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PHARMACY / MEDICAL POLICY – 3.03.01

Prescription Digital Health Diagnostic Aid for Autism Spectrum Disorder

BCBSA Ref. Policy:	3.03.01
Effective Date:	Oct. 1, 2024
Last Revised:	Sept. 9, 2024
Replaces:	N/A

RELATED MEDICAL POLICIES:

- 3.03.03 Prescription Digital Therapeutics for Attention Deficit/Hyperactivity Disorder
- 13.01.500 Prescription Digital Therapeutics

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Digital health technologies use computer software and devices in health care. One of the ways they may be used is to check for the presence of a specific medical condition. Some digital technologies are known as software as a medical device (SaMD). Autism spectrum disorder (ASD) is a developmental condition of the brain. It leads to problems with social communication, interaction, and behavior patterns. ASD can range from mild to severe. It begins in early childhood. If a child's doctor finds developmental delays, a specialist will usually diagnose ASD. Another possible way to help diagnose ASD is with the use of prescription digital health technologies. The use of prescription digital health technologies to help diagnose autism spectrum disorder is unproven (investigational). More studies are needed to see if this technology results in improved health outcomes.

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

Service	Investigational
Prescription digital health technologies	**Prescription digital health technologies that have received clearance for marketing by the FDA as a diagnostic aid for autism spectrum disorder (e.g., Canvas Dx) are considered investigational.**

Coding

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

Benefit Application

Digital therapeutics that are available "over the counter" or without a prescription are generally excluded from most Plans, even if they are ordered by a licensed healthcare practitioner. Please see the individual contract Plan language for specific benefit determination.

Some health plans or employer groups may choose to cover digital therapeutics that do not meet the criteria of this policy or are excluded from coverage under the health plan benefits. Such coverage is considered to be separate from benefits available under the health plan. If

coverage is requested utilizing benefits under the health plan, the criteria of this policy will apply.

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 policy includes only those digital technologies that are intended to be used for diagnostic application (detecting the presence or absence of a condition, the risk of developing a condition in the future, or treatment response [beneficial or adverse]) and meet the following three criterion:

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.

Background

Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a biologically based neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction and restricted, repetitive patterns of behavior, interests, and activities. ASD can range from mild social impairment to severely impaired functioning; as many as half of individuals with autism are non-verbal and have symptoms that may include debilitating intellectual disabilities, inability to

change routines, and severe sensory reactions. The American Psychiatric Association's Diagnostic and Statistical Manual, Fifth Edition (DSM-5) provides standardized criteria to help diagnose ASD.[1]

Diagnosis of ASD in the United States generally occurs in two steps: developmental screening followed by comprehensive diagnostic evaluation if screened positive. The American Academy of Pediatrics (AAP) recommends general developmental screening at 9, 18 and 30 months of age and ASD specific screening at 18 and 24 months of age.[2,3] Diagnosis and treatment in the first few years of life can have a strong impact on functioning as it allows for treatment during a key window of developmental plasticity.[4,5] However, early diagnosis in the US remains an unmet need even though studies have demonstrated a temporal trend of decreasing mean ages at diagnosis over time.[6,7] According to a 2020 study by Autism and Developmental Disabilities Monitoring (ADDM) Network, an active surveillance system that provides estimates of ASD in the US, reported median age of earliest known ASD diagnosis ranged from 36 months in California to 63 months in Minnesota.[8]

Scope of Policy

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

1. Software used in the manufacture or maintenance of a medical device (example 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 (example 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) (example, 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".[9] 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.

The scope of this policy includes only those digital technologies that are intended to be used for diagnostic application (detecting presence or absence of a condition, the risk of developing a condition in the future, or treatment response [beneficial or adverse]) and meet the following three criterion:

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 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.[10]

Summary of Evidence

For individuals who are in the age range of 18 to 72 months and in whom there is a suspicion of ASD by a parent, caregiver, or healthcare provider and who receive Canvas Dx, the evidence includes a single double-blind, multicenter, prospective, comparator cohort study of clinical validity. Relevant outcomes are test validity, change in disease status, functional outcomes, and quality of life. The study compared Canvas Dx output to diagnostic agreement by 2 or more independent specialists in a cohort of 18 to 72-month-olds with developmental delay concerns. The majority of study participants (68% or 290/425) were classified as "indeterminates" by Canvas DX. For the 32% of participants who received a determinate output (ASD positive or negative), sensitivity was 98.4% (95% CI, 91.6% to 100%), specificity was 78.9% (95% CI, 67.6% to 87.7%), positive predictive value (PPV) was 80.8% (95% CI, 70.3% to 88.8%) and negative predictive value (NPV) was 98.3% (95% CI, 90.6% to 100%). A major limitation in study relevance is the lack of clarity on how the test fits into the current pathway and the appropriate referral process subsequent to testing. It is unclear if Canvas Dx is a "rule-out" or "rule-in" test or perhaps both. Major limitations in the design and conduct of the study included missing data and lack of generalizability. The estimated drop out rate was 40%. Authors reported that COVID-19 control measures led to changes in study visit schedules, missed visits, patient discontinuations, and site closures (9 out of 14 sites). No clear description of reasons for discrepancy in the number of clinical sites (30 proposed sites versus 14 actual sites), characteristics of missing observations, or sensitivity analyses of missing data assumptions were provided. Issues related to the generalizability of the study findings were also noted. Data on participants stratified by enrollment sites/states and origin of primary concern for developmental delay (whether it was patient/caregiver or healthcare professional) was not reported. Other limitations include differences that may occur between the testing environments of a structured clinical trial setting versus the home setting and lack of data on usability outside of a clinical trial. More clarity on these issues is needed to understand generalizability of this study. Evidence for the Canvas Dx has not directly demonstrated that the test is clinically useful, and a chain of evidence cannot be constructed to support its utility. 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 ongoing and 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
Ongoing			
NCT05223374	Extension for Community Healthcare Outcomes (ECHO) Autism Diagnostic Study in Primary Care Setting	100	Feb 2024
Unpublished			
NCT04326231[a]	Cognoa ASD Digital Therapeutic Engagement and Usability Study	30	Jul 2020

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored 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 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

The AAP guidelines recommend ASD-specific universal screening in all children at ages 18 and 24 months in addition to developmental surveillance and monitoring.[2] Toddlers and children should be referred for diagnostic evaluation when increased risk for developmental disorders (including ASD) is identified through screening and/or surveillance. Children should be referred for intervention for all identified developmental delays at the time of identification and not wait for an ASD diagnostic evaluation to take place. The AAP does not approve nor endorse any specific tool for screening purposes. The AAP has published a toolkit that provides a list of links to tools for developmental surveillance and screening for use at the discretion of the health care professional.[18]

The American Academy of Child and Adolescent Psychiatry

The American Academy of Child and Adolescent Psychiatry recommends that the developmental assessment of young children and the psychiatric assessment of all children should routinely include questions about ASD symptomatology.[19]

US Preventive Services Task Force Recommendations

The US Preventive Services Task Force (USPSTF) published recommendations for ASD in young children in 2016.[20] The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for ASD in young children (children 18 to 30 months of age) for whom no concerns of ASD have been raised by their parents or a clinician.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

Digital health technologies that meet the current scope of the policy are shown in **Table 2**.

Table 2. Digital Health Technology for Diagnostic Applications

Application	Manu-facturer	FDA Cleared Indication	Description	FDA Product Code	FDA Marketing Clearance	Year
Canvas DX (formerly known as Cognoa App)	Cognoa	"Canvas Dx is intended for use by healthcare providers as an aid in the diagnosis of Autism Spectrum Disorder (ASD) for	Artificial intelligence app for use by health care providers as an adjunct in the diagnosis of autism spectrum	QPF	DEN200069	2021

Application	Manu-facturer	FDA Cleared Indication	Description	FDA Product Code	FDA Marketing Clearance	Year
		patients ages 18 months through 72 months who are at risk for developmental delay based on concerns of a parent, caregiver, or healthcare provider. The device is not intended for use as a stand-alone diagnostic device but as an adjunct to the diagnostic process. The device is for prescription use only (Rx only)."	disorder for patients ages 18 to 72 months. Canvas DX includes 3 questionnaires: parent/caregiver, a video analyst, and a health care provider, with an algorithm that synthesizes the 3 inputs for use by the primary care provider.			

FDA: US Food and Drug Administration

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5), 5th ed. Washington, DC: American Psychiatric Association; 2013
2. Lipkin PH, Macias MM, Norwood KW, et al. Promoting Optimal Development: Identifying Infants and Young Children With Developmental Disorders Through Developmental Surveillance and Screening. Pediatrics. Jan 2020; 145(1). PMID 31843861
3. Hyman SL, Levy SE, Myers SM, et al. Identification, Evaluation, and Management of Children With Autism Spectrum Disorder. Pediatrics. Jan 2020; 145(1). PMID 31843864
4. Dawson G, Bernier R. A quarter century of progress on the early detection and treatment of autism spectrum disorder. Dev Psychopathol. Nov 2013; 25(4 Pt 2): 1455-72. PMID 24342850
5. Dawson G, Rogers S, Munson J, et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. Pediatrics. Jan 2010; 125(1): e17-23. PMID 19948568
6. Hertz-Picciotto I, Delwiche L. The rise in autism and the role of age at diagnosis. Epidemiology. Jan 2009; 20(1): 84-90. PMID 19234401

7. Leigh JP, Grosse SD, Cassady D, et al. Spending by California's Department of Developmental Services for Persons with Autism across Demographic and Expenditure Categories. PLoS One. 2016; 11(3): e0151970. PMID 27015098

8. Maenner MJ, Shaw KA, Bakian AV, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2018. MMWR Surveill Summ. Dec 03 2021; 70(11): 1-16. PMID 34855725

9. International Medical Device Regulators Forum. Software as a Medical Device (SaMD): Key Definitions. 2013. **http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf**. Accessed August 12, 2024.

10. National Institute for Health and Care Excellence (NICE). Evidence standards framework for digital health technologies. 2022. **Section A: Technologies suitable for evaluation using the evidence standards framework | Evidence standards framework for digital health technologies | Guidance | NICE**. Accessed August 12, 2024.

11. Zwaigenbaum L, Bauman ML, Choueiri R, et al. Early Intervention for Children With Autism Spectrum Disorder Under 3 Years of Age: Recommendations for Practice and Research. Pediatrics. Oct 2015; 136 Suppl 1(Suppl 1): S60-81. PMID 26430170

12. Zwaigenbaum L, Bryson S, Lord C, et al. Clinical assessment and management of toddlers with suspected autism spectrum disorder: insights from studies of high-risk infants. Pediatrics. May 2009; 123(5): 1383-91. PMID 19403506

13. Kleinman JM, Ventola PE, Pandey J, et al. Diagnostic stability in very young children with autism spectrum disorders. J Autism Dev Disord. Apr 2008; 38(4): 606-15. PMID 17924183

14. Canvas Dx Website. Available at **https://cognoa.com**. Accessed on August 12, 2024.

15. Abbas H, Garberson F, Liu-Mayo S, et al. Multi-modular AI Approach to Streamline Autism Diagnosis in Young Children. Sci Rep. Mar 19 2020; 10(1): 5014. PMID 32193406

16. Randall M, Egberts KJ, Samtani A, et al. Diagnostic tests for autism spectrum disorder (ASD) in preschool children. Cochrane Database Syst Rev. Jul 24 2018; 7(7): CD009044. PMID 30075057

17. Megerian JT, Dey S, Melmed RD, et al. Evaluation of an artificial intelligence-based medical device for diagnosis of autism spectrum disorder. NPJ Digit Med. May 05 2022; 5(1): 57. PMID 35513550

18. Autism Spectrum Disorder: Links to Commonly Used Screening Instruments and Tools (AAP Toolkits). American Academy of Pediatrics. Available at **https://publications.aap.org/toolkits/pages/asd-screening-tools**. Accessed on August 12, 2024.

19. Volkmar F, Siegel M, Woodbury-Smith M, et al. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder. J Am Acad Child Adolesc Psychiatry. Feb 2014; 53(2): 237-57. PMID 24472258

20. Siu AL, Bibbins-Domingo K, Grossman DC, et al. Screening for Autism Spectrum Disorder in Young Children: US Preventive Services Task Force Recommendation Statement. JAMA. Feb 16 2016; 315(7): 691-6. PMID 26881372

History

Date	Comments
10/01/22	New policy, approved September 13, 2022, Policy created with literature review through April 25, 2022. Prescription digital health technologies that have received clearance for marketing by the US Food and Drug Administration as a diagnostic aid for autism spectrum disorder (Canvas Dx) are considered investigational.
10/01/23	Annual Review, approved September 25, 2023. Policy updated with literature review through May 10, 2023; references added. Policy statements unchanged.
11/01/23	Minor update. Removed 5.01.35 Prescription Digital Therapeutics for Substance Use Disorder, from Related policies, due to archival.
10/01/24	Annual Review, approved September 9, 2024. Policy updated with literature review through May 13, 2024; no references added. Policy statements unchanged.

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.