

## **Medical Coverage Policy**

Effective Date	1/	15/	2025
Next Review Date	12/	15/	2025
Coverage Policy Number			0447

## **Autism Spectrum Disorders/Pervasive Developmental Disorders: Assessment and Treatment**

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Speech Therapy

Transcranial Magnetic Stimulation

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### **Overview**

This Coverage Policy addresses services for the assessment and treatment of autism spectrum disorders (ADD) and pervasive developmental disorders (PDD).

## **Coverage Policy**

A number of states have coverage mandates that require regulated benefit plans to cover services related to an autism spectrum disorder (ASD) or pervasive developmental disorder (PDD). For example, New York law requires regulated benefit plans to provide coverage for the screening, diagnosis and treatment of ASD/PDD.

Please refer to the applicable benefit plan document to determine terms, conditions and limitations of coverage.

Services provided by a psychiatrist, psychologist or other behavioral health professionals may be subject to the provisions of the applicable behavioral health benefit.

Assessment and treatment for comorbid behavioral health and/or medical diagnoses and associated symptoms and/or conditions may be covered under applicable medical and behavioral health benefit plans.

Coverage of medications related to the treatment of autism spectrum disorder (ASD) may be subject to the pharmacy benefit portion of the applicable benefit plan.

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#### **Medically Necessary**

#### **Assessment**

The following services are considered medically necessary for the assessment of a suspected or known ASD:

- behavioral health evaluation including psychiatric examination
- electroencephalogram (EEG) when there is suspicion of a seizure
- evaluation by speech and language pathologist
- lead screening
- autism-specific developmental screening (Current Procedural Terminology [CPT] code 96110, e.g., Checklist for Autism in Toddlers [CHAT], Pervasive Developmental Disorder Screening Test-II) and CPT codes 96112, 96113, e.g., Autism Behavior Checklist [ABC], Childhood Autism Rating Scale [CARS])
- neuroimaging studies when the child is a candidate for specific interventions such as epilepsy surgery
- occupational and/or physical therapy evaluation when motor deficits, motor planning or sensory dysfunction are present
- quantitative plasma amino acid assays to detect phenylketonuria

#### when ANY of the following criteria are met:

- any loss of any language or social skills at any age
- absence of babbling by 12 months
- absence of gesturing (e.g., pointing, waving bye-bye) by 12 months
- absence of single word speech by 16 months
- absence of 2-word spontaneous (not echolalic) phrases by 24 months

#### **Treatment**

Behavioral health treatment (e.g., behavior modification, family therapy, cognitive behavioral therapy or other forms of psychotherapy) for ASD is considered medically necessary when ALL of the following criteria are met:

- individual meets criteria for ASD in the Diagnostic and Statistical Manual of Mental Health Disorders, Fifth Edition (DSM-5 Text Revision [TR]) services are appropriate in terms of type, frequency, extent, site and duration
- treatment is being provided by an appropriate behavioral health care professional
- meaningful and measurable improvement is expected from the therapy

Please refer to the Medical Coverage Policy on Intensive Behavioral Interventions for specific medical necessity criteria for applied behavior analysis (ABA).

Please refer to the Medical Coverage Policies on Neuropsychological Testing, Speech Therapy, and Speech Generating Devices and the Cigna/ASH Medical Coverage Policies for Sensory and Auditory Integration Therapy - Facilitated Communication, Occupational Therapy, and Physical Therapy for specific coverage criteria for these services.

#### **Not Medically Necessary**

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The following procedures/services for the assessment and/or treatment of ASD are considered not medically necessary for this indication (This list may not be all inclusive):

#### **Assessment:**

magnetoencephalography (MEG)

#### **Treatment:**

- chelation therapy
- hyperbaric oxygen therapy
- immune globulin therapy
- transcranial stimulation

#### **Not Covered or Reimbursable Services**

Services that are considered primarily educational or training in nature or related to academic or work performance are not covered under many benefit plans. The following services for the assessment and/or treatment of ASD are considered primarily educational and training in nature and not covered or reimbursable:

- education and achievement testing, including Intelligence Quotient (IQ) testing
- educational interventions (e.g., classroom environmental manipulation, academic skills)

Multi-purpose, general consumer electronic devices such as personal digital assistants (PDAs), computers, tablet devices (e.g., iPads®), smart phones, electronic mail devices and pagers, are not medical in nature and thus are considered not medically necessary.

The following procedures/services for the assessment and/or treatment of ASD are not covered or reimbursable for this indication (This list may not be all inclusive):

#### **Assessment:**

- blood metabolite testing (e.g., NPDX ASD test)
- central carbon metabolites tests (e.g., NPDX ASD test)
- hair analysis

#### **Treatment:**

- art therapy
- BioMat
- equestrian therapy (hippotherapy)
- holding therapy
- music therapy
- recreational therapy
- vision therapy

## **Health Equity Considerations**

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Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

See section below on Health Disparity.

## **General Background**

Autism Spectrum Disorder (ASD) is a developmental disability characterized impairments in reciprocal social communication and social interaction, and restricted, repetitive patterns of behavior, interests, or activities. Deficits often occur across multiple contexts and may result in challenges across multiple areas of functioning. Symptoms associated with ASD must be present in the early developmental period but may not be identified until later. The presentation, impact, and severity of characteristics associated with ASD may vary greatly amongst individuals who meet criteria for the diagnosis.

#### **Etiology**

The precise etiology of ASD is unknown, although there appears to be a high heritability associated with it. The etiology can be identified for between 15% and 20% of individuals with autism; in the others the cause remains unknown. This is a field of active research.

Associations between ASD and a number of other medical conditions have been proposed. Other medical conditions include but are not limited to:

- Epilepsy or seizure disorder
- Tuberous sclerosis
- Fragile X syndrome
- Intellectual disability

American Academy of Child & Adolescent Psychiatry (AACAP): The American Academy of Child & Adolescent Psychiatry (AACAP) 2022 Policy Statement on Autism and Vaccines states "Multiple studies conducted in several different countries have demonstrated that there is no causal association between vaccines or their preservatives and ASD. Further, vaccines do not change the timing of the onset of ASD symptoms, nor do they affect the severity of ASD symptoms. Even in families who have a greater risk for ASD, such as those who already have a child with ASD, there is no increased likelihood that the second child will have ASD if vaccinated" (AACAP, 2022).

American Academy of Pediatrics (AAP): The AAP 2020 Clinical Report on Identification, Evaluation, and Management of Children With Autism Spectrum Disorder states that "The scientific literature does not support an association of vaccination as an environmental factor that increases the risk for ASD. Children with ASD should be vaccinated according to the recommended schedule" (AAP/Hyman, et al., 2020).

#### Screening

Diagnosing autism spectrum disorder (ASD) can be difficult because there is no medical test, like a blood test, to diagnose the disorder. Autism screening is usually administered by a pediatrician

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during a routine well-child checkup. The doctor may observe the child and ask a parent questions about his or her behaviors at home and while interacting with other children on the playground. Doctors evaluate the child's developmental history and behavior to determine whether to make a referral for further formal assessment. Research has shown that intervening as early as possible is associated with more positive outcomes than treatment later in life or not at all.

<u>American Academy of Pediatrics:</u> The American Academy of Pediatrics (AAP) guidelines for identification, evaluation, and management of children with autism spectrum disorder (ASD) recommends screening all children for symptoms of ASD through a combination of developmental surveillance at all visits and standardized autism specific screening tests at 18 and 24 months of age in their primary care visits because children with ASD can be identified as toddlers, and early intervention can and does influence outcomes (AAP/Hyman, et al., 2020).

<u>U.S. Preventive Services Task Force (USPSTF)</u>: The USPSTF published a recommendation statement for screening for ASD in young children (USPSTF, 2016). For children aged 18 to 30 months, the USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for ASD in young children for whom no concerns of ASD have been raised by their parents or a clinician. It should be noted that this recommendation is listed as currently under review.

According to the Autism Research Institute, some of the more commonly used autism screening tools are:

- Modified Checklist for Autism in Toddlers: Revised (M-CHAT), is a popular 20-question test designed for toddlers between 16 and 30 months old.
- The Ages and Stages Questionnaire: (ASQ) is a general developmental screening tool that examines developmental challenges at specific ages.
- Screening Tool for Autism in Toddlers and Young Children: (STAT) is an interactive screening tool comprising of twelve activities that assess play, communication, and imitation.
- Parents' Evaluation of Developmental Status: (PEDS) is a general developmental parent interview designed to identify delays in motor, language, self-help, and more.

If the results of an autism screening indicate a child shows some signs of autism, a pediatrician will likely refer the family to a specialist for a more formal evaluation.

#### **Health Disparity**

The Autism and Developmental Disabilities Monitoring (ADDM) Network is a program funded by Centers for Disease Control and Prevention (CDC) to collect data to better understand the number and characteristics of children with autism spectrum disorder (ASD) and other developmental disabilities living in different areas of the United States. In 2020, there were 11 ADDM Network sites across the United States. Key Findings from the ADDM Network (A Snapshot of Autism Spectrum Disorder in 2020) included:

- More children who were born in 2016 (1.8%) received an ASD diagnosis or special education classification by 4 years of age compared with children born in 2012 (1.1%), suggesting progress in early ASD identification over time.
- Prior to the start of the COVID-19 pandemic, 4-year-old children were receiving more
  evaluations and identifications than 8-year-old children did when they were 4 years of age.
  However, around the start of the COVID-19 pandemic in March 2020, the rate of evaluation
  and ASD identification decreased dramatically among 4-year-old children compared with 8year-old children when they were 4 years of age. Evaluations and ASD identification did not
  return to pre-pandemic levels through the end of 2020.
- About 1 in 36 (2.8%) 8-year-old children were identified with ASD by the ADDM Network.

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- Also in 2020, Black, Hispanic, and Asian or Pacific Islander children had a higher percentage of ASD than White children for the <u>first time</u> among 8-year-olds. Specifically, ASD prevalence was lower among non-Hispanic White children (24.3) and children of two or more races (22.9) than among non-Hispanic Black or African American (Black), Hispanic, and non-Hispanic Asian or Pacific Islander (A/PI) children (29.3, 31.6, and 33.4 respectively).
- Among 8-year-old children, boys were nearly 4 times as likely as girls to be identified with ASD. However, 2020 marked the <u>first time</u> the ADDM Network found the percentage of girls identified with ASD to be over 1%.
- Among 8-year-old children identified with ASD who had intelligence quotient (IQ) scores available, more than one-third (37.9%) also had intellectual disability (CDC, 2023/2024; Maenner, et al., 2023; Shaw, et al., 2023).

#### **Formal Assessment**

<u>American Psychiatric Association:</u> In 2013, the American Psychiatric Association released the fifth edition of its Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The DSM-5 is now the standard reference that healthcare providers use to diagnose mental and behavioral conditions, including autism.

# Diagnostic criteria for Autism Spectrum Disorder from: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5 TR)

- A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by all of the following, currently or by history (examples are illustrative, not exhaustive; see text of DSM-5 TR)
- 1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
- 2. Deficits in nonverbal communicative behaviors used for social interaction, ranging for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a lack of facial expressions and nonverbal communication.
- 3. Deficits in developing, maintaining, and understanding relationships, ranging for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.
- B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text of DSM-5 TR):
- 1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
- 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
- 3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
- 4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling, or touching of objects, visual fascination with lights or movement).

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# Diagnostic criteria for Autism Spectrum Disorder from: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5 TR)

- C. Symptoms must be present in the early developmental period (but may not be fully manifest until social demands exceed limited capacities or may be masked by learned strategies in later life.
- D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- E. These disorders are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnosis of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

The DSM notes that individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specific should be given the diagnosis of autism spectrum disorder. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for autism spectrum disorder, should be evaluated for social (pragmatic) communication disorder.

<u>American Academy of Pediatrics (AAP):</u> The AAP 2020 Clinical Report on Identification, Evaluation, and Management of Children With Autism Spectrum Disorder notes the following:

- Metabolic Testing: The yield of routine metabolic testing for children with ASD is low and not recommended for regular use. However, large population-based studies are lacking, so accurate prevalence and diagnostic yield estimates are not available. There is no evidence at this time for routine testing of hair, blood, or urine for environmental toxins or heavy metals outside of laboratory screening for lead exposure.
- Electroencephalogram (EEG): An EEG is not recommended as a routine baseline evaluation in the absence of clinical concern about seizures, atypical regression, or other neurologic symptoms on history or examination that would suggest an EEG is indicated.
- Genes, Environmental Exposures, and ASD: The potential environmental factors that may
  be related to increased reported prevalence of ASD is an area of active study that, as yet,
  is without firm conclusions.
- Genes, Immunologic Exposures, and ASD: Unless otherwise indicated (eg, history suggestive of autoimmune or immunologic disorder), no immune testing is recommended in the etiologic workup of a child with ASD (AAP/Hyman, et al., 2020).

<u>Centers for Disease Control and Prevention (CDC):</u> The CDC states that diagnosing autism spectrum disorder (ASD) can be difficult because "there is no medical test, like a blood test, to diagnose the disorder" (CDC, 2023).

The use of tests such as hair analysis for trace elements, celiac antibodies, allergy testing (particularly food allergies for gluten, casein, candida and other molds), immunologic or neurochemical abnormalities, micronutrients (e.g., vitamin levels), intestinal permeability studies, stool analysis, urinary peptides, mitochondrial disorders (e.g., lactate and pyruvate), thyroid function tests, erythrocyte glutathione peroxidase studies have not been well studied and no strong conclusions can be made regarding clinical utility for such testing (Chaves-Gnecco, Feldman, 2023).

Metabolomics or blood metabolites has been proposed as a method to be used in the assessment of the diagnosis of autism. The NPDX ASD test (Stemina Biomarker Discovery, Madison, WI) is a blood panel that measures metabolic subtypes (or metabotypes) associated with ASD. According to the product website the NPDX ASD test is a blood panel that measures metabolites in the blood

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of children with differences in metabolism and compares them to specific metabolic imbalances that are associated with autism spectrum disorder (ASD). The test results will include a positive or negative result compared to data from the CAMP study. It is purported that the test can identify a subset of children with autism spectrum disorder (about 30%) who have a metabolic imbalance that is associated with ASD.

Smith et al. (2019) reported on a study that based on evidence that dysregulation of branched-chain amino acids (BCAAs) may contribute to the behavioral characteristics of ASD, tested whether dysregulation of amino acids (AAs) was a pervasive phenomenon in individuals with ASD. The study is reports on the results from the Children's Autism Metabolome Project (CAMP), a large-scale effort to define autism biomarkers based on metabolomic analyses of blood samples from young children. Dysregulation of AA metabolism was identified by comparing plasma metabolites from 516 children with ASD with those from 164 age-matched typically developing children recruited into the CAMP. The ASD subjects were stratified into subpopulations based on shared metabolic phenotypes associated with BCAA dysregulation. Groups of AAs with positive correlations were identified that were, as a group, negatively correlated with BCAA levels in ASD. Imbalances between these two groups of AAs identified three ASD-associated amino acid dysregulation metabotypes. The combination of glutamine, glycine, and ornithine amino acid dysregulation metabotypes identified a dysregulation in AA/BCAA metabolism that is present in 16.7% of the CAMP subjects with ASD and is detectable with a specificity of 96.3% and a positive predictive value of 93.5% within the ASD subject cohort.

There is insufficient evidence in the published peer-reviewed medical literature to support provocative chelation tests for mercury in the assessment of ASD. There has been interest in the relationship of heavy metals, in particular mercury and the etiology of ASD. Testing for heavy metals (e.g., arsenic, barium, beryllium, bismuth, antimony, and mercury) is not supported by evidence in the peer-reviewed medical literature.

#### **Treatment Overview**

There are no medical interventions that are effective in achieving a cure for autism; however, the condition may be managed through a combination of behavioral, pharmacological and educational interventions.

The goal of therapy is to improve an individual's function and well-being. Behavioral interventions are well supported by evidence. No medications have demonstrated efficacy for the core diagnostic symptoms of ASD. Pharmacologic interventions, such as aripiprazole and risperidone, can mitigate behavioral and emotional dysregulation that co-occur in individuals with ASD (Hirota and King, et al., JAMA/2023).

A 2024 a systematic review and meta-analysis of RCTs that examined the efficacy of interventions for the treatment of irritability in individuals of any age with ASD. The interventions assessed were classified as follows: pharmacological monotherapy, risperidone plus adjuvant therapy versus risperidone monotherapy, non-pharmacological intervention, and dietary intervention. Out of 5640 references, 60 eligible articles with 45 different kinds of interventions were identified, including 3531 participants, of which 80.9% were males.

The authors concluded that only risperidone and aripiprazole were pharmacological interventions with promising evidence, while other candidate medications had doubtful results. For non-pharmacological interventions, only parent training showed a significant effect on the reduction of irritability in ASD with moderate certainty of evidence. Several promising candidates as an augmentation to risperidone are found, for which findings should be replicated in additional RCTs (Choi, et al., 2024).

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Agency for Healthcare Research and Quality (AHRQ): The AHRQ published a comparative effectiveness review of therapies for children with autism spectrum (Warren, et al., 2011). The review included 159 unique studies with thirteen studies determined to be good quality, 56 fair quality and 90 trials poor quality. The treatments in the review included behavioral, educational, medical, allied health, and complementary and alternative medicine (CAM) interventions. The CAM interventions included acupuncture and massage. The comparators included no treatment, placebo, and comparative interventions or combinations of interventions. The outcomes included changes in core ASD symptoms and in commonly associated symptoms. The findings of this review included:

#### Behavioral interventions:

- > There were 78 unique behavioral studies. Early intensive behavioral and developmental intervention may improve core areas of deficit for individuals with ASDs; however, few randomized controlled trials (RCTs) of sufficient quality have been conducted, no studies directly compare effects of different treatment approaches, and little evidence of practical effectiveness or feasibility exists.
- Within the behavioral category, the studies of UCLA/Lovaas-based interventions report greater improvements in cognitive performance, language skills, and adaptive behavior skills than broadly defined eclectic treatments available in the community. However, the strength of evidence is currently low. Further, not all children receiving intensive intervention demonstrate rapid gains, and many children continue to display substantial impairment. Although positive results are reported for the effects of intensive interventions that use a developmental framework, such as the Early Start Denver Model (ESDM), evidence for this type of intervention is currently insufficient because few studies have been published to date.
- Less intensive interventions focusing on providing parent training for bolstering social communication skills and managing challenging behaviors have been associated in individual studies with short-term gains in social communication and language use. The current evidence base for such treatment remains insufficient, with current research lacking consistency in interventions and outcomes assessed.
- ➢ Although all of the studies of social skills interventions reported some positive results, most have not included objective observations of the extent to which improvements in social skills generalize and are maintained within everyday peer interactions. Strength of evidence is insufficient to assess effects of social skills training on core autism outcomes for older children or play- and interaction-based approaches for younger children. Several studies suggest that interventions based on cognitive behavioral therapy are effective in reducing anxiety symptoms. The strength of evidence for these interventions, however, is insufficient pending further replication.
- Educational interventions: There were 15 unique studies in this category. Most research on the Treatment and Education of Autistic and Communication related handicapped Children (TEACCH) program was conducted prior to the date cutoff for the review (before 2000). Newer studies continue to report improvements among children in motor, eye-hand coordination, and cognitive measures. The strength of evidence for TEACCH, as well as broad-based and computer-based educational approaches included in this category, to affect any individual outcomes is insufficient because there are too few studies and they are inconsistent in outcomes measured.
- (Pharmaceutical) Medical and related interventions: There were 42 unique studies found, of which 27 were RCTs. Although no current medical interventions demonstrate clear benefit for social or communication symptoms, a few medications show benefit for repetitive behaviors or associated symptoms. The clearest evidence favors the use of medications to address challenging behaviors. The antipsychotics risperidone and aripiprazole each have

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at least two RCTs demonstrating improvement in a parent-reported measure of challenging behavior. A parent-reported hyperactivity and noncompliance measure also showed significant improvement. In addition, repetitive behavior showed improvement with both risperidone and aripiprazole. Both medications also cause significant side effects, however, including marked weight gain, sedation, and risk of extrapyramidal symptoms (side effects, including muscle stiffness or tremor, that occur in individuals taking antipsychotic medications). These side effects limit use of these drugs to individuals with severe impairment or risk of injury. The strength of evidence was rated as high for the adverse effects of both medications, moderate for the ability of risperidone to affect challenging behaviors, and high for aripiprazole's effects on challenging behaviors.

- Allied health: There were 17 unique studies that reported on varied interventions. The
  research provided little support for their use. Specifically, all studies of sensory integration
  and music therapy were of poor quality, and two fair-quality studies of auditory integration
  showed no improvement associated with treatment. Language and communication
  interventions (Picture Exchange Communication System [PECS] and Responsive Education
  and Prelinguistic Milieu Training [RPMT]) demonstrated short-term improvement in word
  acquisition without effect durability, and should be studied further. No other allied health
  interventions had adequate research to assess the strength of evidence.
- CAM: Evidence for CAM interventions (i.e., acupuncture and massage) is insufficient for assessing outcomes (Warren, et al., 2011).

In 2014, the AHRQ published a systematic review that updated the behavioral intervention portion of the comprehensive review of therapies for children with ASD that was published in 2011 (Weitlauf, et al., 2014).

The review focused on behavioral treatments for children ages two through twelve with ASD and children younger than age two at risk of a diagnosis of ASD. The study designs included randomized controlled trials, prospective and retrospective cohort studies, and nonrandomized controlled trials. The 65 new studies include 48 randomized controlled trials (RCTs) and 17 nonrandomized trials or cohort studies (19 good, 39 fair, and 7 poor quality).

The studies in the review were assigned a strength-of-evidence designation. The maximum strength of evidence possible was established based on criteria for each domain: study limitations, consistency in direction of the effect, directness in measuring intended outcomes, precision of effect, and reporting bias. Then the number of studies and range of study designs for a given intervention-outcome pair was assigned and the rating was downgraded when the cumulative evidence was not sufficient to justify the higher rating.

The possible grades for strength of evidence in this report include:

- High: High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.
- Moderate: Moderate confidence that the evidence reflects the true effect. Further research may change confidence in the estimate of effect and may change the estimate.
- Low: Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.
- Insufficient: Evidence is either unavailable or does not permit a conclusion.

The AHRQ report includes the following key questions and findings (Weitlauf, et al., 2014):

- Effects of Behavioral Interventions on Core and Commonly Associated Symptoms in Children With ASD:
  - Studies of Early Intensive Behavioral and Developmental Interventions: the review included 25 new studies that addressed these interventions. The studies included five RCTs of good quality, six of fair quality, and one of poor quality. Individual studies using intensive University of California, Los Angeles (UCLA)/Lovaas-based interventions, the Early Start Denver Model (ESDM), the Learning Experiences and

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Alternate Program for Preschoolers and their Parents (LEAP) program, and eclectic variants reported improvements in outcomes for young children. The improvements were seen mostly in cognitive abilities and language acquisition, with fewer improvements seen in adaptive skills, core ASD symptoms severity, and social functioning. Evidence for the impact of early intensive intervention on core ASD symptoms is limited and mixed. The symptom severity often decreased during treatment, but these improvements often did not differ from those of children in control groups. The better quality studies reported positive effects of intervention on symptom severity, but multiple lower quality studies did not. There was improvement noted in cognitive functioning and language skills in young children receiving high-intensity applied behavior analysis (ABA)-based interventions over extended time frames (i.e., 8 months-2 years) relative to community controls. It was noted that the magnitude of these effects varied across studies and that the variation may reflect subgroups showing differential responses to particular interventions. It is not clear how the intervention response is likely moderated by treatment and child factors and the report notes that even with multiple studies of early intensive treatments, intervention approaches still vary substantially, which makes it difficult to distinguish what these unique treatment and child factors may be. The long-term impact of these early skill improvements is not yet clear, with many studies not following the children beyond late preschool or early school years.

- Social Skills Studies: the review included 13 studies that addressed interventions for social skills including 11 RCTs (two good and 10 fair quality). The interventions varied widely in terms of scope and intensity. A few studies replicated interventions using the Skill streaming model, which uses a published treatment manual to promote a consistent approach. Other studies incorporated peer-mediated and/or group-based approaches, and others described interventions that focused on emotion identification and Theory of Mind training. There was varied intensity, with most consisting of 1-2 hour sessions/week for approximately 4-5 weeks. There were some group-based approaches that lasted 15-16 weeks. Most studies reported short-term gains in either parent-rated social skills or directly tested emotion recognition. However, the confidence or strength of evidence in that effect is low and limited by the diversity of the intervention protocols and measurement tools (i.e., no consistent outcome measures used across studies). In addition, the studies included only participants considered high-functioning and/or with IO test scores >70, which limits generalization of results to children with more significant impairments. The maintenance and generalization of these skills beyond the intervention setting are inconsistent, with variability in performance across environments.
- Play-/Interaction-Focused Studies: The review includes 11 RCTs of good and fair quality and suggests that joint attention interventions may be associated with positive outcomes for toddler and preschool children with ASD, in particular when joint attention skills are targeted as well as related social communication and language skills. Although joint attention intervention studies demonstrated changes within this theoretically important domain, the data is more limited regarding the ability to improve broad developmental skills (e.g., cognition, adaptive behavior, and ASD symptom severity) beyond direct measures of joint attention and related communication and language gains over time.
- > Studies of Interventions Targeting Conditions Commonly Associated With ASD: Six RCTs (five good, one fair quality) of interventions addressing conditions commonly associated with ASD identified for the current update measured anxiety symptoms as a primary outcome. Five studies reported significantly greater improvements in anxiety symptoms in the intervention group compared with controls. Two found positive effects of cognitive behavioral therapy (CBT) on the core ASD symptom of

socialization, and one reported improvements in executive function in the treatment group. The one RCT that did not find a significant benefit of CBT compared it with social recreational therapy rather than with treatment as usual or a wait-listed control group. The studies examining the effects of CBT on anxiety had largely consistent methodologies. Six studies provided follow-up data reflecting treatment effects that lasted beyond the period of direct intervention. Due to the nature of CBT, (language intensive and requires a certain level of reasoning skills to make abstract connections between concepts) most studies included only children with IQs much greater than 70. These studies report positive results regarding the use of CBT to treat anxiety in children with ASD. They also report some positive results in socialization, executive function, and communication; however, less robust results, and unclear in some studies if the improvements exceeded improvements related to the impact of improved anxiety itself.

- Other Behavioral Studies: Two RCTs (one fair, one poor quality) examined neurofeedback and found some improvements on parent-rated measures of communication and tests of executive function. Three fair-quality RCTs reported on sleep-focused interventions, with little positive effect of a sleep education pamphlet for parents in one, improvements in sleep quality in treatment arms in another, and some improvements in time to fall asleep in one short-term RCT of sleep education programs for parents. One poor-quality study of parent education to mitigate feeding problems reported no significant effects.
- Modifiers of Treatment Effects: Among the potential modifiers or moderators of early intensive ABA-based interventions, younger age at intake was associated with better outcomes for children in a limited number of studies. Greater baseline cognitive skills and higher adaptive behavior scores were associated with better outcomes across behavioral interventions, but these associations were not consistent. In general, children with lower symptom severity or less severe diagnoses improved more than participants with greater impairments. Many studies (e.g., social skills, CBT) restricted the range of participants' impairment at baseline (e.g., recruiting only participants with IQs >70), which limits understanding of intervention impact on broader populations. Regarding intervention-related factors, an inconsistent effect was found for duration of treatment. Overall, the report found that most studies were not adequately designed or controlled to identify true moderators of treatment response.
- Treatment Phase Changes That Predict Outcomes: The studies offered little suggestions about what specific early changes from baseline measurements of child characteristics might predict long-term outcome and response.
- Treatment Effects That Predict Long-Term Outcomes: Few studies assessed end-oftreatment effects that may predict outcomes.
- Generalization of Treatment Effects: The majority of the social skills and behavioral
  intervention studies targeting associated conditions attempted to determine outcomes
  based on parent, self, teacher, and peer report of the targeted symptoms at home, at
  school, and in the community. While these ratings outside of the clinical setting may
  suggest generalization in that they improve outcomes in the daily context/life of the child,
  in most cases, these outcomes are parent reported and not confirmed with direct
  observation.
- Treatment Components That Drive Outcomes: there were no studies that met inclusion criteria that addressed this question.
- Treatment Approaches for Children Under Age 2 at Risk for Diagnosis of ASD: In the studies addressing interventions for younger children, children who received behavioral interventions seemed to improve regardless of intervention type. Most outcome measures of adaptive functioning were based on parent report, and the effect of parental perception of treatment efficacy on perception of child functioning was generally not explored.

Limitations of the Evidence Base: the AHRQ report notes that despite improvements, the existing literature has significant methodological concerns that in many ways continue to limit the strength of the conclusions. Evidence for the impact of intensive ABA-based interventions on cognitive, language, and adaptive skills and ASD symptoms emphasizes the important limitations of current treatment modalities. Children who demonstrate clinically significant improvements in these areas often continue to display substantial impairment in these and other areas over time and not all children receiving intensive ABA-based intervention showed robust improvements in these domains. Therefore, it remains challenging to predict long-term functional and adaptive outcomes on an individual level. While children who receive early intensive developmental and behavioral intervention may display substantial improvements, the magnitude of these effects varies across studies and may indicate subgroups showing variable responses to particular interventions. The intervention approaches still vary substantially, which leads to difficulty in determining what the unique treatment and child factors may be. Provider type and qualifications are variably reported, and the impact of this on treatment outcomes is unclear. Study sample sizes are typically small (range from 11 to 284 for studies in the current review, median=40), with some studies considered pilots for larger studies that may respond to questions about intervention intensity and moderators of effects. The report notes that presently the evidence is insufficient to adequately identify and target the children who are most likely to benefit from specific interventions.

In conclusion, the report notes that a growing evidence base suggests that behavioral interventions are associated with positive outcomes for some children with ASD. However, the report concludes that even with improvements in the quality of the included literature, there remains a need for studies of interventions across settings and continued improvements in the methodologic rigor and that substantial scientific advances are needed to improve the understanding of which interventions are most effective for specific children with ASD and to determine the elements or components of interventions most associated with effects. The AHRQ report found for early intensive behavioral and developmental intervention that is ABA based a moderate effect for strength of the evidence in the areas of IO/cognitive and language/communication. In the area of IQ/cognitive, it was found that approaches across the studies varied substantially and not all the improvements were maintained at long-term follow-up. In the area of language/communication, it was found that most studies found a positive effect of treatment on language/communication, however the specific domain of improvement (e.g., receptive vs expressive language) varied across studies and some of the initial between-group differences were not present at long-term follow-up. In addition, in this area of language/communication some studies utilized direct testing, while others used parent-reported measures. The review found a low effect for strength of the evidence in the areas of adaptive behavior, symptom severity, and social skills/social behavior. The intervention approach varied across studies and there is uncertainty regarding which intervention will affect and benefit which sub-group of children with ASD (Weitlauf, et al., 2014).

The AHRQ published a comparative effectiveness review of the effects of available interventions on adolescents and young adults with ASD (ages 13 to 30) (Lounds, et al., 2012). The review focused on the following outcomes: core symptoms of ASD (impairments in social interaction, communication, and repetitive behavior); medical and mental health comorbidities; functional behaviors and independence; the transition to adulthood; and family outcomes. The studies assessed interventions falling into the broad categories of behavioral, educational, adaptive/life skills, vocational, medical, and allied health approaches. The comparators included no treatment, placebo, and comparative interventions or combinations of interventions. Intermediate outcomes included changes in core ASD symptoms and in common medical and mental health comorbidities as well as effects on functional behavior, the transition process, and family outcomes. Long-term outcomes included changes in adaptive/functional independence, academic and occupational

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attainment or engagement, psychological well-being, and psychosocial adaptation. Harms were also assessed.

Across all categories of interventions, most studies (n=27) were of poor quality, and none was good quality. Five randomized controlled trials (RCT) were fair quality: four that investigated pharmacologic agents and one allied health study that assessed a leisure/recreation program. Although positive results may be reported in individual studies, the poor quality of the studies and the lack of replication of the intervention studies mean that the strength of evidence for the body of evidence around any specific intervention is currently insufficient. Findings for the interventions included:

#### Behavioral:

- Individual or group-based social skills training: Four poor-quality studies, with two reporting on manualized (i.e., has a published treatment manual) intervention. Some gains in social skills on largely parent-reported measures in short-term studies. Two studies lacked comparison groups; diagnostic approach, participant characteristics, treatment fidelity not clearly reported.
- Computer-based social skills training: Three poor-quality, short-term studies. Some
  improvements in emotion recognition in treated participants; no differences in measures of
  generalization. Systematic diagnostic approach not reported within studies; concomitant
  interventions and treatment fidelity not reported.
- Intensive behavioral treatment: One poor-quality case series with diverse participants. Some gains in adaptive behavior reported. Intervention not clearly described; treatment fidelity and concomitant interventions not reported; assessors not masked.

#### Adaptive/Life Skills

- Specific life/transitional skills: Three, poor-quality, short-term studies assessing highly specific skills and unique interventions (e.g., shoe lacing, digital device use, rotating classroom schedule). Some gains seen in individual studies but most lacked comparison groups. Systematic diagnostic approach not reported within studies; participants often not clearly characterized; differences in concomitant interventions and treatment fidelity often not reported.
- Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH)-based model: One poor-quality cohort study; desirability of living situation and use of programming rated more highly for TEACCH than other conditions; group homes rated more desirable than institutions. Nonrandom assignment to groups; systematic diagnostic approach not reported within study; inclusion/exclusion criteria not clearly stated; interventions not fully described; assessors not masked.

#### Medical

- Antipsychotics: Two fair-quality RCTs and one poor quality crossover study. Improvements
  in aggression, irritability/agitation, repetitive behavior, sensory motor behaviors, and
  overall behavioral symptoms in participants receiving risperidone. Treatment adherence not
  reported in two studies; assessors not masked and participants not clearly characterized in
  one study.
- Opioid receptor antagonists: One poor-quality crossover study. Significant increase in stereotypy in treated participants. Participants not clearly characterized; adherence and differences in concomitant interventions not reported.
- Serotonin reuptake inhibitors: Two fair-quality RCTs, three poor quality case series. Studies
  had inconsistent results: RCT of fluvoxamine reported decreases in repetitive behavior,
  aggression, autistic symptoms, and language usage. Case series addressing sertraline,
  fluoxetine, and clomipramine reported some benefits, while a crossover study of
  clomipramine vs. placebo reported no significant differences in autistic symptoms between
  groups. Lack of comparison groups in three studies; treatment adherence not reported;
  assessors not masked in some studies.

Allied Health

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- Facilitated communication: Two poor-quality case series. Facilitated communication did not increase participants' communication or literacy abilities over their independent abilities. No comparison groups; differences in concomitant interventions not reported; assessors not masked.
- Music therapy: Two poor-quality case series. Some gains in social skills reported using unvalidated and largely subjective measures. No comparison groups or measures of treatment fidelity; participants not clearly characterized; assessors not masked; differences in concomitant interventions not reported.
- Leisure/recreation program: One fair-quality RCT. Positive effects on stress and quality of life in leisure group participants compared with controls. Attrition and treatment fidelity not reported; randomization method not clearly described; differences in concomitant interventions not reported (Lounds, et al., 2012).

<u>Meta-analysis:</u> Linden et al. (2022) reported results from a meta-analysis of randomized controlled trials including 3243 participants (71 RCTs). The primary analysis objective was to compare relative benefits and harms of different interventions to improve mental health of autistic people. The types of interventions (either alone or in combination) reviewed included the following:

- drugs such as selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), antipsychotics, antioxidants, other medications such as oxytocin, anti-diuretic hormone (ADH).
- psychological therapies such as CBT, mindfulness-based therapy, counselling.
- behavioral therapies such as social skills training, ABA.
- miscellaneous interventions such as music therapy, parent psychoeducation, dietary supplements.
- wait-list (i.e. no additional intervention or placebo intervention until measurement of the outcomes).

The primary outcomes included anxiety or depression using any validated measure, overall health-related quality of life (HRQoL) using any validated measure, and serious adverse events. Sample sizes in the trials varied from 11 to 223 participants. Only six trials had sample sizes of 100 or more participants. The follow-up period in the trials ranged from 1 month to 24 months. Only one trial had a follow-up longer than 12 months. Overall, the reviewed evidence indicates considerable uncertainty about the effects of different interventions for mental health conditions in autistic people. Available evidence suggests that some forms of cognitive behavioral therapy may decrease anxiety and depression scores in autistic children and adults; mindfulness therapy may decrease anxiety and depression scores in autistic adults with previous mental health conditions; and behavioral interventions may provide some benefit for depression in autistic children. The authors noted that few trials specifically studied mental health conditions in autistic people, and those that existed were at high risk of bias. The risk of bias assessment highlighted low study quality, small sample sizes resulting in insufficient statistical power, a lack of blinding of participants and researchers, and few RCTs comparing different interventions (Linden, et al., 2022).

A meta-analysis of RCTs was conducted to investigate the efficacy of early interventions in improving the cognitive ability, language, and adaptive behavior of pre-school children with ASD. The total sample consisted of 2581 children (12–132 months of age). Out of the 33 studies included, 12 studies were categorized as long-term interventions, 9 were categorized as medium-term interventions, and 12 were categorized as short-term interventions. Additionally, 10 studies implemented high-intensity interventions, and 23 studies implemented low-intensity interventions. Results demonstrated early interventions led to positive outcomes for cognitive ability (p = 0.02), daily living skills (p = 0.01), and motor skills (p = 0.001), while no positive outcomes were found

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for the remaining variables. However, when studies without the blinding of outcome assessment were excluded, positive outcomes of early interventions only remained for daily living skills (p = 0.02) and motor skills (p = 0.007). The authors noted that the results should be interpreted with caution considering the great variability in participant and intervention characteristics (Daniolou, et al., 2022).

<u>Cochrane review</u>: A Cochrane review was conducted to assess the effectiveness of behavioral and cognitive behavioral therapy for obsessive compulsive disorder (OCD) in children and adults with ASD. The authors concluded that "Evidence is limited regarding the efficacy of CBT for treatment of OCD in ASD. There is much scope for future study, not only examining the efficacy of CBT for OCD in ASD, but also the particular ways that OCD manifests in and affects people with ASD and the role of the family in treatment response" (Elliott, et al., 2021).

<u>American Occupational Therapy Association (AOTA):</u> The Evidence-Based Practice Program of the AOTA has published seven Systematic Review Briefs in 2023. Each of the following systematic review briefs summarizes the evidence for:

- Interventions to Support Participation in Basic and Instrumental Activities of Daily Living for Autistic Children and Adolescents (2013-2021): This systematic review addressed the question "What are the interventions within the scope of occupational therapy to address participation in activities of daily living, instrumental activities of daily living, rest and sleep, work, education, play, leisure, social participation, and health management among autistic people under the age of 18?" (Baker, et al., 2023).
- Interventions for Developing Positive Mental Health in Autistic Individuals (2013-2021): This systematic review addressed the question "What are the interventions in the scope of occupational therapy to support (or improve) improved self-determination and positive mental health for persons on the autism spectrum?" (Patten, et al., 2023).
- Interventions for Social Participation for Autistic Adults (2013-2020): This systematic review addressed the question "What are the interventions within the scope of occupational therapy to address participation in activities of daily living, instrumental activities of daily living, rest and sleep, work, education, play, leisure, social participation, and health management among autistic people over the age of 18?" (Jirikowic, et al., 2023).
- Interventions for Work/Employment Participation for Autistic Adults (2013-2020): This systematic review addressed the question "What are the interventions within the scope of occupational therapy to address participation in activities of daily living, instrumental activities of daily living, rest and sleep, work, education, play, leisure, social participation, and health management among autistic people over the age of 18?" (Jirikowic, et al., 2023).
- Interventions That Foster Self-Determination in Autistic Individuals (2013-2021): This systematic review addressed the question "What interventions in the scope of occupational therapy support or improve self-determination for autistic individuals?" (Patten, et al., 2023).
- Person-Centered Interventions for Autistic Adults Ages 18+ (2013-2021): This systematic review addressed the question "What are the effects of person-centered, student-centered, or family-centered planning approaches on outcomes within the scope of occupational therapy for autistic persons and families of autistic individuals?" (Benevides, et al., 2023).
- Family-Centered Interventions for Children on the Autism Spectrum (2013-2021): This systematic review addressed the question "What are the effects of person-centered, student-centered or family-centered planning approaches on outcomes within the scope of occupational therapy for autistic persons and families of autistic individuals?" (Watling, et al., 2023).

#### **Pharmacologic Treatment**

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Pharmacological treatments may be useful in the treatment of ASD. Pharmacologic intervention should be targeted toward specific behaviors that significantly interfere with daily functions. In October 2006, the U.S. Food and Drug Administration (FDA) approved Risperdal® (Janssen, L.P., Titusville, N.J.) (risperidone), an adult antipsychotic drug, for the symptomatic treatment of irritability in autistic children and adolescents. The medications used in the treatment of ASD may include, but are not limited to, the following groups:

- Selective serotonin reuptake inhibitors (SSRIs): This is a group of antidepressants. They may be used to reduce the frequency and intensity of repetitive behaviors; decrease irritability, tantrums and aggressive behavior; and improve eye contact.
- Tricyclics and other antidepressants: Tricyclics tend to cause more side effects than the SSRIs; however, they may be more effective in certain individuals. Newer antidepressants that may be an alternative to tricyclics include, but may not be limited to, serotonin norepinephrine reuptake inhibitors (SNRIs).
- Antipsychotics: This group may be used to help control symptoms seen with ASD, including reducing self-injurious behaviors.
- Psychostimulants: This group of medications may be useful in increasing focus and decreasing hyperactivity in people with autism.
- Antianxiety drugs: This group can help relieve anxiety and panic disorders.

Other agents such as antivirals, antifungals, essential oils, vitamin and supplemental therapy, cannabis and marijuana, herbs and homeopathic treatments remain under investigation (Association for Science in Autism Treatment [ASAT]).

<u>American Academy of Child & Adolescent Psychiatry (AACAP):</u> The AACAP Policy Statement on the Use of Medical Marijuana in Children and Adolescents with Autism Spectrum Disorder for Core Autism Symptoms or Co-Occurring Emotional or Behavioral Problems (May 2019) recommends:

- Against the use of medical marijuana or isolated cannabinoids for core symptoms or cooccurring emotional or behavioral problems in children and adolescents with ASD.
- That families should be educated about risks and discouraged from using marijuana and cannabinoids for ASD.
- That State and Federal legislators refrain from approving the use of marijuana and cannabinoids in children with ASD in the absence of scientific evidence in the peer-reviewed medical literature (AACAP, 2019).

<u>Antipsychotics:</u> Deb et al. (2023) conducted a systematic review and meta-analysis of all randomized controlled trials (RCTs) involving antipsychotics for people with autism of all ages, irrespective of the outcomes assessed. Included were 39 papers based on 21 primary RCTs that recruited 1482 people with autism.

- Risperidone: Seven of the 14 RCTs compared risperidone with a placebo, all showing a statistically significant improvement in the risperidone over the placebo group according to the various outcome measures.
- Aripiprazole: Five RCTs compared the efficacy of aripiprazole with a placebo. Four found significantly better outcomes in the aripiprazole group, but one did not. The two large-scale RCTs were conducted by the pharma company that manufactures aripiprazole. Two of the five RCTs were not published in any peer-reviewed journal.
- Lurasidone: Only one RCT has been published on the efficacy of lurasidone. This large-scale (n = 150) multi-center placebo controlled study showed no statistically significant intergroup difference in the outcome.
- Olanzapine: Only one very small (n = 8) placebo-controlled RCT on the efficacy of olanzapine showed significantly better improvement in the intervention group.

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• Adverse effects: Most studies reported significant weight gain, increased appetite, and somnolence in the intervention group. Other adverse effects included raised prolactin levels with and without galactorrhoea, drooling, constipation, and extrapyramidal symptoms (Deb, et al., 2023).

<u>Acetylcholinesterase inhibitors:</u> Ure et al. (2023) evaluated the efficacy and harms of acetylcholinesterase inhibitors for people with the core features (social interaction, communication, and restrictive and repetitive behaviors) of autism. Included were two RCTs totaling 74 participants.

- One study compared the effects of galantamine plus risperidone to placebo plus risperidone (40 participants, aged 4 years to 12 years). Very low-certainty evidence showed there was little to no difference between the two groups postintervention for social communication, and restricted and repetitive behavior. Low-certainty evidence showed a small difference in irritability, with the galantamine plus risperidone group showing a greater decline on the irritability subscale than the placebo group postintervention. There was no evidence of a difference between the groups in hyperactivity postintervention.
- One study compared donepezil to placebo (34 participants aged 8 years to 17 years). Very low-certainty evidence showed no evidence of group differences immediately postintervention in overall autism features, or in the autism symptom domains of social communication, and restricted and repetitive behaviors (Ure, et al., 2023).

<u>D-cycloserine</u>: A Cochrane review on D-cycloserine determined "There appears to be no clear difference between D-cycloserine plus social skills training and social skills training alone, on social and communication skills in individuals with ASD" (Aye, et al., 2021).

<u>Memantine</u>: A Cochrane review on memantine determined "It is unclear if memantine makes any difference to the core symptoms of autism. Additionally, there may be no difference between memantine and placebo in the occurrence of side effects, language ability, memory, adaptive behavior or the autism-related behaviors of hyperactivity and irritability" (Brignell, et al., 2022).

#### **Treatments - Detail**

American Academy of Pediatrics (AAP): Nonbiological interventions used for symptoms of ASD are popular and have also been increasingly studied. There has been conflicting evidence regarding the effect of music therapy, yoga, massage, and equine-assisted therapy on the symptoms of ASD in children, but evidence does not support these therapies for treatment of the core deficits of ASD at this time. Existing studies are insufficient at this time to support dance therapy, drama therapy, and chiropractic therapy.

Medical interventions used for nonstandard purposes also are sometimes prescribed for symptoms of ASD. Clinical trials do not support the use of antifungal agents, immunotherapy, or hyperbaric oxygen treatment, and concern for safety, in addition to lack of supporting data, cautions against chelation therapy for children with ASD (AAP/Hyman, et al., 2020).

**Art Therapy:** Art therapy, or the therapeutic use of art making, has been proposed to address the symptoms of individuals with ASD. The effectiveness of this varied therapy has not been demonstrated in large, well-designed clinical trials in published peer-reviewed scientific literature (Bernier, et al., 2022).

**Augmentative and Alternative Communication:** Augmentative and alternative communication (AAC) includes all forms of communication (other than oral speech) that are used for expression. AAC includes unaided communication systems which rely on the user's body to convey messages—examples include gestures, body language, and/or sign language. Aided

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communication systems require the use of tools or equipment in addition to the user's body. Aided communication methods can range from paper and pencil to communication books or boards to devices that produce voice output (speech generating devices or SGD's) and/or written output. Electronic communication aids allow the user to use picture symbols, letters, and/or words and phrases to create messages. A Picture Exchange Communication System (PECS) uses picture symbols to teach communication skills with the individual taught to use picture symbols to ask and answer questions and hold a conversation.

American Academy of Pediatrics (AAP): When children do not spontaneously speak, augmentative and alternative communication (AAC) may be introduced. Examples of AAC strategies include sign language, the Picture Exchange Communication System, and speech-generating devices. The use of AAC may help promote social interaction and understanding of the purpose of communication and does not delay onset of speech. Indeed, it may enhance emergence of spoken words by pairing nonverbal and verbal communication (AAP/Hyman, et al., 2020).

Please refer to Cigna Coverage Policies (CP) for Speech Therapy (CP 0177) and Speech Generating Devices (CP 0049) for additional information.

Chelation Therapy: Chelation has been proposed for treatment of ASD. The proposal is based on the theory that the chelating agent will remove mercury that is thought to be contained in the tissue after early childhood vaccinations in children with ASD (Levy and Hyman, 2005). While there have been several studies that have examined the relationship of mercury to ASD, no consistent associations have been identified (Levy and Hyman, 2005). A Cochrane review was conducted to assess the potential benefits and adverse effects of pharmaceutical chelation therapy for ASD symptoms (James, et al., 2015). The review included data from one stud with methodological limitations. The review concluded that no clinical trial evidence was found to suggest that pharmaceutical chelation is an effective intervention for ASD. In addition, the review noted that "given prior reports of serious adverse events, such as hypocalcaemia, renal impairment and reported death, the risks of using chelation for ASD currently outweigh proven benefits". There is insufficient evidence in the peer-reviewed literature regarding the efficacy of chelation therapy for treatment of ASD. The AAP guidelines for identification, evaluation, and management of children with ASD note that clinical trials do not support this therapy, and in addition to lack of supporting data, cautions against chelation therapy for children with ASD (AAP/Hyman, et al., 2020).

**Equestrian Therapy:** Equestrian therapy, also referred to as equine therapy, equine-assisted activities and therapies (EAAT), horseback riding or 'hippotherapy' is proposed to offer a person with a disability, including ASD, a means of physical activity that aids in improving balance. Srinivasan et al. (2018) reported on a systematic review for equine therapy for ASD. The review included 15 studies with six to 116 participants, with a variety of study designs, with three randomized studies. The authors note that there is preliminary support for the utility of equine therapy in ASD with beneficial effects on behavioral and to some extent on social communication skills in ASD noted. The studies are limited by small number of participants; further controlled, randomized studies are needed. There is insufficient published evidence regarding the effects of this therapy in children with ASD.

Trzmiel et al. (2019) reported on systematic review to assess the effectiveness of (EAAT) in ASD individuals. The review included 15 studies with 390 participants (aged: 3–16 years). The review noted there appeared to be improved social functioning however it is impossible to draw universal conclusions due to the considerable discrepancies in therapeutic protocols and measurement instruments in the studies. In addition, longitudinal trials, with standardized EAAT protocols and representative large sample groups are necessary and homogeneous tools should be established to measure therapeutic progress and outcomes.

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The 2020 AAP guidelines for identification, evaluation, and management of children with ASD note that there has been conflicting evidence regarding the effect of equine-assisted therapy on the symptoms of ASD in children, but evidence does not support these therapies for treatment of the core deficits of ASD at this time (AAP/Hyman, et al., 2020).

Please refer to Cigna Coverage Policies for Occupational Therapy (CPG 155) and Physical Therapy (CPG 135) for additional information.

**Holding Therapy:** In this intervention the therapist or parent holds the child until they stops resisting or until a fixed amount of time has elapsed. Those who support the technique maintain that it forges a bond between the parent or therapist and child. The effectiveness of this therapy has not been demonstrated in the published peer-reviewed scientific literature.

**Hyperbaric Oxygen Therapy:** Hyperbaric oxygen therapy (HBO or HBOT) is a mode of treatment in which a individual breathes 100% oxygen at pressures greater than normal atmospheric (sea level) pressure. This treatment has been proposed as a treatment for ASD. The published data provided is preliminary and is insufficient to support HBO as a treatment for ASD.

A Cochrane review (Xiong, et al., 2016) of hyperbaric oxygen therapy for people with autism spectrum disorder (ASD) included one trial with a total of 60 children with a diagnosis of ASD who randomly received hyperbaric oxygen therapy or a sham treatment. The authors concluded that, there is no evidence that hyperbaric oxygen therapy improves core symptoms and associated symptoms of ASD. Ghanizadeh (2012) reported on a systematic review of the treatment of children with autism with hyperbaric oxygen therapy. The review found two randomized, doubleblind, controlled clinical trials. The authors concluded that the results supporting the efficacy of HBO therapy are not replicated. In addition, none of these trials used placebo group. These results are not conclusive for the efficacy of HBO therapy for the treatment of autism.

The AAP guidelines for identification, evaluation, and management of children with ASD note that clinical trials do not support the use of HBO at this time (AAP/Hyman, et al., 2020).

Please refer to Cigna Coverage Policy Hyperbaric and Topical Oxygen Therapies (CP 0053) for additional information.

**Immune Globulin:** Intravenous immunoglobulin (IVIG) has been proposed and administered to children with ASD. It is based on the theory that an immune deficiency may exist in ASD. A review of the literature by Levy and Hyman (2005) indicates that there are three small-case series published regarding this treatment. All three studies had a small number of participants and did not demonstrate the efficacy of this treatment. The published literature does not demonstrate the efficacy of IVIG for treatment of ASD.

Rossignol et al. (2021) conducted a meta-analysis examined the studies which assessed immunoglobulin G (IgG) concentrations and the therapeutic use of IVIG for individuals with ASD. The review included 27 publications were identified which examined the use of IVIG in ASD with four studies prospective, controlled studies; six prospective, uncontrolled studies; two retrospective, controlled studies; and 15 retrospective, uncontrolled studies (case reports and series). The authors noted that he quality of the evidence for the use of IVIG is still below what is commonly accepted for a routinely used treatment with the bulk of the studies being uncontrolled. They noted that many studies demonstrated bias, including selection bias (lack of randomization), performance bias (lack of blinding), detection bias (lack of standardized outcomes), attrition bias (retrospective studies are prone to losing individuals to follow-up), and reporting bias (case studies tend to report positive rather than negative outcomes). the authors concluded that the

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current set of studies presented should be used to design and implement well-controlled, blinded randomized clinical trials in the future and that additionally, the populations used in these studies are very heterogeneous with many different immune system abnormalities, making it hard to determine if there is a particular subset of children with ASD in which the treatment may be most effective.

The AAP guidelines for identification, evaluation, and management of children with ASD note that clinical trials do not support the use of immunotherapy at this time (AAP/Hyman, et al., 2020).

Please refer to Cigna Drug and Biologic Coverage Policy Immune Globulin (CP 5026) for additional information.

**Intensive Behavioral Interventions:** Intensive behavioral interventions are comprehensive treatment programs that utilize a combination of interventions with the aim of improving cognitive and intellectual function, social and adaptive skill development and behavior problems. They have been proposed to treat autism spectrum disorders as well as other conditions that involve behavioral difficulties. The programs emphasize early intervention, individualization of treatment and an intensive approach. The programs may also be referred to as early intensive behavior intervention (EIBI), intensive behavior intervention (IBI) or early intensive behavioral treatment (EIBT). At times, the terms EIBI, IBI, EIBT are used interchangeably with applied behavior analysis (ABA), Lovaas therapy or Lovaas University of California Los Angeles (UCLA) Program. The programs are intensive and range from 15 to 40 hours per week, delivered over a long period of time. The intensive behavior programs focus on identifying behaviors that interfere with normal developmental processes, understanding the relationship between a behavior and the child's environment and modifying those behaviors in such a way so as to improve the child's functional capacity. Treatment goals focus on improving adaptive behavior, language/communication skills, decreasing problem behaviors, as well as improving cognitive/intellectual status and academic/developmental achievements.

Please refer to Cigna Coverage Policy Intensive Behavioral Interventions (CP 0499) for additional information.

**Music Therapy:** Music Therapy has been proposed as an intervention for ASD in an attempt to improve coordination and communication skills. The methods can vary and may involve the therapist musically responding to the child's sounds and movements, singing a running commentary to the child's actions, using play routines or stories set to music, or songs involving imitation.

A 2022 Cochrane review assessed on the effects of music therapy, or music therapy added to standard care, for autistic people. The review included 26 studies (1165 participants). These studies examined the short- and medium-term effect of music therapy (intervention duration: three days to eight months) for autistic people in individual or group settings. The authors reported that music therapy compared with 'placebo' therapy or standard care probably increases the chance of overall improvement by the end of therapy, likely improves quality of life and total autism symptom severity immediately after therapy, and probably does not increase adverse events. It remains unclear whether music therapy has an effect on social interaction, non-verbal communication and verbal communication at the end of therapy since the certainty of evidence was low to very low. The authors noted that more research with adequate design (i.e. producing reliable evidence) including long-term outcomes of therapy, is needed (Geretsegger, et al., 2022).

A RCT evaluated effects of improvisational music therapy on generalized social communication skills of children with ASD. In children ages 4-7 years, enhanced standard care (n = 182) versus enhanced standard care plus improvisational music therapy (n = 182) were allocated. Enhanced

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standard care consisted of usual care as locally available plus parent counseling to discuss parents' concerns and provide information about ASD. In improvisational music therapy, trained music therapists sang or played music with each child, attuned and adapted to the child's focus of attention, to help children develop affect sharing and joint attention. A total of 314 (86%) completed the primary end point and 290 (80%) completed the last end point. The authors found that among children with ASD, improvisational music therapy, compared with enhanced standard care, resulted in no significant difference in symptom severity based on the ADOS social affect domain over 5 months (Bieleninik, et al., 2017).

The AAP guidelines for identification, evaluation, and management of children with ASD note that evidence does not support these therapies (music) for treatment of the core deficits of ASD at this time (AAP/Hyman, et al., 2020).

**Recreational Therapy:** Recreational therapy or therapeutic recreation utilizes recreation and other activities as treatment interventions. This therapy has been proposed as a treatment for symptoms off ASD. The effectiveness of this therapy, in its various forms, has not been demonstrated in the published peer-reviewed scientific literature.

**Transcranial stimulation:** Transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) have been proposed for use in ASD. The safety and effectiveness of transcranial stimulation for ASD has not been established in the peer-reviewed scientific literature.

A systematic review of randomized controlled trials evaluating the efficacy and safety of transcranial direct current stimulation in major neurodevelopmental disorders (ADHD, autism, and dyslexia was published in 2022. The authors identified 11 RCTs of tDCS application in children and adolescents with ASD. The authors noted that although preliminary results appear promising, results cannot establish clinical efficacy of tDCS unless proved in large clinical trials with robust experimental design. Large-scale RCTs and translational studies covering the range from basic neurophysiology to application in cognitive-clinical neuroscience are required. Furthermore, stimulation protocols applied in the most studied neurodevelopmental disorders show that we need to develop symptom-specific stimulation protocols that take disorder-specific conditions into account (Salehinejad, et al., 2022).

A meta-analysis that assessed the prevalence of adverse events (AEs) related to TMS in ASD was published in 2022. A total of 11 studies were included in the meta-analysis. The authors found the overall prevalence of reported AEs of TMS among ASD was 25% (headache: 10%; facial discomfort: 15%; irritability 21%; pain at the application site: 6%; light-headedness or dizziness: 8%) (Huashuang, et al., 2022).

**Vision Therapy:** Vision therapy is a proposed optometric treatment method for developing efficient visual skills and processing. A variety of visual therapies, oculomotor exercises, colored filters, irlen lenses and ambient prism lenses have been used in children with autism for the proposed intent to improve visual processing or visual-spatial perception. Studies in the published scientific literature have not provided clear support for this treatment of ASD.

## **Medicare Coverage Determinations**

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No Determination found	
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.

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## **Coding Information**

#### Notes:

- 1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
- 2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

# Considered Medically Necessary for the assessment of suspected or known Autism Spectrum Disorder (ASD) when criteria in the applicable policy statements listed above are met:

CPT®*	Description	
Codes		
83655	Lead	
84030	Phenylalanine (PKU), blood	
90791	Psychiatric diagnostic evaluation	
90792	Psychiatric diagnostic evaluation with medical services	
92521	Evaluation of speech fluency (eg, stuttering, cluttering)	
92522	Evaluation of speech sound production (eg, articulation, phonological process, apraxia, dysarthria)	
92523	Evaluation of speech sound production (eg, articulation, phonological process, apraxia, dysarthria); with evaluation of language comprehension and expression (eg, receptive and expressive language)	
92524	Behavioral and qualitative analysis of voice and resonance	
95705	Electroencephalogram (EEG), without video, review of data, technical description by EEG technologist, 2-12 hours; unmonitored	
95706	Electroencephalogram (EEG), without video, review of data, technical description by EEG technologist, 2-12 hours; with intermittent monitoring and maintenance	
95707	Electroencephalogram (EEG), without video, review of data, technical description by EEG technologist, 2-12 hours; with continuous, real-time monitoring and maintenance	
95711	Electroencephalogram with video (VEEG), review of data, technical description by EEG technologist, 2-12 hours; unmonitored	
95712	Electroencephalogram with video (VEEG), review of data, technical description by EEG technologist, 2-12 hours; with intermittent monitoring and maintenance	
95713	Electroencephalogram with video (VEEG), review of data, technical description by EEG technologist, 2-12 hours; with continuous, real-time monitoring and maintenance	
95717	Electroencephalogram (EEG), continuous recording, physician or other qualified health care professional review of recorded events, analysis of spike and seizure detection, interpretation and report, 2-12 hours of EEG recording; without video	
95718	Electroencephalogram (EEG), continuous recording, physician or other qualified health care professional review of recorded events, analysis of spike and seizure detection, interpretation and report, 2-12 hours of EEG recording; with video (VEEG)	
95812	Electroencephalogram (EEG) extended monitoring; 41-60 minutes	
95813	Electroencephalogram (EEG) extended monitoring; 60-119 minutes	

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CPT®* Codes	Description		
95816	Electroencephalogram (EEG); including recording awake and drowsy		
95819	Electroencephalogram (EEG); including recording awake and asleep		
96110	Developmental screening (eg, developmental milestone survey, speech and language delay screen), with scoring and documentation, per standardized instrument		
96112	Developmental test administration (including assessment of fine and/or gross motor, language, cognitive level, social, memory and/or executive functions by standardized developmental instruments when performed), by physician or other qualified health care professional, with interpretation and report; first hour)		
96113	Developmental test administration (including assessment of fine and/or gross motor, language, cognitive level, social, memory and/or executive functions by standardized developmental instruments when performed), by physician or other qualified health care professional, with interpretation and report; each additional 30 minutes (List separately in addition to code for primary procedure)		
97161	Physical therapy evaluation: low complexity, requiring these components: A history with no personal factors and/or comorbidities that impact the plan of care; An examination of body system(s) using standardized tests and measures addressing 1-2 elements from any of the following: body structures and functions, activity limitations, and/or participation restrictions; A clinical presentation with stable and/or uncomplicated characteristics; and Clinical decision making of low complexity using standardized individual assessment instrument and/or measurable assessment of functional outcome. Typically, 20 minutes are spent face-to-face with the individual and/or family		
97162	Physical therapy evaluation: moderate complexity, requiring these components: A history of present problem with 1-2 personal factors and/or comorbidities that impact the plan of care; An examination of body systems using standardized tests and measures in addressing a total of 3 or more elements from any of the following: body structures and functions, activity limitations, and/or participation restrictions; An evolving clinical presentation with changing characteristics; and Clinical decision making of moderate complexity using standardized individual assessment instrument and/or measurable assessment of functional outcome. Typically, 30 minutes are spent face-to-face with the individual and/or family		
97163	Physical therapy evaluation: high complexity, requiring these components: A history of present problem with 3 or more personal factors and/or comorbidities that impact the plan of care; An examination of body systems using standardized tests and measures addressing a total of 4 or more elements from any of the following: body structures and functions, activity limitations, and/or participation restrictions; A clinical presentation with unstable and unpredictable characteristics; and Clinical decision making of high complexity using standardized individual assessment instrument and/or measurable assessment of functional outcome. Typically, 45 minutes are spent face-to-face with the individual and/or family		
97165	Occupational therapy evaluation, low complexity, requiring these components: An occupational profile and medical and therapy history, which includes a brief history including review of medical and/or therapy records relating to the presenting problem; An assessment(s) that identifies 1-3 performance deficits (ie, relating to physical, cognitive, or psychosocial skills) that result in activity limitations and/or participation restrictions; and Clinical decision making of low complexity, which includes an analysis of the occupational profile, analysis of data from problem-focused assessment(s), and consideration of a limited number		

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CPT®* Codes	Description
	of treatment options. Individual presents with no comorbidities that affect occupational performance. Modification of tasks or assistance (eg, physical or verbal) with assessment(s) is not necessary to enable completion of evaluation component. Typically, 30 minutes are spent face-to-face with the individual and/or family
97166	Occupational therapy evaluation, moderate complexity, requiring these components: An occupational profile and medical and therapy history, which includes an expanded review of medical and/or therapy records and additional review of physical, cognitive, or psychosocial history related to current functional performance; An assessment(s) that identifies 3-5 performance deficits (ie, relating to physical, cognitive, or psychosocial skills) that result in activity limitations and/or participation restrictions; and Clinical decision making of moderate analytic complexity, which includes an analysis of the occupational profile, analysis of data from detailed assessment(s), and consideration of several treatment options. Individual may present with comorbidities that affect occupational performance. Minimal to moderate modification of tasks or assistance (eg, physical or verbal) with assessment(s) is necessary to enable individual to complete evaluation component. Typically, 45 minutes are spent face-to-face with the individual and/or family
97167	Occupational therapy evaluation, high complexity, requiring these components: An occupational profile and medical and therapy history, which includes review of medical and/or therapy records and extensive additional review of physical, cognitive, or psychosocial history related to current functional performance; An assessment(s) that identifies 5 or more performance deficits (ie, relating to physical, cognitive, or psychosocial skills) that result in activity limitations and/or participation restrictions; and Clinical decision making of high analytic complexity, which includes an analysis of the individual profile, analysis of data from comprehensive assessment(s), and consideration of multiple treatment options. Individual presents with comorbidities that affect occupational performance. Significant modification of tasks or assistance (eg, physical or verbal) with assessment(s) is necessary to enable individual to complete evaluation component. Typically, 60 minutes are spent face-to-face with the individual and/or family

# Considered Medically Necessary for the treatment of ASD when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
90785	Interactive complexity (List separately in addition to the code for primary procedure)
90832	Psychotherapy, 30 minutes with individual
90833	Psychotherapy, 30 minutes with individual when performed with an evaluation and management service (List separately in addition to the code for primary procedure)
90834	Psychotherapy, 45 minutes with individual
90836	Psychotherapy, 45 minutes with individual when performed with an evaluation and management service (List separately in addition to the code for primary procedure)
90837	Psychotherapy, 60 minutes with individual

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CPT®*	Description
Codes	
90838	Psychotherapy, 60 minutes with individual when performed with an evaluation and management service (List separately in addition to the code for primary procedure)

#### **Considered Not Medically Necessary for the assessment of ASD:**

HCPCS Codes	Description
S8035	Magnetic source imaging

## **Considered Not Medically Necessary for the treatment of ASD:**

CPT®*	Description
Codes	
64999††	Unlisted procedure, nervous system
99183	Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per session

# <sup>††</sup><u>Note</u>: Not Medically Necessary when used to report transcranial magnetic stimulation for autism.

HCPCS	Description
Codes	
G0277	Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval
J1459	Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g. liquid), 500 mg
J1556	Injection, immune globulin (Bivigam), 500 mg
J1557	Injection, immune globulin, (gammaplex), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1561	Injection, immune globulin, (Gamunex-C - Gammaked), nonlyophilized (e.g., liquid), 500 mg
J1566	Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg
J1568	Injection, immune globulin, (Octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), intravenous, non-lyophilized, (e.g., liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma DIF), intravenous, non-lyophilized (e.g., liquid), 500 mg
S9355	Home infusion therapy, chelation therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

# Considered Educational in Nature/Not Covered or Reimbursable for the assessment and/or treatment of ASD:

HCPCS Codes	Description
G0177	Training and educational services related to the care and treatment of individual's disabling mental health problems per session (45 minutes or more)

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HCPCS	Description
Codes	
H2027	Psychoeducational service, per 15 minutes
S9445	Individual education, not otherwise classified, non-physician provider, individual, per session
S9446	Individual education, not otherwise classified, non-physician provider, group, per session
T1018	School-based individualized education program (IEP) services, bundled

# Considered Not Medically Necessary when used to report multi-purpose, general consumer electronic devices:

HCPCS Codes	Description
E1399	Durable medical equipment, miscellaneous

#### Not Covered or Reimbursable when used to report for the assessment of ASD:

CPT®*	Description
Codes	
83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
95965	Magnetoencephalography (MEG), recording and analysis; for spontaneous brain magnetic activity (eg, epileptic cerebral cortex localization)
95966	Magnetoencephalography (MEG), recording and analysis; for evoked magnetic fields, single modality (eg, sensory, motor, language, or visual cortex localization)
95967	Magnetoencephalography (MEG), recording and analysis; for evoked magnetic fields, each additional modality (eg, sensory, motor, language, or visual cortex localization) (List separately in addition to code for primary procedure)
0063U	Neurology (autism), 32 amines by LC-MS/MS, using plasma, algorithm reported as metabolic signature associated with autism spectrum disorder
0263U	Neurology (autism spectrum disorder [ASD]), quantitative measurements of 16 central carbon metabolites (ie, a-ketoglutarate, alanine, lactate, phenylalanine, pyruvate, succinate, carnitine, citrate, fumarate, hypoxanthine, inosine, malate, S-sulfocysteine, taurine, urate, and xanthine), liquid chromatography tandem mass spectrometry (LC-MS/MS), plasma, algorithmic analysis with result reported as negative or positive (with metabolic subtypes of ASD)
0322U	Neurology (autism spectrum disorder [ASD]), quantitative measurements of 14 acyl carnitines and microbiome-derived metabolites, liquid chromatography with tandem mass spectrometry (LC-MS/MS), plasma, results reported as negative or positive for risk of metabolic subtypes associated with ASD

HCPCS	Description
Codes	
P2031	Hair analysis (excluding arsenic)

#### Not Covered or Reimbursable when used to report for the treatment of ASD:

CPT®* Codes	Description
90283	Immune globulin (IgIV), human, for intravenous use
92065	Orthoptic and/or pleoptic training, with continuing medical direction and evaluation

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HCPCS Codes	Description
G0176	Activity therapy, such as music, dance, art or play therapies not for recreation, related to the care and treatment of individual's disabling mental health problems, per session (45 minutes or more)
H2032	Activity therapy, per 15 minutes
S8940	Equestrian/hippotherapy, per session

<sup>\*</sup>Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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## **Revision Details**

Type of Revision	Summary of Changes	Date
Annual review	<ul> <li>Added policy statement for electronic devices</li> <li>Removed policy statements for:</li> </ul>	1/15/2025
	<ul> <li>audiological evaluation</li> <li>medical evaluation</li> <li>allergy testing</li> <li>celiac antibodies testing</li> <li>erythrocyte glutathione peroxidase studies</li> <li>event-related potentials (i.e., evoked potential studies)</li> <li>heavy metal testing</li> <li>immunologic or neurochemical abnormalities testing</li> <li>intestinal permeability studies</li> <li>micronutrient testing (e.g., vitamin level)</li> <li>provocative chelation tests for mercury</li> <li>stool analysis</li> <li>urinary peptides testing</li> </ul>	

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	<ul> <li>acupuncture</li> <li>auditory integration therapy</li> <li>cognitive rehabilitation</li> <li>craniosacral therapy</li> <li>dietary and nutritional interventions (e.g., elimination diets, vitamins)</li> <li>EEG biofeedback/neurofeedback</li> <li>facilitated communication</li> <li>secretin infusion</li> <li>social skills training</li> <li>Theory of Mind cognitive model</li> <li>weighted blanket/mattress technology</li> </ul>	
Focused review	<ul> <li>Revised policy statements.</li> <li>Removed policy statement for electronic devices.</li> </ul>	12/03/2023

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