

# Life Saving Drugs Program (LSDP)

# Sebelipase alfa (Kanuma<sup>®</sup>) outcome statement

Summary of the consideration of the application from Alexion Australia for the inclusion of sebelipase alfa (Kanuma<sup>®</sup>) on the LSDP for the treatment of infantile-onset lysosomal acid lipase deficiency (LAL-D)

#### **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 Alexion on 24 June 2022 and 14 October 2022 and the CMO recommended sebelipase alfa for listing on the LSDP in December 2022.

# Background:

Sebelipase alfa is approved by the Therapeutic Goods Administration (TGA) for long-term enzyme replacement therapy (ERT) in patients of all ages with lysosomal acid lipase deficiency (LAL-D), including infantile-onset LAL-D (also known as rapidly progressive LAL-D or Wolman disease). Infantile-onset LAL-D is an inherited ultra-rare autosomal recessive lipid metabolism disorder caused by pathogenic variations in the *LIPA* gene, normally responsible for encoding the lysosomal acid lipase (LAL) enzyme. This enzyme normally functions in the lysosomes of cells to break down various types of fats. In infants, mutations to the LIPA gene may result in very little (<1%) or absent LAL enzyme activity, causing infantile-onset LAL-D.

Children with infantile-onset LAL-D generally begin showing signs of the disease shortly after birth as fat molecules begin to accumulate throughout the body. Symptoms typically include multiorgan failure and severe malnutrition due to difficulty absorbing nutrients from food. It is a progressive and rapidly fatal disease.

# Pharmaceutical Benefits Advisory Committee (PBAC) Consideration:

At its March 2022 meeting, PBAC considered a submission from Alexion requesting the listing of sebelipase alfa on the Pharmaceutical Benefits Scheme (PBS) for the treatment of patients with infantile-onset LAL-D. PBAC did not recommend the requested listing of sebelipase alfa as it considered the incremental cost effectiveness ratio (ICER) for sebelipase alfa compared to best supportive care was extremely high and uncertain. Further information on PBAC's consideration of sebelipase alfa including reasons for rejection is available in the <u>PBAC Public Summary</u> <u>Document</u>.

# **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 sebelipase alfa against each criterion is presented below.

LSDP criteria		How sebelipase 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 incidence for the Australian population is one in every 528,000 to 704,000 births which meets the LSDP prevalence criteria.
A2	The disease is identifiable with reasonable diagnostic precision.	Infantile-onset LAL-D can be definitively diagnosed using a LAL enzyme-based blood test in patients with suspected LAL-D. This test forms part of the routine work-up of diagnosing patients with infantile-onset LAL-D. Although not essential for diagnosis, suspected LAL-D patients may also be tested using genetic testing.
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	A natural history study (LAL-1-NH01) was conducted which characterises patient survival and key manifestations of the clinical course of the disease in the absence of sebelipase alfa. Receiving best supportive care only, the median age of death was 3.71 months in the total population (n=35). The Kaplan-Meier estimate for the probability of survival past 12 months of age was 0.114.
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.	Comprehensive data from sebelipase alfa studies LAL-CL03, LAL-CL08, the Alexion-sponsored Global LAL-D Registry and published literature demonstrate that sebelipase alfa substantially extends the life expectancy in patients with infantile-onset LAL-D.
A5	The drug must be accepted as clinically effective but rejected for PBS listing because it fails to meet the required cost effectiveness criteria.	PBAC did not recommend the Section 100 (Highly Specialised Drugs Program) listing of sebelipase alfa for the treatment of infantile-onset LAL-D at its March 2022 meeting. PBAC considered sebelipase alfa was an effective treatment for infantile-onset LAL-D; however, the ICER for sebelipase alfa compared to best supportive care was extremely high and uncertain (5.15.MINS.7.1).

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 or available for public hospital in-patients which can be used as a lifesaving treatment for infantile-onset LAL-D. Current management of infantile-onset LAL-D includes symptom-based treatment only, which fails to address the underlying cause of the disease and does not substantially improve patient outcome. Supportive therapies consist of nutritional support, blood transfusions, steroids and lipid-lowering treatments.
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 infantile-onset LAL-D
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 recommended dosage regimen is 1 mg/kg of body weight, administered as an IV infusion once weekly, with potential dose escalation to 3 mg/kg or 5 mg/kg once weekly in the event of suboptimal response. At the proposed sebelipase alfa price of \$ the annual per patient treatment cost for a 10 kg infant would be \$ the annual per patient treatment cost for a 10 kg infant would be \$ the annual per for a 1 mg/kg weekly dose, 3 mg/kg weekly dose or 5 mg/kg weekly dose, respectively, 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 infantile-onset LAL-D on the LSDP stipulate initial and ongoing eligibility requirements. The diagnosis of infantile-onset LAL-D must be confirmed by evidence demonstrating no detectable or severe deficiency in LAL enzyme activity when tested at the National Referral Laboratory and *LAL (LIPA)* mutations on genetic testing (noting treatment may commence prior to the results of the genetic test being available if necessary). Diagnosis of infantile-onset LAL-D must be confirmed when the patient is under 12 months of age.

# 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, sebelipase alfa will be subject to a post listing review triggered when there are either at least patients accessing sebelipase alfa through the LSDP and all patients have been on the LSDP for at least 12 months, or sebelipase alfa has been on the LSDP for 5 years, whichever comes first.

# 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 Aged Care 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: <u>www.health.gov.au/resources/publications/procedure-guidance-for-medicines-funded-through-the-life-saving-drugs-program-lsdp</u>

# Sponsor's Comment:

Alexion, AstraZeneca Rare Disease, welcomes the Australian Government's decision to list Kanuma<sup>®</sup> (sebelipase alfa) on the Life Saving Drugs Program, giving Australian babies born with infantile-onset LAL-D access to a treatment for this condition. The listing recognises the important value that Kanuma® brings for babies and their families, and is a significant step in creating equitable access to treatments in ultra-rare diseases.