Medical Coverage Policy
Policy Number – MP23-033E
Original review date – 02/09/2023
Effective date – 02/27/2025

Whole exome sequencing

Background

Whole exome sequencing is sequencing of the all the protein coding regions of the genome. This represents approximately 1% of the entire genome, around 20,000 genes. High-throughput next generation sequencing techniques along with bioinformatics are used to identify, by comparison to a reference genome, variations associated with genetic disorders (such as SNPs, insertions, deletions, translocations and so on).

Policy statement

Disclaimer: This policy is applicable to TRICARE Prime and Select beneficiaries and may not apply to Active Duty Service Members (ADSM) under Supplemental Health Care Program (SHCP) or TRICARE Prime Remote (TPR) in accordance with TRICARE Operations Manual (TOM) Ch. 17, Sec. 3. Please review TOM Ch. 17, Sec. 3, Para. 2.0 onwards, regarding SHCP coverage and any TRICARE-specific exclusions included in this coverage policy to accurately determine the benefit for ADSMs.

Whole exome sequencing may be considered medically necessary for the affected person if the following criteria are met:

I. Patient has one of the following:
   a. Unexplained neurodevelopmental disorder, manifesting as developmental delay or intellectual disability
   b. Clinical presentation of a single major (such as hypoplastic left heart syndrome) or multiple minor congenital anomalies
II. Clinical presentation does not fit a well-described syndrome, as indicated by one or more of the following:
   a. Absence of clinically recognizable syndrome caused by single gene disorder or chromosomal disorder; OR
   b. Phenotype suggestive of more than one genetic disorder
III. Genetic etiology is considered the most likely explanation for the phenotype, as indicated by one or more of the following:
   a. Multiple congenital abnormalities affecting unrelated organ systems; OR
   b. Family history strongly suggestive of a genetic etiology (e.g., consanguinity);OR
   c. Period of unexplained developmental regression; OR
   d. Biochemical findings suggestive of an inborn error of metabolism

IV. Results of the test will directly affect treatment and management of the patient
V. Genetic counseling has been performed, as indicated by all of the following:
   a. Counseling is provided by healthcare professional with education and training in genetic issues relevant to the genetic tests under consideration
   b. Counselor is not an employee of the genetics testing laboratory
VI. Family trio testing (whole exome sequencing of the biologic parents or sibling of the affected person) is considered medically necessary when above criteria are met for the affected person

Limitations of coverage

I. Whole exome sequencing for isolated autism spectrum disorders, without signs and symptoms of another condition, is not considered medically necessary due to insufficient evidence of clinical benefit.

Coding information

81415	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis
81416	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (e.g., parents, siblings) (List separately in addition to code for primary procedure)
81417	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); reevaluation of previously obtained exome sequence (e.g., updated knowledge or unrelated condition/syndrome)

References

1. MCG Health. Whole Genome/Exome Sequencing – Developmental Delay and Intellectual Disability. Ambulatory Care 28th edition. ACG: A-0926 (AC). Last updated 3/14/2024
2. MCG Health. Whole Genome/Exome Sequencing – Autism Spectrum Disorders. Ambulatory Care 28th edition. ACG: A-0870 (AC). Last updated 3/14/2024
3. MCG Health. Whole Genome/Exome Sequencing – Congenital Anomalies. 28th edition. ACG: A-0872 (AC). Last updated 3/14/2024
4. MCG Health. Whole Genome/Exome Sequencing – Metabolic, Mitochondrial, and Neurologic Disorders. 28th edition. ACG: A-0871 (AC). Last updated 3/14/2024
5. Uptodate Inc. Autism Spectrum Disorder: Evaluation and diagnosis. Last updated November 5, 2024
6. Uptodate Inc. Intellectual Disability in Children: Evaluation for a Cause. Last updated January 10, 2023

Review history

February 2025:

- Added coverage criteria
- Changed name of policy
- Updated references

September 2024: Updated references

Approved by:

Joseph F. McKeon, MD, MPH

Chief Medical Officer

Date of approval: 02/27/2025