Australian Government
Department of Health and Aged Care

Life Saving Drugs Program (LSDP): Review of Medicines for Mucopolysaccharidosis Type VI (MPS VI)

Review summary and Expert Panel recommendations

Purpose of the MPS VI Review

Galsulfase (Naglazyme®) was listed on the LSDP for MPS VI on 1 August 2008. The Expert Panel considered this review at its October 2020 meeting and out of session.

This review of galsulfase sought to develop a better understanding of this medicine by comparing its current use against the recommendations and expectations at the time of listing.

The review further aimed to assess the clinical benefits achieved through the use of galsulfase; ensure the ongoing viability of the LSDP; and ensure testing and access requirements for galsulfase remains appropriate. It identified immediate and future changes that may be required to the funding criteria for galsulfase and to the LSDP more broadly.

The review of each of the LSDP medicines was supported by an approved disease specific Review Protocol, which was structured around seven Terms of Reference (ToRs). The ToRs were tailored specifically to each disease and the relevant medicine(s).

MPS VI Medicine Review Terms of Reference

1. Review the prevalence of MPS VI in Australia.
2. Review evidence for the management of MPS VI and compare to the LSDP treatment guidelines, patient eligibility and testing requirements for the use of galsulfase on the program (including the validity of the tests).
3. Review clinical effectiveness and safety of galsulfase, including analysis of LSDP patient data and international literature to provide evidence of life extension.
4. Review relevant patient based outcomes that are most important or clinically relevant to patients with MPS VI.
5. Assess the value for money of galsulfase under the current funding arrangements by evaluating the benefit of its treatment outcomes and cost.
6. Review the utilisation of galsulfase including storage, dispensing and evidence of patient compliance to treatment.
7. Investigate developing technologies that may impact future funded access.

Key Findings and Recommendations from the Expert Panel

ToR 1 – Review the prevalence of MPS VI within Australia

The Expert Panel noted the prevalence estimate for MPS VI was likely to be 0.43 cases per 100,000, which was less than the 1:50,000 threshold for a rare disease on the LSDP. Based on the number of patients accessing the LSDP, this was likely to be an overestimate.

Recommendation 1:

The Expert Panel considered that MPS VI meets the LSDP prevalence criterion of less than 1:50,000 and currently remains suitable for inclusion on the LSDP.

ToR 2 – Review evidence for the management of MPS VI and compare to the LSDP treatment guidelines, patient eligibility and testing requirements for the use of galsulfase on the program (including the validity of the tests)

The Expert Panel noted the clinical practice guidelines for MPS VI were relatively consistent, with most recommending early initiation of enzyme replacement therapy (ERT) with galsulfase. There were differences between the published clinical guidelines and LSDP guidelines in the frequency of monitoring and assessments.

There were significant limitations associated with the patient data, which made it difficult to compare the LSDP treatment criteria and the clinical guidelines. Limitations included gaps in the LSDP data and inconsistent clinician interpretation of test results.

The Expert Panel noted the Review suggested improvements such as a reduction in testing burden (this is supported by stakeholders); creation of a more streamlined data entry process (also supported by stakeholders); and linkage of Medicare Benefits Schedule and Pharmaceutical Benefits Scheme databases. The Expert Panel noted the linkage of data with the LSDP data is administratively burdensome and outside the remit of the Panel.

Recommendation 2:

The Expert Panel agreed that the purpose, clinical benefits and frequency of undertaking specific diagnostic/clinical monitoring tests needs to be clarified. The Expert Panel noted the importance of considering analytical validity, clinical validity, and clinical utility when assessing the value of health technologies used in the diagnosis and in monitoring patients with MPS VI. Treating physicians are best placed to provide input on the usefulness of current tests used to diagnose, manage and monitor MPS VI LSDP patients.

The Expert Panel recommended that further clinical advice be sought for review of the following diagnostic/ongoing clinical tests:

- Urinary GAG (glycosaminoglycans)
- Liver and spleen size
- Ophthalmology and neurological examination
- Sleep study.

ToR 3 – Review clinical effectiveness and safety of galsulfase, including analysis of LSDP patient data and international literature to provide evidence of life extension

The Expert Panel noted the additional evidence collected since the original Pharmaceutical Benefits Advisory Committee (PBAC) submission had not substantially changed the conclusions on the safety and efficacy of galsulfase. The evidence indicated galsulfase was associated with potential improvements in urinary GAG, exercise capacity and growth for younger patients. For LSDP patients, there appeared to be signs of deterioration in the clinical test results provided. The Expert Panel noted the degree of deterioration in patients' clinical results was likely to be less significant than those which would have been observed if the patients were untreated.

The Expert Panel noted the published results for galsulfase did not provide evidence of life extension. The LSDP also noted the patients in the LSDP cohort who have died ([redacted] out of [redacted] or [redacted] percent) appeared to have had only relatively short treatment with galsulfase, which limited extrapolation about its effectiveness in those patients to patients in general. Some patients on the LSDP reported improved functional capacity and a reduction in pain with galsulfase treatment (improving their quality of life (QoL)). Overall, the Panel considered it was probable that function was maintained for longer and survival was likely to be modestly improved with galsulfase treatment, particularly in younger MPS VI patients.

Recommendation 3:

The Expert Panel noted the limitations of the available evidence regarding the conclusion that galsulfase likely extends survival for some MPS VI patients. However, on the basis of the evidence identified through the Review, including data on the improvement to patients' QoL, the Expert Panel advised that galsulfase remains suitable for inclusion on the LSDP.

ToR 4 – Review relevant patient based outcomes that are most important or clinically relevant to patients with MPS VI

The Expert Panel noted from the Report the outcomes most important to patients were those that impact patient QoL and capacity to perform activities of daily living with independence and dignity, life expectancy, pain, mobility, range of motion, endurance, fine motor control/grip strength, and frequency of illness/surgery/treatments requiring hospital attendance.

The Expert Panel also acknowledged the stakeholder feedback regarding the administrative burden of testing requirements for MPS VI patients on the LSDP and agreed this should be reviewed. This was also discussed in ToR 2.

Recommendation 4:

The Expert Panel noted that the extent and methods of data collection and the approach to analysis of the data require improvement. The availability of consistent and complete data extracted from initial and ongoing applications to the program is essential. The LSDP should implement a streamlined solution that enables clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Expert Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future reviews of galsulfase.

ToR 5 – Assess the value for money of galsulfase under the current funding arrangements by evaluating the benefit of its treatment outcomes and cost

The Expert Panel noted that while the cost per patient per year for galsulfase was marginally less than anticipated at the time of listing (approximately $[redacted] compared to $[redacted]), this cost was extremely high.

The Expert Panel considered that while the Review found the clinical data did not provide evidence of life extension, it was reasonable to consider a model that includes minor life extension. Indicative Incremental Cost Effectiveness Ratios based on a range of assumed survival improvements (from 0.35 to 3.53 years) were between $[redacted] and $[redacted] per life year gained (with costs and outcomes discounted at five percent). The subjective reports of improvement in QoL outcomes in MPS VI patients treated with galsulfase were indicative of clinical benefit from treatment. A very high cost was being paid for the health gains achieved.

Recommendation 5:

The Expert Panel noted that a survival gain is plausible, with maintenance of function and improvement in QoL from treatment with the medicine in some patients, and that the cost of this medicine remains very high. The Expert Panel therefore recommended that the pricing and listing arrangements for this medicine be reassessed with the goal of improving value for money when:

(i) current deeds of agreements with sponsors expire; and/or

(ii) new medicines for Pompe disease are considered for entry onto the LSDP or other subsidy programs; and/or

(iii) changes in eligibility criteria are being considered.

ToR 6 – Review the utilisation of galsulfase, including the way it is stored and dispensed, and evidence of patient compliance to treatment

The Expert Panel noted patients on the LSDP were heavier on average than expected at the time of listing. However, there have been fewer than predicted patients accessing galsulfase on the LSDP, fewer dispensed vials and lower expenditure. The PBAC had considered the financial estimates to be over-estimated at the time of its consideration.

The Expert Panel noted the high compliance rate for MPS VI patients. The long treatment breaks seen for some patients were likely more reflective of gaps in dispensing data than actual gaps in treatment.

The Expert Panel discussed the lower average dose per patient observed in LSDP patients than recommended in the Product Information may not have been a true reflection of actual administered dose as patients are administered the full vial. The Expert Panel noted the Commonwealth should only be paying for the prescribed dose of a product.

The Review found six patients had a record of receiving a home infusion. The Expert Panel noted the sponsor does not have a home infusion service for galsulfase. As this service would be beneficial to patients, the Expert Panel was supportive of such an initiative should it be in line with the safe use of the product as per the Product Information.

Recommendation 6:

The Expert Panel acknowledged the challenges for sponsors in providing product to satisfy the requirements of different international markets but recognised the significant excess costs to government due to dispensing of greater than approved doses of treatments for MPS VI disease.

The Expert Panel recommended that the value for money aspects of weight-based dosing be reconsidered. Specifically, the funding approach to treatment at above recommended and approved medicine levels should be reassessed. The Expert Panel were of the view that the Commonwealth should only be reimbursing for the dose of drug prescribed by the treating physician within the approved Product Information doses. To account for this, renegotiation of the funding arrangements with medicine sponsors may be required.

The Expert Panel recommended that the sponsor of this medicine should be requested either to make a smaller vial available or to adjust pricing of the single vial to account for use of the medicine in excess of the weight-based dose considered appropriate by the prescriber within the dose limits approved in the Product Information.

Recommendation 7:

The Expert Panel advised that should the Product Information be formally updated to allow for home infusions of galsulfase, the Expert Panel and LSDP would be in support of amending the MPS VI Guidelines to include this service to potentially improve care for patients.

ToR 7 – Investigate developing technologies that may impact future funded access

The Expert Panel noted a new gene therapy and substrate reduction therapy were in development for the treatment of MPS VI. While no new screening and diagnostic procedures were identified in the review, a clinician advised the Expert Panel there were a number of preconception, prenatal and newborn screening programs in the pipeline. Their introduction may increase identification of MPS VI which would affect the utilisation of galsulfase on the LSDP.

Next Steps

The then Minister for Health, the Hon Greg Hunt MP, agreed to these recommendations on 29 March 2022. The implementation of these recommendation is currently being considered and progressed by the Department of Health and Aged Care in consultation with sponsors, treating physicians and patient advocacy groups.