Clinical Policy: Rapid Whole Genome Sequencing of Critically Ill Infants

Reference Number: LA.CP.MP.522c **Implications Coding**

Date of Last Revision: 06/23 **Revision Log**

See Important Reminder at the end of this policy for important regulatory and legal information

Description

To provide guidance for rapid whole genome sequencing performed in the inpatient setting for infants less than 12 months of age with complex illnesses of unknown etiology. Rapid whole genome sequencing includes:

1. **Individual sequencing;**
2. **Trio sequencing of the parents of the infant; and**
3. **Ultra-rapid sequencing.**

Definitions

Genome sequencing (GS) (also known as 'whole genome sequencing' (WGS)) is a comprehensive technique for sequencing the complete DNA sequence, which includes protein coding as well as non-coding DNA elements.

Rapid genome (rGS) sequencing involves sequencing of the genome in an accelerated time frame. Preliminary results can typically be returned in less than seven (7) days, and a final report in less than two (2) weeks. Studies suggest that the use of rGS in acutely ill infants presenting with complex phenotypes that are likely rare genetic conditions can identify a genetic diagnosis more quickly, which allows clinicians and family members to change acute medical or surgical management options and end the diagnostic odyssey.

Trio Testing includes testing of the child and both parents and increases the chances of finding a definitive diagnosis, while reducing false-positive findings.

Ultra-rapid GS involves sequencing of the genome typically in less than seventy-two (72) hours.

Policy/Criteria

I. **It is the policy of Louisiana Healthcare Connections that Rapid whole genome sequencing is considered medically necessary for infants less than twelve (12) months of age who are receiving inpatient hospital services in an intensive care or pediatric unit. Counseling is required before and after all genetic testing and must be documented in the medical record as per Medicaid's "Genetic Testing" policy**

in the Professional Services manual chapter of the Medicaid Services Manual. The criteria are as follows:

1. **Suspected of having a rare genetic condition that is not diagnosable by standard methods;**

2. **Have symptoms that suggest a broad differential diagnosis that requires an evaluation by multiple genetic tests if advanced molecular techniques including, but not limited to, traditional whole genome sequencing, rapid whole genome sequencing, and other genetic and genomic screening are not performed;**

3. **Timely identification of a molecular diagnosis is necessary to guide clinical decision making, and the advanced molecular techniques including, but not limited to, traditional whole genome sequencing, rapid whole genome sequencing, and other genetic and genomic screening results may guide the treatment or management of the infant's condition;**

4. **Have an illness with at least one of the following features:**

a. **Multiple congenital anomalies;**

b. **Specific malformations highly suggestive of a genetic etiology; or**

c. **Abnormal laboratory tests suggesting the presence of a genetic disease or complex metabolic phenotype like but not limited to an abnormal newborn screen, hyperammonemia, or lactic acidosis not due to poor perfusion;**

d. **Refractory or severe hypoglycemia;**

e. **Abnormal response to therapy related to an underlying medical condition affecting vital organs or bodily systems;**

f. **Severe hypotonia;**

g. **Refractory seizures;**

h. **High-risk stratification on evaluation for a brief resolved unexplained event with any of the following:**

    1. **Recurrent event without respiratory infection,**

    2. **Recurrent witnessed seizure-like event, or**

    3. Recurrent cardiopulmonary resuscitation;

i. Abnormal chemistry levels including, but not limited to, electrolytes, bicarbonate, lactic acid, venous blood gas, and glucose suggestive of inborn error of metabolism;
j. Abnormal cardiac diagnostic testing results suggestive of possible channelopathies, arrhythmias, cardiomyopathies, myocarditis, or structural heart disease; or

k. Family genetic history related to the infant's condition.

Coding Implications

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NOTE: Coverage is subject to each requested code's inclusion on the corresponding LDH fee schedule. Non-covered codes are denoted (*) and are reviewed for Medical Necessity for members under 21 years of age on a per case basis.

CPT® Codes	Description
0094U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis
0212U*	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, proband
0213U*	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, each comparator genome (eg, parent, sibling)
81425	Genome (eg, unexplained constitutional or heritable disorder syndrome); sequence analysis
81426	Genome (eg, unexplained constitutional or heritable disorder syndrome); sequence analysis
81427	Genome (eg, unexplained constitutional or heritable disorder syndrome); sequence analysis

Reviews, Revisions, and Approvals	Revision Date	Approval Date
New Policy	6.23	

References

1.) *Louisiana Department of Health (LDH) Hospital Service Provider Manual*. Chapter 25:25.2 Rapid Whole Genome Sequencing of Critically Ill Infants Pg. (12-18). Issued 5/16/23, Replaced 3/09/23. https://www.lamedicaid.com/provweb1/providermanuals/manuals/Hosp/Hosp.pdf

2.) Medicaid's "Genetic Testing" policy in the Professional Services manual chapter of the Medicaid Services Manual.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as any state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy

is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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