



VIMIZIM[®]
(elosulfase alfa)

VIMIZIM[®] (elosulfase alfa)—
**THE FOUNDATION OF
MORQUIO A MANAGEMENT**



**A comprehensive guide to help
you manage your condition**

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 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.

Please see Important Safety Information throughout, important warning for risk of anaphylaxis, and full [Prescribing Information](#).



BIOMARIN



YOU PLAY A KEY ROLE IN YOUR MORQUIO A MANAGEMENT



Get the best care possible

This guide is designed to help you understand Morquio A management strategies. This information is based on the “Recommendations for the Management of MPS IVA: Systematic Evidence- and Consensus-Based Guidance.” These guidelines were created by a panel of expert doctors with experience managing the full range of symptoms associated with Morquio A.

These experts recommend managing Morquio A with a combined approach:

- Initiation of enzyme replacement therapy (ERT) to slow or stop glycosaminoglycan (gly-koh-sah-meen-o-gly-can), or GAG, buildup
- Routine assessments and treatment of specific symptoms

The information in this guide can help you and your healthcare team be better prepared to make critical decisions about your health.

“It’s never too late, even at age 40.”

—FANNY, AGE 40

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VIMIZIM® (elosulfase alfa)— The only treatment that addresses the cause of Morquio A

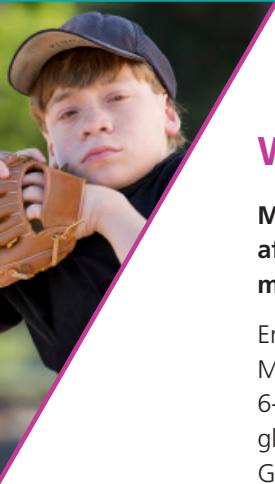
VIMIZIM is an enzyme replacement therapy (ERT) that works to help restore function to cells that have been damaged or weakened by Morquio A.

Use this guide to help you understand how VIMIZIM works and how to make it part of your overall management plan.

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KNOW THE FACTS ABOUT MORQUIO A

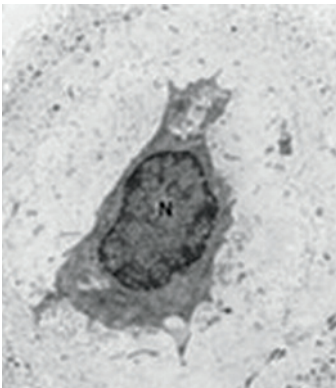


What is Morquio A?

Morquio A 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.

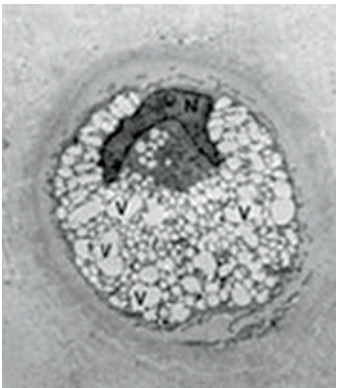
Enzymes are proteins that perform specific jobs in your body. People with Morquio A do not make enough of a specific enzyme called *N*-acetylgalactosamine-6-sulfatase, or GALNS (gal-en-es), which breaks down and recycles cellular waste called glycosaminoglycans (GAGs). When the body doesn't produce enough of the enzyme, GAGs build up in tissues, bones, and major organs.

NORMAL CELL



GALNS breaks down and recycles GAGs.

MORQUIO A CELL



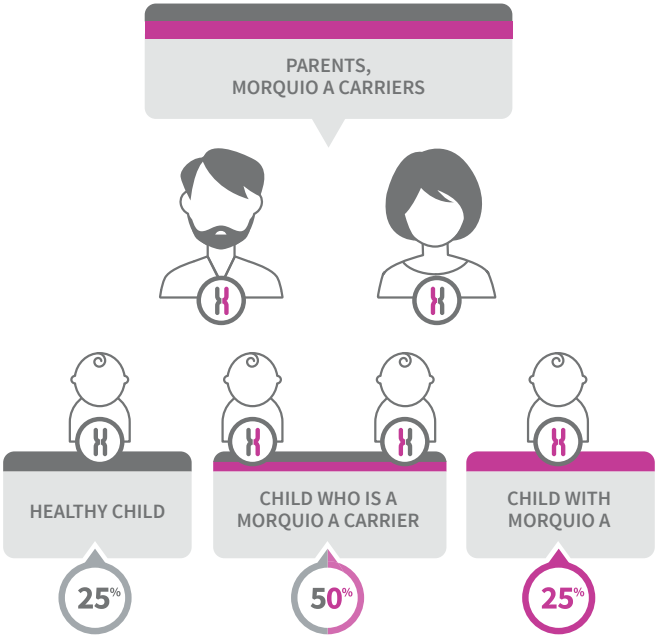
Without enough GALNS, GAGs build up in cells throughout the body.

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What causes Morquio A?

Morquio A is a recessively inherited condition. This means that both parents must have a genetic mutation, also called a variant, in the *GALNS* gene for their children to be affected by Morquio A syndrome.



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.

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SIGNS AND SYMPTOMS OF MORQUIO A



How will Morquio A affect me?

Morquio A is a progressive condition, which means that symptoms get worse over time. It is also heterogeneous (het-er-o-ge-ne-ous), which means that the signs, symptoms, and severity are different for each person.



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

While Morquio A affects each person differently, it is common to have complications such as oddly shaped bones, a curved spine, knock knees, and irregular chest growth.

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

SIGNS AND SYMPTOMS

SKELETAL

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

NONSKELETAL

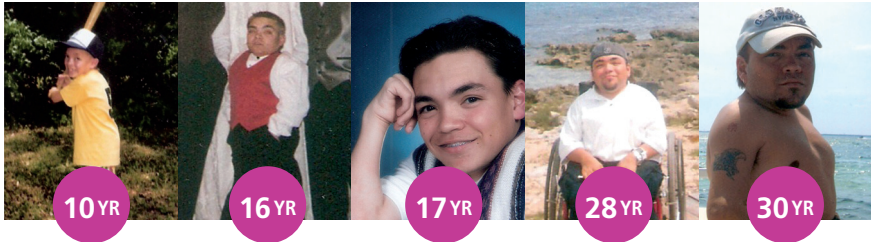
- Breathing problems
- Heart valve problems
- Muscle weakness
- Eye problems
- Hearing loss
- Dental problems
- Enlarged liver
- Enlarged spleen
- Limited energy

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The symptoms of Morquio A progress over time

The buildup of GAGs in the cells of the body can affect multiple body systems. 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 to slow or stop GAG buildup.

People with Morquio A who have reduced endurance may have difficulty with regular activities. 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. And, because Morquio A affects multiple parts of your body, it's critical that you have a team of specialists in place to help manage your care.



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 in individuals after 2 years, compared with baseline measurements.

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

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TAKE CHARGE OF YOUR MORQUIO A WITH VIMIZIM® (elosulfase alfa)

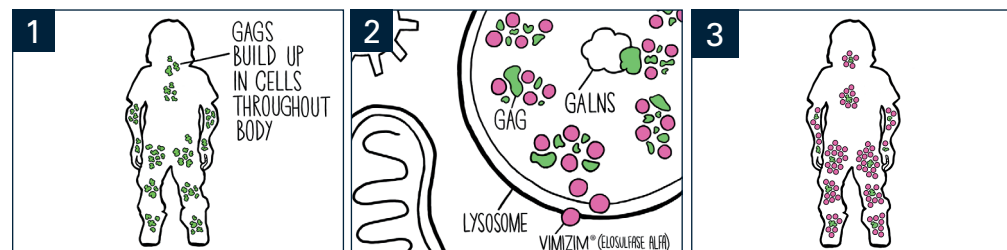


What is VIMIZIM?

VIMIZIM 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 work?

If you have Morquio A, you don't have enough GALNS enzyme activity. VIMIZIM can replace the deficient enzyme to 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.

How is VIMIZIM administered?

VIMIZIM 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.



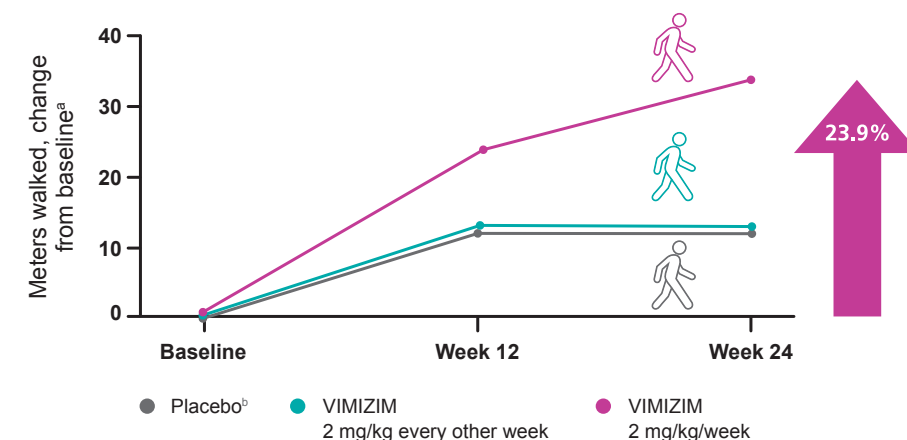
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VIMIZIM IMPROVES ENDURANCE AS MEASURED BY THE 6MWT



VIMIZIM is the only ERT to address the cause of Morquio A and may be able to help you go farther

In a 6-month clinical trial, people who received VIMIZIM 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 those of the people who took a placebo

Select Important Safety Information

Anaphylaxis can occur during any VIMIZIM infusion, as early as 30 minutes from the start and up to 3 hours after infusion, and as late into treatment as the 47th infusion. Hypersensitivity reactions have been observed as early as 30 minutes from the start of infusion but as late as 6 days after infusion.

^aA baseline is a measurement of a person's performance before beginning treatment in a clinical trial. In order to participate in the clinical trial for VIMIZIM, people had to be able to walk between 30 and 325 meters.

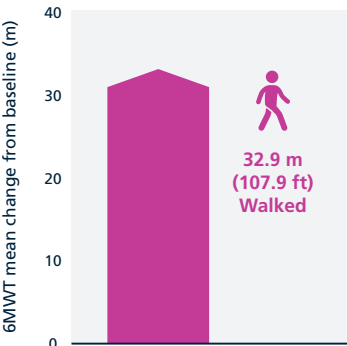
^bA placebo is a substance that does not contain medicine.

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VIMIZIM® (elosulfase alfa) CAN PROVIDE LONG-LASTING BENEFITS

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



Endurance increased

Results from a 2-year extension study showed a 32.9-meter increase in the 6MWT compared with baseline.

Being able to walk farther indicates your whole body is working better—from your heart and lungs to bones and muscles.

Breathing ability improved

The 2-year extension study showed that breathing function, as measured by pulmonary function tests, improved for individuals compared with baseline.

Being able to exhale a greater volume of air indicates that your respiratory system is working better—from your lungs to your muscles.



The 2-year extension study showed that the benefits of VIMIZIM 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.

6MWT, test to measure the distance that can be walked in 6 minutes; FEV₁, maximum volume of air that can be forcibly blown out in 1 second; FVC, volume of air that can be forcibly exhaled from the lungs after taking as deep a breath as possible.

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What are the possible side effects of VIMIZIM?

The most common side effects seen with VIMIZIM 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%)

You should know that serious and severe reactions are also associated with VIMIZIM. These include hypersensitivity reactions as well as life-threatening allergic reactions (anaphylaxis) with symptoms such as hives, swelling, cough, shortness of breath, and flushing. In 6 clinical trials, 18.7% of patients treated with VIMIZIM experienced hypersensitivity reactions, and 7.7% experienced signs and symptoms consistent with anaphylaxis.

As a precautionary measure, 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.

Anaphylaxis can happen as a result of sensitivity to protein-based molecules (like enzymes) when delivered through an IV. Your infusion nurse will check on you while you receive treatment to make sure everything is going well. If you have a reaction, the nurse will stop the infusion immediately and give you medicine to treat the reaction.

Anaphylaxis can occur during any VIMIZIM infusion and up to 3 hours after any infusion. It's important to be aware of how you are feeling after the infusion and once you are home. If you notice any signs that you are experiencing anaphylaxis, call your doctor immediately.

If you have a respiratory illness, it may become worse due to a hypersensitivity reaction, and you may require additional monitoring by your nurse.

These are not all of the possible side effects of VIMIZIM. Talk to your doctor if you have any symptoms that bother you or that do not go away. Safety and effectiveness in pediatric patients below 5 years of age have not been established and are currently being evaluated.

What are the possible long-term side effects of VIMIZIM?

No new serious adverse reactions were reported in the long-term extension study. Of 176 patients enrolled in the 24-week phase 3 study, 173 continued into the 120-week extension study. The most common adverse reactions were injection-associated and were managed with symptomatic treatment and/or modification of infusion rate. In the VIMIZIM 2 mg/kg/week group (who received 120 weeks of treatment), the rate of drug discontinuation due to adverse events was 1.8%.

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MANAGING MORQUIO A

A personalized management plan is your key to success

The signs, symptoms, and severity of Morquio A are different for every person. For this reason, consider working with your healthcare team to develop a management plan to establish realistic treatment expectations.

Your personalized Morquio A management plan includes

- Setting goals and developing a plan with your treatment team
- Following your plan and treatment schedule
- Measuring how you respond over time

While some individuals will experience improvement in endurance, preventing further decline is also a measure of success. Before you start treatment, consider talking to your doctor to determine an individual plan.

Your doctor may also conduct assessments before you start treatment. For many individuals with Morquio A, the following assessments are used:



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

- ✓ **Forced vital capacity (FVC)** measures the volume of air that can be forcibly exhaled after taking the deepest breath possible
- ✓ **Forced expiratory volume (FEV₁)** measures the maximum volume of air that can be forcibly exhaled in 1 second
- ✓ **Maximum voluntary ventilation (MVV)** is the total volume of air that can be exhaled over 12-15 seconds of rapid, deep breathing

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Partnering with your healthcare team

Because different parts of your body are affected by Morquio A, you will need different doctors and specialists to help manage your condition. 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® (elosulfase alfa) treatment.

The more you understand about how each member of your healthcare team can help you, and the more your specialists know about Morquio A, the better you will be able to partner with them to manage your overall care.



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MANAGING MORQUIO A: DOCTORS AND SPECIALISTS

Each member of your healthcare team helps you manage Morquio A in specific ways. Get to know what each doctor and specialist does so that, together, you can help ensure you receive the best possible care.



Geneticist/Pediatrician

*A geneticist looks at how genes affect the body
A pediatrician specializes in treating children*

These specialists primarily focus on

- Medical history
- Endurance (6MWT)
- Growth
- Disease burden (pain assessment and reproducible, age-appropriate quality-of-life questionnaires)



Orthopedist

Specializes in correcting problems related to the skeletal system, and conducts spinal cord compression evaluation

The most common bone and joint conditions are

- Curvature of the spine (scoliosis)
- Short height
- Knock knees
- Overly flexible joints
- Difficulty walking

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.

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Cardiologist

Focuses on the heart and circulatory health

Heart health (to look for abnormalities)

Morquio A can cause abnormalities in the heart valves, which limit the amount of blood the heart can pump. As a result, the heart may speed up to keep up with the body's demand for blood. Dramatic increases in blood pressure can occur when going from lying down to sitting up.



Pulmonologist

Responsible for the lungs and breathing

Respiratory function tests (to measure lung function)

Breathing problems can be caused by

- Narrow, crooked airways
- Abnormally shaped rib cage
- Thickening of mucus
- Obstructive or restrictive disease
- Obstructive sleep apnea (OSA)



Neurosurgeon

Surgeon focused on issues with the brain, spinal cord, and nerves

Neurological function (tests to evaluate spinal cord compression)

Symptoms of spinal cord compression include

- Unsteady gait
- Upper and lower extremity weakness
- Pain or abnormal sensations in the body (dysesthesia)
- Urinary problems
- Paralysis



Ophthalmologist

Specializes in eye health

Vision (eye exams)

Some people with Morquio A have irregularities in the shape of their lenses and corneas that can cause blurry vision and sensitivity to light.



ENT

Focuses on ear, nose, and throat health

Hearing

It is important to quickly treat any infections you may get in your respiratory tract or middle ear. These infections can sometimes lead to hearing loss. Hearing loss can also occur because of abnormalities in the structure of the ear.



Dentist

Specializes in maintaining the mouth and teeth

Dental (teeth evaluation)

Your teeth may look a little different from people around you who do not have Morquio A. Morquio A might weaken your enamel and cause other problems that can lead to cavities.



Gastroenterologist

Specializes in diseases of the digestive system

Manages symptoms related to the digestive tract, including constipation or diarrhea, hernias, problems with the spleen, or swelling of the liver.



Physiotherapist

Specializes in management of physical disabilities, malfunction, or pain

Physical evaluation

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MANAGING MORQUIO A WITH YOUR HEALTHCARE TEAM



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

This chart has been adapted from the latest Morquio A management guidelines, published in 2019. It provides an overview of some of the assessments that your healthcare team may use, as well as recommendations about how often they should be undertaken.

Specialist	Assessment to consider	Suggested frequency
Geneticist/ Pediatrician	Endurance (6-minute walk test or timed 25-foot walk test)	At baseline and then annually
	Growth	Every visit
	Urine test (urinary glycosaminoglycan or uGAG levels)	At baseline and then every 6 months
	Disease burden (pain, quality of life, activities of daily living, fatigue, wheelchair/walking aid use)	Annually
Radiologist	Brain (MRI or CT scan)	At diagnosis and annually or more frequently if clinically indicated
	Hips, lower extremities, and skeletal abnormalities	At diagnosis and as clinically indicated
	Whole spine (MRI or CT scan for injury and changes to spinal canal/cord)	Annually, as clinically indicated
	Standing or sitting plain radiography of the cervical and thoracolumbar spine	At diagnosis and then every 2-3 years, as clinically indicated
Cardiologist	Assessments of vital signs including oxygen saturation, right arm and leg blood pressure measurements, careful auscultation, echocardiogram, and ECG	At diagnosis and then annually, as clinically indicated
Pulmonologist	Respiratory function tests by spirometry in children ages 5 and up. Respiratory rate and arterial oxygen saturation before and after annual endurance testing	At baseline and then annually until child stops growing, then every 2-3 years
	Overnight sleep study	At diagnosis and then every 3 years

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Specialist	Assessment to consider	Suggested frequency
Neurologist	Neurological function and spinal exams to detect any issues	Every visit (minimally every 6 months)
Ophthalmologist	Eye exam including visual acuity, refraction, slit-lamp examination of cornea, funduscopy evaluation including optic nerve, and measurement of intraocular pressure	At baseline and every 6 months or at least annually
ENT (ear, nose, throat)	Hearing evaluation including tympanometry	Every 3-6 months (children) Every 6-12 months (adults)
	Visualization of the upper airway with fiberoptic examination	At diagnosis and then annually
Dentist	Dental evaluation with consideration of subacute endocarditis prophylaxis for certain procedures	Annually
Physical therapist/ Occupational therapist/ Speech therapist	Assessment and support of limb function and speech problems as needed	As clinically indicated

CT, computed tomography; ECG, electrocardiogram; MRI, magnetic resonance imaging.
Adapted from "Recommendations for the Management of MPS IVA: Systematic Evidence- and Consensus-Based Guidance" (Akyol et al. *Orphanet J Rare Dis.* 2019;14:137).

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

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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 specialty pharmacy to coordinate delivery and administration of VIMIZIM
- Providing you with ongoing product support

To learn more about BioMarin RareConnections,
call **1-866-906-6100**
Monday through Friday, 6 AM to 5 PM PT
or email support@biomarin-rareconnections.com

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Managing your care in an emergency

In the event of an emergency, it is critically important to let healthcare providers know that you have Morquio A and that there are special risks associated with emergency care.

Direct healthcare providers who are unfamiliar with the disorder to MPSER.com. This website is dedicated to informing healthcare professionals about the special risks associated with emergency care for people with Morquio A. The website offers

- Steps to help prevent cervical cord injury
- Techniques to protect the airways when a person with Morquio A needs assistance with his or her breathing
- Ways to monitor for signs of heart problems

"I've learned that you really can't focus on the past—you've got to think about your future. You've got to be strong."

—SARAH, AGE 17

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INDICATION

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IMPORTANT SAFETY INFORMATION

Life-threatening allergic reactions, known as anaphylaxis, can occur during VIMIZIM 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.

Anaphylaxis can occur during any VIMIZIM infusion, as early as 30 minutes from the start and up to 3 hours after infusion, and as late into treatment as the 47th infusion. Hypersensitivity reactions have been observed as early as 30 minutes from the start of infusion but as late as 6 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.

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 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 at 1-866-906-6100 and the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

For more information, call BioMarin RareConnections™ at 1-866-906-6100.

Please see full [Prescribing Information](#), including important warning.