MSAC Application 1774

Newborn bloodspot screening for glycogen storage disease, type II (Pompe disease)

Application or referral for other medical service or health technology

MSAC Application Number:
1774

Application title:
Newborn bloodspot screening for glycogen storage disease, type II (Pompe disease)

Submitting organisation:
Department of Health and Aged Care Newborn bloodspot screening

Application description

Succinct description of the medical condition/s:
Glycogen storage disease, type II (GSD II), also known as Pompe disease, is an autosomal inherited lysosomal storage disease caused by a genetic alteration in the α-glucosidase (GAA) gene. It causes deterioration of muscle strength and growth and leads to early death. Early treatment with enzyme replacement therapy can reduce deterioration and extend life to some degree.

Succinct description of the service or health technology:
It is proposed that a screening test for glycogen storage disease, type II (GSD II) is added to newborn bloodspot screening programs (NBS) in Australia.

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 GSDII 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 are 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 first-degree relatives

Application PICO set 1: Population 1: Newborns

Population

Describe the population in which the proposed health technology is intended to be used:
All newborns in Australia are eligible for screening under NBS programs. NBS is normally performed within 48-72 hours of birth as per the newborn bloodspot screening National Policy framework.

Select the most applicable medical condition terminology (SNOMED CT):
237967002

Intervention

Name of the proposed health technology:
National newborn bloodspot screening for Glycogen storage disease type 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 GSD 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:

It is proposed that with early identification of GSD II, treatment with enzyme replacement therapy (ERT) can be started earlier and as a result, a baby's deterioration due to alglucosidase alpha deficiency will be reduced and/or delayed. Patients may live longer, however there may be safety issues associated with ERT. There are also benefits and harms associated with testing.

Health benefits (effectiveness)

- Improvement in clinical outcomes from early diagnosis and intervention (survival, ventilator free survival, vital capacity, forced vital capacity, gross motor function measures)
- Quality of life (both the disease and the treatment may impact on quality aspects)
- Disease specific patient reported outcomes (PROs)
- Value of knowing (family planning)

Health harms (safety)

- Impact of false positive results
- Impact of false negative results (noting this would mean the newborn is diagnosed clinically, which is the comparator. There is a potential that a diagnosis of GSD II may be overlooked if it is assumed it will be detected through NBS)
- Impact of diagnosing cases that are late-onset or have mild symptoms, pseudodeficiency cases, or variants of unknown significance
- Safety of 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 pre-symptomatically, genetic counselling, and other support services)
- Financial impact of ongoing monitoring and surveillance
- Cost effectiveness (cost per diagnosis; cost per QALY)

Other relevant considerations

- 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)
- Family impacts (value of knowing, emotional benefits/harms to family, social benefits/harms to family, noting these are secondary to the outcomes delivered to the baby)

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 GSD Type 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:

[redacted]

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

[redacted]

Provide details and explain:
If using a commercially available kit, such as the NeoLSD™ MSMS Kit from Revvity, which would enable the detection of GSD II plus five additional LSDs (Gaucher Disease, Niemann-Pick A/B Disease, MPS I, Krabbe Disease and Fabry Disease), the estimated costs could be as follows.

National procurement of the kit is estimated to cost approximately [redacted], according to expert advice. The incremental cost of screening per child would be [redacted] as some of the reactions would be required for quality control samples. The detection of other LSDs simultaneously, would presumably improve the cost-effectiveness of an assessment of NBS for multiple conditions, but does not alter the assessment of NBS for Pompe alone.

How is the technolog /service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payment):
NBS for GSD II disease 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:
It is proposed that NBS for GSD II by MS will be superior to no testing of newborns.

This claim is based on evidence that earlier treatment is more effective than late treatment for newborns with GSD II. If treatment is begun prior to the appearance of symptoms (and therefore prior to symptomatic diagnosis), the onset of symptoms can be delayed, prolonging life without severe effects of GSD II.

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, for 2024−2028.

Year 1 estimated uptake (%):
The estimated number of babies born 2024-2025 was 313,993 babies.

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

Year 2 estimated uptake (%):
The estimated number of babies born 2025-2026 was 314,727 babies.

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

Year 3 estimated uptake (%):
The estimated number of babies born 2026-2027 was 315,462 babies.

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

Year 4 estimated uptake (%):
The estimated number of babies born 2027-2028 was 316,196 babies.

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

The ABS registered births (ABS 2022) was used to project the estimated number of births per year, for 2024−2028.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%). The estimated number of babies who uptake NBS in the 2025-2026 financial year would be 312,380 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 0.015% of tests as positive (Kemper et al. 2013), meaning an estimated 47 newborns will require second-tier testing.

- Of the newborns identified as positive or borderline positive from the first-tier test, 23.5% will receive a positive second-tier test result (Kemper et al. 2013), meaning an estimated 11 newborns will be referred for confirmatory diagnostic testing.
- The total number of true positives diagnosed with Pompe disease following confirmatory testing, based on condition incidence (Chin & Fuller, 2022), is 7.

Will the technology be needed more than once per patient?
No, once only

Application PICO set 2: Population 2: Cascade testing of first-degree relatives

Population

Describe the population in which the proposed health technology is intended to be used:
GSD II has a recessive mode of inheritance, therefore both parents of an affected newborn with two pathogenic/likely pathogenic (P/LP) variants can be assumed to be carriers, with one in four chance that future offspring would also be affected.

When a newborn is diagnosed with GSD II, it is proposed that cascade testing is offered to parents to allow for further reproductive planning.

Older siblings of the affected newborn may themselves also be affected or carriers and would also receive cascade testing. If the sibling is a carrier, reproductive planning and partner testing would be available in the future, as required.

Select the most applicable medical condition terminology (SNOMED CT):
237967002

Intervention

Name of the proposed health technology:
Cascade testing of close relatives of a baby diagnosed GSD 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 with genetic counselling would occur after diagnosis of a symptomatic direct family member (including a sibling or child) within the hospital system.

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 siblings of the affected newborn who may themselves also be affected would receive biochemical testing (urine GAG analysis). If the sibling tests positive, genetic testing would be offered. It is proposed that with early identification of GSD II, treatment with enzyme replacement therapy (ERT) can be started earlier and as a result, a baby's deterioration due to alglucosidase alpha deficiency will be reduced and/or delayed. Patients may live longer.

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: AAAAA

Is the proposed item restricted:
No - unrestricted

Provide a short description of the restriction:
NBS for GSD Type 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 GSD 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 testing for GSD II carriers would be conducted in families suspected to be carriers, 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:
The proposed NBS test is likely to have non-inferior safety and superior effectiveness in newborns with GSD II, compared to no testing.

The proposed cascade genetic testing for GSD II test is likely to identify more carriers than phenotypic of family members.

It is proposed that NBS for GSD II by MS will be superior to no testing of newborns.

This claim is based on evidence that earlier treatment is more effective than late treatment for newborns with GSD II. If treatment is begun prior to the appearance of symptoms (and therefore prior to symptomatic diagnosis), the onset of symptoms can be delayed, prolonging life without severe effects of GSD II.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:
An incidence of 2.14 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 7 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 3 (mum, dad and 0-1 sibling). Therefore, approximately 14-21 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:
~33

Optionally, provide details:
The ABS registered births (ABS 2022) was used to project the estimated number of births per year, for 2024−2028 -www.abs.gov.au/statistics/people/population/births-australia/latest-release

The average number of dependent children in Australian households data was 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
- NSW Newborn Bloodspot Screening Program
- NT Newborn Bloodspot Screening Program
- Public Pathology Australia
- QLD Newborn Bloodspot Screening Program
- SA Newborn Bloodspot Screening Program
- TAS Newborn Bloodspot Screening Program
- The Royal College of Pathologists of Australasia
- VIC Newborn Bloodspot Screening Program
- WA Newborn Bloodspot Screening Program

List all appropriate professional bodies/0rganisations 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
- Revvity Pty. Ltd.
- Sanofi-Aventis Australia Pty Ltd

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

- Australian Pompe Association Inc.
- Genetic Alliance Australia
- 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
- SA Metabolic Clinic
- 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?
Yes

Has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?
Yes

Is the therapeutic good classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?
No

Please enter all relevant ARTG ID's:
29295864 – Revvity Pty Ltd - Multiple clinical chemistry constituent IVDs

Is the intended purpose in this application the same as the intended purpose of the ARTG listing(s)?
Yes