



Australian Government

Department of Health

**Life Saving Drugs Program medicines: miglustat (Zavesca®) for the
treatment of Fabry disease**

Review Plan

1. Introduction

1.1 BACKGROUND AND PURPOSE OF THE REVIEW

The Life Savings Drugs Program (LSDP), administered by the Commonwealth Department of Health, was established in the mid-1990s to provide individuals with rare and life-threatening diseases access to expensive medicines that were not considered to be cost effective for Pharmaceutical Benefits Scheme (PBS) listing. Currently, the LSDP fully subsidises 14 life-saving high-cost medicines for approximately 400 patients for the treatment of nine rare diseases. In January 2018, following a review of the LSDP, the Australian Government committed to a number of program improvements, including a review of the medicines currently funded under the LSDP and the establishment of an Expert Panel to provide advice to the Commonwealth Chief Medical Officer (CMO).

The purpose of each of the LSDP reviews (i.e., nine disease-based reviews undertaken in three tranches) is to develop a better understanding of the real-world use of a medicine by comparing the current use and performance of the medicine against the recommendations and expectations at the time of listing. The reviews will aim to assess the clinical benefits achieved through the use of LSDP medicines, ensure the ongoing viability of the program, and ensure testing and access requirements for the medicines remain appropriate.

There are currently four medicines available on the LSDP for the treatment of Gaucher disease:

1. imiglucerase (Cerezyme®);
2. velaglucerase (VPRIV®);
3. taliglucerase (Elelyso®); and
4. miglustat (Zavesca®).

HealthConsult Pty Ltd (HealthConsult) has been contracted to conduct the review of the enzyme replacement medicines for Gaucher disease, which will include imiglucerase, velaglucerase, and taliglucerase.

The uptake of miglustat through the LSDP has been considerably lower than predicted at the time it was added to the program (and significantly less than the use of the enzyme replacement therapies available). As such, a separate review will be conducted in order to better understand any drivers behind this low usage; and to investigate whether there is new evidence to inform the usage parameters of miglustat on the LSDP.

The miglustat review will focus on the following:

- 1) the place of miglustat in the treatment pathway for patients with Gaucher disease at the time it was added to the LSDP compared to now;
- 2) whether any new evidence for the safety and efficacy of miglustat is available compared to what was considered at the time it was recommended to be added to the LSDP; and
- 3) the actual observed usage of miglustat in the time it has been available through the LSDP compared to the predicted usage.

1.2 PURPOSE OF THIS DOCUMENT

This Review Plan is intended to give an overview of how the review of LSDP funded miglustat will be conducted.

The draft Review plan was available for review and comment to all interested stakeholders until 5 March 2019.

2. Review of miglustat

The purpose of this review is to explore any new and emerging evidence of the clinical place and effectiveness of miglustat compared to expectations at the time of listing, and to better understand the real-world application of LSDP subsidised miglustat.

The proposed methodology to conduct this review is outlined below.

2.1 CLINICAL PLACE OF MIGLUSTAT IN THE MANAGEMENT OF GAUCHER DISEASE

The review of Gaucher disease currently being undertaken by HealthConsult includes reviewing the evidence for the management of Gaucher disease (ToR 2). HealthConsult's review will include consideration of the clinical indications for, and management of Gaucher disease within the domestic and international space. Treatment algorithms, guidance documents, testing regimes and treatment modalities will be investigated to inform an evidence based evaluation on the best-practice treatment of Gaucher disease.

The outcome of this investigation will be used to provide evidence on the current clinical importance/place of miglustat in the clinical management of Gaucher disease. This will be compared to the projections made at the time it was listed to identify any contradictions or changes.

2.2 LITERATURE REVIEW

A literature review will be undertaken that focuses on identifying any new evidence available on the effectiveness, safety and performance of miglustat. Relevant data published after 2010 will be searched to ensure that any publications that were not indexed at the time of the 2014 review are captured.

Data previously considered by either the Pharmaceutical Benefits Advisory Committee (PBAC) or within the 2014 post-market review are out of scope for this review.

Key databases (EMBASE, PubMed and Cochrane etc) will be searched, as well as key regulatory agency and health statistic websites. Methods of identification of relevant evidence; selection criteria; critical appraisal; and data extraction will be consistent with those outlined within the Pharmaceutical Benefits Advisory Committee Guidelines¹.

Due to the rarity of Gaucher disease, it is expected that there will be limited literature available for review. Literature review search terms will be kept broad to maximise the number of citations retrieved.

2.3 UTILISATION OF MIGLUSTAT ON THE LSDP AND ANALYSIS OF LSDP PATIENT DATA

The LSDP contains monitoring and outcome data on patients who have received LSDP subsidised medicines. To be found eligible, a treating physician will apply with all required test results and patient details. This data is updated through an annual reapplication process. Any data available on patients who have received LSDP subsidised miglustat, including clinic notes and contact with physicians, will be analysed to supplement the literature review.

¹ Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee version 5.0

Potential information that can be extrapolated from LSDP patient data include:

- patient demographics;
- test/result improvements or stabilisation;
- rates of adverse events; and
- changes in patient outcomes.

All outcomes demonstrated will be compared against the original pivotal trial estimates that informed the LSDP listing.

The LSDP holds data on the dosage regime each patient has followed. This includes data on:

- prescribed dose;
- dosage intervals; and
- dispensing.

This data will be used to conduct an analysis of utilisation and patient compliance to miglustat treatment. Both the patient and dispensing data is linked through a unique patient identifier, allowing any changes in key individual endpoints to be linked with utilisation statistics.

The observed utilisation of miglustat on the LSDP will be compared with the utilisation predicted at the time it was added to the program.

2.4 KEY FINDINGS and NEXT STEPS

Evidence gathered within the review will be used to inform the development of a draft report that will be considered by the Expert Panel. The draft report will outline any changes in the evidence base for the prescription and performance of miglustat, supplemented by outcomes obtained from LSDP patient data. This evidence will also be compared against the original data that informed the listing on the LSDP. Evidence obtained through this review will be used to inform the consideration of miglustat listing arrangements.

The draft report will be provided to key stakeholders for comment prior to consideration by the Expert Panel.