

MSAC Application 1776

**Newborn bloodspot screening for
mucopolysaccharidosis type II (MPS II)**

Application or referral for other medical service or health technology

MSAC Application Number

1776

Application title:

Newborn bloodspot screening for Mucopolysaccharidosis type II (MPS II)

Submitting organisation:

Department of Health and Aged Care Newborn bloodspot screening

Application description

Succinct description of the medical condition/s:

MPS II (Hunter syndrome) is a rare X-linked recessive lysosomal storage disorder (LSD). MPS II is caused by a mutation of the IDS gene which results in dysfunction of the enzyme iduronate-2-sulfatase (ID2S). ID2S normally causes a breakdown of waste materials in the cells of the body (dermatan sulphate (DS) and heparan sulphate (HS)). In MPS II, insufficient ID2S enzyme causes a toxic build-up of DS and HS resulting in cellular damage in affected individuals. This leads to development of symptoms which includes an enlarged liver and spleen, umbilical or inguinal hernia, hearing loss, narrowing of the spinal canal compressing the spinal cord, and heart valve abnormalities leading to heart rhythm abnormalities and heart failure. The severe form characterised by earlier onset of symptoms, more rapid disease progression and neuronopathic involvement, leading to symptoms of significant neurological impairment including cognitive disability and behavioural problems.

Succinct description of the service or health technology:

It is proposed that a screening test for MPS II be added to existing newborn bloodspot screening programs in Australia to support early diagnosis and intervention to improve clinical outcomes.

Application contact details

Are you applying on behalf of an organisation, or as an individual?

Organisation

Is the applicant organisation the organisation you are representing in the HPP today?

Yes

Applicant organisation name:

Department of Health and Aged Care Newborn bloodspot screening

Application details

Please select the program through which the health technology would be funded:

Other

Specify the funding program:

NBS funding

Please provide justification for selecting the above program:

Australian NBS programs are funded and delivered through public hospital services in all Australian jurisdictions. Patients and families can choose to utilise services through the private system at their own cost for postpartum care and any necessary ongoing intervention for rare diseases. However, all NBS samples are tested by the newborn screening laboratories which are managed and funded within the public system.

Each jurisdiction has unique arrangements for the funding and delivery of NBS services to align with specific local health system structures. Funding for the Australian NBS programs comes from a mix of jurisdictional and national funds. The Australian government contributes funds for public hospital services, including typical sample collection, testing and downstream care in the NBS programs, under the 2020-25 National Health Reform Agreement (NHRA). The NHRA recognises the states and territories as system managers of public hospitals. Changes to the NBS laboratories (either directly for state-run pathology services or via contract negotiation as required) will be funded through standard jurisdictional budgetary measures and supported by the NHRA.

There are no Medical Benefits Scheme (MBS) items specifically for the delivery of NBS services; however, MBS items may be used in the delivery of downstream medical care or to confirm diagnoses. Funding for the ongoing delivery of interventions for MPS II is also provided for by the Australian government through the LSDP. The LSDP covers medicines for ultra-rare conditions (1 case per 50000 or fewer) which are not listed on the Pharmaceutical Benefits Scheme (PBS) but which have clinically effective.

In addition to these standard funding mechanisms, the Australian government is directly contributing \$25.3 million to states and territories to support the expansion of the NBS programs. This funding can be used by jurisdictions at their discretion.

What is the type of service or health technology?

Investigative

PICO sets:

PICO set	PICO set name
1	Population 1: Newborns
2	Population 2: Cascade testing of family

Application PICO set 1: Population 1: Newborns

Population

Describe the population in which the proposed health technology is intended to be used:

The target population for MPS II screening as part of Australian NBS programs is all babies born in Australia. The NBS National Policy Framework states that NBS is to be performed within 48 to 72 hours after birth.

Select the most applicable medical condition terminology (SNOMED CT):

70737009

Intervention

Name of the proposed health technology:

Newborn bloodspot screening for mucopolysaccharidosis type II (MPS II)

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This include identifying health care resources that are needed to be delivered at the same time as the comparator service:

The comparator for the proposed health technology is no universal screening for MPS II through NBS programs. Diagnosis would occur as per current clinical practice, following presentation with symptoms or through cascade screening following diagnosis of a family member.

Outcomes

Outcome description - please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Screening of MPS II via NBS programs would enable earlier diagnosis of the condition, and support timely access to intervention. There is some evidence to indicate that earlier initiation of MPS II treatment prior to development of the somatic and neuronopathic manifestations of the disorder can improve health outcomes assessed as improvement or stabilization of symptoms, general functioning and quality of life. There is some evidence

that earlier initiation of enzyme replacement therapy (ERT) or haemopoietic stem cell transplantation (HSCT) can slow the progression of the disease and increase life-expectancy.

Health benefits

- Health outcomes from early diagnosis and intervention (improvement in morbidity and mortality, general functioning and disease manifestations)
- Quality of life (both the disease and the treatment may impact on quality aspects)
- Disease specific patient reported outcomes (PROs)

Health harms

- Impacts from false positive results
- Impacts from false negative results leading to a delayed or missed diagnosis of MPS II (noting this would mean the newborn is diagnosed clinically, which is the comparator. There is a potential that a diagnosis of MPS II may be overlooked if it is assumed it will be detected through NBS)
- Impacts from identifying variants of unknown significance in the IDS gene where the impact of the variant on phenotype is uncertain
- Safety of HSCT and ERT, prior to or after symptom onset, short and long-term effects

Resources

- Financial impact of screening
- Financial impact of diagnosis, relative to existing practice (including false positives)
- Financial impact (including savings) of early intervention, relative to existing practice
- Financial impact of any change in clinical management following NBS (e.g., change in treatment approach when treatment occurs presymptomatically, requirements for MPS II symptom monitoring and surveillance, genetic counselling, and other support services)
- Financial impact of ongoing monitoring and surveillance of patients with MPS II
- Cost effectiveness (cost per diagnosis; cost per QALY)

Other relevant considerations

- Value of knowing (family planning, emotional benefits/harms to family, social benefits/harms to family, noting these are secondary to the outcomes delivered to the baby)
- Accuracy of the screening test (sensitivity, specificity, positive predictive value and diagnostic yield)
- Ethical considerations (equity of access, considerations regarding consent, considerations regarding cascade testing, including notification of carrier status)

Specified restrictions for funding

Please add one or more items, with specified restriction for funding, for each Population/Intervention:

Proposed item: AAAAA

Is the proposed item restricted:

No - unrestricted

Provide a short description of the restriction:

NBS for MPS II is not on the MBS and this intervention is not proposed for addition to the MBS.

Please draft a proposed restriction to define the population and health technology usage characteristics that would define eligibility for funding:

-

Proposed price of supply:

██████████

Indicate the overall cost per patient of providing the proposed health technology:

██████████

Provide details and explain:

MPS II is currently not screened anywhere in Australia. There is also no commercially available kit for this condition. Laboratories would need to develop a screening protocol first to be able to estimate costs for this. Further information on this may be gathered from screening labs during the consultation phase. The test cost of ██████████ is estimated based on the commercial kit cost of ██████████ for MPS I which is a closely related condition to MPS II.

How is the technology / service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payment):

NBS for MPS I is currently not funded or performed in Australia. See attachment for more details on funding for NBS programs.

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

Superior

Please state what the overall claim is, and provide a rationale:

In terms of health outcomes, the proposed NBS for early diagnosis of MPS II is claimed to be superior to the comparator of no NBS and diagnosis upon symptomatic presentation. Early diagnosis allows earlier treatment which improves health outcomes.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:

The number of babies who uptake NBS was taken from Huynh et al. (2022). The total number of babies screened through NBS programs 2016–2020 was divided by the number of registered births over the same time period to estimate the rate of uptake of NBS (99.3%).

Provide the percentage uptake of the proposed health technology by the proposed population:

Year 1 estimated uptake (%):

99.3

Year 2 estimated uptake (%):

99.3

Year 3 estimated uptake (%):

99.3

Year 4 estimated uptake (%):

99.3

Estimate the number of patients who will utilise the proposed technology for the first full year:

311,651

Optionally, provide details:

The ABS registered births (ABS 2022) was used to project the estimated number of births per year, 2024–2028.

Year 1 estimated uptake:

The estimated number of babies born 2024-2025 is 313,993 babies.

The estimated number of babies who uptake NBS 2024-2025 is 311,651 babies.

Year 2 estimated uptake:

The estimated number of babies born 2025-2026 is 314,727 babies.

The estimated number of babies who uptake NBS 2025-2026 is 312,380 babies.

Year 3 estimated uptake:

The estimated number of babies born 2026-2027 is 315,462 babies.

The estimated number of babies who uptake NBS 2024-2025 is 313,109 babies.

Year 4 estimated uptake:

The estimated number of babies born 2027-2028 is 316,196 babies.

The estimated number of babies who uptake NBS 2027-2028 is 313,873 babies.

The number of babies receiving each tier of testing in Year 1 has been estimated as follows:

- The number of babies provided first-tier testing is 311,651.
- First-tier screening would identify 0.009% of tests as positive (including borderline positive) using I2S enzyme testing, based on data from Burton et al (2020), meaning an estimated 28 newborns will require second-tier testing.
- Of the newborns identified as positive or borderline positive from the first-tier test, 78% will be false positives due to pseudodeficiency as identified by the 2nd tier GAG testing, meaning an estimated 6 newborns will be referred for confirmatory diagnostic testing.
- The total number of true positives diagnosed with MPS II following confirmatory testing, based on condition incidence of 0.57 per 100,000 live births (Chin & Fuller, 2022), is 2.

Will the technology be needed more than once per patient?

No, once only

Application PICO set 2: Population 2: Cascade testing of family

Population

Describe the population in which the proposed health technology is intended to be used:

MPS II is an X-linked recessive disorder, primarily affecting males. Based on this inheritance pattern, it is proposed that cascade testing of male newborns diagnosed with pathogenic or likely pathogenic variants of MPS II be offered to the mother only.

Older male siblings of a newborn diagnosed with MPS II with the same mother may also be affected. It is proposed that these individuals receive biochemical testing. If this test is positive for MPS II, the male sibling would then be offered genetic testing.

Cascade testing of unaffected siblings to determine carrier status will not be offered.

It is proposed that the assessment consider the appropriateness of offering cascade testing to the biological father in the rare case that a female with MPS II is diagnosed.

Select the most applicable medical condition terminology (SNOMED CT):

70737009

Intervention

Name of the proposed health technology:

Cascade testing of biological mothers and older male siblings of a baby diagnosed with MPS II

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e., how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This include identifying health care resources that are needed to be delivered at the same time as the comparator service:

Currently, cascade testing is offered to families after diagnosis of a symptomatic child within the hospital system. There are no genetic counsellors associated with metabolic clinics in current practice in Australia. If the parents wish for further family planning advice, they may be referred to an appropriate clinic.

Outcomes

Outcome description - please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Cascade testing enables the parents to undertake reproductive planning. Further, older male siblings of the affected newborn who may themselves also be affected would receive biochemical testing. If the sibling tests positive, genetic testing would be offered. It is proposed that with early identification, intervention could commence sooner and improve health outcomes.

Health benefits

- Improvement in clinical outcomes from an earlier diagnosis and intervention (for affected siblings)

Health harms

- Impact of diagnosing siblings with mild or benign forms of the condition that may not become symptomatic (overdiagnosis)

Resources

- Financial impact of cascade testing
- Health care resources involved in testing and counselling
- Diagnosis and management for an affected sibling
- Total health care costs, including cost effectiveness

Other relevant considerations

- Value of knowing (for parents, siblings and broader family members, emotional benefits/harms to family, social benefits/harms to family)
- Accuracy of the test
- Ethical considerations (equity of access, notification of carrier status)

Specified restrictions for funding

Please add one or more items, with specified restriction for funding, for each Population/Intervention:

Proposed item: BBBBB

Is the proposed item restricted:

No - unrestricted

Provide a short description of the restriction:

NBS for MPS II is not on the MBS and this intervention is not proposed for addition to the MBS.

Please draft a proposed restriction to define the population and health technology usage characteristics that would define eligibility for funding:

NA

Proposed price of supply:

400.00

Indicate the overall cost per patient of providing the proposed health technology:

400.00

Provide details and explain:

Cascade testing is available on the MBS for other conditions, such monogenic conditions (73361), familial hypercholesterolaemia (73353) and mitochondrial disease (73462). The cost of testing a close biological relative of a child with a known pathogenic or likely pathogenic disease variant for all three of these conditions is \$400.00 (Benefit: 75% = \$300.00 85% = \$340.00). Therefore cascade testing for MPS II is likely to be around \$400. These figures may be updated further during the PICO development stage.

How is the technology / service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payment):

Currently cascade testing would be conducted in families suspected to be carriers of MPS II, or when symptoms arise in an infant. Funding would be covered by the state or territory or by the patient undergoing testing (or their parents).

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

Superior

Please state what the overall claim is, and provide a rationale:

Cascade testing may support improved outcomes if an affected sibling is identified through cascade testing, but this would be limited to a small number of cases. It also supports reproductive planning for parents, who are unaffected by the condition.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:

An incidence of 0.57 per 100,000 live births, taken from Chin and Fuller (2022), was used to estimate the number of affected babies that would be identified by screening. This would result in up to 2 babies being diagnosed with MPS II each year.

The family of these babies would be offered cascade testing. The average number of dependent children in an Australian household was reported to be 1.2 in 2020 (see 'optionally provide details' section for reference). Based on this, assuming each family has 1-2 siblings, the number of family members who would need cascade testing per positive baby is 1-2 (mum and 0-1 sibling). Therefore, approximately 2-4 individuals are expected to be offered cascade testing each year.

Provide the percentage uptake of the proposed health technology by the proposed population:

Year 1 estimated uptake (%):

100

Year 2 estimated uptake (%):

100

Year 3 estimated uptake (%):

100

Year 4 estimated uptake (%):

100

Estimate the number of patients who will utilise the proposed technology for the first full year:

2-4

Optionally, provide details:

The average number of dependent children in Australian households data were sourced from <https://www.ceicdata.com/>

Will the technology be needed more than once per patient?

No, once only

Consultation

List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the health technology/service:

- ACT Newborn Bloodspot Screening Program
- Northern Territory Newborn Bloodspot Screening Program
- NSW Newborn Bloodspot Screening Program
- Public Pathology Australia
- Queensland Newborn Bloodspot Screening Program
- South Australian Newborn Bloodspot Screening Program

- Tasmanian Newborn Bloodspot Screening Program
- The Royal College of Pathologists Of Australasia
- Victorian Newborn Bloodspot Screening Program
- West Australian Newborn Bloodspot Screening Program

List all appropriate professional bodies / organisations representing the group(s) of health professionals who request the health technology/service:

- Australian College of Midwives Ltd.

List all appropriate professional bodies / organisations representing the group(s) of health professionals that may be impacted by the health technology/service:

- Department for Health and Wellbeing
- Sanofi-Aventis Australia Pty Ltd

List the patient and consumer advocacy organisations or individuals relevant to the proposed health technology:

- Genetic Alliance Australia
- Mucopolysaccharide & Related Diseases Society Aust. Ltd.
- Rare Voices Australia Ltd

List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed service or health technology:

- ACT Genetics Service
- ACT Paediatric Clinic
- Centre for Genetics Education, NSW Health
- Genetic Services of WA
- Northern Territory Clinical Genetics Service
- NSW Genetic Metabolic Disorders Service
- Queensland Genomics
- Queensland Paediatric Metabolic Medicine clinic
- SA Clinical Genetics Service
- Tasmanian Clinical Genetics Service (TCGS)
- Tasmanian Dietitian Clinic: General Paediatrics
- The Human Genetics Society of Australasia Incorporated
- Victorian Clinical Genetics Services
- Victorian Metabolic Medicine department
- WA Metabolic Medicine Department

Regulatory information

Would the proposed health technology involve the use of a medical device, in-vitro diagnostic test, radioactive tracer or any other type of therapeutic good?

No