Kanuma® ▼ (sebelipase alfa) 2 mg/ml concentrate for solution for infusion

A GUIDE FOR HEALTHCARE PROFESSIONALS

Important Safety Information:

Please read this guide carefully and use it when prescribing Sebelipase alfa as it contains essential safety information.

This guide was created as part of the KANUMA® Risk Management Plan and includes risk-minimising measures for the safe and effective use of the medical product.

This guide is a mandatory part of the approval process for Sebelipase alfa, to help ensure that healthcare professionals consider the special safety requirements of prescribing this medicinal product.

This medicinal product is subject to additional monitoring. This allows rapid identification of new evidence on safety. Healthcare professionals are encouraged to report any suspected case of an adverse reaction. For further information on the reporting of adverse reactions, see page 7.

Read the Summary of Product Characteristics (SmPC) carefully before you prescribe or administer Sebelipase alfa.

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.

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INTRODUCTION

Sebelipase alfa is indicated for long-term enzyme replacement therapy (ERT) in patients of all ages with lysosomal acid lipase (LAL) deficiency.

Please read the Summary of Product Characteristics (SmPC) carefully before prescribing or administering Sebelipase alfa. The complete and current text of this SmPC is available at **https://sdi.sfda.gov.sa/**

LAL Deficiency Registry

To provide additional data on long-term safety of Sebelipase alfa administration, healthcare professionals are strongly encouraged to participate in and enroll all patients diagnosed with LAL deficiency in the LAL deficiency registry. Please note that the registry is a general disease registry not restricted to patients treated with Sebelipase alfa and aims to generate information on disease progression and treatment effects not restricted to exposure to Sebelipase alfa. For information on how to participate, see page 7.

HYPERSENSITIVITY REACTIONS, INCLUDING ANAPHYLAXIS

In clinical studies of patients being treated with Sebelipase alfa, hypersensitivity reactions occurred in 59 of 125 patients (47%) and anaphylactic reactions in 5 of 125 patients (4%). The frequency of the reactions decreased with an increased treatment period, but they were also observed one year after the start of treatment.

The signs and symptoms of the hypersensitivity/anaphylactic reactions included the following:

- chest discomfort, dyspnea, tachypnea, severe respiratory distress
- pruritus, rash, eczema, lip swelling, urticaria
- bronchospasm, rhinorrhea, flushing
- conjunctival hyperaemia, hyperaemia
- stridor, hypoxia
- facial edema, edema of the eyelid, laryngeal edema, edema
- tachycardia, hypertension
- pallor
- abdominal pain, nausea, diarrhea, vomiting
- agitation, irritability
- pyrexia, chills

The majority of these reactions occurred during or within 4 hours of the end of infusion.

PREVENTION AND TREATMENT OF HYPERSENSITIVITY REACTIONS, INCLUDING ANAPHYLAXIS

1. Ensure that **appropriate medical support**, including any required medicine, is readily available when Sebelipase alfa is administered.

2. **Observe patients for 1 hour** in order to monitor for any signs or symptoms of anaphylaxis or a severe hypersensitivity reaction following the first Sebelipase alfa infusion, including the first infusion after a dose escalation.

3. If, during administration of Sebelipase alfa, signs of hypersensitivity occur, the infusion can be slowed or discontinued at the discretion of the healthcare professional.

4. **In case of anaphylaxis, the infusion must be stopped immediately!** Leave the cannula in place for the potential administration of drugs.

5. Initiate the **standard appropriate medical treatment** for the management of hypersensitivity reactions, this may include treatment with:
   - Antihistamines
   - Antipyretics
   - Corticosteroids

6. For patients who have experienced allergic reactions during infusion, **caution should be exercised upon re-administration**. Start with a lower infusion rate and increase until the tolerance limit of the patient is reached.

7. **After severe reactions the risks and benefits** of a further Sebelipase alfa administration should be considered.

8. **Consider pre-treatment** with antipyretics and/or antihistamines to prevent subsequent reactions in those cases where symptomatic treatment was required.

Contact information for adverse event reporting is provided on page 7.

IMMUNOGENICITY

In pivotal clinical studies, anti-drug antibodies (ADA), have been observed in 15% (19/125) of patients receiving Sebelipase alfa, at some timepoint after starting treatment. Of these, a total of 11 patients showed the presence of inhibitory antibody activity (NAbs) at some postbaseline timepoint.

- Collection of information on anti-drug antibodies to Sebelipase alfa is important to evaluate the impact of development of ADA on a potential loss of effect or development of potential hypersensitivity, including anaphylaxis, and to support identification of ADA development related risk factors.
- Therefore patients should be tested for anti-drug antibodies to Sebelipase alfa in the event of severe infusion reactions and in cases of lack or loss of effect.
- To date, no conclusion on the relationship between development of ADAs/NAbs and associated hypersensitivity reactions or suboptimal clinical response can be made. In clinical studies, 3 patients homozygous for a deletion affecting both alleles of genes Lipase A, lysosomal acid [LIPA] and cholesterol 25-Hydroxylase developed inhibitory antibody activity associated with a suboptimal clinical response. These patients underwent either immunomodulary therapy alone or in combination with hematopoietic stem cell transplant (HSCT) or bone marrow transplant (BMT) resulting in improved clinical response to Sebelipase alfa.

Anti-drug Antibody Testing

Information on ADA testing is provided as follows:

- It is recommended that healthcare professionals test their patients for ADA to Sebelipase alfa in the event of severe infusion associated reactions and in cases of lack or loss of effect.
- As there are no marketed tests for ADA to Sebelipase alfa, the Marketing Authorisation Holder will provide testing free of charge through a central laboratory.
- An ADA testing kit and accompanying instruction manual will be provided by Alexion. Please see page 7 for contact information. The instruction manual contains information on how to collect, process, and ship ADA samples.
- Results will be provided to the health care provider via the central laboratory portal of the logistics provider.
- Anonymised ADA testing results will be shared with Alexion research and development team.

CONTACT INFORMATION

Call for Reporting Adverse Events

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

To report any side effect(s), please contact:

The National Pharmacovigilance Centre (NPC):
SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

Or

AstraZeneca Pharmacovigilance Department
Website: https://contactazmedical.astrazeneca.com
Email: ksa.ae@astrazeneca.com
Telephone: +966 11 2249235

Anti-drug Antibody (ADA) Testing

For information on ADA testing, contact Alexion Medical Information team at SMKanuma@quintiles

For more information about KANUMA®, please contact Biologix at medinfoksa@astrazeneca.com

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