KAMADA
High Quality Pharmaceuticals

מאי 2023

רופא/ה, רוקח/ת נכבד/ה,

חברת קמהדע מבקשת להודיע על עידכון עלון כמפורט להלן, עבור התכשיר:

למזיד ;Lamzede

Powder for solution for Infusion, I.V

מרכיבים פעילים: **Velmanase alfa 10 mg/vial**

התוויה מאושרת:

Enzyme replacement therapy for the treatment of non-neurological manifestations in patients with mild to moderate alpha mannosidosis.

מהות השינוי: החמרות ועדכונים בעלון לרופא בסעיפים המפורטים מטה.

בהודעה זו מצוינים השינויים המהווים החמרה (החמרות-הודגשו בצהוב, מידע חדש-הודגש באפור; מחיקות-בקו חוצה). בעלון שינויים נוספים שאינם החמרה.

4.4 Special warnings and precautions for use

…Traceability:

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Immunogenicity :

…In a paediatric clinical study in patients below 6 years, 4 patients out of 5 (80%) developed IgG-class antibodies to velmanase alfa. In this study, the immunogenicity test was performed with a different and more sensitive method and therefore the incidence of patients developing IgG-class antibodies to velmanase alfa was higher but not comparable to data of the previous studies.

4.6 Fertility, pregnancy and lactation

Pregnancy:

…. As velmanase alfa aims at normalizing alpha-mannosidase in alpha-mannosidosis patients, Lamzede ~~should~~ is not recommended to be used during pregnancy ~~only when strictly needed~~ unless the clinical condition of the woman requires treatment with velmanase alfa.

4.8 Undesirable effects

The most common adverse reactions observed were weight increase (~~15~~18%), IRRs (13~~9~~%), diarrhoea (10~~12~~%), headache (7~~9~~%), arthralgia (7~~9~~%), increased appetite (~~5~~6%) and pain in extremity (~~5~~6%). The majority ~~All~~ of these adverse reactions were non-serious.

…A total of 4~~2~~ serious adverse reactions (loss of consciousness in 1 patient~~, and~~ acute renal failure in 1 patient, chills and hyperthermia in 1 patient) were observed. In all~~both~~ cases the patients recovered without sequelae.

System organ class […]	**Adverse reaction** […]	**Frequency** […]
Infections and infestations	Bacterial disease carrier	Not known
	Endocarditis	Not known

System organ class […]	**Adverse reaction** […]	**Frequency** […]
	Furuncle	Not known
	Staphylococcal infection	Not known
Metabolism and nutrition disorders	Decreased appetite	Not known
Psychiatric disorders	Agitation	Not known
	Encopresis	Not known
	Psychotic disorder	Not known
	Nervousness	Not known
Nervous system disorders	Ataxia	Not known
	Nervous system disorder	Not known
	Somnolence	Not known
Eye disorders	Lacrimation increased	Not known
Ear and labyrinth disorders	Deafness	Not known
Cardiac disorders	Cyanosis(1)	Common
	Aortic valve incompetence	Not known
	Palpitations	Not known
	Tachycardia	Not known
Vascular disorders	Hypotension	Not known
	Vascular fragility	Not known
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Not known
	Pharyngeal oedema	Not known
	Wheezing	Not known
Gastrointestinal disorders	Odynophagia	Not known
Skin and subcutaneous tissue disorders	Angioedema	Not known
	Erythema	Not known
	Rash	Not known
Musculoskeletal and connective tissue disorders	Joint swelling	Not known
	Joint warmth	Not known
General disorder and administration site conditions	Asthenia	Not known
Injury, poisoning and procedural complications	Infusion related reaction	Not known

Description of selected adverse reactions - see sec. 4.8 in the SmPC

Paediatric population

Children age below 6 years old

A total of 5 patients with alpha-mannosidosis below 6 years received velmanase alfa in a clinical study. The safety profile was similar to that observed in the previous studies, with similar frequency, type and severity of adverse events.

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Children age group 6 to 17 years old

The safety profile of velmanase alfa in clinical studies involving children and adolescents was similar to that observed in adult patients. Overall, 58% of patients (19 out of 33) with alpha-mannosidosis receiving velmanase alfa in clinical studies were aged 6 to 17 years at the start of the study.

5.1 Pharmacodynamic properties

…Paediatric population

Children below 6 years old

Use of velmanase alfa in the children below 6 years is supported by the evidence of the clinical study rhLAMAN08.

Overall, there were no safety issues from use of velmanase alfa in paediatric patients below 6 years of age with alpha-mannosidosis. Four of 5 patients developed anti-velmanase alfa antibodies during the study, and 3 patients developed neutralising/inhibitory antibodies. Two Patients (both anti-velmanase alfa antibodies positive) experienced a total of 12 IRRs, all manageable, with no event leading to discontinuation of study treatment. Two IRRs were assessed as serious and resolved on the same day of occurrence. Premedication before infusion was used, when necessary, as a measure to further reduce risks related to IRRs. Efficacy analysis demonstrated reduction in concentrations of serum oligosaccharides, increase in IgG levels, and suggested improved endurance and hearing. Lack of accumulation of velmanase alfa at steady state and the safety/efficacy results confirm that the dose of 1 mg/kg is appropriate in paediatric patients (aged below 6 years). The study suggests benefits of early treatment with velmanase alfa in children aged below 6 years.

Children age group 6 to 17 years old

Use of velmanase alfa in the age group 6 to 17 years is supported by evidence from clinical studies in paediatric (19 out of 33 patients enrolled in the exploratory and pivotal studies) and adult patients. ~~No clinical data are available in children below the age of 6 years.~~

5.2 Pharmacokinetic properties

…Paediatric population

Pharmacokinetic data from paediatric patients recapitulate the data from the adult population. In particular, lack of accumulation of velmanase alfa at steady state, as well as the safety/efficacy data, confirm that the dose of 1 mg/kg is appropriate also in patients younger than 6 years.

6.4 Special precautions for storage

Store and transport refrigerated (2°C - 8°C). Do not freeze.

העלון לרופא המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס ע"י פניה לבעל הרישום, חברת קמהדע בע"מ (טל' 08-9406472). להלן הקישור למאגר התרופות: https://israeldrugs.health.gov.il/#!/byDrug

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