Anthem

Medical Policy

Subject: Digital Therapy Devices for Treatment of Amblyopia
Document #: MED.00145
Status: Reviewed
Publish Date: 09/27/2023
Last Review Date: 05/11/2023

Description/Scope

This document addresses digital therapy devices for the treatment of amblyopia. These devices incorporate dichoptic (viewing a separate and independent field through each eye) presentations to improve visual acuity of individuals with amblyopia.

Position Statement

Investigational and Not Medically Necessary:

Digital therapy devices for treatment of amblyopia are considered **investigational and not medically necessary**.

Rationale

Current amblyopia treatment involves re-training the brain to force it to use the weaker eye. This can be accomplished by wearing an eye patch over the stronger eye or the use of eye drops in the stronger eye.

Recently developed digital therapy devices have the potential to address compliance issues that may occur with patching or drops. These digital therapy devices use noninvasive, computerized systems such as 3-dimensional glasses or virtual reality headsets. Participants watch videos on a tablet-like device in which eye-tracking technology blurs images in the center of vision for the stronger eye, while the weaker eye sees clear content. This is proposed as a way to help the eyes learn to work together.

A 2016 randomized trial by Holmes and colleagues studied whether treatment of amblyopia using a binocular video game was noninferior than treatment with eye patching. The primary outcome measure was the change in visual acuity (VA) from baseline to 16 weeks. The eye patch group (n=195) was prescribed to wear the patch 2 hours per day, 7 days per week. The binocular video game group (n=190) was prescribed play for 1 hour per day, 7 days per week. Compliance was measured by parental recording of the number of hours the participant played the game or wore the patch. The video game device recorded the duration of game play, contrast, and performance. There were 172 participants (92.5%) in the eye patch group who completed more than 75% of the prescribed treatments in the 16-week treatment period. In the video game group, there were 176 participants (66.7%) available for evaluation at the 16-week visit from the video game group. Only 39 participants of these 176 participants (22.2%) completed more than 75% of their prescribed treatments, as measured by the video game log file data. The mean amblyopic VA improved from 1.08 lines at baseline in the video game group and by 1.32 lines in the eye patch group. There were no significant between-group differences found for changes in amblyopic eye VA. Limitations include lack of occlusion dose monitors, adherence data reliance on parental report (particularly for eye patch wearing), low adherence among the video game participants, and lack of monitoring of wearing the red-green glasses required to play the video game.

A Cochrane Intervention Review of binocular treatments compared to standard treatments for amblyopia cited the Holmes study described above as the only randomized controlled trial eligible for their analysis (Tailor, 2022). The authors concluded with moderate certainty that 16 weeks of this binocular treatment improved vision comparably to patching. They noted that,

> due to the limited sample size and lack of long term (52 week) follow- up data, it is not yet possible to draw robust conclusions regarding the overall safety and sustained effectiveness of binocular treatment… Further research, using acknowledged methods of visual acuity and stereoacuity assessment with known reproducibility, is required to inform decisions about the implementation of binocular treatments for amblyopia in clinical practice, and should incorporate longer term follow-up to establish the effectiveness of binocular treatment.

In a 2018 randomized, double-masked trial by Gao and colleagues, the authors evaluated efficacy of a home-based digital therapy video game compared to a placebo video game to improve visual function. The study included children age 7 years and older and adults. Participants were prescribed video game play for a minimum of 1 hour per day for 6 weeks.The primary outcome was the change in VA from baseline to 6 weeks. Treatment compliance was recorded by the video game software as well as a written diary completed by study participants. There were 56 participants randomized to the active group and 59 participants who participated in a placebo video game. At the 6 week follow-up, there were 50 participants available in the active group and 57 participants in the placebo group. In the active group, there were 36 participants (64%) who met the study definition of compliance compared to 49 (83%) in the placebo group. At 6 weeks, the mean improvement of VA from baseline was 0.06 logMAR (3 letters) in the active group and 0.07 logMAR (3.5 letters in the placebo group. No significant differences were found between the two groups.

A 2018 randomized clinical trial by Manh and colleagues compared improvement of VA in participants with amblyopia following either treatment with binocular video game play or wearing an eye patch. Participants were 13-16 years old and were followed for 16 weeks after treatment. Those in the binocular video game group (n=40) were prescribed 1 hour of game play each day for 7 days each week. Those in the eye patch group (n=60) were prescribed to wear the patch 2 hours per day. Parents or participants recorded the number of hours of treatment each day. The video game device also recorded the duration of game play. There were 39 participants (98%) in the video game group and 58 participants (97%) in the eye patch group who completed the 16 weeks of treatment. Adherence after 16 weeks was assessed to be adequate in 24 video game participants (62%) and 42 eye patch participants (75%). However, in the video game group, the game device recorded only 13% of participants who completed 75% of their prescribed treatments. At 16 weeks, mean VA in the amblyopic eye improved by 3.7 letters at baseline and by 6.3 letters in the eye patch group. While a major limitation of this study is poor treatment adherence, the authors reported more improvement in VA in the eye patch group compared to the binocular vision treatment group.

In a 2022 prospective, multi-center, randomized non-inferiority trial by Wygnanski-Jaffe, 103 participants with amblyopia received either digital therapy (n=51) or eye patch (n=52). Digital therapy consisted of passively watching vidual content streamed separately to each eye. The system software blurred central vision in the non-amblyopic eye to encourage use of the amblyopic eye. Those who received the digital therapy used the treatment for 90 minutes per day, 5 days per week for 16 weeks. The eye patch group wore their patch for 2 hours per day, 7 days per week. The primary outcome was mean improvement of VA from baseline at 16 weeks (a non-inferiority of no more than 0.10 logMAR). Assessments were performed at 4, 8, 12, and 16 weeks. The baseline mean amblyopic eye

visual acuity in the digital treatment group was 0.37±0.15 logMAR and 0.37±0.14 logMAR in the eye patch group. At 16 weeks, the mean change from baseline was 0.26 logMAR in the digital therapy treatment group and 0.23 logMAR in the eye patch group (standard error 0.02). The authors considered digital therapy to be non-inferior to eye patching. There were no serious adverse events reported. While improvement was noted in the digital therapy treatment group, further studies are necessary to explore longer treatment durations and effects for those treated with digital therapy.

In 2022, Xiao and colleagues reported the results of a phase 3 randomized controlled trial in which 105 participants with amblyopia were treated either with a digital therapeutic device or wore glasses. The digital devices in this study employed dichoptically-transmitted streaming images of popular television shows. Differences in contrast and masking between the eyes required the use of both eyes to fully understand the content. The digital therapy group used their device at home for 1 hour per day, 6 days per week and wore glasses. Those in the comparison group wore refraction-correcting glasses full-time. The primary outcome was the change in VA from baseline to 12 weeks after treatment. There were 51 participants randomized to digital treatment and 54 participants randomized to the comparison group. At 12 weeks following treatment, those in the digital treatment group had improved visual acuity by 1.8 lines while those in the glasses-only group had visual acuity improvement by 0.8 lines. There were no serious adverse events reported. The study was stopped after 12 weeks as a success according to protocol. This study did not compare this digital therapy with eye patching, the current standard treatment for amblyopia. Further studies are needed to understand how this treatment compares to patching and to determine the treatment's long-term effects.

Another randomized clinical trial compared VA changes in participants with amblyopia who were treated with binocular vision video game or spectacle correction. In 2022 Manny and colleagues reported on children aged 4 to 6 years who received 8 weeks treatment with either a video game (n=92) or spectacle correction (n=90). Before the study, those who wore spectacles were required to have had a minimum of 16 weeks of wear. Primary outcome was change in VA from baseline to 4 weeks and to 8 weeks. Participants in the spectacle group were prescribed to wear them during all waking hours. Those in the video game group were prescribed play for 1 hour per day, 5 days per week. At the 4 week visit, there were 85 participants (92%) in the video game group and 84 participants (93%) in the spectacle group available for analysis. Parents reported adherence of greater than 75% for 74 spectacle group participants (95%) and 66 (78%) video game participants. At 8 weeks, 75% adherence was reported for78 (95%) in the spectacle-wearing group and 69 participants (78%) in the video game group. At 4 weeks, mean VA improved 1.1 logMAR lines in the video game group and 0.6 logMAR lines in the group who wore spectacles. At 8 weeks, the mean VA improvement for the video game group was 1.3 and 1.0 in the spectacle group. Additional study is needed to compare this treatment to eye patching and to understand the long-term effectiveness of this treatment.

A 2022 retrospective review by Abdal and colleagues reported on 161 participants with refractive amblyopia who received digital treatment. Digital treatment was provided by dichoptic training in a game format. Participants wore goggles that presented scenes most visible to the dominant eye. A crucial stimulus for game play was only presented to the non-dominant eye. Participants used the therapy 30 minutes per day, 5 times a week, for 6 weeks. The primary outcome was the mean change in best-corrected visual acuity after 6 weeks of treatment. Following treatment, best-corrected visual acuity in the non-dominant eye mean change was 0.39 logMAR. Best-corrected visual acuity in the dominant eye had a mean change of 0.08 logMAR following treatment. Limitations include lack of control or comparison group and a 6 week treatment period. Further study is needed to validate these results.

A 2022 American Academy of Ophthalmology Preferred Practice Pattern for amblyopia states that the evidence to recommend binocular therapy for treatment of amblyopia remains limited.

The currently accepted standard treatments for amblyopia are vision correction with spectacles, patching, blurring vision in the better-seeing eye, or some combination of these three. Decades of research have evaluated the initiation, dosing, and cessation of these treatments as well as their long-term outcomes. Further randomized controlled trials and long-term follow-up is needed to compare digital therapy to eye patching and to demonstrate long-term results and recurrence rates after cessation when used in clinical practice.

Background/Overview

Amblyopia occurs when there is abnormal development of the visual system in early life. Normal development of the visual cortex requires interpretation of clearly focused images from both eyes. When a developing child's two eyes do not transmit the same image to the brain, the brain will suppress the image from one eye to prevent diplopia or unclear perception. Causes include unequal refractive errors between the eyes (refractive amblyopia), obstructed vision (such as from a cataract) that is worse in one eye (obstructive amblyopia), or misalignment of the eyes (strabismic amblyopia). Over time, the brain relies more on the stronger eye while vision in the weaker eye gets worse. Amblyopia typically affects one eye but can also be a bilateral condition. The difference between amblyopia and simple refractive error, visual obstruction, or strabismus is that, in amblyopia, the visual cortex is suppressing the images received from one or both eyes.

Amblyopia usually occurs in one eye and affects approximately 3% of the population. It is the most common cause of vision loss in children. Early treatment therapy is over 90% effective and prevents long-term vision problems.

Treatment of amblyopia begins with correction of visual refraction, obstruction, or misalignment. This is combined with treatments that encourage use of the amblyopic eye. The most commonly used methods for this are to occlude the better-seeing eye, such as with periodic patching, or by blurring vision in the better-seeing eye, such as with atropine drops. Better results are seen when therapy is started as soon as possible after diagnosing amblyopia. Treatment is continued until visual acuity is normal or is no longer improving on multiple observations taken several months apart.

Holmes and colleagues (2004) in the Pediatric Eye Disease Investigator Group (PEDIG) reported on the risk of amblyopia recurrence one year after cessation of amblyopia treatment. Out of 145 children whose vision had improved at least 3 logMAR levels during 3 months of patching or atropine drops, 35 (24%) had a recurrence of amblyopia at their 1-year follow up. Recurrence rates were similar for the patching and atropine groups. Recurrence was more common among children who had been treated with moderately intense patching (6-8 hours per day) and whose treatment was abruptly stopped (11 of 26 children, 42%). The recurrence rate was lower for children whose moderately intense patching was reduced to 1-2 hours per day prior to stopping therapy (3 of 22 children, 14%).

In 2014, Repka and others in the PEDIG reported long-term outcomes of a randomized clinical trial that compared amblyopia treatment with patching to treatment with atropine drops. The trial was started in 1999. It included 419 children under the age of 7 with moderate amblyopia (20/40 to 20/100) due to strabismus, anisometropia, or both. Participants were randomly assigned to patching or to atropine drops. Patching was worn every day for durations between 6 hours and full-time. Atropine treatments were instilled every day. Both study groups received their assigned treatment for at least 6 months and for up to 2 years at the treating provider's discretion. A masked outcome assessment was conducted 2 years after randomization. After that time, 188 children continued in a long-term followup study with further evaluations at 10 and 15 years of age. There were 147 participants who remained in the study through their 15-year-old follow up visit. Their average visual acuity in the amblyopic eye was 0.14 logMAR. This roughly equates to 20/25 acuity. Visual acuity was 20/25 or better for 59.9%, and 20/20 or better for 33.3%, of the amblyopic eyes. Vision at age 15 was better for children who began treatment for amblyopia before the age of 5 (mean logMAR 0.009) than for those starting treatment at

the age of 5 or 6 (mean logMAR 0.18). There were no significant vision differences between the group who had been treated with patching and the group who had received atropine drops. Selection bias may have influenced this study's results. Children who had better vision improvements after their initial treatment were more likely to return for follow-up when they were 15.

Several digital devices have received 510(k) clearance from the United States Food and Drug Administration for treatment of amblyopia including the RevitalVision System (Talshir Medical Technologies LTD, Modi'in, Israel); Luminopia One, (Luminopia, Cambridge, MA); and CureSight (NovaSight, Airport City, Israel).

Definitions

Amblyopia: A type of poor vision that develops when there is a breakdown in how the brain and the eye work together, and the brain can't recognize the sight from one eye.

Dichoptic training: Training that uses simultaneous and separate stimulation of both eyes to encourage use of the non-dominant eye.

logMAR: the Logarithm of the Minimum Angle of Resolution is measurement of visual acuity obtained by asking an individual to read a chart made up of letters of decreasing size. It is considered to be more reliable and precise than the Snellen chart for measurement of visual acuity. In the logMAR, visual acuity is reported as a single number where 0.0 is standard vision. Visual acuity decreases as the number increases and improves as the number decreases.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
For the following procedure codes; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

0687T	Treatment of amblyopia using an online digital program; device supply, educational set-up, and initial session
0688T	Treatment of amblyopia using an online digital program; assessment of patient performance and program data by physician or other qualified health care professional, with report, per calendar month
0704T	Remote treatment of amblyopia using an eye tracking device; device supply with initial set-up and patient education on use of equipment
0705T	Remote treatment of amblyopia using an eye tracking device; surveillance center technical support including data transmission with analysis, with a minimum of 18 training hours, each 30 days
0706T	Remote treatment of amblyopia using an eye tracking device; interpretation and report by physician or other qualified health care professional, per calendar month

HCPCS

A9292	Prescription digital visual therapy, software-only, FDA cleared, per course of treatment

ICD-10 Diagnosis

	All diagnoses

References

Peer Reviewed Publications:

1. Abdal MO, Bhombal F, Nankani GJ, et al. Evaluation of the efficacy of a new dichoptic digital platform to treat the anisometropic and isometropic amblyopia. Brain sciences. 2022; 12 (7).
2. Gao TY, Guo CX, Babu RJ, et al. Effectiveness of a binocular video game vs placebo video game for improving visual functions in older children, teenagers, and adults with amblyopia: A randomized clinical trial. JAMA Ophthalmol. 2018;136:172-181.
3. Holmes JM, Beck RW, Kraker RT, et al. Risk of amblyopia recurrence after cessation of treatment. Journal of AAPOS: the official publication of the American Association for Pediatric Ophthalmology and Strabismus. 2004; 8(5):420-428.
4. Holmes JM, Manh VM, Lazar EL, et al. Effect of a binocular iPad game vs part-time patching in children aged 5 to 12 years with amblyopia: a randomized clinical trial. JAMA ophthalmology. 2016; 134(12):1391-1400.
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6. Manny RE, Holmes JM, Kraker RT, et al. A randomized trial of binocular Dig Rush game treatment for amblyopia in children aged 4 to 6 years. Optometry and vision science : official publication of the American Academy of Optometry. 2022; 99(3):213-227.
7. Repka MX, Kraker RT, Holmes JM, et al. Atropine vs patching for treatment of moderate amblyopia: follow-up at 15 years of age of a randomized clinical trial. JAMA ophthalmology. 2014; 132(7):799-805.
8. Wygnanski-Jaffe T, Kushner BJ, Moshkovitz A, et al. An eye-tracking-based dichoptic home treatment for amblyopia: a multicenter randomized clinical trial. Ophthalmology. 2023; 130(3):274-285.
9. Xiao S, Angjeli E, Wu HC, et al. Randomized controlled trial of a dichoptic digital therapeutic for amblyopia. Ophthalmology. 2022; 129(1);77-85.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Academy of Ophthalmology. Preferred Practice Pattern: Amblyopia. 2022. Available at: https://www.aao.org/preferred-practice-pattern/amblyopia-ppp-2022. Accessed on April 3, 2023.
2. Pineles SL, Aakalu VK, Hutchinson AK, et al. Binocular treatment of amblyopia: a report by the American Academy of Ophthalmology. Ophthalmology. 2020: 127(2):261-272.
3. Tailor V, Ludden S, Bossi M, et al. Binocular versus standard occlusion or blurring treatment for unilateral amblyopia in children aged three to eight years. Cochrane Database Syst Rev. 2022; (2):CD011347.

4. U.S. Food and Drug Administration 510(k) Premarket Notification Database. CureSight Summary of Safety and Effectiveness No. K221375. Rockville, MD: FDA. September 25, 2022. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf22/K221375.pdf. Accessed on April 3, 2023.
5. U.S. Food and Drug Administration 510(k) Premarket Notification Database. Luminopia One Summary of Safety and Effectiveness No. DEN210005. Rockville, MD: FDA. October 20, 2021. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf21/DEN210005.pdf. Accessed on April 3, 2023.
6. U.S. Food and Drug Administration 510(k) Premarket Notification Database. RevitalVision Summary of Safety and Effectiveness. No. K012530. Rockville, MD: FDA. August 31, 2001. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf/k012530.pdf. Accessed on April 3, 2023.

Websites for Additional Information

1. National Eye Institute. Amblyopia (Lazy Eye). Last updated: September 22, 2022. Available at:https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/amblyopia-lazy-eye. Accessed on April 3, 2023.

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CureSight™
Luminopia
RevitalVision
Vivid Vision

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
	09/27/2023	Updated Coding section with 10/01/2023 HCPCS changes; added A9292.
Reviewed	05/11/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, Background/Overview, and References sections.
New	02/16/2023	MPTAC review. Initial document development.

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