

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

- I. 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 **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.

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/>