PRESS RELEASE

# NICE recommends Lamzede®▼ (velmanase alfa) as first ever enzyme replacement therapy for initiation in children with alpha-mannosidosis in England and Wales in final evaluation document

- *Velmanase alfa is the first and only enzyme replacement therapy for the non-neurological signs and symptoms of mild to moderate alpha-mannosidosis.*[1]
- *Alpha-mannosidosis is an extremely rare inherited condition, with only around 25 people affected in England.*[1]

MANCHESTER, UK, 9th November 2023 – Chiesi, the international research-focused biopharmaceutical and healthcare group, today announced that the National Institute for Health and Care Excellence (NICE) has recommended Lamzede® (velmanase alfa) in their final evaluation document as an option for treating the non-neurological signs and symptoms of mild to moderate alpha-mannosidosis.[1] The treatment must be started in people under 18 years of age, and can be continued in people who turn 18 while on treatment, in line with a commercial agreement.[1]

Velmanase alfa becomes the first and only enzyme replacement therapy recommended by NICE for alpha-mannosidosis and is given to patients once-a-week by intravenous infusion.[1] It is designed to supplement or replace an enzyme that is missing in patients with alpha-mannosidosis.[2]

*"We are pleased that eligible patients in England and Wales will now be able to access velmanase alfa on the NHS for the first time,"* said Dr Kamran Iqbal, Head of Medical Affairs, Global Rare Diseases, Chiesi UK&I. *"The discovery and availability of new treatment options is crucial for those affected by this progressive disease, and we have worked tirelessly over several years with key stakeholders including NICE, patient groups and clinicians to address uncertainties that are common in rare diseases and ensure access for those in need. We are immensely grateful for the hard work and commitment of all involved."*

Alpha-mannosidosis is an extremely rare, genetic condition – for example, it is thought to affect around 25 people in England, with many of these children and young people.[1] People with the condition have a shortage of the enzyme alpha-mannosidase, which is needed to break down certain sugars in the body.[2] When this enzyme is missing or does not work properly, these sugars build up inside the cells and may lead to varying levels of signs and symptoms including skeletal abnormalities, hearing loss, intellectual disability, and dysfunction of the immune system.[1] People with alpha-mannosidosis may experience increasing problems as their disease progresses which require a high level of care, with more severe cases associated with poor survival rates.[1]

*"On behalf of our alpha-mannosidosis community, I am pleased at the news that NICE has made the decision to make velmanase alfa available to suitable patients in our community in England and Wales,"* said Bob Stevens, Group Chief Executive, MPS Society. *"This marks a real change for this community because now they have the possibility of treatment and this is another example of innovative science benefitting our rare patients."*

For more information on Chiesi, please visit: www.chiesi.uk.com

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## About alpha-mannosidosis

Alpha-mannosidosis is a lysosomal storage disorder caused by inheriting a faulty copy of the MAN2B1 gene from both parents, resulting in impaired production of the enzyme alpha-mannosidase.[1] Alpha-mannosidosis is an extremely rare disorder with an estimated prevalence of 1 in 500,000-1,000,000, equating to approximately 25 people in England.[1]

Alpha-mannosidosis may cause a broad range of progressive signs and symptoms including difficulty controlling movement, breathing problems, deafness, speech difficulties, infections, bone abnormalities, muscle pain and weakness, and cognitive impairment.[1] People living with alpha-mannosidosis can experience increasing problems with mobility and movement, severe infections and liver enlargement as their disease progresses, which, in severe cases, can lead to early death.[1] The condition can have a considerable impact on people's ability to perform daily activities and also affects their carers who support their daily living.[1]

## About velmanase alfa

Velmanase alfa is a once-weekly enzyme replacement therapy (ERT) used for the treatment of non-neurological manifestations in patients with mild to moderate alpha-mannosidosis, administered by intravenous infusion.[2]

A total of 33 patients enrolled in the exploratory and pivotal studies (20 males and 13 females, ranging in age from 6 to 35 years) were exposed to velmanase alfa in five clinical studies.[2] Patients were diagnosed based on alpha-mannosidase activity <10% of normal activity in blood leukocytes.[2] Patients with the most severe rapidly progressing phenotype (with a deterioration within one year and central nervous system involvement) were excluded.[2] Based on this criteria mild to moderate patients, presenting heterogeneous severity with ability to perform endurance tests, large variability of clinical manifestations and age of onset were enrolled.[2]

Overall effects of treatment were evaluated in the domains of pharmacodynamics (reduction of serum oligosaccharides), functional (three-minute stair climbing test (3MSCT), six-minute walking test (6MWT), and forced vital capacity (FVC) % predicted) and quality of life (childhood health assessment questionnaire (CHAQ) disability index (DI) and CHAQ VAS pain (visual analogue scale)).[2]

In the phase 3 pivotal multi-centre, double-blind, randomised, placebo-controlled, parallel group study rhLAMAN-05, the efficacy and safety of repeated administrations of velmanase alfa over 52 weeks at a dose of 1 mg/kg given weekly as intravenous infusion were investigated.[2] A total of 25 patients were enrolled, including 12 paediatric subjects (age range: 6 to 17 years; mean: 10.9 years) and 13 adult subjects (age range: 18 to 35 years; mean: 24.6).[2] All but one patient were naïve to the treatment with velmanase alfa.[2] In total 15 patients (7 paediatrics and 8 adults) received active treatment and 10 patients received placebo (5 paediatrics and 5 adults).[2] A pharmacodynamic effect with statistically significant decrease of serum oligosaccharides in comparison to placebo was demonstrated.[2] The results observed in patients below 18 years of age showed an improvement. In patients over 18 years old a stabilisation has been demonstrated.[2] The numerical improvement of most clinical endpoints over placebo (2 to 8%) observed in the year of observation could be suggestive of the ability of velmanase alfa to slow down the existing disease progression.[2]

Use of velmanase alfa in children below six years is supported by the evidence of the clinical study rhLAMAN-08.[2] Overall, there were no safety issues from use of velmanase alfa in paediatric patients below six years of age with alpha-mannosidosis.[2] Four of five patients developed anti-velmanase alfa antibodies during the study, and three patients developed neutralising/inhibitory antibodies.[2] Two patients (both anti-velmanase alfa antibodies positive) experienced a total of 12 infusion-related reactions (IRRs), all manageable, with no event leading to discontinuation of study treatment.[2] Two concomitant 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.[2] Efficacy analysis demonstrated reduction in concentrations of serum oligosaccharides, increase in immunoglobulin G (IgG) levels, and suggested improved endurance

and hearing.[2] 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 young paediatric patients (aged below six years).[2] The study suggests benefits of early treatment with velmanase alfa in children aged below six years.[2] 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.[2]

Summarising the safety profile, the most common adverse reactions observed were weight increase (15%), infusion-related reactions (IRRs) (13%), diarrhoea (10%), headache (7%), arthralgia (7%), increased appetite (5%) and pain in extremity (5%).[2]

The majority of these adverse reactions were non-serious.[2] IRRs include hypersensitivity in three patients and anaphylactoid reaction in one patient. These reactions were mild to moderate in intensity.[2]

A total of four serious adverse reactions (loss of consciousness in one patient, acute renal failure in one patient, chills and hyperthermia in one patient) were observed.[2] In all cases the patients recovered without sequelae.[2]

In children age below six years old, a total of five patients with alpha-mannosidosis below six years received velmanase alfa in a clinical study.[2] The safety profile was similar to that observed in the previous studies, with similar frequency, type and severity of adverse events.[2] In 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.[2] 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. [2]

Velmanase alfa is approved in the European Union, Northern Ireland, and Great Britain for the treatment of non-neurological manifestations in patients with mild to moderate alpha-mannosidosis.[2,3] The US Food and Drug Administration (FDA) approved velmanase alfa for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and paediatric patients in February 2023.[4] Velmanase alfa is reimbursed in France, Germany, Italy, Romania, Scotland (via the SMC ultra-orphan framework for 3 years until 2026), Serbia, Slovakia and Spain.[5]

The Great Britain Summary of Product Characteristics for velmanase alfa can be found at https://www.medicines.org.uk/emc/product/12836/smpc#about-medicine.

## About Chiesi Group

Chiesi is an international, research-focused biopharmaceuticals group that develops and markets innovative therapeutic solutions in respiratory health, rare diseases, and specialty care. The company's mission is to improve people's quality of life and act responsibly towards both the community and the environment.

By changing its legal status to a Benefit Corporation in Italy, the US, and France, Chiesi's commitment to create shared value for society as a whole is legally binding and central to company-wide decision-making. As a certified B Corp since 2019, we're part of a global community of businesses that meet high standards of social and environmental impact. The company aims to reach Net-Zero greenhouse gases (GHG) emissions by 2035.

With over 85 years of experience, Chiesi is headquartered in Parma (Italy), operates in 31 countries, and counts more than 6,500 employees. The Group's research and development centre in Parma works alongside 6 other important R&D hubs in France, the US, Canada, China, the UK, and Sweden.

For further information please visit: www.chiesi.uk.com.

## About Chiesi Global Rare Diseases

Chiesi Global Rare Diseases is a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people affected by rare diseases. As a family business,

Chiesi Group strives to create a world where it is common to have a therapy for all diseases and acts as a force for good, for society and the planet. The goal of the Global Rare Diseases unit is to ensure equal access so as many people as possible can experience their most fulfilling life. The unit collaborates with the rare disease community around the globe to bring voice to underserved people in the health care system.

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