Mitochondrial Genome Sequencing, Deletion/Duplication, and/or Nuclear Gene Panel

I. Mitochondrial genome sequencing, deletion/duplication, and/or nuclear genes analysis 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, deletion/duplication, and/or nuclear genes analysis 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/