RAPID GENOME SEQUENCING

I. Rapid genome sequencing (rGS) (81425, 81426, 0094U, 0425U, 0426U), 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:

1. The member has unexplained epilepsy, **OR**

2. The member has multiple congenital abnormalities (functional and/or structural) affecting unrelated organ systems, **OR**

3. The member has epileptic encephalopathy, **OR**

4. 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.

II. Rapid genome sequencing (rGS) (81425, 81426, 0094U, 0425U, 0426U) 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

1. **Genome Sequencing (GS)**: A genomic technique for sequencing the complete DNA sequence, which includes protein coding as well as non-coding DNA elements.
2. **Trio Testing**: Testing of the child and both biological/genetic parents, which increases the chances of finding a definitive diagnosis while reducing false-positive findings.
3. **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.
4. **Global Developmental delay:** An individual that 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)
5. **Intellectual disability (ID):** Defined by the DSM-V as an individual who meets all of the following:
    a. 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.
    b. 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.

c. Onset of intellectual and adaptive deficits during the developmental period.

REFERENCES

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