VIMIZIM®▼ (ELOSULFASE ALFA) DOSING AND ADMINISTRATION GUIDE

This Dosing and Administration Guide is part of the VIMIZIM® marketing authorisation, and it has been approved by the HPRA.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

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VIMIZIM®
(elosulfase alfa)

GETTING READY TO ADMINISTER VIMIZIM® (elosulfase alfa)

VIMIZIM® is indicated for the treatment of mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome) in patients of all ages.[1]

The following steps are recommended for the dosing and administration of VIMIZIM®. Please also refer to the Summary of Product Characteristics for information.

VIMIZIM® treatment should be supervised by a physician experienced in the management of patients with Morquio A or other inherited metabolic diseases. Administration of VIMIZIM® should be carried out by an appropriately trained healthcare professional with the ability to manage medical emergencies.

WARNINGS AND PRECAUTIONS

Anaphylaxis and severe allergic reactions[1]

Anaphylaxis and severe allergic reactions have been reported in patients in clinical studies. Therefore, appropriate medical support must be readily available when VIMIZIM® is administered.

If these reactions occur, immediately stop the infusion and initiate appropriate medical treatment.[1]

Infusion reactions (IRs)[1]

Most adverse reactions in clinical trials were IRs, which are defined as reactions occurring after initiation of infusion until the end of the day following the infusion.

Serious IRs were observed in clinical trials and included:

- Anaphylaxis
- Hypersensitivity
- Vomiting

The most common symptoms of IRs (occurring in ≥10% of patients treated with VIMIZIM® and ≥5% more when compared to placebo) were:

- Headache
- Nausea
- Vomiting
- Pyrexia
- Chills
- Abdominal pain

IRs were generally mild or moderate, and the frequency was higher during the first 12 weeks of treatment and tended to occur less frequently with time.

If severe IRs occur, immediately stop the infusion and initiate appropriate treatment. Re-administration of VIMIZIM® after a severe reaction should be carried out with caution and close monitoring by the treating physician.

Because of the potential for hypersensitivity reactions, patients should receive antihistamines with or without antipyretics 30-60 minutes prior to start of infusion.

RECOMMENDED DOSE

- VIMIZIM® is an injectable solution for infusion and comes in 5 ml, single use vials[1]
- The recommended dose of VIMIZIM® is 2 mg/kg of body weight administered once a week as an intravenous infusion over approximately 4 hours[1]
- Patients should receive antihistamines with or without antipyretics 30-60 minutes prior to the start of infusion[1]

CALCULATING THE DOSE

Perform the following steps to determine how many ml of VIMIZIM® your patient requires:

1 PATIENT DOSE:

Patient weight (kg)	×	2 mg/kg dose	=	**Patient dose** (mg of reconstituted VIMIZIM® required)

2 ML OF VIMIZIM®:

Patient dose (mg)	÷	1 mg/ml concentrate of VIMIZIM®	=	**Total ml of VIMIZIM®**

3 NUMBER OF VIALS OF VIMIZIM®:

Total ml of VIMIZIM®	÷	5 ml per vial	=	**Total number of vials** (round up to the next whole vial)

Dose calculation example for patient weighing <25 kg[1]

Patients weighing less than 25 kg should receive a total volume of 100 ml.

Patient weight (16 kg) x dose (2 mg/kg) = patient dose (32 mg)

Patient dose (32 mg) divided by 1 mg/ml concentrate of VIMIZIM® = total ml of VIMIZIM® (32 ml).

Total amount of VIMIZIM® (32 ml) divided by 5 ml per vial = total number of vials when rounded up to the next whole vial (7 vials).

NOTE: To convert kilograms (kg) to pounds (lb), multiply by 2.2. Then, use 0.9 ml of VIMIZIM® 1 mg/ml per pound of body weight.

Dose calculation example for patient weighing ≥25 kg[1]

Patients weighing 25 kg, or more should receive a total volume of 250 ml.

Patient weight (28 kg) x dose (2 mg/kg) = patient dose (56 mg)

Patient dose (56 mg) divided by 1 mg/ml concentrate of VIMIZIM® = total ml of VIMIZIM® (56 ml).

Total amount of VIMIZIM® (56 ml) divided by 5 ml per vial = total number of vials when rounded up to the next whole vial (12 vials).

NOTE: To convert kilograms (kg) to pounds (lb), multiply by 2.2. Then, use 0.9 ml of VIMIZIM® 1 mg/ml per pound of body weight.

CALCULATING INFUSION RATES BY VOLUME

Dose calculation example for patient weighing <25 kg[1]

When diluted in 100 ml, the initial infusion rate should be 3 ml/h. The infusion rate may be increased as tolerated, every 15 minutes as shown in Table 1; first increase the rate to 6 ml/h, then increase the rate every 15 minutes by 6 ml increments until a maximum rate of 36 ml/h is reached.[1]

Dose calculation example for patient weighing ≥25 kg[1]

When diluted in 250 ml, the initial infusion rate should be 6 ml/h. The infusion rate may be increased as tolerated, every 15 minutes as shown in Table 1; first increase the rate to 12 ml/h, then increase the rate every 15 minutes by 12 ml increments until a maximum rate of 72 ml/h is reached.[1]

Table 1: Recommended infusion volumes and rates[1]*

INTERVALS FOR INCREASING RATE OF VIMIZIM® INFUSION	Patient weight (kg)	
	<25	≥25
	Total infusion volume (ml)	
	100	250
	Rate of infusion (ml/h)	
Step 1: Initial infusion rate 0–15 minutes	3	6
Step 2: 15–30 minutes	6	12
Step 3: 30–45 minutes	12	24
Step 4: 45–60 minutes	18	36
Step 5: 60–75 minutes	24	48
Step 6: 75–90 minutes	30	60
Step 7: 90+ minutes	36	72

*Infusion rate may be increased as tolerated by patient.[1]

SUPPLIES NEEDED

- VIMIZIM® 5 ml, single-use vials[1]
- Sodium chloride 9 mg/ml (0.9%) solution for injection **100 ml** or **250 ml**[1]
- Infusion set equipped with an in-line 0.2 µm filter can be used[1]

DILUTION PRIOR TO ADMINISTRATION

Prepare VIMIZIM® for dilution using aseptic techniques[1]

VIMIZIM® must be diluted with sodium chloride 9 mg/ml (0.9%) solution for injection to a final volume of 100 ml or 250 ml (based on the patient's weight) prior to infusion and delivered intravenously.

For patients weighing ≥25 kg, VIMIZIM® should be prepared in 250 ml of sodium chloride 9 mg/ml (0.9%) solution for injection. For patients weighing <25 kg, VIMIZIM® should be prepared in 100 ml of sodium chloride 9 mg/ml (0.9%) solution for injection.

STORAGE AND CARE OF PRODUCT

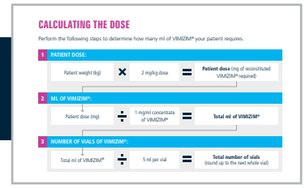
- Vials are for single-use only[1]
- Do not freeze or shake[1]
- Protect from light[1]
- Discard any unused product[1]
- VIMIZIM® does not contain preservatives therefore, the product should be used immediately after dilution. If immediate use is not possible, the diluted product may be stored for up to 24 hours at 2-8°C (36-27F) followed by up to 24 hours at 23-27°C (73-81F).[1]

PREPARE AND ADMINISTER VIMIZIM® ACCORDING TO THE FOLLOWING STEPS:

This product should be prepared and administered under the supervision of a healthcare professional with the ability to manage medical emergencies.[1]

AVOID AGITATION DURING PREPARATION

1



COMPLETE THE DOSE CALCULATION explained previously to determine how many vials of VIMIZIM® you will need.[1]

2

REMOVE the appropriate number of vials from the refrigerator. Do not heat or microwave vials.[1]

3

OBTAIN AN INFUSION BAG
containing sodium chloride 9 mg/ml (0.9%) solution for injection. The total volume of the infusion is determined by the patient's body weight.[1]

4

INSPECT EACH VIAL for particulate matter or discolouration before withdrawing VIMIZIM® from the vial. Because this is a protein solution, slight flocculation (thin translucent fibres) may occur. The VIMIZIM® solution should be clear to slightly opalescent and colourless to pale yellow. Do not use if the solution is discoloured or if there is particulate matter in the solution.[1]

5

WITHDRAW AND DISCARD a volume of the sodium chloride 9 mg/ml (0.9%) solution for injection from the infusion bag equal to the volume of VIMIZIM® concentrate to be added.

6

SLOWLY WITHDRAW the calculated volume of VIMIZIM® from the appropriate number of vials and slowly add to the infusion bag. Gently rotate the infusion bag to ensure proper distribution of VIMIZIM®. Do not shake the solution.[1]

7

ADMINISTER THE DILUTED VIMIZIM® solution to patients using an infusion set, which may be equipped with an in-line 0.2µm filter.[1]

TRACEABILITY

Please ensure you record the product name and batch number in the patient file.

NOTES

NOTES

Adverse events should be reported. Reporting forms and information can be found at: www.hpra.ie.

Adverse events should also be reported to BioMarin at +1 415 506 6179 or via email to: drugsafety@bmrn.com

BIOMARIN®

BioMarin International Limited

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Reference: 1. VIMIZIM® Summary of Product Characteristics (SmPC) .

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