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.

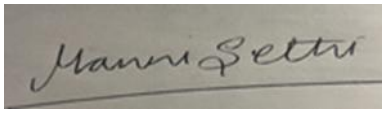
Plan: AmeriHealth Caritas Pennsylvania & Keystone First	Submission Date: 10/1/2025
Policy Number: CCP.1470	Effective Date: 10/1/2020 Revision Date: 9/1/2025
Policy Name: Prescription digital therapeutics for attention deficit hyperactivity disorder	

Type of Submission:

☐ New Policy	☒ Prior Authorization Policy
☒ Revised Policy*	☐ Base Policy
☐ Annual Review- no revisions	☒ Experimental/Investigational Policy
	☐ Statewide PDL
	☐ Other:

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

Please provide any clarifying information for the policy below:

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

Prescription digital therapeutics for attention deficit hyperactivity disorder

Clinical Policy ID: CCP.1470

Recent review date: 9/2025

Next review date: 1/2027

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

Keystone First- CHIP has developed clinical policies to assist with making coverage determinations. Keystone First- CHIP's 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 Keystone First- CHIP, on a case by case basis, 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. Keystone First- CHIP's 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. Keystone First- CHIP's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First- CHIP will update its clinical policies as necessary. Keystone First- CHIP's clinical policies are not guarantees of payment.

Coverage policy

The following prescription digital therapeutics for attention deficit hyperactivity disorder are investigational/not clinically proven and, therefore, not medically necessary:

- EndeavorRx® (Akili Interactive Labs, Inc., Boston, Massachusetts).
- Prismira™ (Aepis Medical, Shingle Springs, California).

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 affects a child'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 usually before age 12. Symptoms interfere

with daily living activities and last six months or longer. Although the condition begins in childhood, it frequently extends into adulthood. The three main subtypes are predominantly inattentive, predominantly hyperactive-impulsive, and a combination of the two (Magnus, 2023).

An estimated seven million (11.4%) of U.S. children have been diagnosed with attention deficit hyperactivity disorder, typically between ages three and 17 years. The condition's prevalence is higher in boys than in girls (15% compared to 8%), and 78% of children with the condition have at least one other co-occurring condition (Centers for Disease Control and Prevention, 2024a).

Causes have remained elusive, but several risk factors have been implicated. Studies of twins have identified a genetic link in some cases. Other suspected risk factors include brain injury; exposure to environmental toxins (e.g., lead) during pregnancy or at a young age; alcohol and tobacco use during pregnancy; and parental mental health and family environment (Centers for Disease Control and Prevention, 2024a).

Treatment is age-specific and can include medication with or without behavioral therapy. Among children with attention deficit hyperactivity disorder, approximately 32% received both medication treatment and behavior treatment, but 30% received no treatment (Centers for Disease Control and Prevention, 2024b).

Current therapies do not help all children with attention deficit hyperactivity disorder, and alternative treatments may be sought. Digital therapeutics (software applications for clinical use) have been proposed to improve attention problems.

The U.S. Food and Drug Administration has issued 510(k) clearance to three digital therapeutic devices to improve attention function in individuals with primarily inattentive or combined type attention deficit hyperactivity disorder. It is used as part of a therapeutic program that may include clinician directed therapy, medication, and/or educational programs, which further address symptoms of the disorder. Of note, patients who engage with these devices may demonstrate improvements in attention functioning but may not display benefits in other behavioral symptoms such as hyperactivity:

- EndeavorRx, the predicate device, is indicated for children ages eight to 17 years and available by prescription only (U.S. Food and Drug Administration, 2023).
- EndeavorOTC is indicated for patients ages 18 and older and available over-the-counter. (U.S. Food and Drug Administration, 2024).
- Prismira is indicated for patients ages 22 to 55 years and available by prescription only (U.S. Food and Drug Administration, 2025).

Findings

Guidelines

Current guidelines for treatment of pediatric attention deficit hyperactivity disorder do not include the use of digital therapeutics, including the EndeavorRx video game or Prismira (Barbaresi, 2020; Wolraich, 2019).

Evidence review

Prescription digital therapeutics are attractive as non-pharmacological therapeutic options for improving attentional function in individuals with attention deficit hyperactivity disorder. EndeavorRx is the first and only digital therapeutic indicated for pediatric populations. The newly approved Prismira is marketed for adult populations as substantially equivalent to EndeavorRx in terms of safety and efficacy but, to date, has no independently published studies supporting its clinical use.

The evidence for EndeavorRx consists of two reported studies performed in children under controlled conditions. EndeavorRx appears safe and well-tolerated and offers short-term improvement in inattention and hyperactivity, but its effectiveness in real world settings and over the long term is unclear.

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).

Regulatory approval for EndeavorRx was based on five studies, with a total of more than 600 participants. The primary study was a controlled trial (n = 348) of children ages eight to 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:

	Cases (n = 180)	Controls (n = 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	*

* Significance at $P < .05$.

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 ages eight to 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. Inattention 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 examined the effects of game-based therapeutics, including EndeavorRx, in randomized controlled trials on children and adolescents with attention deficit hyperactivity disorder. The investigators indirectly compared the outcomes of game-based digital therapeutics, medication, and controls. Outcomes were reported as standard mean difference (95% confidence interval). Both digital therapeutics and controls improved inattention (0.28 [0.14 to 0.41] and 0.21 [0.03 to 0.39], respectively) and hyperactivity/impulsivity (0.28 [0.03 to 0.53] and 0.30 [0.05 to 0.55], respectively). However, medication had outcomes superior to digital therapeutics for these indicators (Oh, 2023).

Video games, such as EndeavorRx, may improve treatment adherence, as they are perceived as enjoyable activities. Drop-out rates for EndeavorRx were 5.45% (Kollins, 2020) and 12.13% (Kollins, 2021), lower than most other video game-based treatments. However, long-term efficacy is uncertain (Caselles-Pina, 2023).

In 2024, we added a systematic review (Caselles-Pina, 2023) and guideline references, and deleted several older references. No policy changes are warranted.

In 2025, we updated the references and added a new prescription digital therapeutic, Prismira, to the policy. There are no published studies supporting its use. No policy changes are warranted.

References

On July 28, 2025, 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 disorder with hyperactivity” (MeSH),” “attention deficit and hyperactivity disorder,” “digital therapeutics,” “EndeavorOTC,” “EndeavorRx,” and “Prismira.” 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.

Barbaresi WJ, Campbell L, Diekroger EA, et al. Society for Developmental and Behavioral Pediatrics clinical practice guideline for the assessment and treatment of children and adolescents with complex attention-deficit/hyperactivity disorder. *J Dev Behav Pediatr*. 2020;41 Suppl 2S:S35-S57. Doi: 10.1097/DBP.0000000000000770.

Caselles-Pina L, Sujar A, Quesada-Lopez A, Delgado-Gomez D. Adherence, frequency, and long-term follow-up of video game-based treatments in patients with attention-deficit/hyperactivity disorder: A systematic review. *Brain Behav*. 2023;13(11):e3265. Doi: 10.1002/brb3.3265.

Centers for Disease Control and Prevention. About attention-deficit / hyperactivity disorder (ADHD). https://www.cdc.gov/adhd/data/index.html. Dated November 19, 2024. (a)

Centers for Disease Control and Prevention. Treatment of ADHD. https://www.cdc.gov/adhd/treatment/index.html. Dated May 16, 2024. (b)

Davis NO, Bower J, Kollins SH. Proof-of-concept study of an at-home, engaging, digital intervention for pediatric ADHD. *PLoS One*. 2018;13(1):e0189749. Doi: 10.1371/journal.pone.0189749.
Kollins SH, DeLoss DJ, Canadas E, et al. A novel digital intervention for actively reducing severity of paediatric ADHD (STARS-ADHD): A randomized controlled trial. *Lancet Digit Health*. 2020;2(4):E168-E178. Doi: 10.1016/S2589-7500(20)30017-0.

Kollins SH, Childress A, Heusser AC, Lutz J. Effectiveness of a digital therapeutic as adjunct to treatment with medication in pediatric ADHD. *NPJ Digit Med*. 2021;4(1):58. Doi: 10.1038/s41746-021-00429-0.
Magnus W, Nazir S, Anilkumar AC, Shaban K. Attention deficit hyperactivity disorder. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK441838/. Last updated August 8, 2023.
Oh S, Choi J, Han DH, Kim EY. Effects of game-based digital therapeutics on attention deficit hyperactivity disorder in children and adolescents as assessed by parents or teachers: A systematic review and meta-analysis. *Eur Child Adolesc Psychiatry*. 2024;33(2):481-493. Doi: 10.1007/s00787-023-02174-z.

U.S. Food and Drug Administration. 510(k) summary approval letter K231337 to Akili Interactive Labs, Inc. https://www.accessdata.fda.gov/cdrh_docs/pdf23/K231337.pdf. Decision date December 14, 2023.

U.S. Food and Drug Administration. 510(k) summary approval letter K233496 Akili Interactive Labs, Inc. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K233496. Decision date June 14, 2024.

U.S. Food and Drug Administration. 510(k) summary approval letter K243729 to Lumos Labs, Inc. https://www.accessdata.fda.gov/cdrh_docs/pdf24/K243729.pdf. Date prepared June 15, 2025.

Wolraich ML, Hagan JF, Jr., Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2019;144(4):e20192528. Doi: 10.1542/peds.2019-2528.

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.

9/2024: Policy references updated.

9/2025: Policy references updated. New product added to Coverage with no policy changes.