopia One.

• Final analysis (N=117, n=88): mean change in fellow eye BCVA from baseline to 12 weeks was -0.036 logMAR in therapeutic group and -0.017 in control group. The difference between groups was -0.018 logMAR with upper 95% confidence limit of 0.006 and p-value <0.0001 for non-inferiority

LABELING

Directions for Use (DFU) labeling provides product description, Indications for Use, software (the operating system) and hardware requirements for device operation, the compatible HMD, and instructions for how to operate the device. The DFU also provides a brief description of the clinical study design including the treatment duration and a summary of the study outcomes including the adverse events. The DFU includes warnings and precautions describing limitations and risks of the device, The DFU labeling is sufficient and satisfies the requirements of 21 CFR § 801.109 for prescription devices.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a digital therapy device for amblyopia and the measures necessary to mitigate these risks.

Identified Risks to Health	**Mitigation Measures**
Adverse events due to device treatment (e.g., headache, new or worsening heterotropia, worsened vision in either eye, eye strain, eye twitching, facial redness, increased night terrors, thermal injury, dizziness, seizure, nausea, or double vision)	Clinical performance testing Labeling
Ineffective treatment leading to worsening of condition	Clinical performance testing Software verification, validation, and hazard analysis Labeling
Therapeutic effect not sustained leading to delay of treatment	Clinical performance testing Labeling
Software malfunction leading to delay of treatment	Software verification, validation, and hazard analysis Labeling
Improper use of the device including HMD or other visual display leading to ineffective treatment or adverse events	Labeling Labeling comprehension testing

Performance variations among different brands/models of visual displays leading to ineffective treatment and/or adverse events	Clinical performance testing Non-clinical performance testing Labeling Software verification, validation, and hazard analysis

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the digital therapy device for amblyopia is subject to the following special controls:

(1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use with labeled compatible visual display devices, including evaluation of all adverse events and device performance to improve measures of visual function.

(2) Software verification, validation, and hazard analysis must be performed. Documentation must include characterizations of the technical specifications of the software.

(3) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. All visual displays intended for use must undergo compatibility testing to ensure adequate display resolution, luminance, contrast, field of view, image quality, appropriate optical image distance, and verify their compatibility with the software and intended user (such as appropriate interpupillary distance).

(4) Labeling must include the following:

  (i) The minimum hardware and operating system requirements that support the software of the device;

  (ii) The models of the visual displays validated to be compatible with this device;

  (iii) The length of treatment and/or retreatment supported by clinical performance testing; and

  (iv) A summary of the clinical performance testing conducted with the device.

(5) Labeling comprehension testing with intended users must be performed.

BENEFIT-RISK DETERMINATION

The risks of the device are based on the clinical performance testing data collected in a clinical study described above.

The clinical study has shown that the treatment with Luminopia One was associated with several adverse events with moderate probability. These adverse events include diplopia (double vision), new or worsening heterotropia (strabismus, "eye turn" or "crossed eyes"), worsened vision in in the amblyopic eye and/or in the fellow eye, headaches, nausea, eye strain (asthenopia), and other events. These events were reversable and considered non-serious. DFU labeling notes that patients should stop using Luminopia One and contact doctor for evaluation and permission to continue treatment if they experience any of these during or after using the device.

The probable benefits of the device are also based on data collected in the clinical study as described above.

The clinical study clearly demonstrated that treatment with Luminopia One improved the visual acuity of the amblyopic eye more than the control (refractive correction alone). Significantly more subjects experienced improvement of the amblyopic eye by BCVA 2 lines or more in the treatment group than in the control group. No reduction in BCVA in the fellow eye was observed between the treatment and control group suggesting no additional risk for fellow eye vision and reverse amblyopia associated with Luminopia One. In addition, Luminopia One provides an alternative for patients who have exhausted currently available treatments.

Although it is unknown whether the benefits of treatment with Luminopia One can be retained beyond 12 weeks, the overall probable benefits of visual acuity improvement in the amblyopic eye outweigh the probable risks of non-serious adverse events associated with the use of Luminopia One.

PATIENT PERSPECTIVES

Patient perspectives considered for Luminopia One included: Questionnaires during the clinical study provided to patients and caregivers during visits and through phone calls. The adverse events reported during the clinical study in Table 5 a demonstrated a clinically meaningful higher rate in the Luminopia One treatment group than in the control group.

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

> Luminopia One is a software-only digital therapeutic designed to be used with commercially available Head-Mounted Displays (HMDs) which are compatible with the software application. Luminopia One is indicated for improvement in visual acuity in amblyopia patients, aged 4-7, associated with anisometropia and/or with mild strabismus, having received treatment instructions (frequency and duration) as prescribed by a trained eye-care professional. Luminopia One is intended for both previously treated and untreated patients; however, patients with more than 12 months of prior treatment (other than refractive correction) have not been studied. Luminopia One is intended to be used as an adjunct to full-time refractive correction, such as glasses, which should also be worn under

the HMD during Luminopia One therapy. Luminopia One is intended for prescription use only, in an at-home environment.

The probable benefits outweigh the probable risks for the Luminopia One. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Luminopia One is granted and the device is classified as follows:

Product Code: QQU
Device Type: Digital therapy device for amblyopia
Regulation Number: 21 CFR 886.5500
Class: II