New Clinical Guideline for Rapid Whole Gene Sequencing

Tennessee | Medicaid

At-a-glance:

- This notice outlines guidelines and information regarding the coverage and clinical implications of Rapid Whole Genome Sequencing (rWGS).
- By adopting rWGS, care providers can enhance their ability to deliver precise, personalized medicine to young patients with genetic conditions while navigating the complexities of modern genomic testing and its associated clinical and administrative demands.
- rWGS can benefit members by leading to faster diagnosis, targeted treatment plans, and informed decision making.

Benefit

Clinical Guideline:	CG-TN-02
Publish date:	July 1, 2025
Status:	New
Last review date:	April 17, 2025

Description

This document provides the rWGS coverage for the Wellpoint plan enacted by Public Chapter 1020, Senate Bill No. 1762.

rWGS means an investigation of the entire human genome, including coding and non-coding regions and mitochondrial deoxyribonucleic acid, to identify disease-causing genetic changes that return the preliminary positive results within seven days and results within 15 days from the date of receipt of the sample by the lab performing the test. Includes patient-only whole genome sequencing, duo whole genome sequencing of the patient and one biological parent, and trio whole genome sequencing of the patient and both biological parents.

https://provider.wellpoint.com/tn

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Clinical indications

Medically necessary

It is medically necessary when all the following criteria are met:

- The beneficiary is under 21 years of age.
- The beneficiary has a complex or acute illness of unknown etiology that is not confirmed to be caused by environmental exposure, toxic ingestion, an infection with a normal response to therapy, or trauma.
- The beneficiary is receiving hospital services in an intensive care unit or other high-acuity care unit within the hospital.
- The parent of the member will also be eligible if covered by Wellpoint benefits and all other conditions in one to three are met.

Not medically necessary

It is considered not medically necessary if the above criteria are not met.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis, or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Services may be medically necessary when criteria are met:

HCPCS	
0425U	Genome (for example, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis, each comparator genome (for example, parents, siblings)
0094U	Genome (for example, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis
ICD-1O Diagnosis	
All diagnoses	

General information

The following provides general information for cases where the criteria are not met in the listed procedure codes above or for situations specified in the clinical indications.

Genetic testing involves risk that accompanies its potential benefits. The clinical team and the patient should consider the balance of risks and potential benefits before testing is pursued through informed consent. As with any procedure, the clinical utility of the genetic test must be considered along with its psychological and sociological implications. Counseling, performed by a genetic counselor or team clinician, provides a patient-centered approach to the care of people who are undergoing a diagnostic genetic test.

It is also recognized that accessibility to genetic counselors is limited by available resources and other social drivers of health. Therefore, as it relates to screening, counseling, such as informed consent, should be prioritized in a general sense, as noted above.

Genomic technologies generate large amounts of data, and this increases the potential for uncertainty in managing and adapting to this information. Clinicians are tasked with accurately interpreting and communicating information about test validity and the reliability of test results, as well as the probability of individual patient benefit. Uncovering incidental findings and being overwhelmed with information are important barriers to genetic testing, particularly among vulnerable patient subgroups. Genetic counseling is an invaluable resource for patients undergoing genetic testing, but there are practical limitations because of the scarcity of genetic counselors relative to the current need, as noted above.

Whereas whole-exome sequencing (WES) involves sequencing all protein-coding regions of the DNA (about 1.5% of the human genome), whole-genome sequencing (WGS) entails sequencing all coding (exons) and noncoding (introns) nuclear DNA as well as mitochondrial DNA. In WES, the use of DNA samples from both biological parents, in addition to the proband (trio testing), is recommended when available. Trio WES analysis reduces analytic cost, highlights de novo changes, precludes the need for numerous low-throughput Sanger co-segregation analyses, and reduces overall turnaround time.[6] The rationale for exploring the role of WGS rather than WES is that some rare genetic diseases involve noncoding structural rearrangements and break points in non-coding regions, which are not detected in routine exome analyses.

Research related to WGS testing typically involves careful selection of severely ill patients (often neonates). Congenital 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, and physical or social functioning.[7] In this setting, clinical geneticists and experienced multidisciplinary teams are typically involved, and when a specific illness phenotype is suspected, single gene testing or multi-gene panel testing, and sometimes chromosomal microarray testing, is pursued with turnaround times of around 4 weeks. WGS testing typically takes 8 to 12 weeks and has been explored mostly in situations where all other testing is negative or when the seriously ill infant has multiple nonspecific phenotypic features.[8] Importantly, pre- and post-test genetic counseling is critically important in this setting. There is research evaluating WGS in highly selected cases as an early single-pass test that includes all single-nucleotide variants, copy number variations, structural variations, and mitochondrial DNA. Trio analysis is sometimes included, which involves WGS testing not only the affected child but also both parents.

The feasibility of a rWGS testing approach was tested using a payor-funded, prospective, real-world quality improvement project in the regional ICUs of five tertiary care children's hospitals—Project Baby Bear. Participation was limited to acutely ill Medi-Cal beneficiaries who were admitted November 2018 to May 2020, were < 1 year old, and within one week of hospitalization or had just developed an abnormal response to therapy. The primary outcomes evaluated were changes in medical care reported by physicians and changes in the cost of care. Of 184 infants enrolled, 74 (40%) received a diagnosis by rWGS that explained their admission in a median time of 3 days. In 58 (32%) affected individuals, rWGS led to changes in medical care. Testing and precision medicine cost $1.7 million, but modeled data suggested cost savings associated with this approach when commercial costs were considered. The savings were not attributable to the diagnostic capability of the rWGS testing as much as acceleration of the diagnostic journey and reduced length of stay in the newborn intensive care unit. The applicability of this ultra-rapid testing to the real world is limited by the limited availability of this testing and the necessity of trio testing (meaning both parents submit specimens along with the child), which enables the rapid 3-day turnaround time. In 2020, the Pediatric Exome Sequencing/Genome Sequencing Guideline Work Group (Peds ES/GS GWG) was convened to develop an evidence-based guideline for the clinical use of ES/GS in patients with congenital anomalies, developmental delay, or intellectual disability. This working group addressed the question "Should exome sequencing or genome sequencing be used in the evaluation of patients with more than one congenital anomaly apparent before one year of age, or in patients with developmental disability/intellectual disability diagnosed prior to 18 years of age, compared to standard testing without exome or genome

sequencing?" The evidence review involved 36 studies where the patient population was greater than 20. The authors concluded that WES or WGS testing has a higher diagnostic yield and may be more cost-effective when ordered early in the diagnostic evaluation.[7]

A more recent systematic review examining the role of genomic medicine with WES or WGS testing in critically ill infants was conducted with data from 21 studies reflecting results from 1,654 patients. A mean of 46% (range, 15%-72%) of patients had a positive genetic test result, and a mean of 37% (range, 13%-61%) met the criteria for experiencing utility. This review found that studies disproportionally highlighted patient cases that resulted in treatment change, and larger studies reported substantially lower utility. The authors concluded that a more complete definition of utility that is used consistently may improve understanding of the potential benefits and harms of this testing of critically ill infants. An editorial related to this systematic review emphasized that strengthening the rigor with which utility is measured is critically important and may serve as the foundation for the evaluation of genomic medicine in other clinical contexts outside of neonatal intensive care.

Per Tennessee Public Chapter 1020 Senate Bill No. 1762: rWGS means an investigation of the entire human genome, including coding and non-coding regions and mitochondrial deoxyribonucleic acid, to identify diseases causing genetic changes that returns the preliminary positive results within seven days and within 15 days from the date of receipt of the sample by the lab performing the test. Includes patient-only whole genome sequencing, duo whole genome sequencing of the patient one biological parent, and trio whole genome sequencing of the patient and both biological parents.

History

Status	Date	Action
New	April 2, 2025	New Clinical Guideline for TN Public Chapter 1020 Senate Bill No. 1762.

Federal and state law, as well as contract language including definitions and specific coverage provisions/exclusions, and Medical Policies take precedence over Clinical Utilization Management (UM) Guidelines and must be considered first in determining eligibility for coverage. The members' contract benefits, according to the date that services are rendered, must be used. Clinical UM Guidelines, which address medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical

technology is constantly evolving, and we reserve the right to review and update Clinical UM Guidelines periodically. Clinical UM Guidelines are used when the plan performs utilization review for the subject. Due to variances in utilization patterns, each plan may choose whether to adopt a particular Clinical UM Guideline. To determine if a review is required for this Clinical UM Guideline, please contact the customer service number on the back of the member's ID card.