Life Saving Drugs Program (LSDP)

Olipudase alfa (Xenpozyme®) outcome statement

Summary of the consideration of the application from Sanofi Australia and New Zealand for the inclusion of olipudase alfa (Xenpozyme®) on the LSDP for the treatment of acid sphingomyelinase deficiency (ASMD) types A/B and B

Overview

The LSDP Expert Panel (the Expert Panel) advises the Chief Medical Officer (CMO) on new medicine applications to the LSDP. The Expert Panel considered the application from Sanofi Australia and New Zealand (Sanofi) on 20 October 2023 and 13 December 2024 and the CMO recommended olipudase alfa for listing on the LSDP in February 2025.

Background

Olipudase alfa is approved by the Therapeutic Goods Administration (TGA) for the treatment of non-central nervous system (non-neurological) manifestations of acid sphingomyelinase deficiency (ASMD) in paediatric and adult patients with type A/B (Niemann-Pick type A/B) or type B (Niemann-Pick type B). ASMD is an ultra-rare lysosomal storage disorder resulting from deficiency of the lysosomal enzyme acid sphingomyelinase (ASM) due to bi-allelic mutations in the sphingomyelin phosphodiesterase 1 (*SMPD1*) gene. The ASM enzyme normally functions to break down a fat called sphingomyelin within a lysosome. When there is a deficiency with this enzyme, sphingomyelin accumulates in the body which can result in organ damage and a variety of symptoms, including neurological issues, organ enlargement, and other systemic effects.

Olipudase alfa is a copy of the normal ASM enzyme. It is expected to replace the deficient enzyme in a patient and reduce the build-up of fats within lysosomes. However, olipudase alfa is unable to cross the blood-brain barrier and is therefore not expected to improve the neurological aspects of ASMD. As such patients with ASMD type A, who present with severe neurological symptoms are not expected to benefit from treatment.

Pharmaceutical Benefits Advisory Committee (PBAC) Consideration

At its July 2023 meeting, PBAC considered a submission from Sanofi requesting the listing of olipudase alfa on the Pharmaceutical Benefits Scheme (PBS) for the treatment of patients with ASMD type A/B or type B. PBAC did not recommend the requested listing of olipudase alfa as it

considered the incremental cost effectiveness ratio (ICER) for olipudase alfa compared to best supportive care was extremely high and uncertain. Further information on PBAC's consideration of olipudase alfa including reasons for rejection is available in the PBAC Public Summary Document.

Expert Panel Consideration

Funding Criteria

To be listed on the LSDP, a medicine must meet each of the LSDP funding criteria A1-A8. A summary of the claims for olipudase alfa against each criterion is presented below.

LSDP criteria		How olipudase alfa meets the criteria
A1	**There is a rare but clinically definable disease for which the drug is regarded as a proven therapeutic modality, i.e. approved for that indication by the TGA (prevalence of ≤1 per 50,000 people).**	The estimated birth prevalence for the Australian population is 0.3 per 100,000 live births respectively which meets the LSDP prevalence criteria.
A2	**The disease is identifiable with reasonable diagnostic precision.**	ASMD can be diagnosed biochemically by reduced acid sphingomyelinase (ASM) activity with simultaneous testing of glucocerebrosidase activity to distinguish it from Gaucher disease. Gene sequencing of the ASM gene (*SMPD1*) can follow a biochemical diagnosis. Diagnosis based on gene sequencing is definitive for ASMD and will not misdiagnose Gaucher disease or lysosomal acid lipase deficiency.
A3	**Epidemiological and other studies provide evidence that the disease causes a significant reduction in age-specific life expectancy for those suffering from the disease**	There is significant literature available supporting the reduced life expectancy for patients with ASMD types A/B and type B. Data from the SPHINGO-100 single arm study documented that 15% of patients (9/59) died during the study duration with recorded deterioration in patients' splenomegaly, hepatomegaly, interstitial disease, diffusing capacity of the lung for carbon monoxide (DLco) and dyslipidaemia.
A4	**There is evidence to predict that a patient's lifespan will be substantially extended as a direct consequence of the use of the drug.**	Data from olipudase alfa studies ASCEND, ASCEND-peds, DFI13412, LTS13632 and SPHINGO-100 and published literature demonstrate that olipudase alfa decreases in spleen volume, liver volume, DLco and alanine aminotransferase, which may be surrogates for overall survival. Olipudase alfa is approved by the TGA as an enzyme replacement therapy for the treatment of non-central nervous system (CNS) manifestations of ASMD in paediatric and adult patients with type A/B or type B. Olipudase alfa does not cross the

		blood-brain barrier and has no effect on neurological symptoms of ASMD.
A5	**The drug must be accepted as clinically effective but rejected for PBS listing because it fails to meet the required cost effectiveness criteria.**	The PBAC did not recommend the Section 100 (Highly Specialised Drugs Program) listing of olipudase alfa for the treatment of ASMD type A/B or type B. The PBAC considered olipudase alfa was an effective treatment for ASMD type A/B or type B; however, the ICER for olipudase alfa compared to best supportive care was extremely high and uncertain. (5.08 Public Summary Document July 2023).
A6	**There is no alternative drug listed on the PBS or available for public hospital in-patients which can be used as lifesaving treatment for the disease. However, the availability of an alternative drug under the LSDP does not disqualify the proposed drug from consideration for inclusion on the LSDP.**	There are no alternative medicines listed on the PBS, LSDP or available for public hospital in-patients which can be used as a lifesaving treatment ASMD type A/B or type B.
A7	**There is no alternative nondrug therapeutic modality (eg surgery, radiotherapy) which is recognised by medical authorities as a suitable and cost-effective treatment for this condition.**	There is no alternative non-drug therapeutic modality which is recognised by medical authorities as a suitable treatment for ASMD type A/B or type B.
A8	**The cost of the drug, defined as the cost per dose multiplied by the expected number of doses in a one-year period for the patient, would constitute an unreasonable financial burden on the patient or his/her guardian.**	The TGA approved Product Information states that the recommended starting dose for paediatric patients is 0.03 mg/kg and 0.1 mg/kg in adults. In both populations a series of non-uniform dose escalations every 2 weeks is recommended up to the final maintenance dose of 3 mg/kg every 2 weeks. At the proposed prices of a 4 mg vial ($[redacted]) and 20 mg vial ($[redacted]) for olipudase alfa the annual per patient treatment cost for a [redacted] kg patient on a maintenance dose would be $[redacted]., representing an unreasonable financial burden on the patient or guardian.

Pricing Issues

The price of all LSDP medicines are subject to commercial in confidence arrangements.

Consumer Input

The Expert Panel noted the stakeholder input from the PBAC application.

Treatment Guidelines

The Guidelines for the treatment of ASMD types A/B and type B on the LSDP stipulate initial and ongoing eligibility requirements. The diagnosis of ASMD type A/B or type B must be confirmed by either evidence demonstrating deficiency of ASM and normal activity of the glucocerebrosidase enzyme to rule out a different condition called Gaucher disease, or by molecular genetic testing indicating biallelic disease-causing variants in the *SMDP1* gene.

Eligibility is also dependent on the presentation of clinical markers demonstrating the severity of the condition in a patient such as their spleen volume or interstitial lung disease.

Management of Uncertainties

To address uncertainties, clinical data will be collected through initial and ongoing applications to the LSDP. In line with LSDP policy and to manage uncertainties, a review of olipudase alfa will be conducted 24 months after listing to ensure use and performance of the medicine is in line with the expectations at the time of listing.

Context

The LSDP provides access for eligible patients with ultra-rare and life-threatening diseases to essential and very expensive medicines. The LSDP provides eligible patients with access to these life saving medicines at no expense to the patients or their families.

Before being considered for inclusion on the LSDP, a drug must first be considered by PBAC and accepted as clinically effective but rejected for PBS listing because it fails to meet the required cost effectiveness criteria.

All applications for new medicines seeking funding through the LSDP are considered by the Expert Panel. The role of the Expert Panel is to provide advice and assistance to the CMO on a range of matters relating to new medicines seeking funding, including assessment of how the medicine addresses the LSDP criteria, guidelines for medicine use and testing requirements, suitable pricing arrangements, and data collection required for future reviews.

After receiving advice from the Expert Panel, the CMO advises the Minister for Health and Ageing on medicines proposed to be included on the LSDP.

This document aims to provide an overview of the evidence considered by the Expert Panel and CMO during their assessment of medicines.

For more information on the process for new medicines seeking funding through the LSDP, refer to the LSDP Procedure guidance: www.health.gov.au/resources/publications/procedure-guidance-for-medicines-funded-through-the-life-saving-drugs-program-lsdp

Sponsor's Comment

Sanofi welcomes the Government's decision to list Xenpozyme (olipudase alfa) and supports the long-term sustainability of the LSDP. This is a significant decision for ASMD patients in Australia whose life expectancy is affected by this devastating disorder.