Cigna Medical Coverage Policy

Subject: Autism Spectrum Disorders/Pervasive Developmental Disorders: Assessment and Treatment

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The following Coverage Policy applies to health benefit plans administered by Cigna companies. Coverage Policies are intended to provide guidance in interpreting certain standard Cigna benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2013 Cigna

Coverage Policy

Some benefit plans specifically exclude therapy and nonmedical ancillary services for learning disabilities, developmental delays, autism, and mental retardation or for care which is not restorative in
nature. In addition, many benefit plans specifically exclude behavioral training or services that are considered educational and/or training in nature. In benefit plans where these exclusions are present, services that are considered behavioral training or such as intensive behavioral interventions would not be covered.

In addition, coverage of intensive behavioral interventions and/or treatment of autism spectrum disorders (ASD) may be governed by state and/or federal mandates.

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

Aids or devices that assist with nonverbal communications, including but not limited to communication boards and prerecorded speech devices, are specifically excluded under many benefit plans. Therefore, speech generating devices that use prerecorded messages (HCPCS codes E2500-E2506) are generally not covered. If covered, coverage for speech generating devices is subject to the terms, conditions and limitations of the applicable benefit plan’s Durable Medical Equipment (DME) benefit and schedule of copayments. Please refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage. Under many benefit plans, coverage for DME is limited to the lowest-cost alternative.

Please refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage. Under some benefit plans, coverage for genetic screening and/or testing may be excluded or restricted.

Under many benefit plans formerly administered by Great-West Healthcare, speech therapy, occupational therapy, and physical therapy are only covered when the therapy services are performed for acute injuries, diseases or conditions and are expected to result in significant clinical improvement within two months.

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.

Assessment

Cigna covers the following services as medically necessary for the assessment of a suspected or known ASD:

- audiological evaluation
- behavioral health evaluation including psychiatric examination
- electroencephalogram (EEG) when there is suspicion of a seizure
- evaluation by speech and language pathologist
- lead screening
- medical evaluation including history and physical examination
- 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 code 96111, 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

Cigna covers behavioral health treatment (e.g., behavior modification, family therapy, or other forms of psychotherapy) for ASD as 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)
- 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 Cigna Coverage Policies on Speech/Language Therapy, Occupational Therapy and Physical Therapy for specific coverage criteria for these therapies.

Speech Generating Device

Cigna covers a speech generating device for ASD as medically necessary when ALL of the following criteria are met:

- The individual has a permanent and severe expressive speech impairment.
- A speech evaluation, conducted by a speech-language pathologist, has documented the severity of the individual’s disability, specific to their primary language.
- Speaking needs cannot be met using natural communication methods.
- Other forms of treatment have failed, are contraindicated, or are otherwise not appropriate.
- A speech generating device is available in the individual’s primary language
- A speech generating device is being requested for the sole purpose of speech generation.

Genetic Testing

Comparative genomic hybridization testing (chromosomal microarray analysis)

Cigna covers comparative genomic hybridization testing (chromosomal microarray analysis) as medically necessary in a child age 13 years or younger for ASD in which the phenotypic characteristics of a specific genetic disorder are absent.

Please refer to the Cigna Coverage Policy Comparative Genomic Hybridization Testing (Chromosomal Microarray Analysis) for Autism Spectrum Disorders, Developmental Delay, Intellectual Disability and Multiple or Unspecified Congenital Anomalies for specific coverage criteria of this test.

FMR1 Genetic Testing

Cigna covers confirmatory (diagnostic) genetic testing for FMR1 gene mutations as medically necessary with targeted mutation analysis and methylation analysis when fragile X is suspected in the presence of intellectual disability, developmental delay, or autism.

Cigna covers genetic testing for a known familial mutation (i.e., testing for the known familial variant) for FMR1 gene mutations as medically necessary for EITHER of the following indications:
• carrier status of a prospective biologic parent when there is an identified mutation in a blood relative and the couple has the capacity and intention to reproduce
• prenatal testing of a fetus (i.e., amniocentesis or chorionic villus sampling [CVS]) or preimplantation genetic diagnosis (PGD) testing when the mother is a known carrier of a disease-causing mutation in the FMR1 gene

Cigna covers genetic testing of FMR1 gene mutations as medically necessary with ANY of the following genetic testing methods when targeted mutation analysis and methylation analysis is negative and the clinical suspicion of fragile X syndrome remains high:

• deletion/duplication analysis
• sequence analysis

**MECP2 Genetic Testing**

Cigna covers confirmatory (diagnostic) genetic testing for MECP2 gene mutations as medically necessary with sequence analysis when a MECP2-related disorder is suspected.

Cigna covers genetic testing for a known familial mutation (i.e., testing for the known familial variant) for MECP2 gene mutations as medically necessary for EITHER of the following indications:

• preconception prenatal genetic testing to determine carrier status of a prospective biologic female parent when there is an identified mutation in a blood relative and the couple has the capacity and intention to reproduce
• prenatal testing of a fetus (i.e., amniocentesis or chorionic villus sampling [CVS]) or preimplantation genetic diagnosis (PGD) testing when the mother is a known carrier of a disease-causing mutation in the MECP2 gene.

Cigna covers genetic testing for MECP2 gene mutations as medically necessary with deletion/duplication analysis when sequence analysis is negative and the clinical suspicion of a MECP2-related disorder remains high.

**Not Covered Services**

Services that are considered primarily educational or training in nature or related to improving academic or work performance are not covered under many benefit plans. Cigna does not cover the following services for the assessment and/or treatment of ASD because they are primarily educational and training in nature (this list may not be all-inclusive):

• education and achievement testing
• educational interventions (e.g., classroom environmental manipulation, academic skills training and parental training)

Cigna does not cover neuropsychological testing for the assessment and/or treatment of ASD because such testing is considered educational in nature and not medically necessary.

Cigna does not cover 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, because they are not medical in nature.

Cigna does not cover ANY of the following procedures/services for the assessment and/or treatment of ASD because they are considered experimental, investigational or unproven for this indication (these lists may not be all-inclusive):

**Assessment:**

• allergy testing (e.g., food allergies for gluten, casein, candida, molds)
• celiac antibodies testing
• erythrocyte glutathione peroxidase studies
• event-related potentials (i.e., evoked potential studies)
• hair analysis
• heavy metal testing
• immunologic or neurochemical abnormalities testing
• intestinal permeability studies
• magnetoencephalography (MEG)
• micronutrient testing (e.g., vitamin level)
• mitochondrial disorders testing (e.g., lactate and pyruvate)
• provocative chelation tests for mercury
• stool analysis
• urinary peptides testing

Treatment:

• acupuncture
• art therapy
• auditory integration therapy
• chelation therapy
• cognitive rehabilitation
• craniosacral therapy
• dietary and nutritional interventions (e.g., elimination diets, vitamins)
• EEG biofeedback/neurofeedback
• equestrian therapy (hippotherapy)
• facilitated communication
• holding therapy
• hyperbaric oxygen therapy
• immune globulin therapy
• intensive behavioral interventions for autism (e.g., early intensive behavior intervention [EIBI] intensive behavior intervention [IBI], Lovaas therapy, applied behavior analysis [ABA])
• music therapy
• recreational therapy
• secretin infusion
• sensory integration therapy
• vision therapy

Cigna does not cover genetic screening for ASD in the general population because such screening is considered not medically necessary.

All individuals undergoing genetic testing for the above indications should have both pre- and post-test genetic counseling with a board-certified or board-eligible medical geneticist or a licensed or certified genetic counselor.

General Background

The essential features of autism spectrum disorder are persistent impairment in reciprocal social communication and social interaction and restricted, repetitive patterns of behavior, interests or activities. These symptoms are present from early childhood and limit or impair everyday functioning. Manifestations of the disorder vary greatly depending on the severity of the autistic condition, developmental level, and chronological age, which leads to the term spectrum. Autism spectrum disorder encompasses disorders previously referred to as early infantile autism, childhood autism, Kanner's autism, high-functioning autism, atypical autism, pervasive developmental disorder not otherwise specified, childhood disintegrative disorder, and Asperger's disorder (American Psychiatric Association, 2013)
In March 2012, the Centers for Disease Control and Prevention (CDC) published updated data regarding the prevalence of autism spectrum disorder (ASD). The CDC estimates that approximately one in 88 children has been identified with an ASD. ASDs are reported to occur in all racial, ethnic, and socioeconomic groups. ASDs are almost 5 times more common among boys (1 in 54) than among girls (1 in 252) (CDC, 2012).

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 (Miles, et al., 2003/2010). This is a field of active research.

Associations between ASD and a number of medical conditions have been proposed. Several other disorders are associated with ASD. These include (National Institute of Child Health and Human Development [NICHD], 2005a):

- Epilepsy or seizure disorder: Nearly one-third of those with autism also show signs of a seizure disorder.
- Tuberous sclerosis: Approximately six percent of those with autism also have this rare multi-systemic, genetic disease that causes noncancerous tumors to grow in the brain and other vital organs. It may result in symptoms that include: seizures, developmental delay, behavioral problems, skin abnormalities and kidney disease.
- Fragile X syndrome: About 2.1% of those with autism also have this condition that is the most common inherited form of intellectual disability.
- Intellectual disability: Approximately 25% of persons with autism also have some degree of intellectual disability.

**Diagnostic criteria for 299.00 Autism Spectrum Disorder from:**
Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, no exhaustive; see text of DSM-5)

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.

Specify current severity:

**Severity is based on social communication impairments and restricted, repetitive patterns of behavior.**

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, no exhaustive; see text of DSM-5):

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).

Specify current severity:
Severity is based on social communication impairments and restricted, repetitive patterns of behavior.

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 specified 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.

Assessment

It has been suggested that early identification and initiation of early interventions results in improved management for most children with ASD. Routine developmental surveillance should be conducted by all providers at every well-child visit. Indications for immediate evaluation of ASD include (Filipek, et al., 2000/2006/2010):

- no babbling or pointing or other gesture by 12 months
- no single words by 16 months
- no two-word spontaneous (not echolalic) phrases by 24 months
- any loss of any language or social skills during the preadolescent years

The evaluation for ASD often requires a multidisciplinary team approach and will be dependent on the impairments that are present. The team may include a pediatrician, psychiatrist, psychologist, neurologist, speech therapist, occupational therapist, and social worker. There is no specific test that can confirm a diagnosis of ASD. The evaluation must include the following (Tuchman, 2003; Filipek, et al., 2000/2006/2010):

- Clinical history: This includes parental report, family history, pregnancy, neonatal and developmental history of the child. Use of standardized questionnaires may be used.
- Clinical examination

The evaluation may include the following (Tuchman, 2003; Filipek, et al., 2000/2006/2010):

- audiologic evaluation
- communication assessment performed by speech and language pathologist
- assessment by occupational or physical therapist if there are motor deficits, motor planning or sensory dysfunction present
- lead screening should be performed, particularly when pica is present
- magnesium screening
- cognitive assessment

There is consensus that the following tests are not needed for the evaluation of ASD; however, they may be considered appropriate for the evaluation of associated conditions:

- Chromosome tests may be performed to detect a syndromic condition such as fragile-X or other genetic etiology.
- Metabolic tests may be needed if the history or examination suggest.
- Neuroimaging studies are indicated only if the child is a candidate for specific interventions (e.g., epilepsy surgery).
- Electroencephalogram (EEG) may be performed if there is suspicion of a seizure.
The American Academy of Neurology (AAN) and Child Neurology Society (CNS) have developed evidenced-based practice parameters for the screening and diagnosis of autism. These parameters include the following developmental and assessment screening instruments that may be used in the evaluation process (Filipek, et al., 2000/2006/2010):

- The Ages and Stages Questionnaire
- The BRIGNACE® screens
- The Child Development Inventories
- The Parents’ Evaluation of Developmental Status

The AAN/CNS practice parameters also note that screening for autism should be performed on all children failing routine developmental surveillance procedures and may include these tools (Filipek, et al., 2000/2006/2010):

- Checklist for Autism in Toddlers (CHAT): This test is used for children 18 months of age.
- Autism Screening Questionnaire: This test is used for children four years of age and older.

The AAN/CNS practice parameters noted that the Denver II (formerly the Denver Developmental Screening Test-Revised) is not recommended as a developmental screening tool for autism (Filipek, et al., 2000/2006/2010). It is also noted in the practice parameters that, “There is insufficient evidence to support the use of other 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 such as vitamin levels, intestinal permeability studies, stool analysis, urinary peptides, mitochondrial disorders (including lactate and pyruvate), thyroid function tests, or erythrocyte glutathione peroxidase studies” (Filipek, et al., 2000/2006/2010). The practice parameters note that recording of event-related potentials and magnetoencephalography currently are research tools and there does not appear to be evidence of routine clinical utility.

The American Academy of Pediatrics (AAP) guidelines for identification and evaluation of children with ASD recommend that surveillance for risk factors is performed at every preventive visit throughout childhood. When the surveillance yields concerns then developmental screening with autism-specific screening tools should be used (Johnson, et al., 2007/2010). Screening tools that include a direct clinical observation component have the benefit of providing some potentially more objective information, and aspects of behavior that parents may not have noticed can be sampled. The guidelines note that some measures, such as the Checklist for Autism in Toddlers (CHAT), Modified Checklist for Autism in Toddlers (M-CHAT), and Pervasive Developmental Disorder Screening Test-II Primary Care Screen were designed specifically for early detection of ASDs in young children. Other extended testing includes: Autism Behavior Checklist [ABC], Childhood Autism Rating Scale [CARS]). The guidelines note that autism specific screening should be performed at the 18-month visit.

It has been proposed that neuropsychological testing be used in the assessment of ASD and to assist with the educational planning process. The medical necessity for the standard use of neuropsychological testing in the assessment and/or management of ASD is not supported in the medical literature. The use of neuropsychological testing in these settings is primarily used for educational purposes and is not medically necessary for the assessment or treatment of the conditions.

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.

**Genetic Testing for Autism Spectrum Disorders (ASD)**

The cause of autism is not known, but it appears that there may be a wide variety of genetic and non-genetic causes. This has been an area of ongoing research regarding autism as a genetic condition. It has been estimated that there is a sibling recurrence risk of approximately 5% (2–8%) (Freitag, 2007). Although it is thought that there is a genetic cause, the identity and number of genes involved remain unknown (Muhle, et al., 2004). Research indicates that that there is no single biological or clinical marker for autism or that a single gene
is responsible for the condition (Santangelo and Tsatsanis, 2005). The wide phenotypic variability of the ASDs is thought to be due to the interaction of multiple genes within an individual's genome and the existence of distinct genes and gene combinations among those affected (Muhle et al., 2004). The exception is Rett's disorder, where mutations in the MECP2 gene are thought to be responsible for the majority of cases with this condition.

Genetic testing for the majority of patients will have a very low yield unless the family history, medical history, presence of intellectual disability, or dysmorphic or other findings on examination are suggestive of a diagnosable condition. Genetic counseling should assist in providing information to parents and children and estimate the recurrence risk. Conditions that may warrant genetic testing include situations where the results will directly impact clinical decision-making and/or clinical outcome, and the testing method is considered a proven method for the identification of a genetically-linked inheritable disease. The presence of dysmorphic features or other specific findings may suggest obtaining genetic screening for inherited metabolic disorders or chromosome analysis. It may be appropriate to perform genetic testing in the following situations:

- **MECP2-Related Disorders/Rett's disorder/Rett syndrome:** Molecular testing for MECP2 mutations is clinically available. Classic Rett syndrome is a progressive neurodevelopmental disorder primarily affecting girls. It is characterized by apparently normal psychomotor development during the first six to 18 months of life, followed by a short period of developmental stagnation, then rapid regression in language and motor skills, followed by long-term stability. The diagnosis of all MECP2-related disorders relies on molecular genetic testing. It is inherited in an X-linked dominant manner. It will usually result from either a de novo mutation in the child or inheritance of disease-causing mutation from one parent who has somatic or germline mosaicism. Testing is generally performed initially with sequence analysis has a mutation detection frequency of 80% for classic Rett syndrome and 40% for atypical Rett syndrome. When sequence analysis is negative, testing with deletion/duplication analysis can be performed and has a mutation detection frequency of 8% for classic Rett syndrome and 3% for atypical Rett syndrome (Christodoulou, 2012).

- **Fragile X syndrome/fragile X-associated disorders (FXD)** refers to a family of conditions all caused by changes in FMR1 gene. This is the most common cause of inherited intellectual disability and is due to a mutation on the X-linked FMR1 gene. A small percentage of children with autism will have fragile X syndrome; however, approximately 50% of children with this syndrome have autistic behaviors (Miles, et al., 2003/2010). More than 99% of individuals with fragile X syndrome have a loss-of-function mutation in the FMR1 gene (Saul, et al., 2012). Fragile X syndrome occurs in individuals with an FMR1 full mutation or other loss-of-function mutation and is nearly always characterized by moderate intellectual disability in affected males and mild intellectual disability in affected females. Because FMR1 mutations are complex alterations involving non-classic gene-disrupting alterations and abnormal gene methylation, affected individuals occasionally have an atypical presentation with an IQ above 70, the traditional demarcation denoting intellectual disability. Males with an FMR1 full mutation accompanied by aberrant methylation may have a characteristic appearance (e.g., large head, long face, prominent forehead and chin, protruding ears), connective tissue findings (joint laxity), and large testes after puberty (Saul, et al., 2012). Molecular genetic testing of FMR1 gene is appropriate for individuals of either sex with intellectual disability, developmental delay, or autism (Saul, et al., 2012). Targeted mutation analysis and methylation analysis have a mutation detection frequency for FMR1 of 99%–100%. Deletion/duplication analysis and sequence analysis have a mutation detection frequency of less than 1% and may be used when the targeted mutation analysis and methylation analysis are negative and clinical suspicion of the fragile X remains high (Saul, et al., 2012).

Chromosomal microarray analysis (CMA) includes comparative genomic hybridization (CGH) and single nucleotide polymorphism (SNP) arrays. CGH is a microarray based cytogenetic technology used for the detection of submicroscopic genomic copy number variations (CNVs: e.g., deletion and duplication) of DNA. Conditions that may warrant CGH testing include situations where the results will directly impact clinical decision-making and/or clinical outcome, and the testing method is considered a proven method for the identification of a genetically-linked inheritable disease. CGH is a recognized genetic test for individuals with diagnosed ASDs in which a specific genetic disorder is unknown.

Please refer to the Cigna Coverage Policy Comparative Genomic Hybridization Testing (Chromosomal Microarray Analysis) for Autism Spectrum Disorders, Developmental Delay, Intellectual Disability and Multiple or Unspecified Congenital Anomalies for further information regarding this type of testing.
Genetic Counseling
Genetic testing should be undertaken only after independent genetic counseling has been provided to patients in order to assist in complex clinical decision-making. Post-genetic testing counseling should be planned. The genetic counseling should be provided by an independent specialty-trained genetics professional such as a medical geneticist or a genetic counselor who is an American Board of Medical Genetics or American Board of Genetic Counseling certified genetic counseling professional who is unaffiliated with the genetic testing lab performing the test(s).

Treatment
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.

Communication deficits are often present with ASD; however, speech pathology treatment is considered behavioral and training in nature. When these deficits overlap with an impairment of speech due to a separate neurological cause, speech therapy may be medically necessary.

Occupational and physical therapy may be needed to address specific fine or gross motor deficits or a comorbid physical impairment when there is potential for functional improvement.

The Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review of therapies for children with autism spectrum disorders. The review was prepared by the Vanderbilt Evidence-based Practice Center (Warren, et al., 2011). The review included 183 articles, representing 159 unique studies. Thirteen studies were determined to be good quality, 56 were fair quality and 90 trials were 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 our 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.

- 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 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 patients 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.

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 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

- 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.

Pharmacologic Treatment: Pharmacological treatments may be useful in the treatment of ASD. Pharmacologic intervention should be targeted toward specific behaviors that significantly interfere with daily functions (Filipek, et al., 2006). 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 FDA states that the approval is the first for the use of a drug to treat behaviors associated with autism in children. These behaviors are included under the general heading of irritability and include aggression, deliberate self-injury, and temper tantrums (FDA, 2006). The medications used in the treatment of ASD may include, but are not limited to, the following groups (NICHD, 2005a):

- 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.
Secretin: Secretin has been proposed as a treatment for autism. Secretin is a hormone produced by the small intestine that assists in digestion. Secretin currently is approved by the U.S. Food and Drug Administration (FDA) for a single dose only for use in diagnosing digestive problems. The AACAP issued a policy statement on the use of secretin in the treatment of autism and noted that the available evidence does not suggest that secretin is a useful treatment for autism, and use of this medication remains unproven (AACAP, 2002).

Williams et al. (2012) reported on a Cochrane review of intravenous secretin for ASD, an update of a 2005 review. Randomized, controlled trials (RCT) of intravenous secretin compared to a placebo treatment in children or adults diagnosed with ASD were included, where at least one standardized outcome measure was reported. Sixteen studies, with over 900 children, met the inclusion criteria but for two of these, the only available multisite data were reported in press releases. All outcome data from the other 14 trials were continuous. Twenty-five established standardized outcome measures were reported to assess core features of ASD, communication, behavior, visuospatial skills, affect and adverse events. One standardized measure of global impression was also used. No more than four studies used any one outcome measure with a similar approach. Meta-analysis of data was not possible. There is now consistency of findings, with RCTs of the efficacy of secretin in autism not showing improvements for core features of ASD. The authors concluded that there is no evidence that single or multiple dose intravenous secretin is effective and as such currently it should not be recommended or administered as a treatment for ASD.

Krishnaswami et al. (2011), reported on a systematic review of the evidence regarding the use of secretin in children with ASDs who are aged 12 years and younger. Evidence from seven randomized controlled trials supports a lack of effectiveness of secretin for the treatment of ASD symptoms including language and communication impairment, symptom severity, and cognitive and social skill deficits. No studies have resulted in significantly greater improvements in measures of language, cognition, or autistic symptoms when compared with placebo; study authors who reported improvement over time did so equally for both the intervention and placebo groups.

Toda et al. (2006) conducted a single-blind crossover study to evaluate the clinical effects of intravenously administered secretin in 12 children with autism. Association between improvement in symptoms and changes in cerebrospinal fluid (CSF) were measured. After administration of secretin, the Autism Diagnostic Interview-Revised (ADI-R) score improved in seven of the 12 children. Behaviors were evaluated before administration and two, four, six, and eight weeks after the administration. The score deteriorated in two of the 12 children. Elevation in the levels in CSF was noted with improvement in the ADI-R score. The authors theorized that that these findings suggest that secretin activated metabolic turnover of dopamine in the central nervous system, thereby improving symptoms. They noted that, in the future, the detailed mechanism of this effect should be further investigated.

Sandler et al. (1999) conducted a double-blind placebo-controlled trial of a single dose of secretin in 60 children with ASD. The children were randomly assigned to receive a single intravenous infusion of secretin or a placebo of saline. Fifty-six children completed the study. As compared with the placebo, secretin treatment was not associated with significant improvement in any of the outcome measures. The authors concluded that a single dose of secretin is not an effective treatment for ASD. In 2003, Levy et al. conducted a randomized, crossover, double-blind and placebo-controlled trial of a single intravenous dose of human synthetic secretin involving 62 subjects. Sixty-one children completed the study. Compared with placebo, secretin treatment was not associated with significant improvement measured with the Communication and Symbolic Behavior Scale (CSBS). Five children showed clinical improvement in standard scores: two after the secretin and three after placebo.

Acupuncture: Acupuncture is a procedure where specific body areas the meridian points, are pierced with fine needles for therapeutic purposes. It is theorized that by stimulating various meridian points acupuncture may be able to correct the disharmony and dysregulation of organ systems, which might be involved in various dimensions of ASD, relieve symptoms and restore the mind and body (Cheuk, et al., 2011). A Cochrane review was conducted to determine the effectiveness of acupuncture for ASD (Cheuk, et al., 2011). The review included 10 randomized and quasi-randomized controlled trials that involved 390 children with ASD. The duration of treatment ranged from four weeks to nine months. Two trials compared needle acupuncture with sham acupuncture and found no difference in primary outcome of core autistic features, although results suggested needle acupuncture might be associated with improvement in some aspects of the secondary
outcomes of communication and linguistic ability, cognitive function and global functioning. Six trials that compared needle acupuncture plus conventional treatment with conventional treatment alone used different primary outcome measures and most could not demonstrate effectiveness of acupuncture in improving core autistic features in general. Four trials reported some adverse effects; though there was little quantitative information, and at times both intervention and control groups experienced them—the adverse effects included bleeding, crying due to fear or pain, irritability, sleep disturbance and increased hyperactivity. The limitations included the trials were few in number and included only children; six trials were at high risk of bias; they were heterogeneous in terms of participants and intervention; they were of short duration and follow-up; inconsistent and imprecise results were reported, and due to carrying out large numbers of analyses they were at risk of false positivity. The authors concluded that the current evidence does not support the use of acupuncture for treatment of ADS and that there is no conclusive evidence that acupuncture is effective for treatment of ADS in children. Further high quality trials of larger size and longer follow-up are needed.

**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 therapy has not been demonstrated in the published peer-reviewed scientific literature.

**Auditory Integration Training (AIT):** AIT refers to listening to music that has been computer-modified to remove frequencies to which an individual demonstrates hypersensitivities and to reduce the predictability of auditory patterns. A special device is used to modify the music for the treatment sessions. Auditory thresholds are determined via audiograms. The audiogram is then reviewed for evidence of hyperacusis (i.e., an abnormal sensitivity to sound). A clinical history of sound sensitivities and behavior is also reviewed. Audiograms are repeated midway and at the end of the training session to document progress and to determine whether further treatment sessions are necessary. AIT is usually provided by a speech-pathologist or audiologist. This treatment has been proposed for improving abnormal sound sensitivity in individuals with behavioral disorders, including autism spectrum disorders. Evidence supporting the use of this technique is limited, thus the role of AIT in the treatment of ASD has not been established.

A comparative effectiveness review of therapies for children with autism spectrum disorders was published by the Agency for Healthcare Research and Quality (AHRQ), prepared by the Vanderbilt Evidence-based Practice Center (Warren, et al., 2011). Among the allied health therapies in the review were sensory and auditory integration therapy and it was found that the research provided little support for their use. Specifically, two fair-quality studies of auditory integration showed no improvement associated with treatment.

A Cochrane review was conducted with the objective of determining the effectiveness of AIT or other methods of sound therapy in individuals with autism spectrum disorders (Sinha, et al., 2004). Six randomized controlled trials of AIT were identified, including one crossover trial. Four trials had fewer than 20 patients involved in the study. Seventeen different outcome measures were used. It was noted in the review that due to the high heterogeneity or presentation of data in unusable forms, a meta-analysis was not possible. It was noted that three studies did not demonstrate benefit of AIT over the control conditions. Three trials reported improvements at three months for the AIT group with the Aberrant Behavior Checklist (ABC), which is of questionable validity. The reviewers concluded, “Further research is needed to determine the effectiveness of sound therapies. In the absence of evidence, the treatment must be considered experimental and care must be taken not to risk hearing loss” (Sinha, et al., 2004).

Several professional organizations have determined that evidence is insufficient regarding the efficacy of AIT. The American Speech-Language-Hearing Association (ASHA) prepared an evidenced-based technical report regarding AIT treatment (ASHA, 2004). They noted that, despite approximately one decade of practice, this method has not met scientific standards for efficacy and safety that would justify its inclusion as a mainstream treatment for a variety of communication, behavioral, emotional and learning disorders. The American Academy of Audiology (AAA) has published a position statement regarding AIT (AAA, 1993). The statement notes that, “that there are no published results of peer-reviewed studies using controlled populations and using scientific methods that demonstrated whether this auditory training program provides significant improvement in any dimension for any population.” It is also noted that the organization believes this training to be entirely investigational, and further research is needed to demonstrate the efficacy. The Educational Audiology Association (EAA) issued a position statement regarding AIT (EAA, 1997). They stated that “Auditory integration therapy has not been proven to be a viable treatment for any disability. Only inconsistent, uncontrolled anecdotal evidence has been provided to support claims of changes in auditory performance.” In addition, the
position statement noted that without controls to protect against excessively loud auditory stimuli, AIT may cause harm to the auditory system. The American Academy of Pediatrics (AAP) has published a statement regarding two treatments proposed for autism (i.e., AIT and facilitated communication) (AAP, 1998/2010). They have noted that as yet there are no good controlled studies to support the use of AIT for children with autism. It is also noted that until further information is available, the use of these treatments does not appear warranted at this time, except within research protocols.

**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 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 Speech-Language-Hearing Association (ASHA) notes in their guidelines for speech-language pathologists in the diagnosis, assessment, and treatment of ASDs note that, “Decisions about the integration of modes of communication (e.g., spoken language, gestures, sign language, picture communication, speech generating devices [SGDs], and/or written language) should be individualized according to specific capabilities and contexts of communication, as well as cultural issues.” (ASHA, 2006b) ASHA also notes, the available research literature does not predict which forms of AAC will be most beneficial for which individuals with ASD (ASHA, 2006a).

A speech evaluation is performed in order to determine the severity and motor deficit of each individual. This evaluation is conducted by a speech-language pathologist (SLP). The evaluation consists of: a case history, the examination of the oral mechanism during nonspeech activities, an assessment of perceptual speech characteristics, an assessment of intelligibility, and acoustic physiological analyses. The SLP will be able to determine, based on these factors and on the natural course of the disease or condition, when a speech generating device or treatment is necessary and what type of device or treatment would best meet the needs of the specific patient in question. Upon completion of the evaluation, a speech generating device may be recommended according to the permanence and severity of expressive speech impairment, as well as the short- and long-term goals for these individuals.

For further information regarding speech generating devices, please refer to the Cigna Coverage Policy for Speech Generating Devices.

**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). There is insufficient evidence in the peer-reviewed literature regarding the efficacy of chelation therapy for treatment of ASD.

**Cognitive Rehabilitation:** Cognitive rehabilitation has been proposed as an intervention for ASD. This therapy involves a systematic, goal-oriented treatment program designed to improve cognitive functions and functional abilities, and increase levels of self-management and independence following neurological damage to the central nervous system. It is primarily used in rehabilitation of traumatic brain injury and stroke. There is insufficient evidence in the published medical literature to support the use of cognitive rehabilitation for ASD.

**Craniosacral Therapy:** Craniosacral therapy is a form of massage that involves using gentle pressure on the plates of the patient’s skull. It is considered a complementary and alternative medicine (CAM) intervention. There is a lack of evidence that supports the efficacy of this treatment for ASD and it would be considered unproven.
**Dietary and Nutritional Interventions:** Various dietary interventions involving elimination diets, nutritional supplements and vitamins have been proposed for treatment of ASD. These include gluten and casein-free diets, a ketogenic diet, and providing diet supplements with vitamin B6 and magnesium (B6-Mg). There is insufficient evidence in the published, peer-reviewed medical literature to support the use of dietary and nutritional interventions in the management of ASD.

The proposal of a gluten and/or casein-free diet is based on the thought that the peptides from gluten and casein may have a role in the physiology of autism and that a diet free from these substances may reduce the symptoms associated with the condition. Millward et al. (2004) conducted a Cochrane review to examine the effectiveness of gluten and/or casein-free diets on symptoms of individuals with ASD. Only one trial met inclusion criteria. This trial was a small, single-blinded trial of combined gluten and casein-free diet versus a normal diet. It was noted that three of the four outcomes (i.e., cognitive skills, linguistic ability and motor ability) that were reported on were not significant; however, the fourth outcome, reduction in autistic traits did show a significant beneficial treatment effect for the combined gluten and casein-free diet. The authors concluded that, “Though the results of one small trial adds weight to the existing anecdotal evidence for a gluten and/or casein-free diet for autism, there is not yet sufficient evidence for clinicians to advise the use of such diets in cases of autistic spectrum disorder” (Millward, et al., 2004). In 2008, an update to the 2004 Cochrane review was published (Millward, et al., 2008). A second study was identified and included in the review—a small pilot, randomized, crossover trial with 15 children. There was not sufficient homogeneity of outcomes to perform a meta-analysis. In the second study there was no significant difference between the diet and control group for outcomes which were reported on the Childhood Autism Rating Scale (CARS). The authors note the second trial did appear to be well-designed and provides a blueprint for future studies in this area.

Another dietary intervention, the use of ketogenic diets, has also been proposed. A study regarding this intervention (Erickson, et al., 2005) included 30 autistic children, all concurrently taking haloperidol on a ketogenic diet. The study found that 60% of the children tolerated the diet and, within this group, improvement was noted on the Childhood Autism Rating Scale, with the less severely impaired children showing more improvement. Since the study lacked a control group, it is difficult to interpret the results.

Interventions utilizing vitamin B6 and magnesium (B6-Mg) have been proposed. A Cochrane review was conducted to determine the efficacy of B6-Mg to treat the social, communication, and behavioral responses of children and adults with ASD (Nye and Brice, 2005). Nineteen studies were identified; however, only three studies were included in the review. The three studies each included a small number of participants. The reviewers concluded that due to the small number of studies, the methodological quality of studies, and the small sample size, no recommendation can be made regarding the use of B6-Mg as a treatment for autism. The review noted that there is insufficient evidence to demonstrate treatment efficacy.

**EEG Biofeedback/neurofeedback:** is electroencephalogram (EEG) biofeedback, also called neurofeedback or neurotherapy, is a form of biofeedback which measures alpha (associated with relaxation and meditation) and theta (associated with focused attention) brainwave activity. It is proposed to counterbalance genetic and environmental tendencies by learning to alter brain wave patterns. EEG biofeedback has been proposed for the treatment of ASD. The evidence in the published peer-reviewed scientific literature does not support the efficacy of EEG biofeedback.

**Equestrian Therapy:** Equestrian therapy, also referred to as 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, posture, coordination, the development of a positive attitude and a sense of accomplishment. There is insufficient published evidence regarding the effects of this therapy in children with ASD.

**Facilitated Communication (FC):** This treatment is a method of providing assistance to a nonverbal person in typing out words using a typewriter, computer keyboard, or other communication device. FC involves supporting the individual’s hand to make it easier for him or her to indicate the letters that are chosen sequentially to develop the communicative statement. Proponents claim that this manual prompting by a trained facilitator provides expressive language abilities in a wide range of individuals, including those with severe intellectual disabilities or autism. FC has been at the center of a growing controversy, because several scientific studies have suggested that facilitators may unintentionally influence the communication, perhaps to the extent of actually selecting the words themselves. The scientific literature indicates many controlled studies with consistently negative findings, indicating that the technique is neither reliably replicable nor valid.
Several professional organizations have published statements regarding FC that indicates this treatment is unproven. The AAP has published a statement regarding two treatments proposed for autism: AIT and facilitated communication. According to the AAP, there is good scientific data showing FC to be ineffective; therefore, its use does not appear warranted at this time (AAP, 1998/2010). The AACAP published a policy statement regarding facilitated communication that notes that studies have repeatedly shown that FC is not a scientifically valid technique for individuals with autism or intellectual disability and that “In particular, information obtained via (FC) should not be used to confirm or deny allegations of abuse or to make diagnostic or treatment decisions” (AACAP, 1993/2008). The American Psychological Association (APA) has adopted the position that facilitated communication is a controversial and unproven communicative procedure with no scientifically demonstrated support for its efficacy (APA, 1994).

**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 patient breathes 100% oxygen at pressures greater than normal atmospheric (sea level) pressure. This treatment has been proposed as a treatment for ASD. The Agence d’évaluation des technologies et des modes d’intervention en santé (AETMIS) reviewed the published scientific data and current studies to determine the therapeutic potential of HBO for the treatment of autism. The review included three case series, one randomized controlled trial and five unpublished studies. The studies were limited by small patient populations (n=10–60) and variations in the oxygen and pressure parameters. Although the studies seemed to indicate a reduction in autism symptoms, AETMIS concluded that “there is insufficient evidence to build a strong case for the efficacy of hyperbaric oxygen therapy in the management of autistic disorders” (AETMIS, 2007). In 2008, AETMIS published an update to their recommendations for the indications for HBO and noted that the role of HBO remains experimental treatment for autism (AETMIS, 2008).

Ghanizadeh (2012) reported on a systematic review of the treatment of children with autism with hyperbaric oxygen therapy. The review found two randomized, double-blind, 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.

Jepson et al. (2011) reported on the effect of HBOT on 11 topographies of behavior, representing a wide sample of behaviors characteristics of autism, across five replications of multiple baselines, in 16 children with autism. The study found no consistent effects (positive or negative) observed as a result of the treatment.

Rossignol et al. (2009) performed a multicenter, randomized, double-blind, controlled trial to assess the efficacy of hyperbaric treatment in children with autism. The study included 62 from 6 centers. They were randomly assigned to 40 hourly treatments of either hyperbaric treatment or slightly pressurized room air. Outcome measures included Clinical Global Impression (CGI) scale, Aberrant Behavior Checklist (ABC), and Autism Treatment Evaluation Checklist (ATEC). After 40 sessions, mean physician CGI scores improved in the treatment group compared to controls in overall functioning (p=0.0008), receptive language (p<0.0001), social interaction (p=0.0473), and eye contact (p=0.0102). Nine children (30%) in the treatment group were rated as "very much improved" or "much improved" compared to two (8%) of controls (p=0.0471); 24 (80%) in the treatment group improved compared to 10 (38%) of controls (p=0.0024). Mean parental CGI scores significantly improved in the treatment group compared to controls in overall functioning (p=0.0336), receptive language (p=0.0168), and eye contact (p=0.0322). On the ABC, significant improvements were observed in the treatment group in total score, irritability, stereotypy, hyperactivity, and speech (p<0.03 for each), but were not seen in the control group. In the treatment group compared to the control group, mean changes on the ABC total score and subscales were similar except a greater number of children improved in irritability (p=0.0311). On the ATEC, sensory/cognitive awareness significantly improved (p=0.0367) in the treatment group compared to the control group.

Rossignol et al. (2007) reported on a prospective study of 18 children with autism who were treated with HBOT at atmospheric pressures and oxygen concentrations to determine the effects of HBOT on oxidative stress.
markers before and after the treatment and to determine the impact of HBOT on an inflammatory marker (C-reactive protein). The children underwent 40 hyperbaric sessions of 45 minutes duration. Neither group showed statistically significant changes in mean plasma GSSG levels, which appeared to indicate that intracellular oxidative stress appears unaffected by either regimen. There was a trend towards improvement in mean CRP noted in both groups. The largest improvements were observed in children with initially higher elevations in CRP. When all 18 children were pooled, a significant improvement in CRP was noted (p= 0.021). Pre- and post-parenteral observations indicated statistically significant improvements in both groups, including motivation, speech, and cognitive awareness (p< 0.05). In 2006, Rossignol and Rossignol reported on a retrospective case series of 6 children, aged 2 to 7 years, diagnosed with autism and treated with low-pressure hyperbaric oxygenation. The patients received treatment 40 1-hour sessions of HBOT at 1.3 atmospheres absolute and 28% to 30% oxygen. One patient completed only 25 sessions but was included in the analysis. Three parent-reported behavior evaluation instruments were used to measure outcomes. Modest improvement was noted in all scoring systems, with greater changes recorded for the younger children.

Data provided by these studies is preliminary and is insufficient to support HBO as a treatment for ASD.

**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 AAP’s technical report on the pediatrician’s role in the diagnosis and management of ASD notes that larger controlled investigations would be needed to assess this kind of treatment; however, there is no scientific evidence to justify the use of infusions of immune globulin to treat children with ASD (AAP, 2001). The published literature does not demonstrate the efficacy of IVIG for treatment of ASD.

**Intensive Behavioral Interventions:** Intensive behavioral interventions or programs are also 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 start of these programs was in the 1980s, as researchers began to report positive outcomes of early intensive behavior intervention programs, including increases in developmental levels, gains in intelligence quotient (IQ) scores, improvements in social behavior, and decreases in signs of autism. These programs incorporated behavior modification and applied behavior analysis. Behavior analysis is a behavioral assessment of the child and environmental conditions that may be used to help the child develop higher skills through behavioral procedures. These methods are based on research in the application of learning principles to the education of autistic children and incorporate behavior modification, training and education. Procedures that strengthen desired behaviors and/or decrease undesirable behaviors are used as part of an individualized intervention plan. The programs are increasingly prescribed by school systems as an intervention that is part of the individualized educational plan (IEP). In younger children these treatments may also be provided in the home. 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.

Intensive intervention programs other than those that focus on behavior analytic treatment have also been developed. These include, but are not limited to:

- **TEACCH program:** The TEACCH program (Treatment and Education of Autistic and Related Communication Handicapped Children) is an educational intervention focused on improving motor coordination and cognitive skills and has been implemented in many special education programs for autistic children. It includes behavioral analytic approaches for some skills but uses other interventions as well.

- **Denver Model:** The focus of the Colorado Health Sciences program (Denver Model) is learning through play based on Piaget and object relations theories. Behavior analytic techniques are included for behavior management.

- **Rutgers program:** The Rutgers program is known as the Douglas Developmental Disabilities Center (based at Rutgers University), has three programs small-group segregated preschool, and integrated preschool and intensive home-based intervention, and uses ABA techniques and similarities to the Lovaas program. Families are trained in the program and provide the treatment when they are available and or hire staff trained in the program.
• Learning Experiences and Alternative Program (LEAP): LEAP program includes both a preschool program and a behavioral skill training program for parents, as well as national outreach activities. The program includes an individualized curriculum that targets goals in social, emotional, language, adaptive behavior, cognitive, and physical developmental areas (National Research Council [NRC], 2001).

• Relationship Development Intervention (RDI): RDI is a program designed to empower and guide parents of children, adolescents and young adults with ASD and similar developmental disorders to function as facilitators for their children’s mental development (Gutstein, 2009). RDI is based on instructing the parents to have an important role in improving critical emotional, social and meta-cognitive abilities through carefully graduated, guided interaction in daily activities.

• Floortime: this is also referred to as DIR® (Developmental, Individual Difference, Relationship-based model), DIR® Floortime, or Greenspan Floor-Time Model. This is a developmentally-based, one-on-one treatment program delivered 10 to 25 hours per week. The primary intervention method used in this model is intensive interactive “floor-time” play sessions, in which an adult follows a child’s lead in play and interaction. The program consists of three components: home-based play sessions, individual therapies, and early education programs. The intense floor-time sessions at home are intended to help children reach what has been described as the key elements of early development: self-regulation and shared attention, engagement and relating, two-way intentional communication, problem solving, symbolic and creative use of ideas, and logical and abstract use of ideas and thinking. Parents or caregivers typically participate in the floor-time sessions. The program may also involves speech, occupational, and physical therapists; educators; and/or psychotherapists who work one-on-one with the child using specialized techniques informed by floor-time principles to deal with the child’s specific challenges (ECRI, 2011)

• Pivotal Response Therapy: This is also known as Pivotal Response Treatment (PRT)®, Pivotal Response Training®, Pivotal Response Teaching® or Pivotal Response Intervention. It is a behavioral intervention model based on the principles of ABA. The treatment focuses on altering gateway/pivotal behaviors considered central to broad areas of functioning and in which improvements would lead to improvements in behaviors; pivotal behaviors include motivation to initiate or and respond to stimuli, self-direction of behavior, and responsiveness to cues/stimuli; typically involves extensive parent/family training components (Warren, et al., 2011).

While there are published studies regarding the effectiveness of intensive behavioral interventions for ASD, they are limited by small size and insufficient length of follow-up time. The majority of the studies are non-randomized. Due to quality of published studies no conclusion can be drawn regarding the effectiveness of this treatment. There is insufficient evidence in the published medical literature to demonstrate the long-term effectiveness and impact on health outcomes of intensive early intervention programs for children with autism. The effectiveness of specific intervention strategies, the duration and intensity of the interventions and the characteristics of children who respond have not been established.

Please refer to the Cigna Coverage Policy on Intensive Behavioral Interventions for further information regarding this treatment.

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 (Ball, 2004).

Gold et al. (2006) conducted a Cochrane review to evaluate the effects of music therapy for individuals with autistic spectrum disorders. Three small studies (n=24) were included in the review. The studies examined the short-term effect of brief music therapy interventions (daily sessions over one week) for children with autism. Music therapy was superior to placebo therapy with respect to verbal and gestural communications skills. The effect on behavioral problems was not significant. The authors concluded that the studies were of limited applicability to clinical practice; the findings indicate that music therapy may help children with ASD to improve their communicative skills and that further research is needed to examine whether the effects of music therapy are enduring and to investigate the effects of music therapy in typical clinical practice.

A review done by the Wessex Institute of Health Research and Development (Ball, 2004) noted that children with ASD may demonstrate slight improvement in speech and imitation during music therapy sessions, but the
clinical importance of these changes may be negligible. The review also noted that the impact on behavior or social interaction outside the sessions is unclear, as are any long-term effects. The report concluded that there was insufficient evidence regarding the effects of music therapy on behavior in children with ASD.

**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 of ASD. The effectiveness of this therapy has not been demonstrated in the published peer-reviewed scientific literature.

**Sensory Integration Treatment:** Sensory integration treatment (SIT) has been proposed as a treatment for ASD. This treatment has been proposed as a method to improve the way the brain processes and organizes external stimuli, such as touch, movement, body awareness, sight and sound. The therapy is usually performed by occupational or physical therapists. Pfeiffer et al. (2011) reported on a randomized study to address the effectiveness of sensory integration (SI) intervention in children with ASD. The children were randomized to SI intervention or fine motor intervention and received three sessions per week for six weeks. The study included 21 children diagnosed with autism and 16 with PDD-NOS. Pretests and posttests measured social responsiveness, sensory processing, functional motor skills, and social–emotional factors. Results identified significant positive changes in Goal Attainment Scaling scores for both groups; more significant changes occurred in the SI group, and a significant decrease in autistic mannerisms occurred in the SI group. No other results were significant. The results are preliminary and further research is needed.

The American Academy of Pediatrics (AAP) published a policy statement regarding sensory integration therapies for children with developmental and behavioral disorders (AAP, 2012). The report included the following recommendations:

- At this time, pediatricians should not use sensory processing disorder as a diagnosis. When these sensory symptoms are present, other developmental disorders—specifically, autism spectrum disorders, attention deficit/hyperactivity disorder, developmental coordination disorder, and anxiety disorder—must be considered and thoroughly evaluated, usually by appropriate referral(s) to a developmental and behavioral pediatrician, child psychiatrist, or child psychologist.
- Pediatricians should recognize and communicate with families about the limited data on the use of sensory-based therapies for childhood developmental and behavioral problems.
- If the pediatrician is managing a child whose therapist is using sensory-based therapies, the pediatrician can play an important role in teaching families how to determine whether a therapy is effective.
  - Help families design simple ways to monitor effects of treatment (e.g., behavior diaries, pre-post behavior rating scales). Help the family be specific and create explicit treatment goals, designed at the onset of therapy, focused on improving the individual's ability to engage and participate in everyday activities (e.g., ability to focus, tolerate foods, and be in a room with loud noises).
  - Set a time limit for seeing the family back to discuss whether the therapy is working to achieve the stated goals.
- Pediatricians should inform families that occupational therapy is a limited resource, particularly the number of sessions available through schools and through insurance coverage. The family, pediatrician, and other clinicians should work together to prioritize treatment on the basis of the effects the sensory problems have on a child’s ability to perform daily functions of childhood.

Dawson and Watling (2000) conducted a systematic review of the research regarding the effectiveness of interventions for sensory and motor abnormalities in autism. Four studies on the effectiveness of sensory integration therapy in autism that utilized objective measures of behavior to assess outcome were found. All but one had a sample size of fewer than six subjects. None of the studies had a comparison group. One study that had a larger sample size and better design found no change in vocal behavior following brief participation in sensory activities. The review concluded that although sensory and motor impairments are commonly found in autism, the interventions developed to address them have not been well validated. In the case of SIT, it was noted, “there exist so few studies that conclusions cannot be drawn” (Dawson and Watling, 2000). Little is known regarding which ages or subgroups of individuals are most likely to benefit from therapies addressing sensory and motor difficulties, and further research is recommended.

The NRC Committee on educational intervention for children with autism assessment concluded that there is insufficient evidence of the effectiveness of SIT for autism. It is noted in the report that there is a paucity of research concerning SIT for autism and that these interventions have not yet been supported by empirical
there is insufficient evidence found in the published scientific literature regarding the efficacy of SIT in children with autism.

**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 (NRC, 2001). Studies in the published scientific literature have not provided clear support for this treatment of ASD.

**Professional Societies/Organizations**

**American Academy of Child and Adolescent Psychiatry (AACAP):** The AACAP updated their practice parameters for the assessment and treatment of children and adolescents with autism spectrum disorders. These guidelines are found at the AACAP website, are noted to be in press and not yet published. The guidelines include the following regarding assessment (AACAP, 2013):

- The developmental assessment of young children and the psychiatric assessment of all children should routinely include questions about autism spectrum disorder symptomatology (CS).
- If the screening indicates significant autism spectrum disorder symptomatology, a thorough diagnostic evaluation should be performed to determine the presence of ASD (CS).
- Clinicians should coordinate an appropriate multi-disciplinary assessment of children with ASD [CS].

**Recommendations for treatment include:**

- The clinician should help the family obtain appropriate, evidence-based and structured educational and behavioral interventions for children with ASD (CS).
- There is a lack of evidence for most other forms of psychosocial intervention, though cognitive behavioral therapy (CBT) has shown efficacy for anxiety and anger management in high functioning youth with ASD.
- Studies of sensory oriented interventions, such as auditory integration training (AIT), sensory integration therapy (SIT) and touch therapy/massage, have contained methodological flaws and have yet to show replicable improvements.
- There is also limited evidence thus far for what are usually termed developmental, social-pragmatic models of intervention, such as Developmental-Individual Difference-Relationship Based (DIR)/Floortime, Relationship Development Intervention (RDI), Social Communication Emotional Regulation and Transactional Support (SCERTS) and Play and Language for Autistic Youths (PLAY), which generally use naturalistic techniques in the child’s community setting to develop social communication abilities.
- Pharmacotherapy may be offered to children with ASD where there is a specific target symptom or comorbid condition (CS).
- The clinician should maintain an active role in long term treatment planning and family support as well as support of the individual (CS).
- Clinicians should specifically inquire about the use of alternative/complementary treatments, and be prepared to discuss their risk and potential benefits (CS).

*evidence base for practice parameters:*

Recommendations for best assessment and treatment practices are stated in accordance with the strength of the underlying empirical and/or clinical support, as follows:

Clinical Standard (CS) is applied to recommendations that are based on rigorous empirical evidence (e.g., meta-analyses, systematic reviews, individual randomized controlled trials) and/or overwhelming clinical consensus.

**Technical Expert Panel (TEP) and HRSA Autism Intervention Research–Behavioral (AIR-B) Network:** TEP published recommended guidelines and further research needs for nonmedical interventions for children with ASD based on evidence and the expert panel (Maglione, et al., 2012). The TEP included practitioners, researchers, and parents. The report notes that the strength of evidence of efficacy varied by intervention type from insufficient to moderate, with none reaching high strength. The evidence included studies with a sample size of at least 10; control group not necessary and observational studies were included. The scientific literature
is not clear as to which individual participant characteristics are associated with success of various approaches. The TEP noted that:

- According to commonly accepted standards, the evidence that comprehensive intervention programs, often referred to as “intensive” interventions, are effective at improving core deficits of ASD is moderate strength. Even though controlled studies have been conducted, few have randomly selected their subjects or enrolled large samples. Several meta-analyses of programs based on applied behavioral analysis or the Lovaas method have been conducted to increase statistical power; they have found promising results in the areas of language, adaptive skills, and IQ.
- Evidence is insufficient to suggest the superiority of one behavioral curriculum over others. There is moderate evidence that greater intensity of treatment (hours per week) and greater duration (in months) lead to better outcomes.
- Regarding developmentally based intensive programs and environmental programs such as TEACCH, the strength of evidence is lower.
- Overall, autonomous social skills programs for high-functioning children and adolescents have a moderate strength of evidence of efficacy; however, our analyses could not determine which approaches, settings, and modalities were superior.
- For children with little or no verbal language, the Picture Exchange Communication System (PECS) has moderate strength of evidence of efficacy, and no controlled trials or uncontrolled observational studies of augmentative communication devices were identified.
- Auditory integration training was found ineffective in four of five.

The review identified future research priorities:

- There was significant heterogeneity in outcome measures used in trials of interventions for ASD. Research priority: assessment and monitoring of outcomes
- The needs of preverbal children may differ considerably from those of verbal children, but exiting studies rarely focus on preverbal children (or minimally verbal or nonverbal). Research priority: understanding and addressing the needs of pre-verbal and nonverbal individuals with ASD.
- The appropriate intensity, duration and type of program for adolescents with ASDs cannot be determined from the current literature, since few studies report on interventions for this age group. Research priority: understanding and addressing the needs of adolescents and adults with ASDs.
- While some reviews found that applied behavioral analysis is a highly effective component of a comprehensive intervention in addressing IQ and communication skills, it is unclear which other components affect which specific core deficits. Research priority: Identifying the most effective strategies to impact the specific core deficits of ASDs.
- Comparative effectiveness studies of different intensities and durations of ASD interventions are relatively lacking from the existing literature, but are important. Research priority: Identification of the most effective dose and duration of interventions.

Use Outside of the US
National Institute for Health and Clinical Excellence (NICE): NICE published guidelines for the management and support of children and young people on the autism spectrum (NICE, 2013). The recommendations for treatment include:

Psychosocial interventions

- Consider a specific social-communication intervention for the core features of autism in children and young people that includes play-based strategies with parents, carers and teachers to increase joint attention, engagement and reciprocal communication in the child or young person. Strategies should:
  - be adjusted to the child or young person's developmental level
  - aim to increase the parents', carers', teachers' or peers' understanding of, and sensitivity and responsiveness to, the child or young person's patterns of communication and interaction
  - include techniques of therapist modeling and video-interaction feedback
  - include techniques to expand the child or young person's communication, interactive play and social routines

The intervention should be delivered by a trained professional. For pre-school children consider parent, carer or teacher mediation. For school-aged children consider peer mediation.

Pharmacological and dietary interventions
• Do not use the following interventions for the management of core features of autism in children and young people:
  - antipsychotics
  - antidepressants
  - anticonvulsants
  - exclusion diets (such as gluten- or casein-free diets)

Interventions that should not be used for autism in children and young people:
• neurofeedback to manage speech and language problems in children and young people with autism
• auditory integration training to manage speech and language problems in children and young people with autism
• omega-3 fatty acids to manage sleep problems in children and young people with autism
• the following interventions should not be used to manage autism in any context in children and young people:
  - secretin
  - chelation
  - hyperbaric oxygen therapy

National Institute for Health and Clinical Excellence (NICE): NICE published clinical guidelines for the recognition, referral, diagnosis and management of adults on the autism spectrum. The guidelines include the following recommendations (NICE, 2012):

Psychosocial interventions for the core symptoms of autism
• For adults with autism without a learning disability or with a mild to moderate learning disability, who have identified problems with social interaction, consider:
  - a group-based social learning program focused on improving social interaction
  - an individually delivered social learning program for people who find group-based activities difficult
• Social learning programs to improve social interaction should typically include:
  - modeling
  - peer feedback (for group-based programs) or individual feedback (for individually delivered programs)
  - discussion and decision-making
  - explicit rules
  - suggested strategies for dealing with socially difficult situations
• Do not provide facilitated communication for adults with autism.

Psychosocial interventions focused on life skills
• For adults with autism of all ranges of intellectual ability, who need help with activities of daily living, consider a structured and predictable training program based on behavioral principles.
• For adults with autism without a learning disability or with a mild to moderate learning disability, who are socially isolated or have restricted social contact, consider:
  - a group-based structured leisure activity program
  - an individually delivered structured leisure activity program for people who find group-based activities difficult
• A structured leisure activity program should typically include:
  - a focus on the interests and abilities of the participant(s)
  - regular meetings for a valued leisure activity
  - for group-based programs, a facilitator with a broad understanding of autism to help integrate the participants
  - the provision of structure and support
• For adults with autism without a learning disability or with a mild to moderate learning disability, who have problems with anger and aggression, offer an anger management intervention, adjusted to the needs of adults with autism.
• Anger management interventions should typically include:
  - functional analysis of anger and anger-provoking situations
  - coping-skills training and behavior rehearsal
  - relaxation training
  - development of problem-solving skills
For adults with autism without a learning disability or with a mild learning disability, who are at risk of victimization, consider anti-victimization interventions based on teaching decision-making and problem-solving skills.

Anti-victimization interventions should typically include:
- identifying and, where possible, modifying and developing decision-making skills in situations associated with abuse
- developing personal safety skills

For adults with autism without a learning disability or with a mild learning disability, who are having difficulty obtaining or maintaining employment, consider an individual supported employment program.

Biomedical (pharmacological, physical and dietary) interventions and the core symptoms of autism

Do not use the following:
- anticonvulsants for the management of core symptoms of autism in adults
- chelation for the management of core symptoms of autism in adults
- the following interventions for the management of core symptoms of autism in adults:
  - exclusion diets (such as gluten- or casein-free and ketogenic diets)
  - vitamins, minerals and dietary supplements (such as vitamin B6 or iron supplementation)
- drugs specifically designed to improve cognitive functioning (for example, cholinesterase inhibitors) for the management of core symptoms of autism or routinely for associated cognitive or behavioral problems in adults
- oxytocin for the management of core symptoms of autism in adults
- secretin for the management of core symptoms of autism in adults
- testosterone regulation for the management of core symptoms of autism in adults
- hyperbaric oxygen therapy for the management of core symptoms of autism in adults
- antipsychotic medication for the management of core symptoms of autism in adults
- antidepressant medication for the routine management of core symptoms of autism in adults

Academy of Medicine Singapore–Ministry of Health (AMS–MOH): this organization published clinical practice guidelines for autism spectrum disorders in pre-school children (AMS–MOH, 2010). The recommendations include:

- All professionals involved in diagnosing ASD in children should consider using either the ICD-10 or DSMIV-TR systems of classification (Grade C, Level 2+)
- Professionals should aim to identify ASD early. Early identification provides opportunity for early referral and intervention, so that the child with ASD may have improved functioning in later life (Grade D, Level 3)
- Active surveillance by healthcare professionals is recommended at 18 months and again at 24–36 months for key signs of ASD (Grade D, Level 3)
- Children with one or more of the following clinical features must be referred promptly for comprehensive developmental evaluation (Grade D, Level 4):
  - No babble, pointing or other gestures by 12 months.
  - No single words by 18 months.
  - No spontaneous (non-echoed) 2-word phrases by 24 months.
  - Any loss of language or social skills at any age

Assessment

- Diagnostic evaluation of a child suspected to have ASD should be carried out by a multi-disciplinary team or professional who is trained and experienced with diagnosis of ASD. Evaluation includes:
  - An ASD-specific developmental history
  - Direct observations
  - Obtaining wider contextual and functional information
- Children with ASD with the following features should have a genetic evaluation (Grade D, Level 3):
  - Microcephaly or macrocephaly
  - A positive family history (of a genetic syndrome)
  - Dysmorphic features
- Children with ASD may be offered high-resolution chromosomal studies and DNA analysis to look for an associated medical condition following diagnosis (Grade D, Level 3).
- Children with ASD may be offered selective metabolic testing when an inborn error of metabolism is suspected (Grade C, Level 2+).
- Brain imaging is not routinely recommended in children with ASD (Grade C, Level 2+)
• Electro-encephalography (EEG) is not routinely recommended in children with ASD but should be considered if any of the following are present (Grade C, Level 2+):
  ➢ Clinical seizures
  ➢ Symptoms suggestive of sub-clinical seizures
  ➢ such as staring spells
  ➢ A history of developmental regression

• Serum lead screening is not routinely indicated in children with ASD but may be considered where there is clinical suspicion of pica (Grade D, Level 4)

• Food allergy tests are not recommended in the routine assessment of children with ASD (Grade C, Level 2+)

• Hair mineral analysis is not recommended in the evaluation of children with ASD (Grade C, Level 2+)

• Immunologic investigation is not routinely indicated in children with ASD (Grade C, Level 2+)

• Assay of vitamin B6 and magnesium levels is not recommended in children with ASD (Grade C, Level 2+)

• Investigations to identify yeast over-growth in the gastro-intestinal tract are not recommended in children with ASD (Grade C, Level 2+)

Management: Interventions

• Every pre-school child diagnosed with ASD should have an individualized intervention plan with goals, types, frequency and intensity of intervention (Grade D, Level 4)

• Should undergo early intervention as soon as significant developmental need is recognized (Grade C, Level 2+)

• There is no single language or communication intervention for an individual child with ASD. The optimal communication intervention depends on the needs of that particular child (Grade D, Level 4)

• Alternative-augmentative communication systems maybe recommended because they expand communication, may stimulate speech acquisition in non-verbal children and enhance expression in verbal children (Grade A, Level 1+)

• When presenting with perceptual distortions, fine and gross motor co-ordination difficulties, impaired play skills and impaired self-care and adaptability may benefit from consultation with appropriate specialists, such as occupational therapy and/or physiotherapists (Grade B, Level 2+)

• Sensory integration intervention is not recommended as standard therapy in management of children with ASD but may be considered where child has sensory difficulties that affect daily functioning (Grade D Level 3)

• Early intensive Behavior Intervention (EIBI) can be recommended as an intervention option for children with ASD (Grade A, Level 1++)

• Developmental models, such as Developmental, Individual-difference, Relationship-based (DIR)/Floortime and Relationship Developmental Intervention (RDI) may be considered options (Grade D, Level 3)

Management: Complementary alternative therapies

• Parents and caregivers should not replace mainstream interventions for pre-school children with ASD with complementary and alternative therapies (GPP).

• Healthcare professionals caring for pre-school children with ASD should advise and counsel parents and caregivers about relevant, safe and effective health services and therapies regardless of whether the therapies are mainstream or complementary alternative therapies (GPP).

• The following complementary alternative therapies are not recommended in pre--school children with ASD because of potential for harm or adverse effects:
  ➢ Acupuncture
  ➢ Antibiotics and Anti--yeast medication
  ➢ Ascorbic acid (vitamin C) supplementation
  ➢ Auditory Integration Therapy
  ➢ Chelation therapy
  ➢ Chiropractic
  ➢ Cranio--sacral therapy
  ➢ Digestive enzymes
  ➢ Facilitated Communication
  ➢ Folate supplementation
Grade of recommendation:
A: At least one meta-analysis, systematic review of RCTs, or RCT rated as 1+ + and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1+ + or 1+
C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2+ +
D: Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
GPP: (good practice points) Recommended best practice based on the clinical experience of the guideline development group.

Levels of evidence:
1+ +: High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias.
1+: Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2+ +: High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3: Non-analytic studies, e.g. case reports, case series
4: Expert opinion

Summary
The autism spectrum disorders (ASD) are a range of complex behavioral disorders that are also referred to as pervasive developmental disorders (PDD). The disorders include: autism or autistic disorder, Asperger’s syndrome, Rett’s disorder, childhood disintegrative disorder and pervasive developmental disorder not otherwise specified (PDD-NOS). The disorders are characterized by varying degrees of impairment in communication skills, reciprocal social interactions, and restricted, repetitive and stereotyped patterns of behavior, speech and interests.

ASD is associated with many genetic conditions; however, genetic testing for the majority of patients will have a very low yield unless the family history, medical history, presence of intellectual disability, or dysmorphic or other findings on examination are suggestive of a diagnosable condition. In the presence of intellectual disability or dysmorphic features, it is appropriate to test for fragile X syndrome. If Rett’s disorder is suspected, then testing for mutations on gene MECP2 is appropriate.

There are no medical interventions that have been proven to be effective in achieving a cure for autism; however, the condition may be managed through a combination of behavioral, pharmacological and educational interventions. Educational services (e.g., including special education, some forms of behavior modification and other services) are the central and integral aspect of the treatment for ASD. Psychosocial interventions include parent training that involves behavior modification techniques and referral to support groups. It has been noted in the literature that there is no single approach that is best for all individuals with ASD.
Therapies that have not yet been proven to be effective in the treatment of ASD include, but are not limited to: acupuncture, art therapy, auditory integration therapy, chelation therapy, cognitive rehabilitation, craniosacral therapy, dietary and nutritional interventions (e.g., elimination diets, vitamins), EEG biofeedback/neurofeedback, equestrian therapy, facilitated communication, holding therapy, hyperbaric oxygen therapy, immune globulin therapy, intensive behavioral intervention programs for autism, music therapy, recreational therapy, secretin infusion, sensory integration therapy, and vision therapy.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Covered when medically necessary for the assessment of ASD:

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81228</td>
<td>Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (e.g., Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)</td>
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<tr>
<td>81229</td>
<td>Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities</td>
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<tr>
<td>81243</td>
<td>FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles</td>
</tr>
<tr>
<td>81244</td>
<td>FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; characterization of alleles (e.g., expanded size and methylation status)</td>
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<td>81302</td>
<td>MECP2 (methyl CpG protein 2) (e.g., Rett Syndrome) gene analysis; full sequence analysis</td>
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<td>MECP2 (methyl CpG protein 2) (e.g., Rett Syndrome) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81304</td>
<td>MECP2 (methyl CpG protein 2) (e.g., Rett Syndrome) gene analysis; duplication/deletion variants</td>
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<td>83655</td>
<td>Lead</td>
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<td>84035</td>
<td>Phenylketones, qualitative</td>
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<td>90791</td>
<td>Psychiatric diagnostic evaluation</td>
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<td>90792</td>
<td>Psychiatric diagnostic evaluation with medical services</td>
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<td>92506</td>
<td>Evaluation of speech, language, voice, communication, and/or auditory processing (code deleted 12/31/2013)</td>
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<td>92521</td>
<td>Evaluation of speech fluency (e.g., stuttering, clattering) (code effective 01/01/2014)</td>
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<td>92522</td>
<td>Evaluation of speech sound production (e.g., articulation, phonological process, apraxia, dysarthria) (Code effective 01/01/2014)</td>
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<td>92523</td>
<td>Evaluation of speech sound production (e.g., articulation, phonological process, apraxia, dysarthria); with evaluation of language comprehension and expression (e.g., receptive and expressive language) (Code effective 01/01/2014)</td>
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<td>92524</td>
<td>Behavioral and qualitative analysis of voice and resonance (Code effective 01/01/2014)</td>
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<td>95812</td>
<td>Electroencephalogram (EEG) extended monitoring; 41-60 minutes</td>
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<td>95813</td>
<td>Electroencephalogram (EEG) extended monitoring; greater than 1 hour</td>
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<td>95816</td>
<td>Electroencephalogram (EEG); including recording awake and drowsy</td>
</tr>
<tr>
<td>95819</td>
<td>Electroencephalogram (EEG); including recording awake and asleep</td>
</tr>
<tr>
<td>95827</td>
<td>Electroencephalogram (EEG); all night recording</td>
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| 96110      | Developmental screening, with interpretation and report, per standardized
Developmental testing, (includes assessment of motor, language, social, adaptive, and/or cognitive functioning by standardized developmental instruments) with interpretation and report

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**Physical therapy evaluation**

**Occupational therapy evaluation**

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<th>ICD-9-CM Diagnosis Codes</th>
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<td>299.00-299.91</td>
<td>Pervasive developmental disorders</td>
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**Covered when medically necessary for the treatment of ASD:**

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<th>CPT* Codes</th>
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<td>Interactive complexity (List separately in addition to the code for primary procedure)</td>
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<td>90832</td>
<td>Psychotherapy, 30 minutes with patient and/or family member</td>
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<tr>
<td>90833</td>
<td>Psychotherapy, 30 minutes with patient and/or family member when performed with an evaluation and management service (List separately in addition to the code for primary procedure)</td>
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<td>Psychotherapy, 45 minutes with patient and/or family member</td>
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<td>90836</td>
<td>Psychotherapy, 45 minutes with patient and/or family member when performed with an evaluation and management service (List separately in addition to the code for primary procedure)</td>
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<td>90837</td>
<td>Psychotherapy, 60 minutes with patient and/or family member</td>
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<tr>
<td>90838</td>
<td>Psychotherapy, 60 minutes with patient and/or family member when performed with an evaluation and management service (List separately in addition to the code for primary procedure)</td>
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<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
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<td>E2500</td>
<td>Speech generating device, digitized speech, using pre-recorded messages, less than or equal to eight minutes recording time</td>
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<tr>
<td>E2502</td>
<td>Speech generating device, digitized speech, using pre-recorded messages, greater than 8 minutes but less than or equal to 20 minutes recording time</td>
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<td>E2504</td>
<td>Speech generating device, digitized speech, using pre-recorded messages, greater than 20 minutes but less than or equal to 40 minutes recording time</td>
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<td>E2506</td>
<td>Speech generating device, digitized speech, using pre-recorded messages, greater than 40 minutes recording time</td>
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<tr>
<td>E2508</td>
<td>Speech generating device, synthesized speech, requiring message formulation by spelling and access by physical contact with the device</td>
</tr>
<tr>
<td>E2510</td>
<td>Speech generating device, synthesized speech, permitting multiple methods of message formulation and multiple methods of device access</td>
</tr>
<tr>
<td>E2511</td>
<td>Speech generating software program, for personal computer or personal digital assistant</td>
</tr>
</tbody>
</table>

Educational in nature, not medically necessary and not covered for the assessment and/or treatment of ASD:
### CPT* Codes

<table>
<thead>
<tr>
<th>CPT* Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96116</td>
<td>Neurobehavioral status exam (clinical assessment of thinking, reasoning and judgment, eg, acquired knowledge, attention, language, memory, planning and problem solving, and visual spatial abilities), per hour of the psychologist's or physician's time, both face-to-face time with the patient and time interpreting test results and preparing the report</td>
</tr>
<tr>
<td>96118</td>
<td>Neuropsychological testing (eg, Halstead-Reitan Neuropsychological Battery, Wechsler Memory Scales and Wisconsin Card Sorting Test), per hour of the psychologist's or physician's time, both face-to-face time administering tests to the patient and time interpreting these test results and preparing the report</td>
</tr>
<tr>
<td>96119</td>
<td>Neuropsychological testing (eg, Halstead-Reitan Neuropsychological Battery, Wechsler Memory Scales and Wisconsin Card Sorting Test), with qualified health care professional interpretation and report, administered by technician, per hour of technician time, face-to-face</td>
</tr>
<tr>
<td>96120</td>
<td>Neuropsychological testing (eg, Wisconsin Card Sorting Test), administered by a computer, with qualified health care professional interpretation and report</td>
</tr>
</tbody>
</table>

**Experimental/Investigational/Unproven/Not Covered when used to report for the assessment of autism spectrum disorders:**

<table>
<thead>
<tr>
<th>CPT* Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>82705</td>
<td>Fat or lipids, feces; qualitative</td>
</tr>
<tr>
<td>83018</td>
<td>Heavy metal (eg, arsenic, barium, beryllium, bismuth, antimony, mercury); quantitative, each</td>
</tr>
<tr>
<td>83615</td>
<td>Lactate dehydrogenase (LD) (LDH)</td>
</tr>
<tr>
<td>86001</td>
<td>Allergen specific IgG quantitative or semiquantitative, each allergen</td>
</tr>
<tr>
<td>86003</td>
<td>Allergen specific IgE; quantitative or semiquantitative, each allergen</td>
</tr>
<tr>
<td>86005</td>
<td>Allergen specific IgE; qualitative, multiallergen screen (dipstick, paddle, or disk)</td>
</tr>
<tr>
<td>86485</td>
<td>Skin test; candida</td>
</tr>
<tr>
<td>92585</td>
<td>Auditory evoked potentials for evoked response audiometry and/or testing of the central nervous system; comprehensive</td>
</tr>
<tr>
<td>92586</td>
<td>Auditory evoked potentials for evoked response audiometry and/or testing of the central nervous system; limited</td>
</tr>
<tr>
<td>95004</td>
<td>Percutaneous tests (scratch, puncture, prick) with allergenic extracts, immediate type reaction, including test interpretation and report by physician, specify number of tests</td>
</tr>
<tr>
<td>95017</td>
<td>Allergy testing, any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal), sequential and incremental, with venoms, immediate type reaction, including test interpretation and report, specify number of tests</td>
</tr>
<tr>
<td>95018</td>
<td>Allergy testing, any combination of percutaneous (scratch, puncture, prick) and intracutaneous (intradermal), sequential and incremental, with drugs or biologicals, immediate type reaction, including test interpretation and report, specify number of tests</td>
</tr>
<tr>
<td>95076</td>
<td>Ingestion challenge test (sequential and incremental ingestion of test items, eg, food, drug or other substance); initial 120 minutes of testing</td>
</tr>
<tr>
<td>95079</td>
<td>Ingestion challenge test (sequential and incremental ingestion of test items, eg, food, drug or other substance); each additional 60 minutes of testing (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>95930</td>
<td>Visual evoked potential (VEP) testing central nervous system, checkerboard or flash</td>
</tr>
<tr>
<td>95965</td>
<td>Magnetoencephalography (MEG), recording and analysis; for spontaneous brain magnetic activity (eg, epileptic cerebral cortex localization)</td>
</tr>
<tr>
<td>95966</td>
<td>Magnetoencephalography (MEG), recording and analysis; for evoked magnetic fields, single modality (eg, sensory, motor, language, or visual cortex localization)</td>
</tr>
<tr>
<td>95967</td>
<td>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)</td>
</tr>
<tr>
<td>HCPCS Codes</td>
<td>Description</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td>P2031</td>
<td>Hair analysis (excluding arsenic)</td>
</tr>
</tbody>
</table>

**Experimental/Investigational/Unproven/Not Covered when used to report for the treatment of autism spectrum disorders:**

<table>
<thead>
<tr>
<th>CPT* Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>90281</td>
<td>Immune globulin (Ig), human, for intramuscular use</td>
</tr>
<tr>
<td>90283</td>
<td>Immune globulin (IgIV), human, for intravenous use</td>
</tr>
<tr>
<td>90284</td>
<td>Immune globulin (SCIg), human, for use in subcutaneous infusions, 100 mg, each</td>
</tr>
<tr>
<td>90399</td>
<td>Unlisted immune globulin</td>
</tr>
<tr>
<td>90875</td>
<td>Individual psychophysiological therapy incorporating biofeedback training by any modality (face-to-face with the patient), with psychotherapy (eg, insight oriented, behavior modifying or supportive psychotherapy); approximately 20-30 minutes</td>
</tr>
<tr>
<td>90876</td>
<td>Individual psychophysiological therapy incorporating biofeedback training by any modality (face-to-face with the patient), with psychotherapy (eg, insight oriented, behavior modifying or supportive psychotherapy); approximately 45-50 minutes</td>
</tr>
<tr>
<td>90901</td>
<td>Biofeedback training by any modality</td>
</tr>
<tr>
<td>92065</td>
<td>Orthoptic and/or pleoptic training, with continuing medical direction and evaluation</td>
</tr>
<tr>
<td>97532</td>
<td>Development of cognitive skills to improve attention, memory, problem solving (includes compensatory training), direct (one-on-one) patient contact by the provider, each 15 minutes</td>
</tr>
<tr>
<td>97533</td>
<td>Sensory integrative techniques to enhance sensory processing and promote adaptive responses to environmental demands, direct (one-on-one), patient contact by the provider, each 15 minutes</td>
</tr>
<tr>
<td>97810</td>
<td>Acupuncture, 1 or more needles; without electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient</td>
</tr>
<tr>
<td>97811</td>
<td>Acupuncture, 1 or more needles; without electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>97813</td>
<td>Acupuncture, 1 or more needles; with electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient</td>
</tr>
<tr>
<td>97814</td>
<td>Acupuncture, 1 or more needles; with electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>99183</td>
<td>Physician attendance and supervision of hyperbaric oxygen therapy, per session</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
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</tr>
</thead>
<tbody>
<tr>
<td>A4575</td>
<td>Topical hyperbaric oxygen chamber, disposable</td>
</tr>
<tr>
<td>A1300</td>
<td>Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval</td>
</tr>
<tr>
<td>C9130</td>
<td>Injection, immune globulin (Bivigam), 500 mg</td>
</tr>
<tr>
<td>G0176</td>
<td>Activity therapy, such as music, dance, art or play therapies not for recreation, related to the care and treatment of patient's disabling mental health problems, per session (45 minutes or more)</td>
</tr>
<tr>
<td>J1459</td>
<td>Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g. liquid), 500 MG</td>
</tr>
<tr>
<td>J1557</td>
<td>Injection, immune globulin, (Gammaphex), intravenous, non-lyophilized (e.g., liquid), 500 mg</td>
</tr>
<tr>
<td>J1559</td>
<td>Injection, immune globulin (Hizentra), 100 mg</td>
</tr>
<tr>
<td>J1561</td>
<td>Injection, immune globulin, (Gamunex/Gamunex-C/Gammaked), nonlyophilized (e.g., liquid), 500 mg</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>J1562</td>
<td>Injection, immune globulin (Vivaglobin), 100 mg</td>
</tr>
<tr>
<td>J1566</td>
<td>Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg</td>
</tr>
<tr>
<td>J1568</td>
<td>Injection, immune globulin, (Octagam), intravenous, nonlyophilized (e.g., liquid), 500 mg</td>
</tr>
<tr>
<td>J1569</td>
<td>Injection, immune globulin, (Gammagard liquid), intravenous, nonlyophilized, (e.g., liquid), 500 mg</td>
</tr>
<tr>
<td>J1572</td>
<td>Injection, immune globulin, (Flebogamma/Flebogamma Dif), intravenous, nonlyophilized (e.g., liquid), 500 mg</td>
</tr>
<tr>
<td>J1599</td>
<td>Injection, immune globulin, intravenous, non-lyophilized (e.g. liquid), not otherwise specified, 500 mg</td>
</tr>
<tr>
<td>J2850</td>
<td>Injection, secretin, synthetic, human, 1 mcg</td>
</tr>
<tr>
<td>S8940</td>
<td>Equestrian/hippotherapy, per session</td>
</tr>
<tr>
<td>S9355</td>
<td>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</td>
</tr>
</tbody>
</table>


References


