Rapid Exome Sequencing

I. 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 criteria:

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

2. The member has global developmental delay, **OR**

3. The member was diagnosed with at least one congenital anomaly (functional and/or structural), **OR**

4. 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) Severe neuropsychiatric condition (e.g., schizophrenia, bipolar disorder, Tourette syndrome, self-injurious behavior, reverse sleep-wake cycles), **OR**

f) Period of unexplained developmental regression (unrelated to epilepsy or autism).

II. Rapid exome sequencing (rES) is considered **investigational** for all other indications, including screening asymptomatic/healthy individuals for genetic disorders.

DEFINITIONS

1. **Congenital anomalies** (according to ACMG) 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.
2. **Genome Sequencing** (GS) is a genomic technique for sequencing the complete DNA sequence, which includes protein coding as well as non-coding DNA elements.
3. **Global Developmental delay** is diagnosed when a child under age 5 is slow-to-meet or not reaching milestones in the expected way for their age in at least two areas of development (communication, gross/fine motor, cognition, social-emotional, or adaptive skills).
4. **Trio Testing** is testing of the child and both biological/genetic parents, which increases the chances of finding a definitive diagnosis while reducing false-positive findings.

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