

MITOCHONDRIAL GENOME SEQUENCING, DELETION/DUPLICATION, AND/OR NUCLEAR GENES

- I. Mitochondrial genome sequencing (81460), deletion/duplication (81465), and/or nuclear genes analysis (0417U, 81440) to establish or confirm a diagnosis of a primary mitochondrial disorder is considered **medically necessary** when:
 - A. The member has a classic phenotype of one of the maternally inherited syndromes (e.g., Leber hereditary optic neuropathy, mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes [MELAS], myoclonic epilepsy with ragged red fibers [MERRF], maternally inherited deafness and diabetes [MIDD], neuropathy, ataxia, retinitis pigmentosa [NARP], Kearns-Sayre syndrome/CPEO); or of a nuclear DNA mitochondrial disorder (e.g., mitochondrial neurogastrointestinal encephalopathy [MNGIE]); **OR**
 - B. The member has non-specific clinical features suggestive of a primary mitochondrial disorder and meets **ALL** of the following:
 1. Clinical findings of at least two of the following:
 - a) Ptosis, **OR**
 - b) External ophthalmoplegia, **OR**
 - c) Proximal myopathy, **OR**
 - d) Exercise intolerance, **OR**
 - e) Cardiomyopathy, **OR**
 - f) Sensorineural deafness, **OR**
 - g) Optic atrophy, **OR**
 - h) Pigmentary retinopathy, **OR**
 - i) Diabetes mellitus, **OR**
 - j) Fluctuating encephalopathy, **OR**
 - k) Seizures, **OR**
 - l) Dementia, **OR**
 - m) Migraine, **OR**
 - n) Stroke-like episodes, **OR**
 - o) Ataxia, **OR**
 - p) Spasticity, **OR**

- q) Chorea, **OR**
 - r) Multiple late term pregnancy loss, **AND**
2. Conventional biochemical laboratory studies have been completed and are non-diagnostic, including at least: plasma or CSF lactic acid concentration, ketone bodies, plasma acylcarnitines, and urinary organic acids, **AND**
 3. Additional diagnostic testing indicated by the member's clinical presentation (e.g., fasting blood glucose, electrocardiography, neuroimaging, electromyography, echocardiography, audiology, thyroid testing, electroencephalography, exercise testing) have been completed and are non-diagnostic.
- II. Mitochondrial genome sequencing (81460), deletion/duplication (81465), and/or nuclear genes analysis (81440) to establish or confirm a diagnosis of a primary mitochondrial disorder is considered **investigational** for all other indications.

DEFINITIONS

1. **Mitochondrial disease** refers to a heterogenous group of disorders caused by dysfunctional mitochondria, the organelles responsible for oxidative phosphorylation within the cell.

REFERENCES

1. Parikh S, Goldstein A, Koenig MK, et al. Diagnosis and management of mitochondrial disease: a consensus statement from the Mitochondrial Medicine Society. *Genet Med.* 2015;17(9):689-701. doi:10.1038/gim.2014.177

2. Chinnery PF. Primary Mitochondrial Disorders Overview. 2000 Jun 8 [Updated 2021 Jul 29]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1224/>