Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: AmeriHealth Caritas Pennsylvania	**Submission Date**: 10/1/2023
Policy Number: ccp.1470	**Effective Date:** 10/2020 **Revision Date:** September 1, 2023
Policy Name: EndeavorRx video for ADHD	

Type of Submission – Check all that apply:

- **New Policy**
- x **Revised Policy***
- **Annual Review – No Revisions**
- **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

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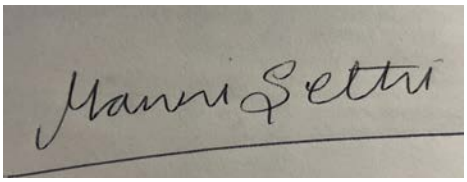
Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Manni Sethi, MD, MBA, CHCQM	

EndeavorRx video for ADHD

Clinical Policy ID: CCP.1470

Recent review date: 9/2023

Next review date: 1/2025

Policy contains: Attention deficit and hyperactivity disorder; digital therapeutics; EndeavorRx video.

AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania clinical policies are not guarantees of payment.

Coverage policy

EndeavorRx™ video for attention deficit hyperactivity disorder is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Medication (stimulants and non-stimulants); behavior management.

Background

Attention deficit hyperactivity disorder is a psychiatric and neurodevelopmental condition that has been identified as affecting children's ability to function. Symptoms generally include developmentally inappropriate loss of concentration and focus, inattentiveness, hyperactivity and impulsivity. The disorder is usually first suspected in childhood during elementary school with children demonstrating difficulty completing tasks, becoming disorganized and forgetful, and losing things. A diagnosis is made based on these symptoms before age 12. Symptoms interferie with daily living activities and last six months or longer. Although the condition begins in childhood, it frequently extends into adulthood (Magnus, 2023). The Diagnostic and Statistical Manual (DSM IV) defines three main subtypes which are predominantly inattentive, predominantly hyperactive-impulsive, or a combination of the two (Centers for Disease Control and Prevention, 2022a).

In 2016, a national parent survey estimated that 6.1 million (9.4%) of U.S. children have been diagnosed with attention deficit hyperactivity disorder, typically between ages 6 and 17. The disease's prevalence in boys is more than double than that of girls (12.9% compared to 5.6%). Sixty-two (62) percent of U.S. children with the disorder were taking medications, while 47% were receiving behavioral therapy and 23% received no treatment (Centers for Disease Control and Prevention, 2022b; Danielson, 2018). Other treatments include symptom management through appropriate eating, physical activity, and sleep, and limited screen time in front of television and computers (Centers for Disease Control and Prevention, 2022b).

While a large temporal increase in prevalence is perceived, precisely calculating this change is difficult due to lack of understanding and correctly diagnosing/assigning codes for the condition until recently. A study by Kaiser Permanente Northern California of 867,453 children ages 5 to 11 found that from 2007 to 2016, the prevalence of the disease rose 26%, from 2.96 to 3.74 cases per 100 (Chung, 2019).

The causes of the condition have remained elusive. Studies of twins have identified a genetic link in some cases. Other suspected causes include brain injury; exposure to environmental toxins (e.g., lead) during pregnancy or at a young age; alcohol and tobacco use during pregnancy; premature delivery; and low birth weight (Centers for Disease Control and Prevention, 2022a).

Current therapies do not help all children with attention deficit hyperactivity disorder. A shortage of pediatric mental health specialists (Health Resources and Services Administration, 2023) limits safe and effective use of medication and behavioral therapy.

Researchers are continually searching for different means of treatment for attention deficit hyperactivity disorder. One of these is digital therapeutics, which can potentially improve attention problems (Engelhard, 2019). Children with the disorder have been observed to have fewer problems with concentration and engagement when playing digital games, which has prompted development of such games that might have a positive impact on the health of these children (Bul, 2015).

Akili Interactive Labs of Boston has developed video games for affected children with a staff of neuroscientists and video game experts. Akili has developed five research program studies, namely STARS-ADHD; STARS-Adjunct; ADHD-POC; sensory processing disorder; and autism spectrum disorder. The last two are pilot programs for conditions that are comorbid to attention deficit hyperactivity disorder as of late July 2020 (Biospace.com, 2020):

On April 22, 2020, the Food and Drug Administration granted Akili marketing for use permission of the video game EndeavorRx under the Administration's COVID-19 enforcement discretion guidance. The approval is for children ages 8 – 12 years old with primarily inattentive or combined-type attention deficit hyperactivity disorder who have a demonstrated attention issue. The game is designed to target and activate specific neural systems to treat brain disease with associated cognitive dysfunction. Participants steer a flying craft through obstacle courses to avoid hazards in EndeavorRx (Biospace.com, 2020).

On June 15, 2020, the Administration approved EndeavorRx for use with a prescription, for children ages 8 – 12, for 25 – 30 minutes a day, five days a week, for four weeks. EndeavorRx is the first game-based digital therapeutic granted approval by the federal government for the condition (Food and Drug Administration, 2020).

Findings

No professional guidelines exist as of this writing governing use of digital therapeutics for attention deficit hyperactivity disorder, including the EndeavorRx video game.

Before developing EndeavorRx, Akili Interactive tested prototype digital treatments. In one of these, 80 children were randomized into those with and without attention deficit hyperactivity disorder. Significant neuropsychological improvements were observed for the 40 cases, but not for the 40 controls (Davis, 2018).

The Food and Drug Administration's decision to approve EndeavorRx was based on five studies, with a total of over 600 participants. The primary study was a controlled trial (n = 348) of children ages 8 – 12 years old. All participants were required to have a definitive diagnosis of attention deficit hyperactivity disorder, scores on several ratings scales indicating attention problems, an intelligence quotient above 80, no comorbid psychiatric conditions, and no use of medications for the disease that could not be discontinued (Kollins, 2020).

Children in the case group played the EndeavorRx video game for five five-minute sessions per day, five days a week for four weeks. The control group played a game whose objective was to find and connect letters on a grid to spell words during the same period. Major findings include (an asterisk indicates significance at $P < .05$):

	Cases (180)	Controls (168)	*P* value	
Test of Variables of Attention	47%	32%	.0058	*
Attention Performance Index	11%	4%	.033	*
ADHD Rating Scale (> 2 points)	74%	73%	.77	
ADHD Rating Scale (> 30%)	24%	19%	.23	
Impairment Rating Scale	48%	37%	.049	*
Clinical Global Impressions (< 2 post-intervention)	17%	16%	.86	
Clinical Global Impressions (1 post-intervention)	1%	1%	.96	
Self-Reported Improvement on Exit (patients)	73%	66%	.15	
Self-Reported Improvement on Exit (parents)	56%	44%	.025	*

The percentage of patients experiencing intervention-emergent adverse effects during the study period was higher for cases (7%, n = 12) versus controls (2%, n = 3). Ten of the 12 effects on the test patients were frustration (5), headache (3), and emotional reaction (2). No serious adverse effects were experienced by either group, and there were no discontinuations (Kollins, 2020).

An update to this trial (n = 206) of children 8 – 14 with attention deficit hyperactivity disorder taking or not taking stimulant medication assessed the impact of AKL-T01, an application and video-game-based treatment for inattention. Subjects used the game for four weeks, followed by non-use for four weeks. Impairment improved in groups taking or not taking medication, both significant at $P < .001$) after four weeks, with no side effects, and improvements persisted up to one month (Kollins, 2021).

A systematic review of digital therapeutics, including EndeavorRx, for attention deficit hyperactivity disorder improved inattention and hyperactivity/impulsivity more than controls. However, medication had outcomes superior to digital therapeutics for these indicators (Oh, 2023).

A literature review of digital health interventions to treat attention deficit hyperactivity disorder in children, which discussed EndeavorRx, noted that this approach has potential cognitive, emotional, social, and motivational

benefits. Improvements have been measured in cognitive control, attention, reaction time, and response variability. These, along with good compliance and lack of side effects, mean digital health interventions "can be safely added to the standard of care" (Pandian, 2021).

Other large-scale studies of behavioral improvements, particularly video game therapeutics for attention deficit and hyperactivity, have been published. One systematic review of 22 articles concluded that video games were well accepted and effective in assessment and management of the disease (Penuelas-Calvo, 2022). All others, however, reveal limits that prevent conclusions on effectiveness from being made:

- A systematic review/meta-analysis of 21 studies evaluated the ability of digital health interventions to aid children with mental health problems. It concluded that benefits of these interventions are uncertain, with no evidence of cost-effectiveness. Improvement in methodological flaws, such as non-standard taxonomy, small sample sizes, and lack of blinding, will be crucial in improving understanding (Hollis, 2020).

- A systematic review of 47 studies of technologies to treat neurological disorders included eight studies of attention deficit hyperactivity disorder, four of which used video gaming (n = 274). Authors note that the Qb test of attention and impulsivity shows promise in measuring improvements (Valentine, 2020).

- In a review of digital interactive games, mostly to treat autism, attention deficit hyperactivity disorder, developmental coordination disorder, and disabilities affecting intellectual abilities, 30 of 145 studies were randomized. Authors identified promising results in anxiety reduction, stress regulation, emotion recognition, and rehabilitation, but note clinical evidence is lacking (Kokol, 2020).

- A systematic review/meta-analysis of 190 trials (n = 26,114) analyzed management of attention deficit hyperactivity disorder through pharmacological, psychological, complementary, and alternative medicine. Behavioral therapy was generally more effective than placebo, and stimulants were more effective than behavioral therapy, cognitive therapy, and non-stimulants. Behavioral therapy and stimulants were superior to stimulants alone. Authors observed limits to study heterogeneity, small sample sizes, length of follow-up time, and absence of high-quality evidence (Catala-Lopez, 2017).

- A systematic review of 14 studies addressing video game training for attention deficit hyperactivity disorder reported cognitive and behavioral gains. Multiple biases on choice of outcome instruments, sampling, and blindness of assessors indicate that more and improved studies are needed before conclusions are made (Rivero, 2015).

- Achieving effective results from cognitive measures has proved especially daunting. A review of 16 studies (n = 795) concluded that cognitive training had "limited effects" on symptoms of attention deficit and hyperactivity disorder (Cortese, 2015).

References

On June 9, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "attention deficit and hyperactivity disorder," "digital therapeutics," and "EndeavorRx video." We included the best available evidence according to established

evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Biospace.com. Akili announces Endeavor™ digital attention treatment is now available for children with attention deficit hyperactivity disorder (ADHD) under FDA's COVID-19 enforcement discretion guidance. https://www.biospace.com/article/releases/akili-announces-endeavortm-digital-attention-treatment-is-now-available-for-children-with-attention-deficit-hyperactivity-disorder-adhd-under-fda-s-covid-19-enforcement-discretion-guidance/. Published April 22, 2020.

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Policy updates

9/2020: initial review date and clinical policy effective date: 10/2020.

9/2021: Policy references updated.

9/2022: Policy references updated.

9/2023: Policy references updated.