Whole genome sequencing for the diagnosis of mitochondrial disease

Last updated: 22 November 2023

- From 1 November 2023, seven new pathology items were listed on the Medicare Benefits Schedule (MBS) for testing for genetic variants associated with mitochondrial disease (MD).
- This means better health outcomes for patients, by supporting clinicians to request genetic testing for the diagnosis of MD in patients who are suspected of having either acute or chronic disease. The new items also provide for cascade testing of the patient's biological relatives, as well as reproductive partner testing and fetal testing.

What are the changes?

Effective 1 November 2023, seven new pathology items were listed on the MBS, for testing affected individuals using singleton and trio virtual gene panel-based analysis of whole exome or genome data, data re-analysis, mitochondrial DNA deletion testing, cascade testing of biological relatives, reproductive partner testing, and fetal testing. **Attachment A** to this factsheet lists the new items.

Mitochondrial disease is rare and affects a person's ability to make enough energy for the body. Mitochondrial disease can affect children and adults. It can affect different organs with different severity. Patients with mitochondrial disease can have a wide range of symptoms. Mitochondrial disease is usually diagnosed through tests such as muscle biopsies (minor surgery to take a sample of muscle tissue), but these do not provide a definite result without additional genetic testing.

For private health insurance purposes, the new items were listed under the following clinical category and procedure type:

- New items 73456, 73457, 73458, 73459, 73460, 73461 and 73462:
    - Clinical category: Support List (pathology)
    - Procedure type: Type C

Why are the changes being made?

These tests are aimed at providing genetic testing which is safer and more effective than the current diagnostic process, including muscle biopsy. These tests will provide valuable diagnostic information and inform treatment of patients. Publicly funding these tests will support equitable access to targeted therapies.

There are also new items which allow couples whose genetic tests show these variants to make informed reproductive choices, including choosing to have pre-implantation or prenatal fetal testing if they wish to.

The listing of this service was recommended by the Medical Services Advisory Committee (MSAC) in November 2022 in response to MSAC Application 1675. Further details about MSAC applications can be found under MSAC Applications on the MSAC website (Medical Services Advisory Committee).

What does this mean for requestors and providers?

Specialists or consultant physicians are now able to request publicly funded genetic tests for patients with a strong suspicion of a mitochondrial disease. These tests utilise whole genome sequencing, whole exome sequencing and mitochondrial DNA sequencing as appropriate, to detect germline variants present in nuclear DNA and in mitochondrial DNA of patients. There are also tests for reanalysis and testing of family members to inform reproductive decision making:

- singleton testing of affected patients
- trio testing of affected patients and their biological parents
- re-analysis of data at least 18 months after the previous genetic testing
- testing of a fetus at risk of having MD based on the parents' genotypes
- testing for patients strongly suspected of having a mtDNA deletion and in whom sequencing and analysis was non-informative
- genetic testing of the reproductive partner of an individual with a recessive MD variant
- cascade testing of biological relatives

To be eligible for Medicare benefits, laboratories providing this service must be accredited according to the pathology accreditation standards specified in the *Health Insurance (Accredited Pathology Laboratories-Approval) Principles 2017*.

How will these changes affect patients?

Genetic testing for mitochondrial disease only requires a blood sample. It is also more effective as it can provide a more accurate diagnosis than current test methods, and sooner. This may allow patients to avoid some tests such as biopsies. Public funding for genetic testing will support better access to the treatments that are available for some patients.

Who was consulted on the changes?

The Department received responses from ten organisations and one individual consumer. The feedback was overall supportive of the application. The organisations that provided input were: Australian Genomics (AG), Australian Pathology (AP), Childhood Dementia Initiative (CDI), GUARD Collaborative Australia (GUARD), Human Genetics Society of Australasia (HGSA), Murdoch Children's Research Institute (MCRI), Mito Foundation (Mito), Public Pathology Australia (PPA), The Royal College of Pathologists of Australasia (RCPA), and Rare Voices Australia (RVA).

How will the changes be monitored and reviewed?

All MBS items are subject to compliance processes and activities, including random and targeted audits which may require a provider to submit evidence about the services claimed.

Where can I find more information?

The full item descriptor(s) and information on other changes to the MBS can be found on the MBS Online website at www.mbsonline.gov.au. You can also subscribe to future MBS updates by visiting MBS Online and clicking 'Subscribe'.

The Department of Health and Aged Care provides an email advice service for providers seeking advice on interpretation of the MBS items and rules and the *Health Insurance Act 1973* and associated regulations. If you have a query relating exclusively to interpretation of the Schedule, you should email askMBS@health.gov.au.

Private health insurance information on the product tier arrangements is available at www.privatehealth.gov.au. Detailed information on the MBS item listing within clinical categories is available on the Department's website. Private health insurance minimum accommodation benefits information, including MBS item accommodation classification, is available in the latest version of the *Private Health Insurance (Benefit Requirements) Rules 2011* found on the Federal Register of Legislation. If you have a query in relation to private health insurance, you should email PHI@health.gov.au.

Subscribe to 'News for Health Professionals' on the Services Australia website and you will receive regular news highlights.

If you are seeking advice in relation to Medicare billing, claiming, payments, or obtaining a provider number, please go to the Health Professionals page on the Services Australia website or contact the Services Australia on the Provider Enquiry Line – 13 21 50.

The data file for software vendors when available can be accessed via the Downloads page.

Attachment A:

Amended item descriptors (to take effect 1 November 2023)

Category 6 – Pathology Services

Group P7 - Genetics

73456

Characterisation by whole genome sequencing, or by either or both whole exome sequencing and mitochondrial DNA sequencing, of germline variants present in nuclear DNA and in mitochondrial DNA of a patient with a strong suspicion of a mitochondrial disease, if:

(a) the characterisation is requested by a specialist or consultant physician; and

(b) the characterisation is requested because of the onset of one or more clinical features indicative of mitochondrial disease, including at least one or more of the following:
- (i) meeting the clinical criteria of a probable indicator of mitochondrial disease on a relevant scoring system;
- (ii) evident mitochondrial dysfunction or decompensation;
- (iii) unexplained hypotonia or weakness, profound hypoglycaemia or “failure to thrive” in the presence of a metabolic acidosis;
- (iv) unexplained single or multi-organ dysfunction or fulminant failure (including, but not limited to, neuropathies, myopathies, hepatopathy, pancreatic and/or bone marrow failure);
- (v) refractory or atypical seizures, developmental delays or cognitive regression, or progressive encephalopathy or progressive encephalomyopathy;
- (vi) cardiomyopathy and/or cardiac arrythmias;
- (vii) rapid hearing or painless visual loss or ptosis;
- (viii) stroke-like episodes or nonvasculitic strokes;
- (ix) ataxia, encephalopathy, seizures, muscle fatigue or weakness;
- (x) external ophthalmoplegia;
- (xi) hearing loss, diabetes, unexplained short stature, or endocrinopathy;
- (xii) family history of mitochondrial disease, or any of the above; and

(c) the service is not a service associated with a service to which item 73358, 73359 or 73457 applies

Applicable only once per lifetime

MBS Fee: $2,100.00

Benefit: 75% = $1,575.00 85% = $2,001.30 (Greatest Permissible Gap (GPG) will apply)

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Group P7 - Genetics

Category 6 – Pathology Services

73457

Characterisation by whole genome sequencing, or either or both whole exome sequencing and mitochondrial DNA sequencing, of germline variants present in nuclear DNA and in mitochondrial DNA, of a patient with a strong suspicion of a mitochondrial disease, if:

(a) the characterisation is performed using a sample from the patient and a sample from each of the patient's biological parents; and

(b) the request for the characterisation states that singleton testing is inappropriate; and

(c) the characterisation is requested by a specialist or consultant physician; and

(d) the characterisation is requested because of the onset of one or more clinical features indicative of mitochondrial disease, including at least one or more of the following:

- (i) meeting the clinical criteria of a probable indicator of mitochondrial disease on a relevant scoring system;
- (ii) evident mitochondrial dysfunction or decompensation;
- (iii) unexplained hypotonia or weakness, profound hypoglycaemia or "failure to thrive" in the presence of a metabolic acidosis;
- (iv) unexplained single or multi-organ dysfunction or fulminant failure (including, but not limited to, neuropathies, myopathies, hepatopathy, pancreatic and/or bone marrow failure);
- (v) refractory or atypical seizures, developmental delays or cognitive regression, or progressive encephalopathy or progressive encephalomyopathy;
- (vi) cardiomyopathy and/or cardiac arrythmias;
- (vii) rapid hearing or painless visual loss or ptosis;
- (viii) stroke-like episodes or nonvasculitic strokes;
- (ix) ataxia, encephalopathy, seizures, muscle fatigue or weakness;
- (x) external ophthalmoplegia;
- (xi) hearing loss, diabetes, unexplained short stature, or endocrinopathy;
- (xii) family history of mitochondrial disease; and

(e) the service is not a service associated with a service to which item 73358, 73359 or 73456 applies

Applicable only once per lifetime

MBS Fee: $3,300.00

Benefit: 75% = $2,475.00 85% = $3,201.30 (Greatest Permissible Gap (GPG) will apply)

Category 6 – Pathology Services

Group P7 - Genetics

73458

Re-analysis of whole genome or whole exome or mitochondrial DNA data obtained in performing a service to which item 73456 or 73457 applies, for characterisation of previously unreported germline variants related to the clinical phenotype, if:

(a) the re-analysis is requested by a specialist or consultant physician; and

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(b) the patient is strongly suspected of having a monogenic mitochondrial disease; and

(c) the re-analysis is performed at least 24 months after:
- (i) the service to which item 73456 or 73457 applies; or
- (ii) a service to which this item applies

Applicable twice per lifetime

MBS Fee: $500.00

Benefit: 75% = $375.00 85% = $425.00

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73459

Testing for diagnostic purposes of a pregnant patient, for detection in the fetus of a gene variant or variants present in the parents, if:

(a) the gene variant or variants are:
- (i) a variant or variants in the mitochondrial genome identified in the oocyte donating parent; or
- (ii) autosomal recessive variants identified in both biological parents within the same gene; or
- (iii) an autosomal dominant or X-linked variant identified in either biological parent; or
- (iv) identified in a biological sibling of the fetus; and

(b) the causative variant or variants for the condition of the fetus' first-degree relative have been confirmed by laboratory findings; and

(c) the detection is requested by a specialist or consultant physician; and

(d) the service is not a service associated with a service to which item 73361, 73362, 73363 or 73462 applies

MBS Fee: $1,600.00

Benefit: 75% = $1,200.00 85% = $1,501.30 (Greatest Permissible Gap (GPG) will apply)

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73460

Characterisation of mitochondrial DNA deletion or variant for diagnostic purposes in a patient suspected to have mitochondrial disease, if:

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(a) the characterisation is requested by the specialist or consultant physician managing the patient's treatment; and

(b) the patient displays onset of one or more clinical features indicative of mitochondrial disease, including at least one or more of the following:

(i) meeting the clinical criteria of a probable indicator of mitochondrial disease on a relevant scoring system;
(ii) evident mitochondrial dysfunction or decompensation;
(iii) unexplained hypotonia or weakness, profound hypoglycaemia or 'failure to thrive' in the presence of a metabolic acidosis;
(iv) unexplained single or multi-organ dysfunction or fulminant failure (including, but not limited to, neuropathies, myopathies, hepatopathy, pancreatic and/or bone marrow failure);
(v) refractory or atypical seizures, developmental delays or cognitive regression, or progressive encephalopathy or progressive encephalomyopathy;
(vi) cardiomyopathy and/or cardiac arrythmias;
(vii) rapid hearing or painless visual loss or ptosis;
(viii) stroke-like episodes or nonvasculitic strokes;
(ix) ataxia, encephalopathy, seizures, muscle fatigue or weakness;
(x) external ophthalmoplegia;
(xi) hearing loss, diabetes, unexplained short stature, or endocrinopathy;
(xii) family history of mitochondrial disease; and

(c) the service is performed following a service to which items 73292, 73358, 73359, 73456 or 73457 applies for the same patient if the results were non-informative

Applicable 3 times per lifetime

MBS Fee: $450.00

Benefit: 75% = $337.50 85% = $382.50

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73461

Whole gene testing of a person for the characterisation of all germline gene variants within the same gene in which the person's reproductive partner has a pathogenic or likely pathogenic germline recessive gene variant for mitochondrial disease, if:

(a) the partner's germline recessive gene variant is confirmed by laboratory findings; and

(b) the characterisation is requested by a specialist or consultant physician

MBS Fee: $1,200.00

Benefit: 75% = $900.00 85% = $1,101.30 (Greatest Permissible Gap (GPG) will apply)

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Group P7 - Genetics

73462

Testing of a person for the detection of a single gene variant, if:

(a) the person tested has a biological relative with a known pathogenic or likely pathogenic mitochondrial disease variant confirmed by laboratory findings; and

(b) the testing is requested by a specialist or consultant physician; and

(c) the service is not a service associated with a service to which item 73361, 73362 or 73363 applies

MBS Fee: $400.00

Benefit: 75% = $300.00 85% = $340.00

Please note that the information provided is a general guide only. It is ultimately the responsibility of treating practitioners to use their professional judgment to determine the most clinically appropriate services to provide, and then to ensure that any services billed to Medicare fully meet the eligibility requirements outlined in the legislation.

This factsheet is current as of the Last updated date shown above and does not account for MBS changes since that date.