Genetic testing: exome and genome sequencing for the diagnosis of genetic disorders

These services may or may not be covered by your HealthPartners plan. Please see your plan documents for your specific coverage information. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage.

Administrative Process

Prior authorization is required for the following services:

- Standard exome sequencing
- Reanalysis of exome or genome sequencing data
- Rapid exome sequencing
- Standard genome sequencing
- Rapid genome sequencing
- Testing that is associated with a procedure code listed in “Box A”, below.

Coverage for rapid genome sequencing may vary due to variations in member benefits. Please check member benefits for additional conditions of coverage.

Box A: Genetic testing procedure codes that require prior authorization
Molecular pathology procedures, Tier 2 or unlisted (CPT 81400-81408, 81479)
Unlisted multianalyte assays (CPT 81599)
Any other listed or unlisted laboratory/pathology CPT code when it is used in association with a genetic test.

Tests that require prior authorization will be reviewed for medical necessity of the testing as a whole. That is, a single coverage decision will apply to all of the tests, services, and/or procedure codes associated with the genetic test, whether they are requested/billed together or separately.

Policy Reference Table

Below is a list of higher volume tests and the associated laboratories for each coverage criteria section. This list is not all inclusive.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes
Standard Exome Sequencing	Genomic Unity Exome Analysis - Proband (Variantyx Inc.)	81415	F70-F79, F80.0-F89, Q00.0-Q99.9, R56.9, R62.0, R62.50, R62.51, G40.909
	Genomic Unity Exome Analysis - Comparator (Duo or Trio) (Variantyx Inc.)	81416	
	XomeDx - Proband (GeneDx)	81415	
	Exome - Proband Only (Invitae)		
	XomeDx - Duo (GeneDx)	81415, 81416	
	XomeDx - Trio (GeneDx)		
	Exome - Duo (Invitae)		
	Exome - Trio (Invitae)		
Reanalysis of Exome or Genome Sequencing Data	Exome Reanalysis (Ambry)	81417	F70-F79, F80-F89, Q00.0-Q99.9, R56.9, R62.0, R62.50, R62.51, G40.909
	Whole Genome Reanalysis (ARUP)	81427	
Rapid Exome Sequencing	XomeDxXpress (GeneDx)	81415, 81416	F70-F79, F80-F89, Q00.0-Q99.9, R56.9,
	ExomeNext-Rapid (Ambry)		

	PGxome RAPID Exome Test (PreventionGenetics, part of Exact Sciences)		R62.0, R62.50, R62.51, G40.909
	STAT Whole Exome Sequencing (PerkinElmer Genomics)		
Standard Genome Sequencing	Genomic Unity Whole Genome Analysis - Proband (Variantyx Inc.)	0212U	F70-F79, F80-F89, Q00.0-Q99.9, R56.9, R62.0, R62.50, R62.51, G40.909
	Genomic Unity Whole Genome Analysis - Comparator (Variantyx Inc.)	0213U	
	GenomeSeqDx (GeneDx)	81425, 81426	
	TruGenome Trio (Illumina, Inc)		
	Whole Genome Sequencing (PerkinElmer Genomics)		
	MNGenome (MNG Laboratories)		
	Praxis Whole Genome Sequencing (Praxis Genomics LLC)	0265U	
Rapid Genome Sequencing	Rapid Whole Genome Sequencing (Rady Children's Institute for Genomic Medicine)	0094U	F70-F79, F80-F89, Q00.0-Q99.9, R56.9, R62.0, R62.50, R62.51, G40.909
	Rapid Whole Genome Sequencing, Comparator Genome (Rady Children's Institute for Genome Medicine)	0425U	
	Ultra-Rapid Whole Genome Sequencing (Rady Children's Institute for Genomic Medicine)	0426U	
	STAT Whole Genome Sequencing (PerkinElmer Genomics)	81425, 81426	
	MNGenome STAT (Labcorp/MNG laboratories)		

Coverage

Standard Exome Sequencing

1. Standard exome sequencing, with trio testing when possible, is considered **medically necessary** when:
   - A. The member has not previously had genome sequencing, **and**
   - B. Alternate etiologies have been considered and ruled out when possible (e.g., environmental exposure, injury, infection, isolated prematurity), **and**
   - C. Clinical presentation does not fit a well-described syndrome for which rapid single-gene or targeted multi-gene panel testing is available, **and**
   - D. The member's personal and family histories have been evaluated by a Medical Geneticist, Genetic counselor or an Advanced Practice Nurse in Genetics (APGN), **and**
   - E. The member meets at least one of the following clinical findings:
     - i. The member has unexplained epilepsy diagnosed at any age, **or**
     - ii. The member has global developmental delay or intellectual disability with onset prior to age 18 years, **or**
     - iii. The member was diagnosed with at least one congenital anomaly (functional and/or structural), **or**
     - iv. The member has at least **two** of the following:
       - a) Bilateral sensorineural hearing loss of unknown etiology, **or**
       - b) Symptoms of a complex neurological disorder (e.g., dystonia, hemiplegia, spasticity, epilepsy, myopathy, muscular dystrophy), **or**
       - c) Family history suggestive of a genetic etiology, including consanguinity, **or**

d) Clinical or laboratory findings suggestive of an inborn error of metabolism, **or**
e) Autism, **or**
f) Severe neuropsychiatric condition (e.g., schizophrenia, bipolar disorder, Tourette syndrome, self-injurious behavior, reverse sleep-wake cycles), **or**
g) Period of unexplained developmental regression (unrelated to epilepsy or autism).

2. Repeat standard exome sequencing is considered **investigational**.
3. Standard exome sequencing is considered **investigational** for all other indications, including screening asymptomatic/healthy individuals for genetic disorders.

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Reanalysis of Exome or Genome Sequencing Data

1. Reanalysis of exome or genome sequencing data is considered **medically necessary** when*:
   A. The member had exome or genome sequencing at least 18 months ago, **or**
   B. The member's phenotype has expanded to include clinical findings** that were not present at the time of the initial exome or genome sequencing analysis, **and**
      i. Results of prior exome or genome sequencing do not explain these new clinical findings.
   C. Reanalysis of exome or genome sequencing data is considered **investigational** for all other indications.

*If reanalysis of exome data is not possible, see the genome sequencing criteria for additional coverage information.
**See Standard Exome Sequencing or Standard Genome Sequencing criteria for qualifying clinical findings.

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Rapid Exome Sequencing

1. Rapid exome sequencing (rES), with trio testing when possible, is considered **medically necessary** when:
   A. The member is an acutely-ill infant (12 months of age or younger), **and**
   B. The member has not previously had genome sequencing, **and**
   C. Alternate etiologies have been considered and ruled out when possible (e.g., environmental exposure, injury, infection, isolated prematurity), **and**
   D. Clinical presentation does not fit a well-described syndrome for which rapid single-gene or targeted multi-gene panel testing is available, **and**
   E. The member's personal and family histories have been evaluated by a Medical Geneticist, Genetic Counselor or an Advanced Practice Nurse in Genetics (APGN), **and**
   F. The member meets at least one of the following clinical findings:
      i. The member has unexplained epilepsy, **or**
      ii. The member has global developmental delay **or**
      iii. The member was diagnosed with at least one congenital anomaly (functional and/or structural), **or**
      iv. The member has at least **two** of the following:
         a) Bilateral sensorineural hearing loss of unknown etiology, **or**
         b) Symptoms of a complex neurological disorder (e.g., dystonia, hemiplegia, spasticity, myopathy, muscular dystrophy), **or**
         c) Family history suggestive of a genetic etiology, including consanguinity, **or**
         d) Clinical or laboratory findings suggestive of an inborn error of metabolism, **or**
         e) **or**
         f) Severe neuropsychiatric condition (e.g., schizophrenia, bipolar disorder, Tourette syndrome, self-injurious behavior, reverse sleep-wake cycles), **or**
         g) Period of unexplained developmental regression (unrelated to epilepsy or autism).
2. Rapid exome sequencing is considered **investigational** for all other indications, including screening asymptomatic/healthy individuals for genetic disorders.

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Standard Genome Sequencing

1. Standard genome sequencing, with trio testing when possible, is considered **medically necessary** when:
   A. Alternate etiologies have been considered and ruled out when possible (e.g., environmental exposure, injury, infection, isolated prematurity), **and**
   B. Clinical presentation does not fit a well-described syndrome for which rapid single-gene or targeted multi-gene panel testing is available, **and**

C. The member's personal and family histories have been evaluated by a Medical Geneticist, Genetic Counselor or an Advanced Practice Nurse in Genetics (APGN), **and**
D. The member meets at least one of the following clinical findings:
i. The member previously had uninformative exome sequencing (ES), **and**
a) ES reanalysis is not possible, **or**
ii. The member has unexplained epilepsy diagnosed at any age, **or**
iii. The member has global developmental delay or intellectual disability with onset prior to age 18 years, **or**
iv. The member was diagnosed with at least one congenital anomaly (functional and/or structural), **or**
v. The member has at least **two** of the following:
a) Bilateral sensorineural hearing loss of unknown etiology, **or**
b) Symptoms of a complex neurological disorder (e.g., dystonia, hemiplegia, spasticity, epilepsy, myopathy, muscular dystrophy), **or**
c) Family history suggestive of a genetic etiology, including consanguinity, **or**
d) Clinical or laboratory findings suggestive of an inborn error of metabolism, **or**
e) Autism, **or**
f) Severe neuropsychiatric condition (e.g., schizophrenia, bipolar disorder, Tourette syndrome, self-injurious behavior, reverse sleep-wake cycles), **or**
g) Period of unexplained developmental regression (unrelated to epilepsy or autism).

2. Repeat standard genome sequencing is considered **investigational**.
3. Standard genome sequencing is considered **investigational** for all other indications, including screening asymptomatic/healthy individuals for genetic disorders.

Note: When genome sequencing is performed, the mitochondrial genome is assumed to be included as a part of the analysis.

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Rapid Genome Sequencing

1. Rapid genome sequencing (rGS), with trio testing when possible, is considered **medically necessary** when:
A. The member is an acutely-ill infant (12 months of age or younger), **and**
B. Alternate etiologies have been considered and ruled out when possible (e.g., environmental exposure, injury, infection, isolated prematurity), **and**
C. Clinical presentation does not fit a well-described syndrome for which rapid single-gene or targeted multi-gene panel testing is available, **and**
D. The member's personal and family histories have been evaluated by a Medical Geneticist, Genetic Counselor or an Advanced Practice Nurse in Genetics (APGN), **and**
E. The member meets at least one of the following clinical findings:
i. The member has multiple congenital abnormalities (functional and/or structural) affecting unrelated organ systems, **or**
ii. The member has epileptic encephalopathy, **or**
iii. The member has unexplained epilepsy
iv. The member has at least **two** of the following:
a) Abnormality affecting at least one organ system, **or**
b) Symptoms of a complex neurological condition (e.g., dystonia, hemiplegia, spasticity, epilepsy, hypotonia, myopathy, muscular dystrophy, global developmental delay, intellectual disability), **or**
c) Family history suggestive of a genetic etiology, including consanguinity, **or**
d) Laboratory findings suggestive of an inborn error of metabolism, **or**
e) Abnormal response to standard therapy.

2. Rapid genome sequencing (rGS) is considered **investigational** for all other indications, including screening asymptomatic/healthy individuals for genetic disorders.

Note: When genome sequencing is performed, the mitochondrial genome is assumed to be included as a part of the analysis.

Definitions

Exome Sequencing (ES): A genomic technique for sequencing all of the protein-coding regions of genes in the genome (also known as the exome).

Genome Sequencing (GS): A genomic technique for sequencing the complete DNA sequence, which includes protein coding as well as non-coding DNA elements.

Trio Testing: Testing of the child and both biological/genetic parents and increases the chances of finding a definitive diagnosis, while reducing false-positive findings.

Comparator Exome Sequencing: Used only for comparison with the proband (individual undergoing exome sequencing) and is used to inform the pathogenicity of variants. A comparator exome is typically one or both biological/genetic parents to the proband.

Congenital anomalies: According to ACMG, congenital anomalies are multiple anomalies not specific to a well-delineated genetic syndrome. These anomalies are structural or functional abnormalities usually evident at birth, or shortly thereafter, and can be consequential to an individual's life expectancy, health status, physical or social functioning, and typically require medical intervention.

Global developmental delay: When an individual is slow-to-meet or not reaching milestones in the expected way for a child's age in at least two of the areas of development (communication, gross/fine motor, cognition, social-emotional, or adaptive skills)

Intellectual disability (ID): Defined by the DSM-V as:

1. Deficits in intellectual functions, such as reasoning, problem solving, planning, abstract thinking, judgment, academic learning, and learning from experience, confirmed by both clinical assessment and individualized, standardized intelligence testing.
2. Deficits in adaptive functioning that result in failure to meet developmental and sociocultural standards for personal independence and social responsibility. Without ongoing support, the adaptive deficits limit functioning in one or more activities of daily life, such as communication, social participation, and independent living, across multiple environments, such as home, school, work, and community.
3. Onset of intellectual and adaptive deficits during the developmental period.

Exome sequencing (ES) reanalysis: May not be possible in some situations. Sequencing platforms may have changed substantially enough that the performing lab can no longer use the data from the original ES in their pipeline. Specifically, ES reanalysis may not be possible if there have been improvements in technology/chemistry (e.g., new methods for DNA capture and/or sequencing), bioinformatics advancements, or there is new information regarding the genetic etiology of a condition that could explain the patient's clinical features and would not have been able to be detected by the previous exome sequencing.

Products

This information is for most, but not all, HealthPartners plans. Please read your plan documents to see if your plan has limits or will not cover some items. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage. These coverage criteria do not apply to Medicare Products. For more information regarding Medicare coverage criteria or for a copy of a Medicare coverage policy, contact Member Services at 952-883-7272 or 1-877-778-8384.

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