COVERAGE AUTHORIZATION GUIDE

VIMIZIM® (elosulfase alfa)

NAGLAZYME® (galsulfase)

INDICATIONS:

NAGLAZYME® (galsulfase) is a hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme indicated for patients with Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome). NAGLAZYME has been shown to improve walking and stair-climbing capacity.

VIMIZIM® (elosulfase alfa) is a hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)

VIMIZIM Important Safety Information
BOXED WARNING: RISK OF ANAPHYLAXIS
Life-threatening anaphylactic reactions have occurred in some patients during VIMIZIM infusions.
See included full prescribing information for complete boxed warning.

BioMarin manufactures therapies to treat individuals with certain diagnosed lysosomal storage disorders (LSDs). VIMIZIM is the only enzyme-replacement therapy (ERT) approved for Morquio A (MPS IVA). NAGLAZYME is the only approved ERT for the treatment of Mucopolysaccharidosis VI (MPS VI, also known as Maroteaux-Lamy syndrome).

VIMIZIM® (elosulfase alfa)

Naglazyme® (GALSULFASE)

BIOMARIN®

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM.
Click here for full Prescribing Information for NAGLAZYME.

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

TABLE OF CONTENTS

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

3

INTRODUCTION AND DISCLAIMER

BioMarin, the manufacturer of VIMIZIM® (elosulfase alfa) and NAGLAZYME® (galsulfase), would like to help every individual who is medically appropriate for the product to have access to it. We can provide assistance with managing the process of getting patients on VIMIZIM or NAGLAZYME. We offer assistance to patients, their caregivers, and healthcare providers through our support services hub, BioMarin RareConnections™, and work directly with patients to help educate them on the safe and appropriate use of BioMarin products.

Every patient's insurance plan and health benefits are different, so it is very important to contact each patient's plan for assistance when interpreting drug policies, billing and coding, and payment. These items vary greatly among insurance plans and are subject to change without notice because of frequently changing guidelines, laws, rules, and regulations. Some patients may change insurance plans during the year, so verify current insurance information at each patient visit. If your patient receives a denial, consult the insurance plan to help interpret the denial language, and provide the necessary information and documentation requested by the plan in a timely manner.

Some patients may change insurance plans during the year, so verify current insurance information at each patient visit.

THIS COVERAGE AUTHORIZATION GUIDE PROVIDES IMPORTANT INFORMATION FOR GAINING ACCESS TO BIOMARIN THERAPIES INCLUDING:

- WORKING WITH BIOMARIN RARECONNECTIONS
- RECORDING RELEVANT BASELINES
- SAMPLE LETTERS OF MEDICAL NECESSITY
- SAMPLE APPEAL LETTERS
- SPECIALTY PHARMACY COORDINATION
- APPROPRIATE CODING

Disclaimer:

BioMarin compiled this guide with information gathered from third-party sources and experienced insurance reimbursement experts to serve as a source of information to educate your practice around the process for obtaining approval and ongoing authorization for VIMIZIM or NAGLAZYME. While we have included some best practices for working with BioMarin RareConnections™, insurance companies, and specialty pharmacies in this guide, BioMarin makes no guarantee that the use of this information will prevent denials, delays, or differences of opinion with insurance plans as to the correct information to submit for VIMIZIM or NAGLAZYME authorization, or forms of billing that will expedite payment to providers of service. BioMarin provides this information as a convenience; it does not constitute legal advice or a recommendation regarding medical practice.

This guide provides an overview of the process for obtaining coverage authorization for FDA-approved indications that are documented in the enclosed VIMIZIM and NAGLAZYME Prescribing Information documents (in the inside pocket). If reimbursement is sought for prescribed use and/or administration of this product that may be inconsistent with, or not expressly specified in, the FDA-cleared or FDA-approved labeling outlined in the VIMIZIM or NAGLAZYME Prescribing Information, consult with your billing advisers or the patient's insurance plan on handling such issues.

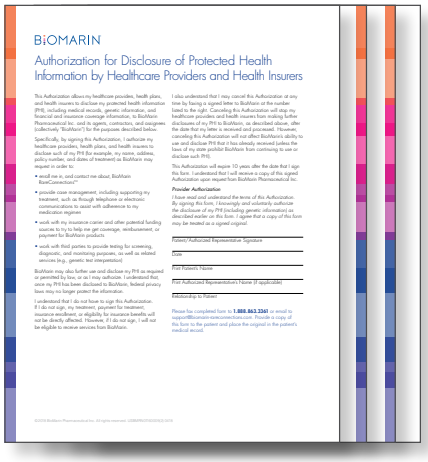
Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

COORDINATE WITH BIOMARIN RARECONNECTIONS™

BioMarin RareConnections helps patients navigate the difficulties of managing serious and rare genetic diseases through a wide array of product support services throughout the treatment journey. Our dedicated and experienced Case Managers will provide guidance and answer questions about how to gain access to VIMIZIM® (elosulfase alfa) and NAGLAZYME® (galsulfase).

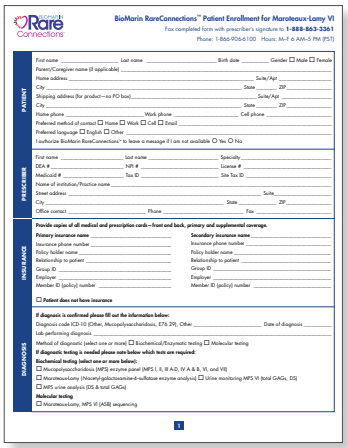
In order to access BioMarin RareConnections product support services, submit both the BioMarin RareConnections Patient Enrollment Form (PEF) and the BioMarin Patient Authorization Form (PAF) and copies of the Insurance Cards (front and back).

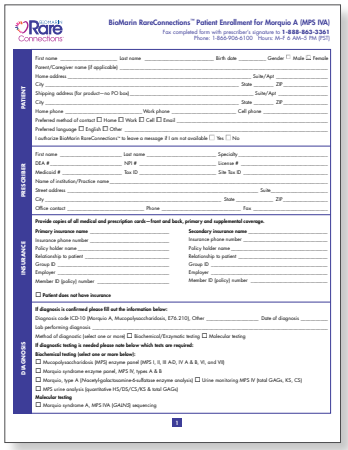
- **PAF:** The Patient Authorization Form provides authorization from the patient for the provider/clinic to provide patient-level information to BioMarin and for BioMarin to use this patient-level information to communicate with payers and SPs to secure access to the prescribed product


BIOMARIN

Authorization for Disclosure of Protected Health Information by Healthcare Providers and Health Insurers

- **PEF:** The Patient Enrollment Form serves as the prescription and provider authorization for BioMarin RareConnections to work on a patient's case


BioMarin RareConnections™ Patient Enrollment for Maroteaux-Lamy VI


BioMarin RareConnections™ Patient Enrollment for Morquio A (MPS IVA)

BioMarin RareConnections helps patients managing serious and rare genetic diseases with product access support services throughout the treatment journey. Our dedicated and experienced Case Managers:

- Help patients understand their insurance coverage and financial assistance options
- Provide ongoing support for access to VIMIZIM and NAGLAZYME
- Coordinate with a specialty pharmacy and schedule delivery of the patient's medication

BioMarin RareConnections™

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

MPS BIOMARIN RARECONNECTIONS™ ROADMAP

Patient Enrollment: PAF + PEF

- ✓ HCP notification of PEF receipt
- ✓ Follow-up with HCP on missing information
- ✓ Patient notification of PAF received

Securing Coverage

- ✓ Benefits Investigation (BI) and prior authorization (PA) requirements assessed
- ✓ Patient welcome call
- ✓ Patient notification of BI results
- ✓ HCP notification of BI results & PA requirements

Financial Assistance Support*

- ✓ Referrals to independent foundations if needed
- ✓ BioMarin patient assistance program eligibility screening

Wholesaler or Specialty Pharmacy Shipment Coordination

- ✓ Shipment coordination with patients (medical setting or home)
- ✓ Packaging and delivery logistics
- ✓ Home health nurse coordination

Maintaining Therapy†

- ✓ PA reauthorization
- ✓ Infusion relocation support
- ✓ Monitoring

VIMIZIM® (elosulfase alfa)

Important Safety Information for VIMIZIM: Patients with acute febrile or respiratory illness at the time of VIMIZIM infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Careful consideration should be given to the patient's clinical status prior to administration of VIMIZIM and consider delaying the VIMIZIM infusion.

*As appropriate for eligible patients.
†Specialty Pharmacy-depending processes.
HCP, Healthcare Provider; PAF, BioMarin RareConnections™ Patient Authorization Form; PEF, BioMarin RareConnections™ Patient Enrollment Form.

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

INSURANCE VERIFICATION AND WORKING WITH BIOMARIN RARECONNECTIONS™

Does your patient have insurance coverage for VIMIZIM® (elosulfase alfa) and NAGLAZYME® (galsulfase)?

Now that your patient and you have decided to use VIMIZIM to treat their Mucopolysaccharidoses type IVA (MPS IVA; Morquio A Syndrome) or NAGLAZYME to treat their Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome), it is important to understand how to gain coverage for the treatment. VIMIZIM and NAGLAZYME are injections for intravenous use and specialty treatments. Managing and accessing a specialty drug is quite different from a typical prescription filled at a local retail pharmacy. Additional steps and time are needed to authorize the treatment chosen for the patient. Understanding if and how your patient's insurance covers VIMIZIM or NAGLAZYME is the first step, and BioMarin has included some suggestions below to help you.

Completing the prior authorization requirements

1 

Before a patient can be treated with VIMIZIM or NAGLAZYME, the patient's insurance benefits should be verified

2 

Make copies of the medical and pharmacy benefit insurance cards, and upload the insurance information to your patient's medical record

3 

Always ask if there have been changes to the patient's insurance each time they come to the office

VERIFY THE PATIENT'S INSURANCE BENEFITS

BioMarin RareConnections Field Reimbursement Managers (FRMs) can work directly with you to provide education around managing the VIMIZIM and NAGLAZYME prescription fulfillment process. They can also provide information related to payer requirements for the patient's insurance plan PA form and appeals process. The FRM works in coordination with the patient's BioMarin RareConnections Case Manager and is your 1:1 in-person informational resource for clinics.

- Individualized reimbursement support for patients, including coordinated communication with BioMarin RareConnections Case Managers, and dedicated case-specific support as needed
- BioMarin RareConnections overview (program services and tools, including the ePAF website)
- General reimbursement education (PA/appeal support, regional payer insights/trends, formulary changes)
- Specialty Pharmacy Education & Support

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

TREATMENT AUTHORIZATION AND REAUTHORIZATION

Prescribing VIMIZIM® (elosulfase alfa) or NAGLAZYME® (galsulfase)

VIMIZIM and NAGLAZYME are specialty drugs. Specialty drugs often require additional verification steps from the patient's insurance plan. The insurance plan manages access to specialty drugs because it wants to ensure the drug is used in the appropriate patient population.

After BioMarin RareConnections™ verifies the patient's insurance benefits, your office may be required to complete a Prior Authorization (PA) request from the insurance plan. The insurance plan will review the completed PA and supporting medical documentation, and then provide a determination. A determination is either an approval or denial for the specialty drug, usually obtained within 24–72 hours.

VIMIZIM and NAGLAZYME are dosed based on calculating the patient's body weight and the amount of drug needed. The intravenous infusions are administered once weekly and usually conducted in the physician's office or the hospital outpatient department. Alternatively, if the patient's insurance plan allows it, patients may also have the opportunity to administer their treatment at home. Insurance plans may require additional prior authorization if alternative administration sites are requested by the patient or caregiver(s). It will be very important to monitor the phone, fax, email, and/or mail for any communication from the patient's insurance plan or specialty pharmacy for every patient prescribed VIMIZIM or NAGLAZYME. The insurance plans will expect a high level of monitoring and oversight of these patients by their healthcare providers.

Requesting prior authorization for VIMIZIM or NAGLAZYME

- BioMarin RareConnections can provide the payer-specific PA form to your office (when available), based on its investigation of the patient insurance benefits
- The healthcare provider/clinic must complete the PA paperwork and gather the supporting medical documentation
  - Write a letter of medical necessity to the insurance plan's contact information listed on the PA
  - Provide any baseline data requested by the patient's insurance plan, which may include:

TEST	VIMIZIM	NAGLAZYME
6MWT	✔	✔
T25FW	✔	
FVC	✔	✔
FEV[1]	✔	✔
MVV	✔	
MPS urine analysis GAGs	✔	✔

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

  - Submit the complete PA package (ie, PA and supporting documents) to the patient's insurance plan
- If the insurance plan requests additional documentation, it is important to provide it in a timely manner
- Monitor for any communication from the patient's insurance plan
- If you utilize BioMarin RareConnections™, they can help monitor approvals and denials. Denials may also be communicated by a letter mailed to the patient and the physician's office

If the patient wants the treatment administered at home, the prescriber is strongly advised to document medical necessity to facilitate the approval process.

Examples of supporting medical documentation

- For initiation of treatment
  - ICD-10-CM codes pertinent to the diagnosis of MPS IVA or MPS VI
  - Patient history or consultation report(s) discussing the patient's diagnosis and medical necessity for VIMIZIM® (elosulfase alfa) or NAGLAZYME® (galsulfase) treatment
  - Testing and laboratory results pertinent to diagnosis of MPS IVA or MPS VI
  - Treatment history
  - Baseline data for clinical assessments
  - Healthcare provider chart notes
- Other examples of supporting documentation
  - Any shared decision-making notes from multidisciplinary discussions or case conferences

Reauthorization

Insurance plans typically authorize treatment for 1 year, so each year they may require the prescriber to issue a new prescription and reauthorize treatment with VIMIZIM or NAGLAZYME. The patient's insurance plan may request data that demonstrates stabilization or improvement from baseline, when being treated with VIMIZIM or NAGLAZYME. BioMarin encourages providers to conduct ongoing assessments of their patients using the same instruments with which they gathered baseline measurements.

Specialty pharmacies provide the following services for patients who are receiving their drug through the specialty pharmacy channel. BioMarin RareConnections provides these services for patients who receive their medications via Buy and Bill.

- Inform the patient and the prescriber if treatment reauthorization is required by the patient's health insurance
- Ask the prescriber to submit an updated prescription and request any additional information to include in the PA
- Inform the patient and the prescriber if treatment is reauthorized for another year, or if the insurance plan requires additional information

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

PRIOR AUTHORIZATION CHECKLIST

Checklist for VIMIZIM® (elosulfase alfa) or NAGLAZYME® (galsulfase) treatment

Utilize the following checklist to ensure that all relevant information is obtained before submitting the PA package for VIMIZIM or NAGLAZYME. All services requested by the patient's insurance benefits must be medically appropriate and properly supported by the patient's medical record, and most importantly, based on the medical diagnosis determined by the prescriber.

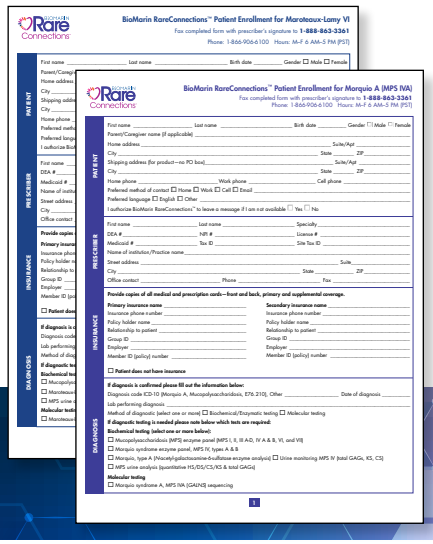
The following items may be requested by the patient's insurance plan to include in the prior authorization or medical necessity request:

Key PA criteria
(information usually requested by insurance plans)

- ☐ ICD-10-CM diagnosis and description
- ☐ Patient weight
- ☐ Patient height
- ☐ Expected location for drug administration
- ☐ Genetic testing
- ☐ Enzyme assays
  (eg, *N*-acetylgalactosamine 6-sulfatase)
- ☐ Baseline testing results

Supporting medical documentation

- ☐ Medical and treatment history
- ☐ Clinical notes
- ☐ Medication record
- ☐ Relevant laboratory tests
- ☐ Medical necessity for home administration



PLEASE REFER TO THE PATIENT ENROLLMENT FORM (PEF) FOR ADDITIONAL DETAILS ON BASELINE TESTING

NAGLAZYME® (galsulfase)

Important Safety Information for NAGALZYME: Life-threatening anaphylactic reactions and severe allergic reactions have been observed in some patients during NAGLAZYME (galsulfase) infusions and up to 24 hours after infusion. If these reactions occur, immediate discontinuation of NAGLAZYME is recommended and appropriate medical treatment should be initiated, which may include resuscitation, epinephrine, administering additional antihistamines, antipyretics or corticosteroids. In patients who have experienced anaphylaxis or other severe allergic reactions during infusion with NAGLAZYME, caution should be exercised upon rechallenge; appropriately trained personnel and equipment for emergency resuscitation (including epinephrine) should be available during infusions.

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

SAMPLE LETTER OF MEDICAL NECESSITY FOR VIMIZIM® (elosulfase alfa) *TREATMENT*

- ✔ Date
- ✔ Patient Name
- ✔ Patient Mailing Address
- ✔ Patient Contact Phone Number
- ✔ Insurance Plan Name
- ✔ Insurance Plan Mailing Address
- ✔ Insurance Subscriber Name
- ✔ Insurance Subscriber ID Number
- ✔ Effective Date of Coverage

RE: Authorization of VIMIZIM® (elosulfase alfa) for MPS IVA Treatment

Dear Sir or Madam:

I am writing on behalf of my patient, [insert patient name], to request approved authorization and coverage from [insert insurance plan name] for VIMIZIM® (elosulfase alfa) injection for intravenous use. My patient has been diagnosed with Mucopolysaccharidosis type IVA, which can also be referred to as MPS IVA or Morquio A Syndrome. Individuals born with MPS IVA have a gene that results in missing or low levels of the *N*-acetylgalactosamine 6-sulfatase (GALNS) enzyme that breaks down certain complex carbohydrates known as glycosaminoglycans (GAGs). Without sufficient quantities of GALNS, the normal breakdown of GAG is incomplete or blocked, and it accumulates in the lysosomes of the cell. This may cause serious problems, including heart disease, skeletal abnormalities, vision and hearing loss, difficulty breathing, and early death.

VIMIZIM is a hydrolytic lysosomal glycosaminoglycan enzyme indicated for patients with Morquio A syndrome. This letter provides information about my patient's medical and treatment history, diagnosis, and details regarding the medical necessity for treatment with VIMIZIM.

Patient's medical history

My patient's current disease state, prior treatment and response to those treatments, as well as other issues that impact my treatment decision, are:

- ✔ Insert brief description of patient: age, height, weight, functional status, MPS IVA history, and prior treatment history
- ✔ Include essential labs and genetic history that verify MPS IVA diagnosis
- ✔ Include other factors that impact the treatment decision (eg, comorbidities, work status, etc)
- ✔ Include supporting medical documentation (eg, patient's medical record, clinical notes, medication records, relevant lab results, etc)

Disease and treatment information

I have attached the prescribing information for VIMIZIM, which was approved by the U.S. Food and Drug Administration (FDA) on February 16, 2014.

VIMIZIM is an intravenous infusion treatment, and patients are weight-dosed at 2 mg per kilogram of body weight, administered once weekly over 3.5–4.5 hours, based on infusion volume. I am requesting approval for all dosages that my patient will require for treatment. VIMIZIM is supplied in 5 mg/5 mL (1 mg/mL) single-use vials.

In conclusion, I am requesting that you approve treatment for my patient, [insert patient name], with VIMIZIM. Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

SUGGESTED ENCLOSURES

- VIMIZIM prescribing information
- VIMIZIM published clinical studies
- Patient medical history, clinical notes, and labs confirming diagnosis
- Relevant labs, eg, genetic tests, baseline testing

SAMPLE LETTER OF MEDICAL NECESSITY FOR VIMIZIM® (elosulfase alfa) *TREATMENT + HOME ADMINISTRATION*

- ✔ Date
- ✔ Patient Name
- ✔ Patient Mailing Address
- ✔ Patient Contact Phone Number
- ✔ Insurance Plan Name
- ✔ Insurance Plan Mailing Address
- ✔ Insurance Subscriber Name
- ✔ Insurance Subscriber ID Number
- ✔ Effective Date of Coverage

RE: Authorization of VIMIZIM® (elosulfase alfa) for MPS IVA Treatment and Home Administration

Dear Sir or Madam:

I am writing on behalf of my patient, [insert patient name], to request approved authorization and coverage from [insert insurance plan name] for VIMIZIM® (elosulfase alfa) injection for intravenous use and home administration. My patient has been diagnosed with Mucopolysaccharidosis type IVA, which can also be referred to as MPS IVA or Morquio A Syndrome. Individuals born with MPS IVA have a gene that results in missing or low levels of the *N*-acetylgalactosamine 6-sulfatase (GALNS) enzyme that breaks down certain complex carbohydrates known as glycosaminoglycans (GAGs). Without sufficient quantities of GALNS, the normal breakdown of GAG is incomplete or blocked, and it accumulates in the lysosomes of the cell. This may cause serious problems, including heart disease, skeletal abnormalities, vision and hearing loss, difficulty breathing, and early death.

VIMIZIM is a hydrolytic lysosomal glycosaminoglycan enzyme indicated for patients with Morquio A syndrome. This letter provides information about my patient's medical and treatment history, diagnosis, and details regarding the medical necessity for treatment with VIMIZIM.

I am also requesting authorization for once-weekly home nursing visits for the administration of VIMIZIM for the management of my patient's MPS IVA diagnosis. The nurse will administer VIMIZIM via intravenous infusion, monitor the patient, and administer any needed interventions during the visit. It is my medical opinion that my patient is a suitable candidate for home infusion.

Patient's medical history

My patient's current disease state, prior treatment and response to those treatments, as well as other issues that impact my treatment decision, are:

- ✔ Insert brief description of patient: age, height, weight, functional status, MPS IVA history, and prior treatment history
- ✔ Include essential labs and genetic history that verify MPS IVA diagnosis
- ✔ Include other factors that impact the treatment decision (eg, comorbidities, work status, etc)
- ✔ Include supporting medical documentation (eg, patient's medical record, clinical notes, medication records, relevant lab results, etc)
- ✔ Include supporting documentation of medical necessity, if the patient wants the treatment administered at home

Disease and treatment information

I have attached the prescribing information for VIMIZIM, which was approved by the U.S. Food and Drug Administration (FDA) on February 16, 2014.

VIMIZIM is an intravenous infusion treatment, and patients are weight-dosed at 2 mg per kilogram of body weight, administered once weekly over 3.5–4.5 hours, based on infusion volume. I am requesting approval for all dosages that my patient will require for treatment. VIMIZIM is supplied in 5 mg/5 mL (1 mg/mL) single-use vials.

In conclusion, I am requesting that you approve treatment and home infusion for my patient, [insert patient name], with VIMIZIM. Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

SUGGESTED ENCLOSURES

- VIMIZIM prescribing information
- VIMIZIM published clinical studies
- Patient medical history, clinical notes, and labs confirming diagnosis
- Relevant labs, eg, genetic tests, baseline testing

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM.
Click here for full Prescribing Information for NAGLAZYME.

SAMPLE LETTER OF MEDICAL NECESSITY FOR NAGLAZYME® (galsulfase) *TREATMENT*

- ✔ Date
- ✔ Patient Name
- ✔ Patient Mailing Address
- ✔ Patient Contact Phone Number
- ✔ Insurance Plan Name
- ✔ Insurance Plan Mailing Address
- ✔ Insurance Subscriber Name
- ✔ Insurance Subscriber ID Number
- ✔ Effective Date of Coverage

RE: Authorization of NAGLAZYME® (galsulfase) for MPS VI Treatment

Dear Sir or Madam:

I am writing on behalf of my patient, [insert patient name], to request approved authorization and coverage from [insert insurance plan name] for NAGLAZYME® (galsulfase) injection for intravenous use. My patient has been diagnosed with Mucopolysaccharidosis type VI, which can also be referred to as MPS VI or Maroteaux-Lamy syndrome. Individuals born with MPS VI have a gene that results in a deficiency of the lysosomal enzyme *N*-acetylgalactosamine 4-sulfatase, an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs).

NAGLAZYME is a hydrolytic lysosomal glycosaminoglycan enzyme indicated for patients with Maroteaux-Lamy syndrome. This letter provides information about my patient's medical and treatment history, diagnosis, and details regarding the medical necessity for treatment with NAGLAZYME.

Patient's medical history

My patient's current disease state, prior treatment and response to those treatments, as well as other issues that impact my treatment decision, are:

- ✔ Insert brief description of patient: age, weight, functional status, MPS VI history, and prior treatment history
- ✔ Include essential labs and genetic history that verify MPS VI diagnosis
- ✔ Include other factors that impact the treatment decision (eg, comorbidities, work status, etc)
- ✔ Include supporting medical documentation (eg, patient's medical record, clinical notes, medication records, relevant lab results, etc)

Disease and treatment information

I have attached the prescribing information for NAGLAZYME, which was approved by the U.S. Food and Drug Administration (FDA) on May 31, 2005.

NAGLAZYME is an intravenous infusion treatment and patients are weight-dosed at 1 mg per kilogram of body weight, administered once weekly. I am requesting approval for all dosages that my patient will require for treatment. NAGLAZYME is supplied in 5 mg/5 mL (1 mg/mL) single-use vials.

In conclusion, I am requesting that you approve treatment for my patient, [insert patient name], with NAGLAZYME. Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

SUGGESTED ENCLOSURES

- NAGLAZYME prescribing information
- NAGLAZYME published clinical studies
- Patient's medical history, clinical notes, and labs confirming diagnosis
- Relevant labs, eg, genetic tests, baseline testing

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

SAMPLE LETTER OF MEDICAL NECESSITY FOR NAGLAZYME® (galsulfase) *TREATMENT + HOME ADMINISTRATION*

- ✔ Date
- ✔ Patient Name
- ✔ Patient Mailing Address
- ✔ Patient Contact Phone Number
- ✔ Insurance Plan Name
- ✔ Insurance Plan Mailing Address
- ✔ Insurance Subscriber Name
- ✔ Insurance Subscriber ID Number
- ✔ Effective Date of Coverage

RE: Authorization of NAGLAZYME® (galsulfase) for MPS VI Treatment for Home Administration

Dear Sir or Madam:

I am writing on behalf of my patient, [insert patient name], to request approved authorization and coverage from [insert insurance plan name] for NAGLAZYME® (galsulfase) injection for intravenous use and home infusion. My patient has been diagnosed with Mucopolysaccharidosis type VI, which can also be referred to as MPS VI or Maroteaux-Lamy syndrome. Individuals born with MPS VI have a gene that results in a deficiency of the lysosomal enzyme *N*-acetylgalactosamine 4-sulfatase, an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs).

NAGLAZYME is a hydrolytic lysosomal glycosaminoglycan enzyme indicated for patients with Maroteaux-Lamy syndrome. This letter provides information about my patient's medical and treatment history, diagnosis, and details regarding the medical necessity for treatment with NAGLAZYME.

I am also requesting authorization for once-weekly home nursing visits for the administration of NAGLAZYME for the management of my patient's MPS VI diagnosis. The nurse will administer NAGLAZYME via intravenous infusion, monitor the patient, and administer any needed interventions during each visit. It is my medical opinion that my patient is a suitable candidate for home infusion.

Patient's medical history

My patient's current disease state, prior treatment and response to those treatments, as well as other issues that impact my treatment decision, are:

- ✔ Insert brief description of patient: age, weight, functional status, MPS VI history, and prior treatment history
- ✔ Include essential labs and genetic history that verify MPS VI diagnosis
- ✔ Include other factors that impact the treatment decision (eg, comorbidities, work status, etc)
- ✔ Include supporting medical documentation (eg, patient's medical record, clinical notes, medication records, relevant lab results, etc)
- ✔ Include supporting documentation of medical necessity, if the patient wants the treatment administered at home

Disease and treatment information

I have attached the prescribing information for NAGLAZYME, which was approved by the U.S. Food and Drug Administration (FDA) on May 31, 2005.

NAGLAZYME is an intravenous infusion treatment and patients are weight-dosed at 1 mg per kilogram of body weight, administered once weekly. I am requesting approval for all dosages that my patient will require for treatment. NAGLAZYME is supplied in 5 mg/5 mL (1 mg/mL) single-use vials.

In conclusion, I am requesting that you approve treatment and home infusion for my patient, [insert patient name], with NAGLAZYME. Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

SUGGESTED ENCLOSURES

- NAGLAZYME prescribing information
- NAGLAZYME published clinical studies
- Patient's medical history, clinical notes, and labs confirming diagnosis
- Relevant labs, eg, genetic tests, baseline testing

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM.
Click here for full Prescribing Information for NAGLAZYME.

MANAGING DENIALS AND APPEALS

Denials can occur when the insurance plans do not have enough information to confirm that a patient is the right candidate for a specialty treatment. They can also occur if the patient does not meet the clinical criteria for approval, as specified by the insurance plan. Specialty drugs can often be denied following an initial authorization request, and can require writing an appeal or conducting a peer-to-peer discussion. The insurance plan will provide a written rationale for the denial to both prescriber and patient, usually by mail. Read these letters carefully, as they will provide the reasons for denial, methods for appealing the denial, and timeframe to request an appeal. If you do not understand the denial letter, contact the patient's insurance plan to request additional information.

Additional insurance plan requests

The denial letter may include additional requests for medical information; this may include additional medical records, laboratory work, genetic testing records, and/or the healthcare provider's medical rationale for selecting VIMIZIM® (elosulfase alfa) or NAGLAZYME® (galsulfase) as medically necessary for your patient.

Evaluate the methods for appealing in the letter or contact the insurance plan directly to understand your appeal options. Often written appeals are the first option provided, but if a peer-to-peer discussion is available, this can be an expeditious means of appealing a denial that the prescriber can use.

Peer-to-peer appeals can be an expeditious means of appealing a denial.

Three types of appeals

1 

Appeal letter: A formal, written letter is the usual and customary first level of appeal. This letter is the first attempt to answer or provide additional information requested by the insurance plan. Adjudication for coverage will be returned in letter format.

2 

Peer-to-Peer discussion: A peer-to-peer appeal is a phone call where the prescriber has the opportunity to verbally provide the missing data for the insurance plan and explain his/her rationale for selecting a particular treatment. Adjudication for coverage could be provided during the call or be issued in a letter format.

3 

External review: If the insurance plan denies authorization for VIMIZIM or NAGLAZYME treatment multiple times, patients have the opportunity to appeal to an external court or administrative law judge for review of treatment authorization. The letter must be written by the patient, and if an in-person meeting is granted, it must be conducted by the patient or the patient's legal representation. The prescriber also attends to provide additional detail to support the appeal. Policies and specifics for this level of denial are state-specific, and it is recommended that patients or caregivers seek legal advice.

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

SAMPLE APPEAL LETTER FOR VIMIZIM® (elosulfase alfa) *TREATMENT*

- ✔ Date
- ✔ Patient Name
- ✔ Patient Mailing Address
- ✔ Patient Contact Phone Number
- ✔ Insurance Plan Name
- ✔ Insurance Plan Mailing Address
- ✔ Insurance Subscriber Name
- ✔ Insurance Subscriber ID Number
- ✔ Effective Date of Coverage

RE: Denial of VIMIZIM® (elosulfase alfa) for MPS IVA Treatment

Dear Sir or Madam:

I am writing on behalf of my patient, [insert patient name] to appeal the [insert date] denial for coverage of VIMIZIM® (elosulfase alfa) for my patient who has been diagnosed with Mucopolysaccharidosis type IVA, which can also be referred to as MPS IVA or Morquio A Syndrome. This letter provides the additional information requested by [insert insurance plan name] in the denial letter and is a formal request for appeal and expedited review of my request for VIMIZIM coverage for [insert patient name].

Disease and treatment information

VIMIZIM is a hydrolytic lysosomal glycosaminoglycan enzyme indicated for patients with Morquio A syndrome. This appeal letter provides additional information about my patient's medical and treatment history, diagnosis, and details regarding the medical necessity for treatment with VIMIZIM. VIMIZIM was approved by the U.S. Food and Drug Administration (FDA) on February 16, 2014.

Individuals born with MPS IVA have a gene that results in missing or low levels of the *N*-acetylgalactosamine 6-sulfatase (GALNS) enzyme that breaks down certain complex carbohydrates known as glycosaminoglycans (GAGs). Without sufficient quantities of GALNS, the normal breakdown of GAG is incomplete or blocked, and it accumulates in the lysosomes of the cell. I am requesting that you reassess the denial decision in light of the additional information I have provided and that you please approve my treatment request for [insert patient name] with VIMIZIM.

Patient's medical history

My patient's current disease state, prior treatment and response to those treatments, as well as other issues that impact my treatment decision, are:

- ✔ Insert brief description of patient: age, height, weight, functional status, MPS IVA history, and prior treatment history
- ✔ Include essential labs and genetic history that verify MPS IVA diagnosis
- ✔ Include other factors that impact the treatment decision (eg, comorbidities, work status, etc)
- ✔ Include supporting medical documentation (eg, patient's medical record, clinical notes, medication records, relevant lab results, etc)

In conclusion, I am asking [insert insurance plan name] to reconsider your decision to deny my patient access to VIMIZIM. I request that [insert insurance plan name] issue a 1-year approval for all dosages my patient will require for treatment.

Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

SUGGESTED ENCLOSURES

- Copy of denial letter
- VIMIZIM prescribing information
- VIMIZIM published clinical studies
- Patient's medical history, clinical notes, and labs confirming diagnosis
- Relevant labs, eg, genetic tests, baseline testing

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM.
Click here for full Prescribing Information for NAGLAZYME.

SAMPLE APPEAL LETTER FOR NAGLAZYME® (galsulfase) *TREATMENT*

- ✔ Date
- ✔ Patient Name
- ✔ Patient Mailing Address
- ✔ Patient Contact Phone Number
- ✔ Insurance Plan Name
- ✔ Insurance Plan Mailing Address
- ✔ Insurance Subscriber Name
- ✔ Insurance Subscriber ID Number
- ✔ Effective Date of Coverage

RE: Denial of NAGLAZYME® (galsulfase) for MPS VI Treatment

Dear Sir or Madam:

I am writing on behalf of my patient, [insert patient name] to appeal the [insert date] denial for coverage of NAGLAZYME® (galsulfase) for my patient who has been diagnosed with Mucopolysaccharidosis type VI, which can also be referred to as MPS VI or Maroteaux-Lamy syndrome. This letter provides the additional information requested by [insert insurance plan name] in the denial letter and is a formal request for appeal and expedited review of my request for NAGLAZYME coverage for [insert patient name].

Disease and treatment information

NAGLAZYME is a hydrolytic lysosomal glycosaminoglycan enzyme indicated for patients with Maroteaux-Lamy syndrome. Individuals born with MPS VI have a gene that results in a deficiency of the lysosomal enzyme *N*-acetylgalactosamine 4-sulfatase, an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs). This appeal letter provides additional information about my patient's medical and treatment history, diagnosis, and details regarding the medical necessity for treatment with NAGLAZYME. NAGLAZYME was approved by the U.S. Food and Drug Administration (FDA) on May 31, 2005.

My patient has been diagnosed with MPS VI. I am requesting that you reassess the denial decision in light of the additional information I have provided and that you please approve my treatment request for [insert patient name], with NAGLAZYME.

Patient's medical history

My patient's current disease state, prior treatment and response to those treatments, as well as other issues that impact my treatment decision, are:

- ✔ Insert brief description of patient: age, weight, functional status, MPS VI history, and prior treatment history
- ✔ Include essential labs and genetic history that verify MPS VI diagnosis
- ✔ Include other factors that impact the treatment decision (eg, comorbidities, work status, etc)
- ✔ Include supporting medical documentation (eg, patient's medical record, clinical notes, medication records, relevant lab results, etc)

In conclusion, I am asking [insert insurance plan name] to reconsider your decision to deny my patient access to NAGLAZYME. I request that [insert insurance plan name] issue a 1-year approval for all dosages my patient will require for treatment.

Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

SUGGESTED ENCLOSURES

- Copy of denial letter
- NAGLAZYME prescribing information
- NAGLAZYME published clinical studies
- Patient's medical history, clinical notes, and labs confirming diagnosis
- Relevant labs, eg, genetic tests, baseline testing

INTRODUCTION
VERIFICATION
AUTHORIZATION
SAMPLE LETTERS
DENIALS and APPEALS
SHIPMENT
CODING
INFORMATION

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

SHIPMENT COORDINATION

VIMIZIM® (elosulfase alfa) or NAGLAZYME® (galsulfase) is delivered by the specialty pharmacy or via Buy and Bill through a wholesaler, directly to the location where the patient is going to have infusions administered in a medical setting or at home. VIMIZIM and NAGLAZYME can be administered by a Healthcare Provider (HCP) either in the hospital, the outpatient or community clinic, physician's office, or at home by a home infusion nurse. BioMarin is contracted with a limited number of Specialty Pharmacies (SPs) and wholesalers to distribute VIMIZIM and NAGLAZYME. The SPs are licensed in all 50 states.

HCP administration

If the prescribing physician chooses a medical setting for infusions, this information will be included in the prior authorization language. The patient's insurance plan will approve that infusions occur in the medical setting.

- If the medication is sent to the medical setting, the hospital, clinic, or HCP office will properly store the medication until the patient comes for the weekly infusion
- The administration sites are expected to have all of the necessary supplies when the patient arrives for the infusion appointment
- During infusion, patients are monitored by the HCP
- HCPs will manage the proper disposal of the used infusion materials and medication vials
- Patients receive infusions once a week

Home administration

In order for the patient to receive administration of the drug at home, the prescribing physician writes the order for home infusion, and it must be approved by the patient's insurance plan. Additionally, home health nursing, drug supplies and expenses related to conducting the infusions at home will need to be approved by the patient's insurance plan.

- BioMarin's clinical nurse coordinators conduct the training for home health infusion nurses
- The specialty pharmacy calls the patient/caregivers to set up delivery for the medication and/or needed supplies; some specialty pharmacies also coordinate scheduling the home health nurse appointments
- The patient/caregivers are responsible for properly storing the drug until it's time for the patient's infusion
- During administration, patients are monitored by their home health nurse and/or caregivers
- The home health nurse manages the proper disposal of the used infusion materials and medication vials
- Patients receive home health infusions once a week

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

CODING

Possible coding for VIMIZIM® (elosulfase alfa) or NAGLAZYME® (galsulfase) intravenous infusion

The following coding examples are provided by BioMarin but are not considered a guarantee for reimbursement:

VIMIZIM

CODE TYPE	Code(s)	Descriptors
ICD-10 Diagnosis Code	E76.210	Mucopolysaccharidoses IVA (MPS IVA; Morquio A Syndrome)
HCPCS	J1322	Injection, elosulfase alfa, 1 mg
VIMIZIM National Drug Code	68135-100-01	One 5 mL vial containing 5 mg of elosulfase alfa
CPT Codes*	96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
	96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (list separately in addition to code for primary procedure)
Revenue Codes (for use in hospital outpatient only)	258	Pharmacy: IV solutions
	261	IV therapy: infusion pump
	262	IV therapy: IV therapy, pharmacy services
	263	IV therapy: IV therapy/drug/supply/delivery
	631	Drugs require specific ID: single-source drug
	636	Drugs require specific ID: drugs requiring detail coding

NAGLAZYME

CODE TYPE	Code(s)	Descriptors
ICD-10 Diagnosis Code	E76.29	Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome)
HCPCS	J1458	Injection, galsulfase, per 1.0 mg
NAGLAZYME National Drug Code	68135-020-01	5 mg of galsulfase, per 1.0 mg
CPT Codes*	96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
	96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour
	Q0081	Non-chemotherapeutic infusion (hospital only)
Revenue Codes (for use in hospital outpatient only)	258	Normal saline IV solutions
	260	General IV therapy service
	261	IV therapy: infusion pump
	636	Drugs require specific ID: drugs requiring detail coding

*VIMIZIM and NAGLAZYME are intravenous infusion drugs and administration(s) will be performed under the supervision of a healthcare provider.

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

IMPORTANT INFORMATION

VIMIZIM® (elosulfase alfa): For additional information about VIMIZIM resources, visit the product website at https://vimizim.com/hcp/resources/ to find the following information:

- VIMIZIM RareConnections Patient Enrollment Form
- BioMarin RareConnections Patient Authorization Form
- VIMIZIM Dosing and Administration Guide
- VIMIZIM Product Fact Sheet
- Assessments Overview Chart

NAGLAZYME® (galsulfase): For additional information about NAGLAZYME resources, visit the product website at https://www.naglazyme.com/hcp/ to find the following information:

- NAGLAZYME RareConnections Patient Enrollment Form
- NAGLAZYME Dosing and Infusion Directions
- Billing and Reimbursement Support

Please see Important Safety Information on Pages 22–23.
Click here for full Prescribing Information including Boxed Warning for VIMIZIM. Click here for full Prescribing Information for NAGLAZYME.

BIOMARIN RARECONNECTIONS™

BioMarin RareConnections™: For additional information about BioMarin RareConnections resources and contact information, visit the website https://www.biomarin-rareconnections.com/ to find the following information:

- All product Patient Enrollment Forms
- BioMarin RareConnections Patient Authorization Form
- Phone: 1-866-906-6100
- Email: support@biomarin-rareconnections.com
- Hours: Mon–Fri, 6 AM–5 PM PT

For your patients to enroll in BioMarin RareConnections and get connected with a Case Manager, they can complete the Patient Authorization Form at www.BioMarinPAF.com.

BIOMARIN Rare Connections™

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 anaphylactic reactions have occurred in some patients during VIMIZIM® (elosulfase alfa) infusions. Anaphylaxis, presenting as cough, erythema, throat tightness, urticaria, flushing, cyanosis, hypotension, rash, dyspnea, chest discomfort, and gastrointestinal symptoms (e.g., nausea, abdominal pain, retching, and vomiting) in conjunction with urticaria, have been reported to occur during VIMIZIM infusions, regardless of duration of the course of treatment. Closely observe patients during and after VIMIZIM administration and be prepared to manage anaphylaxis. Inform patients of the signs and symptoms of anaphylaxis and have them seek immediate medical care should symptoms occur. Patients with acute respiratory illness may be at risk of serious acute exacerbation of their respiratory compromise due to hypersensitivity reactions, and require additional monitoring.

Due to the potential for anaphylaxis, appropriate medical support should be readily available when VIMIZIM is administered and for an appropriate period of time following administration. In clinical trials, cases of anaphylaxis occurred as early as 30 minutes from the start of infusion and up to three hours after infusion, and as late into treatment as the 47th infusion.

In clinical trials, hypersensitivity reactions have been observed as early as 30 minutes from the start of infusion but as late as six days after infusion. Frequent symptoms of hypersensitivity reactions (occurring in more than 2 patients) included anaphylactic reactions, urticaria, peripheral edema, cough, dyspnea, and flushing.

Because of the potential for hypersensitivity reactions, administer antihistamines with or without antipyretics prior to infusion. Management of hypersensitivity reactions should be based on the severity of the reaction and include slowing or temporary interruption of the infusion and/or administration of additional antihistamines, antipyretics, and/or corticosteroids for mild reactions. However, if severe hypersensitivity reactions occur, immediately stop the infusion of VIMIZIM and initiate appropriate treatment.

Consider the risks and benefits of re-administering VIMIZIM following a severe reaction.

Patients with acute febrile or respiratory illness at the time of VIMIZIM infusion may be at higher risk of life-threatening complications from hypersensitivity reactions. Careful consideration should be given to the patient's clinical status prior to administration of VIMIZIM and consider delaying the VIMIZIM infusion.

Sleep apnea is common in MPS IVA patients. Evaluation of airway patency should be considered prior to initiation of treatment with VIMIZIM. Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an acute reaction, or extreme drowsiness/sleep induced by antihistamine use.

Spinal or cervical cord compression (SCC) is a known and serious complication of MPS IVA and may occur as part of the natural history of the disease. In clinical trials, SCC was observed both in patients receiving VIMIZIM and patients receiving placebo. Patients with MPS IVA should be monitored for signs and symptoms of SCC (including back pain, paralysis of limbs below the level of compression, urinary and fecal incontinence) and given appropriate clinical care.

All patients treated with VIMIZIM 2 mg/kg once per week in the placebo-controlled trial developed anti-drug antibodies. The relationship between the presence of neutralizing antibodies and long-term therapeutic response or occurrence of anaphylaxis or other hypersensitivity reactions could not be determined.

VIMIZIM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known if VIMIZIM is present in human milk. Exercise caution when administering VIMIZIM to a nursing mother. There is a Morquio A Registry that collects data on pregnant women and nursing mothers with MPS IVA who are treated with VIMIZIM. Contact MARS@BMRN.com for information and enrollment.

Safety and effectiveness in pediatric patients below 5 years of age have not been established and are currently being evaluated.

In clinical trials, the most common adverse reactions (>10%) occurring during infusion included pyrexia, vomiting, headache, nausea, abdominal pain, chills, and fatigue. The acute reactions requiring intervention were managed by either temporarily interrupting or discontinuing infusion, and administering additional antihistamine, antipyretics, or corticosteroids.

To report SUSPECTED ADVERSE REACTIONS contact BioMarin Pharmaceutical Inc. at 1-866-906-6100, or FDA at 1-800-FDA-1088 or go to www.fda.gov/medwatch.

Please click on link below to see full Prescribing Information, including boxed warning, or visit www.VIMIZIM.com.

Click here for full Prescribing Information including Boxed Warning.

VIMIZIM® (elosulfase alfa)

IMPORTANT SAFETY INFORMATION

INDICATION

NAGLAZYME® (galsulfase) is indicated for patients with Mucopolysaccharidosis VI (MPS VI; Maroteaux-Lamy syndrome). NAGLAZYME has been shown to improve walking and stair-climbing capacity.

IMPORTANT SAFETY INFORMATION

Life-threatening anaphylactic reactions and severe allergic reactions have been observed in some patients during NAGLAZYME (galsulfase) infusions and up to 24 hours after infusion. If these reactions occur, immediate discontinuation of NAGLAZYME is recommended and appropriate medical treatment should be initiated, which may include resuscitation, epinephrine, administering additional antihistamines, antipyretics or corticosteroids. In patients who have experienced anaphylaxis or other severe allergic reactions during infusion with NAGLAZYME, caution should be exercised upon rechallenge; appropriately trained personnel and equipment for emergency resuscitation (including epinephrine) should be available during infusions.

As with other enzyme replacement therapies, immune-mediated reactions, including membranous glomerulonephritis have been observed. In clinical trials, nearly all patients developed antibodies as a result of treatment with NAGLAZYME; however, the analysis revealed no consistent predictive relationship between total antibody titer, neutralizing or IgE antibodies, and infusion-associated reactions, urinary glycosaminoglycan (GAG) levels, or endurance measures.

Caution should be exercised when administering NAGLAZYME to patients susceptible to fluid volume overload because congestive heart failure may result. Consider a decreased total infusion volume and infusion rate when administering NAGLAZYME to these patients.

Consideration to delay NAGLAZYME infusion should be given when treating patients who present with an acute febrile or respiratory illness. Sleep apnea is common in MPS VI patients and antihistamine pretreatment may increase the risk of apneic episodes. Evaluation of airway patency should be considered prior to the initiation of treatment. Patients using supplemental oxygen or continuous positive airway pressure (CPAP) during sleep should have these treatments readily available during infusion in the event of an infusion reaction, or extreme drowsiness/sleep induced by antihistamine use.

Pretreatment with antihistamines with or without antipyretics is recommended prior to the start of infusion to reduce the risk of infusion reactions. If infusion reactions occur, decreasing the infusion rate, temporarily stopping the infusion, or administering additional antihistamines and/or antipyretics is recommended.

During infusion, serious adverse reactions included laryngeal edema, apnea, pyrexia, urticaria, respiratory distress, angioedema, and anaphylactoid reaction; severe adverse reactions included urticaria, chest pain, rash, abdominal pain, dyspnea, apnea, laryngeal edema, and conjunctivitis. The most common adverse events (≥10%) observed in clinical trials in patients treated with NAGLAZYME were rash, pain, urticaria, pyrexia, pruritus, chills, headache, nausea, vomiting, abdominal pain, and dyspnea. The most common adverse reactions requiring interventions are infusion-related reactions.

Spinal/cervical cord compression is a known and serious complication that is expected to occur during the natural course of MPS VI. Signs and symptoms of spinal/cervical cord compression include back pain, paralysis of limbs below the level of compression, and urinary or fecal incontinence. Patients should be evaluated for spinal/cervical cord compression prior to initiation of NAGLAZYME to establish a baseline and risk profile. Patients treated with NAGLAZYME should be regularly monitored for the development or progression of spinal/cervical cord compression and be given appropriate clinical care.

To report SUSPECTED ADVERSE REACTIONS contact BioMarin Pharmaceutical Inc. at 1-866-906-6100, or FDA at 1-800-FDA-1088 or go to www.fda.gov/medwatch.

Please click on link below to see full Prescribing Information.

Click here for full Prescribing Information.

Naglazyme® (GALSULFASE)

23

BioMarin RareConnections™

Phone: 1-866-906-6100

Email: support@biomarin-rareconnections.com

BIOMARIN®

VIMIZIM® (elosulfase alfa)

Naglazyme® (GALSULFASE)