



**VIMIZIM**<sup>®</sup>  
(elosulfase alfa)

## Understanding Morquio A and VIMIZIM<sup>®</sup> (elosulfase alfa)

Life-threatening allergic reactions, known as anaphylaxis, can occur during VIMIZIM<sup>®</sup> (elosulfase alfa) infusions. Typical signs of anaphylaxis include cough, rash, throat tightness, hives, flushing, changes in skin color, low blood pressure, shortness of breath, chest pain, and gastrointestinal symptoms such as nausea, abdominal pain, retching, and vomiting. Contact your doctor or get medical help right away if these symptoms occur during or after VIMIZIM infusions. If you have a respiratory illness, you may be at risk for a sudden worsening of your condition, and you may require additional monitoring.

Additional Important Safety Information will be discussed during this presentation.

**BIOMARIN**

## Morquio A key facts

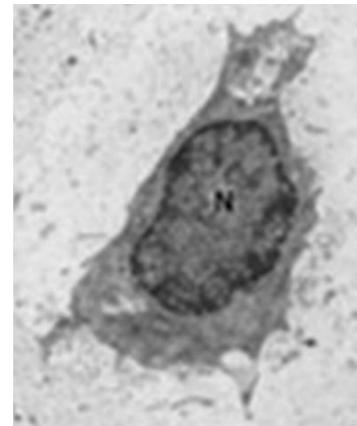
Morquio A (also known as MPS IVA) is a rare and progressive inherited disease that affects major organ systems in the body. It is a form of mucopolysaccharidosis (MPS), a type of **lysosomal storage disorder**.

Enzymes are proteins that perform specific jobs in your body.

People with Morquio A do not make enough of a specific enzyme, called N-acetylgalactosamine-6 sulfatase, or **GALNS (gal·en·es)**, which breaks down and recycles cellular waste called glycosaminoglycans (**GAGs**).

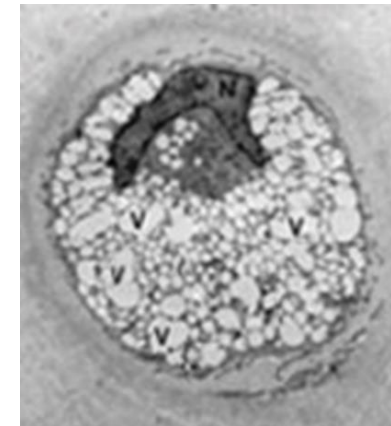
When the body doesn't produce enough of the enzyme, GAGs build up in tissues, bones, and major organs, potentially causing serious physical problems.

**NORMAL CELL**



GALNS breaks down and recycles GAGs.

**MORQUIO A CELL**

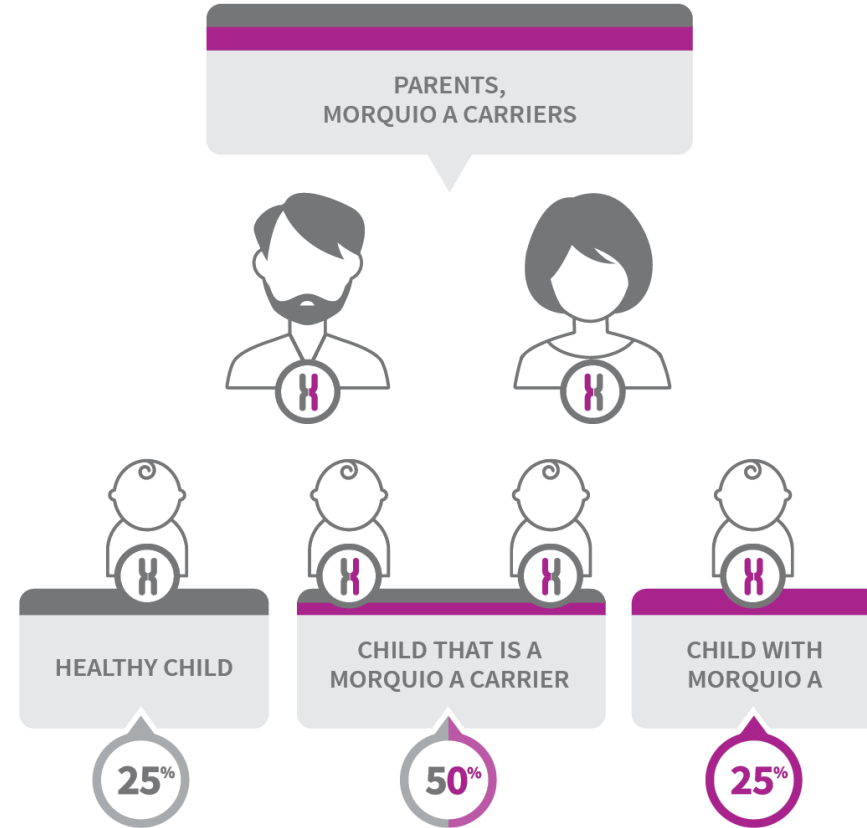


Without enough GALNS, GAGs build up in cells throughout the body.

## How do people inherit Morquio A?

Morquio A is a recessively inherited condition. This means that both parents must have a genetic mutation, or variant, in the *GALNS* gene to pass Morquio A on to their children.

When 2 parents who are carriers have children, each pregnancy presents a 25% chance (1 in 4) of passing Morquio A on to that child.



# What are the signs and symptoms of Morquio A?

Morquio A affects many parts of the body and is **heterogeneous** (het·er·o·ge·ne·ous), which means that the symptoms and severity are different for each person.

Individuals with Morquio A may have:



## SKELETAL SYMPTOMS

Skeletal abnormalities	Overly flexible joints
Short trunk	Abnormal walk
Weakness in the neck	Spinal problems
Spinal cord compression	Chest deformities
Knock knees	

## NONSKELETAL SYMPTOMS

Breathing problems	Dental problems
Heart valve problems	Enlarged liver
Muscle weakness	Enlarged spleen
Eye problems	Limited energy
Hearing loss	

*It is important to know that Morquio A does not affect your ability to think and learn.*

## The symptoms of Morquio A progress over time

Morquio A is **progressive**, which means that symptoms get worse over time, as GAGs build up in the body.

The buildup of GAGs in the cells of the body can affect multiple systems.

For many people with Morquio A, symptoms can appear by age 2 or 3, others may not show initial symptoms (including hip stiffness and pain) until the second decade of life.

*Since the symptoms of Morquio A may worsen over time, it's important to look for early symptoms to ensure that you get timely treatment.*



# The health complications of Morquio A can affect endurance

Endurance is how far a person can push himself or herself physically. It measures how well the whole body performs—from heart and lungs to bones and muscles. People with Morquio A who have reduced endurance may have difficulty with regular activities.



## HEART COMPLICATIONS

**Examples:** Thickening and/or narrowing of valves, valve insufficiency



## BREATHING COMPLICATIONS

**Examples:** Complications with sinuses, sleep apnea, respiratory infections, restricted lungs and airways



## MUSCLE AND SKELETAL COMPLICATIONS

**Examples:** Overly flexible joints, joint pain, hip dysplasia, knock knees, reduced height

## Reduced endurance

- Difficulty with regular daily activities
- Limited mobility
- Reduced quality of life

## How is endurance measured?

- Endurance is how far you can push yourself physically
- Endurance can be measured using a test called the 6-minute walk test (6MWT), which measures how far a person can walk in 6 minutes
  - For people who have difficulty walking, the timed 25-foot walk test (T25FWT) is used to measure endurance
- Medical researchers have used the 6MWT to show that people with Morquio A can have significantly less endurance than people who do not have Morquio A
- The 6MWT has also been used to show that as people with Morquio A get older, their endurance declines



## Endurance declined over time in individuals with Morquio A

In a 2-year observational study, people with Morquio A showed a **continued decline in endurance**.



Individuals with Morquio A walked 21.9 meters less than they did at the start of the study, as measured by the 6-minute walk test (6WMT), which measures how far someone can walk in 6 minutes.

In the same study, people with Morquio A showed a **decline in most measures of breathing ability**.



Breathing function, as measured by pulmonary function tests, showed a decline in most measures of breathing ability after 2 years, compared with baseline measurements.

This study was not designed to measure the impact of treatment with VIMIZIM<sup>®</sup> (elosulfase alfa). It is unknown what impact VIMIZIM may have had on these individuals.



## VIMIZIM® (elosulfase alfa) works at a cellular level to help with deficient enzyme activity

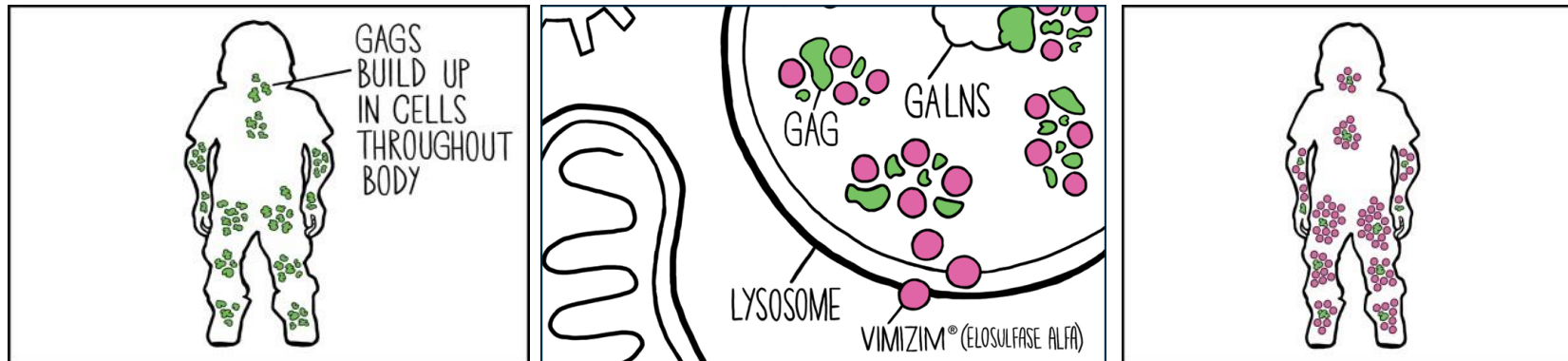
VIMIZIM® (elosulfase alfa) is the only enzyme replacement therapy (ERT) approved by the US Food and Drug Administration for people with Morquio A.

VIMIZIM was made to replace the GALNS enzyme that is missing in people with Morquio A.



## How does VIMIZIM® (elosulfase alfa) work at a cellular level?

If you have Morquio A, you don't have enough GALNS enzyme activity. VIMIZIM® (elosulfase alfa) can replace the deficient enzyme to help restore some cell function.



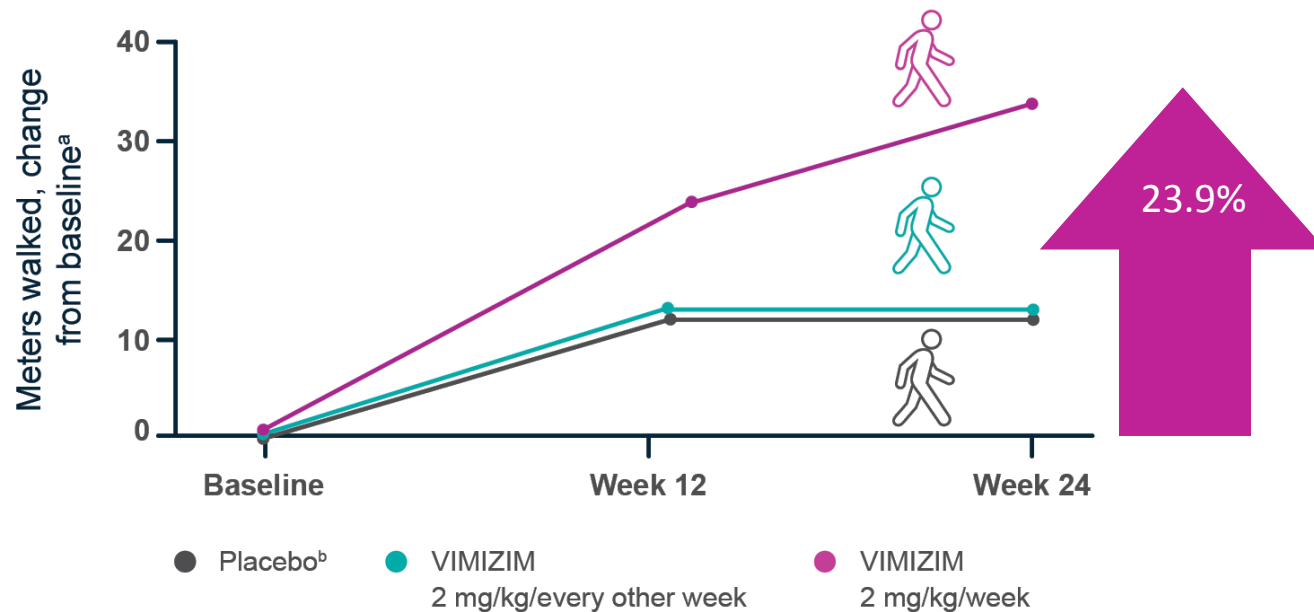
In people with Morquio A, GAGs build up in the lysosomes of cells throughout the tissues and organs of the body, potentially causing serious problems.

A weekly infusion of VIMIZIM replaces the deficient GALNS enzyme your body needs to help reduce the buildup of certain GAGs.

Taking VIMIZIM every week can help people with Morquio A reduce the buildup of certain GAGs.

## VIMIZIM<sup>®</sup> (elosulfase alfa) improves endurance

In a 6-month clinical trial, people who received VIMIZIM<sup>®</sup> (elosulfase alfa) infusions every week improved their endurance as measured by the 6MWT.



This graph shows that by the end of a 24-week trial, people who took VIMIZIM once a week walked an average of 23.9% farther than at baseline

People who took VIMIZIM every other week did not show much improvement, and their results were similar to the people who took a placebo

<sup>a</sup>A baseline is a measurement of a person's performance before they begin treatment in a clinical trial.

To participate in the clinical trial for VIMIZIM, people had to be able to walk more than 30 meters but less than 325 meters in 6 minutes.

<sup>b</sup>A placebo is a harmless substance that does not contain any medicine.

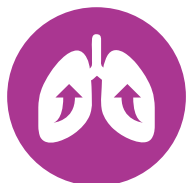
## VIMIZIM<sup>®</sup> (elosulfase alfa) can provide long-lasting benefits

A 2-year extension study showed that the benefits of VIMIZIM<sup>®</sup> (elosulfase alfa) can be maintained over the long term and are consistent with the results of the primary study, though no placebo group was available for comparison.



### Improved endurance

Results from the long-term extension study showed a 32.9-meter mean increase.



### Breathing ability improved

Breathing function, as measured by pulmonary function tests, improved for individuals compared to baseline.

There was a 9.2% increase in FVC (volume of air that can forcibly be exhaled from the lungs after taking the deepest breath possible) and an 8.8% increase in FEV<sub>1</sub> (maximum volume of air that can be forcibly blown out in 1 second), compared to baseline.

Staying on once-weekly VIMIZIM can help maintain or improve endurance and breathing ability

## What are the possible side effects of VIMIZIM® (elosulfase alfa)?

The most common side effects seen with VIMIZIM® (elosulfase alfa) that occurred more often than with a placebo

Side effect	VIMIZIM 2 mg/kg/wk N=58 n (%)	Placebo N=59 n (%)
Fever	19 (33%)	8 (14%)
Vomiting	18 (31%)	4 (7%)
Headache	15 (26%)	9 (15%)
Nausea	14 (24%)	4 (7%)
Abdominal pain	12 (21%)	1 (1.7%)
Chills	6 (10.3%)	1 (1.7%)
Fatigue	6 (10.3%)	2 (3.4%)

### Serious adverse reactions with VIMIZIM® (elosulfase alfa)

- Serious and severe reactions were associated with VIMIZIM® (elosulfase alfa), including hypersensitivity reactions as well as life-threatening allergic reactions (anaphylaxis)
- In clinical trials, 18.7% of patients treated with VIMIZIM experienced hypersensitivity reactions and 7.7% experienced anaphylaxis
- Anaphylaxis can occur during VIMIZIM infusions and up to 3 hours after any infusion

## What are the possible long-term side effects of VIMIZIM<sup>®</sup> (elosulfase alfa)?

No new serious adverse events were reported in the long-term extension study.

- 173 of 176 patients enrolled in the 24-week phase 3 study continued into the 120-week extension study
- The most common adverse reactions were infusion-associated and were managed with symptomatic treatment and/or modification of infusion rate
- In the VIMIZIM<sup>®</sup> (elosulfase alfa) 2 mg/kg/week group (who received 120 weeks of drug), the rate of drug discontinuation due to adverse events was 1.8%

## **Serious adverse reactions associated with VIMIZIM<sup>®</sup> (elosulfase alfa) are manageable with appropriate medical support**

- As a precaution, you should receive medication such as antihistamines with or without antipyretics (fever reducers) before VIMIZIM<sup>®</sup> (elosulfase alfa) infusions to reduce the risk of reactions
- Your infusion nurse should check on you while you receive treatment to make sure everything is going well. If you notice any unusual symptoms, tell your nurse right away
- If a reaction occurs, the infusion should be slowed or stopped, and you may be given additional medication
- Your doctor and nurses will work with you to develop a plan to address any possible reactions that could occur during or after your infusion



Please see Important Safety Information, including important warning, on slides 24-26.

## Once-a-week VIMIZIM<sup>®</sup> (elosulfase alfa) infusions

- VIMIZIM<sup>®</sup> (elosulfase alfa) is administered by intravenous (IV) infusion directly into a vein in your body
- Infusions take place once a week and may take at least 3.5 to 4.5 hours
- To start, you will receive your infusions in an infusion clinic
- Later, you may be able to arrange to have your infusions performed in your home



### What people taking VIMIZIM have to say

*“Before treatment, I felt I had run a marathon because by the end of the day, middle of the day, I was exhausted... Now, I'm able to keep doing other things. I'm back working on Saturdays and Sundays.”*

– Fanny



Please see Important Safety Information, including important warning, on slides 24-26.



## What to expect before your infusion

Infusions can take at least 3.5 hours, be sure to prepare

- Get a good night's sleep and wear comfortable clothing
- Bring a book, a handheld video game, or other activities to pass the time while you get your infusion
- Make a plan with your employer or teachers to cover missed time at work or school
- Drink plenty of water to stay hydrated
- Make sure to follow any pre-infusion medication recommendations from your doctor to help prevent a reaction



### What people taking VIMIZIM® (elosulfase alfa) have to say

*“The clinical trials worked great for me. I have more endurance. Before I started this infusion, I would never have thought about college. But now I’m going to Penn State World Campus, WE ARE!”*

– Sarah

## Committing to VIMIZIM<sup>®</sup> (elosulfase alfa) is a commitment to your health

- Morquio A affects every person in a different way—the results you'll see from VIMIZIM<sup>®</sup> (elosulfase alfa) will be specific to you
- You might not notice a difference right away, but remember that VIMIZIM works by replacing the deficient GALNS enzyme to restore cell function
- Every VIMIZIM infusion is important to help get rid of GAGs in the body—any infusions that are missed should be rescheduled right away



## Working with your healthcare team before starting VIMIZIM<sup>®</sup> (elosulfase alfa)

- Morquio A affects each person differently. It's important to establish an overall management plan with your doctors and develop realistic treatment expectations
- Before you start treatment, your doctor may work with you to determine an individual plan. Your doctor can conduct assessments before you start treatment, such as



### ENDURANCE



#### 6-minute walk test (6MWT)

Measures how far you can walk in 6 minutes



#### The timed 25-foot walk test (T25FWT)

Is used for people who have difficulty walking



### RESPIRATORY



#### Respiratory forced vital capacity (FVC)

Measures the volume of air that can forcibly be exhaled after taking the deepest breath possible



#### Forced expiratory volume (FEV<sub>1</sub>)

Measures the maximum volume of air that can be forcibly exhaled in 1 second



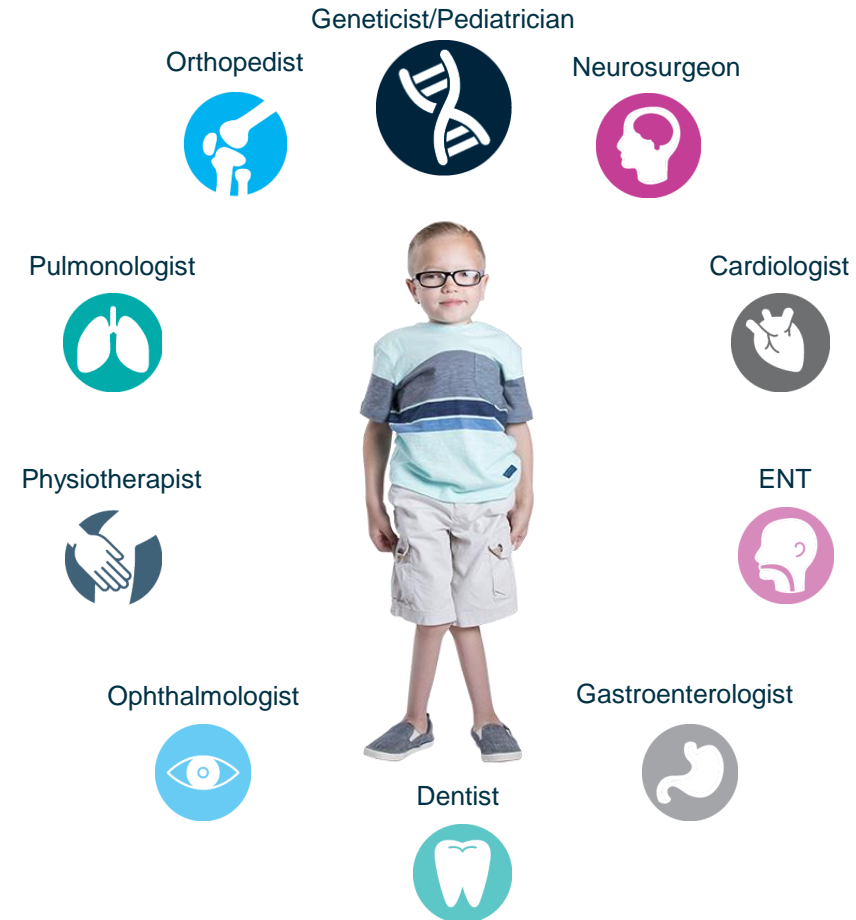
#### Maximum voluntary ventilation (MVV)

Measures the maximum amount of air that can be inhaled and exhaled in 1 minute

## With your geneticist and healthcare team, you can take charge of your Morquio A

Different parts of your body are affected by Morquio A, so you'll need different doctors and specialists to help manage your condition. Your geneticist will help you find and coordinate with the doctors you'll need to see.

- Your geneticist will take the lead in coordinating many aspects of your treatment plan, such as tests and visits, as well as arranging for VIMIZIM<sup>®</sup> (elosulfase alfa) treatment
- Individuals with Morquio A are at increased risk for surgical complications. It is important to talk to your healthcare team to plan for surgical procedures



**VIMIZIM**<sup>®</sup>  
(elosulfase alfa)

Please see Important Safety Information, including important warning, on slides 24-26.

# Know your important health assessments

## ASSESSMENTS<sup>a</sup>



### MUSCULOSKELETAL

Standardized upper extremity function test, radiographs



### RESPIRATORY

FVC, MVV, respiratory rate, oxygen saturation, overnight sleep study



### NEUROLOGICAL

Neurological exam  
plain radiograph  
MRI scan  
CT scan



### CARDIOVASCULAR

Electrocardiogram  
echocardiogram  
heart rate



### OPHTHALMOLOGICAL

Refractive error and intraocular pressure



### AUDIOLOGICAL

Multimodal hearing assessment



### ABDOMINAL

Assessments of gastrointestinal problems



### DENTAL

Evaluation of oral health



### ENDURANCE

6MWT



### QUALITY OF LIFE (QoL)

Reproducible, age-appropriate QoL questionnaires  
(eg, EQ-5D-5L)

## FREQUENCY<sup>a</sup>

- At diagnosis/baseline, annually
- At diagnosis/baseline, annually
- At diagnosis/baseline, every visit (minimum, every 6 months)
- At diagnosis, every 1 to 3 years
- At diagnosis, annually
- As clinically indicated
- At diagnosis, every 1 to 3 years, as clinically indicated
- At diagnosis, every 2 to 3 years, as clinically indicated
- At diagnosis, annually
- At diagnosis, as clinically indicated
- At diagnosis, annually
- As clinically indicated
- At diagnosis, annually
- At diagnosis, annually, before and regularly after initiation of ERT
- At diagnosis, annually

Your healthcare team can help you determine which assessments are most important for you and how often you should have them done

**Abbreviations:** 6MWT, 6-minute walk test; CT, computed tomography; ERT, enzyme replacement therapy; FVC, forced vital capacity; MVV, maximal voluntary ventilation

<sup>a</sup>Note: For additional detail, please consult the Guidelines.



Please see Important Safety Information, including important warning, on slides 24-26.

## BioMarin RareConnections™: Uncommon support for rare diseases

Rare diseases like Morquio A can bring uncommon challenges. BioMarin RareConnections™ is here to help you meet these challenges with the resources and assistance you need to gain access to VIMIZIM® (elosulfase alfa).

When you enroll in BioMarin RareConnections™, you will be connected with a dedicated case manager who can provide a wide array of product support services to help you start and stay on VIMIZIM.

This includes:

- Helping you understand your insurance coverage and financial assistance options
- Working with you and your care team to coordinate delivery and administration of VIMIZIM
- Providing you with ongoing product support

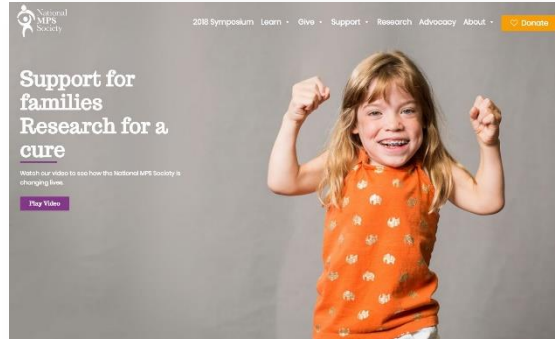
**Contact BioMarin RareConnections™ at 1-866-906-6100  
or email us at [support@biomarin-rareconnections.com](mailto:support@biomarin-rareconnections.com)  
Monday through Friday, 6AM to 5PM PT**



Please see Important Safety Information, including important warning, on slides 24-26.

## Additional resources

Visit these websites to learn more!



### National MPS Society

Making a difference for families through support, research, education, and advocacy

[www.MPSsociety.org](http://www.MPSsociety.org)

1-877-MPS-1001  
info@mpssociety.org



### Morquiosity

A comprehensive resource for information and support in the Morquio A community

[www.Morquiosity.com](http://www.Morquiosity.com)



### VIMIZIM® (elosulfase alfa)

VIMIZIM is the only enzyme replacement therapy (ERT) to address the cause of Morquio A (MPS IVA)

[www.VIMIZIM.com](http://www.VIMIZIM.com)



Please see Important Safety Information, including important warning, on slides 24-26.

# IMPORTANT SAFETY INFORMATION

## INDICATION

VIMIZIM® (elosulfase alfa) is indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome).

## IMPORTANT SAFETY INFORMATION

**Life-threatening allergic reactions, known as anaphylaxis, can occur during VIMIZIM® (elosulfase alfa) infusions. Typical signs of anaphylaxis include cough, rash, throat tightness, hives, flushing, changes in skin color, low blood pressure, shortness of breath, chest pain, and gastrointestinal symptoms such as nausea, abdominal pain, retching, and vomiting. Contact your doctor or get medical help right away if these symptoms occur during or after VIMIZIM infusions. If you have a respiratory illness, you may be at risk for a sudden worsening of your condition, and you may require additional monitoring.**

VIMIZIM is a prescription medicine. Before treatment with VIMIZIM, it is important to discuss your medical history with your doctor. Tell your doctor if you are sick or taking any medication and if you are allergic to any medicines. Also tell your doctor if you are pregnant, planning to become pregnant, or are a nursing mother. Your doctor will decide if VIMIZIM is right for you. If you have questions or would like more information about VIMIZIM, contact your doctor.



Please see additional Important Safety Information on slides 25-26.



## IMPORTANT SAFETY INFORMATION (cont'd)

Anaphylaxis can occur during any VIMIZIM infusion and up to three hours after any infusion, and hypersensitivity reactions have been observed as early as 30 minutes from the start of infusion but as late as six days after infusion.

Serious and severe reactions can happen with VIMIZIM treatment, including life-threatening allergic reactions (anaphylaxis), hives, swelling, cough, shortness of breath, and flushing. You should receive medication such as antihistamines before VIMIZIM infusions to reduce the risk of reactions. If a reaction occurs, the infusion should be slowed or stopped and you may be given additional medication. If a severe reaction occurs, the infusion should be stopped immediately and you will receive appropriate medical treatment.

If you have acute febrile or respiratory illness at the time of VIMIZIM infusion you may be at higher risk of life-threatening complications from hypersensitivity reactions. If you use supplemental oxygen or continuous positive airway pressure (CPAP) you should have it available during your infusion in the event of a sudden reaction, or extreme drowsiness/sleep from antihistamines.



Please see additional Important Safety Information, including important warning, on slides 24 and 26.

## IMPORTANT SAFETY INFORMATION (cont'd)

Spinal cord damage may occur due to the natural MPS IVA disease process. Signs of spinal cord injury include back pain, numbness and paralysis, and loss of bladder and bowel control. Contact your doctor immediately if you develop any of these symptoms.

The most common side effects reported during VIMIZIM infusions included fever, vomiting, headache, nausea, abdominal pain, chills, and fatigue. These are not all of the possible side effects with VIMIZIM. Talk to your doctor if you have any symptoms that bother you or that do not go away.

**Call your doctor for medical advice about side effects. You may report side effects to BioMarin Pharmaceutical Inc. at 1-866-906-6100, or FDA at 1-800-FDA-1088 or go to [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

**Please see full Prescribing Information, including important warning, provided by MPS Specialist or visit [www.VIMIZIM.com](http://www.VIMIZIM.com).**



**Please see additional Important Safety Information, including important warning, on slides 24-25.**

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