Australian Government
Department of Health and Aged Care

Life Saving Drugs Program (LSDP): Review of Medicines for Gaucher Disease (Type 1)

Review summary and Expert Panel recommendations

Purpose of the Gaucher Disease (Type 1) Medicines Review

There are 3 enzyme replacement therapies (ERTs) currently available on the LSDP to treat Gaucher disease (type 1):

- imiglucerase (Cerezyme®) (listed on 1 August 1999)
- velaglucerase (VPRIV®) (listed on 1 August 2012)
- taliglucerase (Elelyso®) (listed on 1 October 2015).

The Expert Panel considered this review at its October 2020 meeting.

This review of the Gaucher disease (type 1) medicines sought to develop a better understanding of these LSDP medicines by comparing their current use against the recommendations and expectations at the times of listing.

The review further aimed to assess the clinical benefits achieved through the use of these medicines; ensure the ongoing viability of the LSDP; and ensure testing and access requirements for these medicines remains appropriate. It identified immediate and future changes that may be required to the funding criteria for the Gaucher disease (type 1) medicines 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 (ToR). The ToRs were tailored specifically to each disease and the relevant medicine(s).

Gaucher Disease (Type 1) Medicines Review Terms of Reference

1. Review the prevalence of Gaucher disease (type 1) in Australia.
2. Review evidence for the management of Gaucher disease (type 1) and compare to the LSDP treatment guidelines, patient eligibility and testing requirements for the use of these medicines on the program (including the validity of the tests).
3. Review clinical effectiveness and safety of medicines for the treatment of Gaucher disease (type 1), 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 Gaucher disease (type 1).
5. Assess the value for money of LSDP Gaucher disease medicines under the current funding arrangements by evaluating the benefit of the medicines' treatment outcomes and cost.

6. Review the utilisation of LSDP Gaucher disease medicines 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 Gaucher disease within Australia

The Expert Panel noted the best prevalence estimate for Gaucher disease (type 1) in Australia was 0.19 per 50,000. The prevalence of all types of Gaucher disease was estimated to be 0.88 per 50,000. The Expert Panel noted the prevalence of Gaucher disease is rising at a rate greater than the rate of growth of the Australian population, potentially due to increased awareness of the disease. Newborn screening studies suggested the prevalence of Gaucher disease (all types) is up to 3.75 per 50,000. However, the Expert Panel noted these studies were not performed in Australia.

LSDP eligibility criteria limit use of available treatments to Gaucher disease (type 1) patients with symptoms of end-organ damage. Approximately 88 percent of patients with Gaucher disease (type 1) in Australia were eligible for treatment on the LSDP. The majority (approximately 90 percent) of those eligible patients accessed treatment on the LSDP.

The Expert Panel noted there were a small number of grandfathered patients with Gaucher disease (type 3) accessing the LSDP. While these patients do respond to treatment despite having more severe symptoms than patients with Gaucher disease (type 1), there is no evidence for improved survival associated use of Gaucher disease medicines in this cohort.

This issue is discussed further under ToR 2.

Recommendation 1:

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

In light of the increasing prevalence of Gaucher disease in Australia, and anticipated increased access to genetic testing, the Expert Panel recommends that the prevalence of Gaucher disease be reviewed in five years, or within five years post implementation of any Government agreed changes to eligibility, to determine whether Gaucher disease continues to meet the prevalence criterion for inclusion on the LSDP (prevalence ≤ 1 in 50,000 considering all stages and genetic subtypes of the condition[1]).

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

The Expert Panel noted the Review found the current LSDP Guidelines for diagnosis are consistent with best practice and ERT is still the standard treatment for Gaucher disease.

[1] Procedure guidance for medicines funded through the LSDP (July 2018)

Eligibility criteria for subsidised ERT are broader in international clinical guidelines compared to those guiding access to treatment under the LSDP, particularly around the inclusion of patients with Gaucher disease (type 3).

Patients with Gaucher disease (type 3) cannot be accurately diagnosed as children and are usually identified later in life. As discussed in ToR 1, there is a small number of grandfathered adult patients with Gaucher disease (type 3) on the program. The LSDP Guidelines do not permit any other patients with Gaucher disease (type 3) access to subsidised treatment as use in this subgroup has not been assessed by the Pharmaceutical Benefits Advisory Committee (PBAC) for clinical effectiveness.

The Expert Panel noted that should this subgroup be permitted to access treatment through the LSDP, both expenditure and patient numbers may increase (around five percent of Gaucher disease patients are this subtype).

The Expert Panel noted that similarly, utilisation and expenditure would increase if patients with severe phenotypes were granted access to LSDP treatment earlier. These patients are ineligible for LSDP funded treatment with these medicines as evidence of life extension in this patient group was not presented at the time of entry to the LSDP.

The Expert Panel discussed the high burden placed on patients and treating physicians through the annual patient assessment and application process. The Expert Panel noted the assessment and application process can be invasive, which is a concern for young children, and may be unnecessary in many adults.

Recommendation 2:

The Expert Panel recognised that LSDP patient eligibility treatment criteria are currently narrower than applied in some other international jurisdictions. In order to evaluate whether Gaucher Disease (type 3) is appropriate for inclusion on the LSDP, the Expert Panel recommended that sponsors submit applications for consideration of amending/ revising the eligibility criteria for commencement and for continued access to treatment for Gaucher disease. Sponsor submissions must include an assessment of the clinical, economic and financial implications if expanded access is a likely consequence of adoption of any proposal.

ToR 3 – Review clinical effectiveness and safety of medicines and evaluate the evidence of comparative effectiveness of LSDP Gaucher disease medicines. This will include analysis of LSDP patient data and international literature to provide evidence of life extension

The Expert Panel noted the Report found all three medicines were effective when compared to placebo (or standard therapy) and no new safety signals were identified. The literature provided evidence of life extension if key reasonable assumptions were accepted. There were too few deaths reported in the LSDP data to determine whether ERT has extended survival in Australian patients.

The Expert Panel considered the LSDP data were broadly consistent with a conclusion that patients on ERT were experiencing outcomes consistent with the expectations at the time of listing.

The Expert Panel noted the international clinical guidelines recommend that dosing in stable adult patients who have met their treatment goals (such as clinical improvement) can be down-titrated to 15-30 units/kg every other week. According to the evidence, if doses were to be reduced after 12 months of therapy (i.e. to 30 units/kg every other week), this would decrease program expenditure without impacting patient outcomes. The Expert Panel was concerned that, as the above dosing guidance is not included in the Product Information or the LSDP Guidelines, treating physicians may not be aware that it is a viable treatment option.

Recommendation 4:

On the basis of the evidence identified through the Review, the Expert Panel recommended that imiglucerase, velaglucerase and taliglucerase remain suitable for inclusion on the LSDP. The Expert Panel considered that there was insufficient evidence to support any claim of a clinically important difference between the three Gaucher disease medicines.

Recommendation 5:

In light of the international clinical guidelines recommending the down-titration of doses after 12 months in stable patients, the Expert Panel recommended that this guidance be included in the LSDP Guidelines for treating physicians to consider in stable adult patients. Dosage adjustments should be made on an individual basis, and may increase or decrease, based on achievement of therapeutic goals as assessed by routine comprehensive evaluations of the patient's clinical manifestations.

ToR 4 – Review relevant patient based outcomes that are most important or clinically relevant to patients with Gaucher disease (type 1)

Consultations with stakeholders, including consumers, indicated the outcomes that were most important to patients included improvement in symptoms (which affect quality of life). The Expert Panel noted improved outcomes are achieved with ERT.

Substantial gaps in the collection of data from LSDP patients were noted, and this limited interpretation. The Expert Panel discussed that a review was necessary to determine:

i. which outcomes warrant data collection;
ii. what data are required to assess those outcomes;
iii. what the appropriate approaches to collection of that data are; and
iv. design of a statistical plan to analyse these data.

The aim of this review would be to limit data collection and its burden while improving monitoring and meaningful reporting of key outcomes for patients treated through the LSDP.

The Expert Panel noted a suggestion from treating physicians that data collected as part of LSDP administration should be collated into a data registry that treating physicians can access.

Recommendation 6:

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 treating physicians 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 treating physician and patient satisfaction and facilitate availability of complete and comprehensive data for any future review of Gaucher disease medicines.

ToR 5 – Conduct an analysis of the value for money of LSDP Gaucher disease medicines under the current funding arrangements by evaluating the benefit of the medicines' treatment outcomes and cost

The average annual cost of treating a patient with imiglucerase, velaglucerase or taliglucerase ranged from approximately $[redacted] to $[redacted]. This was less than estimated at the time of listing, largely due to price reductions.

Using a model that required significant assumptions, the Review calculated a discounted Incremental Cost Effectiveness Ratio of $[redacted] /Life Years Gained (LYG) for paediatric patients and $[redacted]/LYG in adults. These estimates were associated with significant uncertainty. The Expert Panel considered that a very high cost is being paid for the health gains achieved.

Recommendation 7:

The Expert Panel noted that there appears to be a survival gain and improvement in quality of life from treatment with the three medicines, and that the cost of these medicines remains very high. The Expert Panel therefore recommended that the pricing and listing arrangements for these medicines 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 Gaucher 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 LSDP Gaucher disease medicines, including the way they are stored and dispensed, and evidence of patient compliance to treatment

Consultation with patients and treating physicians indicated that, in practice, weight-based doses are rounded to the nearest whole vial of drug and the entire contents of the vials are administered to patients. The Expert Panel did not object to the practice of prescribing and approving dosages in whole vials; however, it noted the practice resulted in expenditure that did not reflect the recommended and approved doses. This was particularly an issue with imiglucerase and velaglucerase that are only available in 400 U vial, more so than with taliglucerase, which is available in a 200 U vial.

Recommendation 8:

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 Gaucher disease.

The Expert Panel recommended that the value for money aspects of a weight-based dosing be reconsidered. Specifically, the funding approach to treatment at above recommended and approved medicine levels should be reassessed. The Expert Panel was 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 sponsors of these medicines should be requested either to make a smaller vial available or to adjust pricing of the single vial to account for use of the medicines in excess of the weight-based dose considered appropriate by the prescriber within the dose limits approved in the Product Information.

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

The Expert Panel noted oral substrate reduction therapies for patients with Gaucher disease were in clinical development and new diagnostic methodologies have been identified. The Expert Panel noted availability of these may have an impact on the LSDP medicines for Gaucher disease (type 1). Stakeholders and the LSDP were supportive of considering novel TGA registered therapies.

Recommendation 9:

The Expert Panel noted that novel therapies and diagnostic methods are in development and their availability may impact the LSDP and patients in the future, however none were imminent. The Expert Panel also noted that the existing TGA registered product eliglustat (Cerdelga®) was not included in this review but is an approved option for some patients with Gaucher disease.

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.