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Summary of the risk management plan (RMP) for Vimizim (elosulfase alfa)

This is a summary of the risk management plan (RMP) for Vimizim, which details the measures to be taken in order to ensure that Vimizim is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Vimizim, which can be found on Vimizim's EPAR page.

Overview of disease epidemiology

Mucopolysaccharidosis type IVA (MPS IVA) is a rare inherited disorder where the body is unable to make an enzyme called N-acetylgalactosamine-6-sulfatase that it needs to break down substances called glycosaminoglycans (or GAGs). Without this enzyme, GAGs build up in the patient's organs and tissues, causing problems with bones and joints and with the ability to breathe normally. Most patients are significantly limited in both the ability to move around and in how much activity they can tolerate without getting tired, and often require multiple surgical procedures to correct problems with bones and joints. Many patients end up using scooters, wheelchairs, or other walking aids by the time they are teenagers. As patients get older, the respiratory problems often lead to pneumonia (lung infection) or respiratory failure, and the bone and joint problems in the back can lead to weakness, numbness, problems with bowel or bladder control, and even paralysis or death. Most patients with MPS IVA will have a shortened lifespan, although this varies depending on how quickly the symptoms worsen.

In the EU, MPS IVA is estimated to affect approximately 0.06 in 10,000 people, which corresponds to 1,300 MPS IVA patients in the EU.

Summary of treatment benefits

Vimizim has been investigated in a double-blind study (meaning the patients and their doctors didn't know which treatment patients were given) involving 176 patients with MPS IVA where Vimizim was compared with placebo (a dummy treatment). The study showed that Vimizim given once a week for approximately 6 months was more effective than placebo at improving the distance patients could walk in 6 minutes. There was also some evidence from the study data to suggest that the medicine could improve how well patients breathe or climb stairs, and in children, how well they grew when compared with children without MPS IVA.

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Unknowns relating to treatment benefits

Because studies so far have only examined use of Vimizim over periods of up to 18 months, the medicine will continue to be studied in patients with MPS IVA to determine whether it remains effective when used for a longer period of time, and also to get more information about its safety.

The clinical studies with Vimizim have included a wide range of patients of different ages, genders, and racial/ethnic and geographical backgrounds. A review of the results of these studies has not shown any difference in terms of safety or effectiveness of Vimizim based on any of those characteristics. There are still groups of patients that have not been closely studied (such as women who are pregnant or breastfeeding, or patients with liver or kidney problems). No older patients (over the age of 65) have received Vimizim. It is not known whether Vimizim will have a different effect or will be less safe when used in these groups.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Infusion reactions (including anaphylaxis and severe allergic reactions)	Infusion reactions are reactions that occur during an infusion or up to the end of the day following an infusion. Over 90% of the subjects in clinical studies had at least one infusion reaction. The most common reactions are headache, fever, vomiting and nausea. Most infusion reactions are not serious and either get better on their own or with basic treatments (like an antihistamine), but some subjects have had more severe reactions that have required treatments with steroids and oxygen to help them breathe. Anaphylaxis is a particularly serious kind of allergic reaction. Common symptoms of anaphylaxis include an itchy rash, swelling, difficulty breathing, flushing, and a drop in blood pressure. Anaphylaxis can be treated but usually requires emergency treatment, such as adrenaline.	Treatment with an antihistamine with or without an antipyretic (a medicine for fever) approximately 30-60 minutes before an infusion reduces the likelihood of infusion reactions. Physicians and other healthcare professionals who will be giving Vimizim to patients will be trained in how to recognise infusion reactions, including anaphylaxis, and in what to do to treat them.

Important potential risks

Risk	What is known
The body may make antibodies that attack the medicine (Immunogenicity)	All patients treated with Vimizim developed antibodies in their blood against the medicine. When the patients' blood was tested in a laboratory, about 80% of the patients had also developed a special kind of antibodies that might block the medicine from attaching to the cells where it is needed. While these special antibodies were found in the lab, there was no evidence that the medicine was unsafe or less effective in patients who developed antibodies when compared with patients who didn't.
Problems with the nerves in the back (Spinal/cervical cord compression, including laxity and unmasking myelopathic symptoms)	Spinal or cervical cord compression has occurred in a small number of patients who have taken Vimizim. Spinal or cervical cord compression is when the nerves that run down the neck and back get pinched or damaged. This damage can cause problems such as weakness, numbness, problems with bowel or bladder control, and even paralysis or death. Spinal cord compression also occurs in patients with MPS IVA who are not taking Vimizim, and there was no evidence that taking the medicine made a patient more likely to develop spinal cord compression.
Medication errors	Medication errors were observed during clinical trials in about 2.8% of all infusions. The most common reason for these errors was the patient not getting the right dose based on his/her current weight (so the patient may have received more or less than the recommended dose). Most of these errors had no impact on the safety of the patient, or on how well the medicine worked.

Missing information

Risk	What is known
Limitations of the safety database	Because MPS IVA is a rare disease, the number of patients who were treated with Vimizim in clinical studies was small (about 235 patients overall). It is possible that uncommon side effects that might be associated with Vimizim have not been seen because not enough patients have yet been treated with the medicine.
Safety in patients with pre-existing organ diseases	There is limited information available on the use of Vimizim in patients who have pre-existing heart, liver or kidney disease. It is not known whether Vimizim will act differently or cause different side effects in these groups.
Safety in pregnancy and lactation	Vimizim has not been studied in women who are pregnant or breastfeeding, or in patients whose partners are pregnant or

Risk	What is known
	breastfeeding.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Vimizim can be found on Vimizim's EPAR page.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published on Vimizim's EPAR page; how they are implemented in each country however will depend upon agreement between the marketing authorisation holder and the national authorities.

These additional risk minimisation measures are for the following risks:

Medication errors

Risk minimisation measure: Healthcare professional education programme
Objective and rationale: Educational material to be provided to healthcare professionals to minimise the risk of medication errors.
Description: The marketing authorisation holder of Vimizim will provide healthcare professionals who are expected to use and/or prescribe Vimizim with educational materials, informing them of the proper storage, preparation and administration of Vimizim, and the risk of severe allergic reactions.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
MPS IVA CRP (registry)	To characterise and describe the MPS IVA population as a whole, including the heterogeneity, progression and natural history of MPS IVA. To evaluate the long-term effectiveness and safety of Vimizim (elosulfase alfa). To help the MPS IVA medical community with the development of recommendations for monitoring subjects and reports on subject outcomes to optimise subject care. To collect data on other treatment paradigms, evaluate the prevalence of their use and their effectiveness. To characterise the effects of 5 years of elosulfase alfa treatment in subjects under 5 years of age.	**Safety:** Additional data collected will help broaden knowledge of identified and potential risks of elosulfase alfa, as well as increase the size of the safety database and possibly provide new information on use in identified subgroups (pregnancy, hepatic and renal impairment, cardiac impairment). **Efficacy:** Additional data collected will help evaluate long-term effectiveness of elosulfase alfa.	Planned to start Q3 2014	Annual interim reports. Final report due in 2025.

Studies which are a condition of the marketing authorisation

The registry described above is a condition of the marketing authorisation.

Summary of changes to the risk management plan over time

None.

This summary was last updated in 04-2014.