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PHARMACY / MEDICAL POLICY – 3.03.03

Prescription Digital Therapeutics for Attention Deficit/Hyperactivity Disorder

BCBSA Ref. Policy:	3.03.03	
Effective Date:	Oct. 1, 2024	RELATED MEDICAL POLICIES:
Last Revised:	Sept. 9, 2024	13.01.500 Prescription Digital Therapeutics
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
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Introduction

Prescription digital therapeutics (PDTs) are software applications that are prescribed by a licensed healthcare provider. They are used on mobile devices such as a mobile phone, tablet, smartwatch, or laptop computer. The goal of prescription digital therapeutics is to evaluate, diagnose, manage symptoms, or treat an illness, injury, or disease. Attention-deficit/hyperactivity disorder (ADHD) is a condition with symptoms of hyperactivity, impulsive behavior, and inattention that is considered excessive for the person's age. Established treatments for ADHD include education, changes to the individual's environment, behavioral therapy, and medication. The use of prescription digital therapeutics to treat ADHD is considered investigational. That means it is still being studied.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Investigational
Prescription digital therapy	**Prescription digital therapeutics are considered investigational for the treatment of attention-deficit/hyperactivity disorder (e.g., EndeavorRx)**

Coding

Note: There is no specific code for this digital therapeutic

Code	Description
CPT	
99199	Unlisted special service, procedure or report
HCPCS	
A9999	Miscellaneous DME supply or accessory, not otherwise specified
E1399	Durable medical equipment, miscellaneous

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

N/A

Evidence Review

Description

Digital health technologies is a broad term that includes categories such as mobile health, health information technology, wearable devices, telehealth and telemedicine, and personalized medicine. These technologies span a wide range of uses, from applications in general wellness

to applications as a medical device, and include technologies intended for use as a medical product, in a medical product, as companion diagnostics, or as an adjunct to other medical products (devices, drugs, and biologics). The scope of this review includes only those digital technologies that are intended to be used for therapeutic application and meet the following three criteria:

1. Must meet the definition of "Software as a medical device", which states that software is intended to be used for a medical purpose, without being part of a hardware medical device or software that stores or transmits medical information.
2. Must have received marketing clearance or approval by the US Food and Drug Administration (FDA) either through the de novo premarket process or 510(k) process or pre-market approval; and
3. Must be prescribed by a healthcare provider.

This review will assess whether digital therapy in the form of a computer game can improve attention in children with attention-deficit/hyperactivity disorder (ADHD).

Background

Scope of Review

Software has become an important part of product development and is integrated widely into digital platforms that serve both medical and non-medical purposes. The three broad categories of software use in medical devices are:

1. Software used in the manufacture or maintenance of a medical device (e.g., software that monitors x-ray tube performance to anticipate the need for replacement),
2. Software that is integral to a medical device or software in a medical device (e.g., software used to "drive or control" the motors and the pumping of medication in an infusion pump),
3. Software, which on its own is a medical device referred to as "Software as a Medical Device" (SaMD) (e.g., software that can track the size of a mole over time and determine the risk of melanoma).

The International Medical Device Regulators Forum, a consortium of medical device regulators from around the world led by the FDA defines SaMD as "software that is intended to be used for one or more medical purposes that perform those purposes without being part of a hardware

medical device".[1] Such software was previously referred to by industry, international regulators, and health care providers as "standalone software," "medical device software," and/or "health software," and can sometimes be confused with other types of software.

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1. Must meet the definition of "Software as a medical device" (SaMD) which states that software is intended to be used for a medical purpose, without being part of a hardware medical device or software that stores or transmits medical information.
2. Must have received marketing clearance or approval by the US FDA either through the de novo premarket process or 510(k) process or pre-market approval and,
3. Must be prescribed by a healthcare provider.

BCBSA Evaluation Framework for Digital Health Technologies

SaMDs, as defined by the FDA, are subject to the same evaluation standards as other devices. The Blue Cross and Blue Shield Association Technology Evaluation Criterion are as follows:

1. The technology must have final approval from the appropriate governmental regulatory bodies.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.
3. The technology must improve the net health outcome.[a]
4. The technology must be as beneficial as any established alternatives.
5. The improvement must be attainable outside the investigational settings.[b]

[a] The technology must assure protection of sensitive patient health information as per the requirements of The Health Insurance Portability and Accountability Act of 1996 (HIPAA).

[b] The technology must demonstrate usability in a real-world setting.

Other regulatory authorities such as the United Kingdom's National Institute for Health and Care Excellence (NICE) have proposed standards to evaluate SaMD.[2]

Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition characterized by core symptoms of hyperactivity, impulsivity, and inattention, which are considered excessive for the person's age. Both the International Classification of Mental and Behavioral Disorders 10th edition (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) require that the symptoms are reported or observed in several settings and that the symptoms of ADHD affect psychological, social, and/or educational/occupational functioning. Prevalence estimates for ADHD vary from 7.2% to 15.5% of children.[3]

For children younger than 17 years of age, the DSM-5 requires at least six symptoms of hyperactivity-impulsivity or at least six symptoms of inattention. The combined type requires a minimum of six symptoms of hyperactivity-impulsivity plus at least six symptoms of inattention. The symptoms must 1) occur often, 2) be present in more than 1 setting, 3) persist for at least six months, 4) be present before 12 years of age, 5) impair function in academic, social, or occupational activities, and 6) be excessive for the developmental level of the child.

Treatment

Established treatments for ADHD in children include educational, environmental, psychological, and behavioral interventions, and medication. Almost two-thirds of children with ADHD take medication, and about one half receive behavioral treatment.[3] The following therapies are currently used to treat ADHD, either individually or in combination:

- Educational intervention involves discussion with parents about symptoms and access to services, environmental modifications such as seating arrangements, changes to lighting and noise, reducing distractions, and the benefit of having movement breaks and teaching assistants at school.
- Parent-child behavioral therapy teaches parenting techniques within the principles of behavior therapy. The therapy programs typically last two to three months and includes rewarding positive behavior, identifying unintentional reinforcement of negative behaviors, limiting choices, and using calm discipline.
- Medication with stimulants, such as methylphenidate, are considered first-line therapy for ADHD in school-age children. However, adverse effects of stimulants may include sleep disturbance, decreased appetite, and weight changes. Combination therapy with medication and behavioral interventions can improve both core ADHD symptoms and non-ADHD symptoms such as social skills and parent-child relations.

The digital technology being considered is EndeavorRx. It is an interactive video game that requires the user to navigate a character through a game-like space while collecting objects. It is designed to be played on a mobile device at home for approximately 25 minutes a day, five days a week. Typical treatment would be for a period of one month, with an extension up to three months allowed per license.

EndeavorRx uses a proprietary technology platform that adjusts the difficulty level based on the user's prior performance. The adaptive algorithm is intended to encourage the user to surpass their previous performance, so that the user would gradually increase their ability to focus attention. No claims are made for behavioral symptoms such as hyperactivity.

Version 1.5 was reviewed by the FDA for de novo marketing clearance. Earlier non-prescription versions were called ProjectEvo and AKL-T01, which were released under the Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the COVID-19 Public Health Emergency.

EndeavorRx is intended to be used as part of a therapeutic program. EndeavorRx is not intended to be used as a stand-alone treatment.

Summary of Evidence

For individuals who are children ages 8 to 12 years with ADHD who receive EndeavorRx , the evidence includes a pivotal randomized controlled trial (RCT) and an open label study.. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The pivotal RCT compared outcomes of EndeavorRx with a word game that targeted different cognitive abilities (digital control intervention). Although the experimental treatment group had significantly greater improvement on a computerized test of attention, both the experimental and control groups improved to a similar extent on parent and clinician assessments. The clinical significance of an improvement in a computerized test of attention without a detectable improvement in behavior by parents and clinicians is uncertain. A second open label study compared EndeavorRx plus stimulant medication with EndeavorRx alone. This study design does not permit conclusions about the adjunctive treatment effect of EndeavorRx as both study arms received EndeavorRx. An appropriate study design would be comparing EndeavorRx plus stimulant medication versus stimulant medication alone. A number of questions remain concerning the efficacy of this treatment, and additional studies to assess the effect of the digital therapy in adolescents and in children on stimulant medication have recently been completed but not yet published. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Unpublished			
NCT02828644	Software Treatment for Actively Reducing Severity of ADHD - Follow Up (STARS-ADHD2)	175	Feb 2018
NCT05183919	Software Treatment for Actively Reducing Severity of ADHD in Adults (STARS ADHD Adult)	223	Jan 2023
NCT04897074	Software Treatment for Actively Reducing Severity of ADHD in Adolescents (STARS-ADHD-Adolescents)	165	Sep 2022
NCT03310281	Software Treatments for Actively Reducing Severity of Cognitive Deficits in MDD (STARS-MDD)	84	Nov 2018
NCT03649074	Software Treatment for Actively Reducing Severity of ADHD as Adjunctive Treatment to Stimulant	203	Sep 2019

NCT: national clinical trial.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or the National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Pediatrics

In 2019, the American Academy of Pediatrics (AAP) updated their 2011 clinical practice guideline on the diagnosis, evaluation, and treatment of ADHD in children and adolescents.[3]

The guidelines were based on a systematic evidence review by the Agency for Healthcare Research and Quality. The AAP gave strong recommendations based on level A evidence for medications and training and behavioral treatment for ADHD implemented with the family and school.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

In April 2020, EndeavorRx (Akili Interactive Labs) received marketing clearance by the FDA through the De Novo premarket review process (DEN200026). EndeavorRx is a prescription device that is indicated to "improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined type ADHD, who have a demonstrated attention issue. Patients who engage with EndeavorRx demonstrate improvements in a digitally assessed measure Test of Variables of Attention (TOVA) of sustained and selective attention and may not display benefits in typical behavioral symptoms, such as hyperactivity." EndeavorRx is intended to be used as part of a therapeutic program that may include clinician-directed therapy, medication, and/or educational programs.

References

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13. Kollins, S.H., Childress, A., Heusser, A.C. et al. Effectiveness of a digital therapeutic as adjunct to treatment with medication in pediatric ADHD. npj Digit. Med. 4, 58 (2021). https://doi.org/10.1038/s41746-021-00429-0

History

Date	Comments
10/01/21	New policy, approved September 14, 2021. Policy created with literature review through June 9, 2021. Prescription digital therapeutics for the treatment of ADHD is considered investigational.
09/01/22	Annual Review, approved August 22, 2022. Policy updated with literature review through June 23, 2022. No references added; policy statements unchanged.
10/01/23	Annual Review, approved September 25, 2023. Policy updated with literature review through May 5, 2023. Reference added. Policy statement unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
10/01/24	Annual Review, approved September 9, 2024. Policy updated with literature review through June 5, 2024. No references added; policy statements unchanged.

local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.