MYOZYME® (alglucosidase alfa)

SAFETY INFORMATION PACKET

Guidance for Health Care Professionals on risks associated with MYOZYME administration, clinical risk management and immunological testing.

Please be aware that this guide does not cover all the risks associated with the use of MYOZYME. Adverse events not listed in this guide may occur. Further information is available in the MYOZYME Product Information (Australia) and Datasheet (New Zealand) which should be consulted prior to prescribing.

Australian version 5.0 Apr 2024

sanofi

Contents

Abbreviations

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
CARM	Centre for Adverse Reactions Monitoring
CIC	Circulating-Immune Complex
CK	Creatine Kinase
CRIM	Cross Reactive Immunologic Material
DS	Data Sheet
ERT	Enzyme Replacement Therapy
GAA	Acid Alfa-Glucosidase
HCP	Health Care Professional
IAR	Infusion-Associated Reaction
IOPD	Infantile-Onset Pompe Disease
IV	Intravenous
LOPD	Late-Onset Pompe Disease
PI	Product Information
PSP	Patient Safety & Pharmacovigilance
rhGAA	Recombinant Human Acid alfa-glucosidase
SIP	Safety Information Packet
TGA	Therapeutic Goods Administration

SUMMARY

Aim of the Safety Information Packet

The MYOZYME (alglucosidase alfa) Safety Information Packet (SIP) is a supplementary educational material provided to physicians involved in managing patients with Pompe disease treated with MYOZYME. Treating physicians may make this material available to other health care professionals (HCPs) involved in the management of the disease as required (pharmacists, non-specialist physicians, allergists, nurses). The main purpose of the SIP is to:

1. Educate and minimise, when possible, the known risks associated with MYOZYME treatment.
2. Guide HCPs on the clinical management of these risks
3. Guide HCPs to carry out immunological testing which will help further characterise the potential mechanism of infusion-associated reactions (IARs) and hypersensitivity reactions.

The SIP also provides information on Sanofi's Rare Disease Specialty Testing Program (RDSTP), for immunological testing, which is provided as a free of charge service by Sanofi.

MYOZYME and Pompe disease

Pompe disease is a lysosomal storage disorder caused by a deficiency of acid α-glucosidase (GAA), an enzyme that degrades lysosomal glycogen to glucose. GAA deficiency leads to glycogen accumulation and the eventual rupture of lysosomes, resulting in cellular dysfunction in many body tissues, particularly muscle fibres.[1]

MYOZYME contains the active ingredient recombinant human acid-α-glucosidase [rhGAA]. MYOZYME is indicated for long-term enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of Pompe disease (acid α-glucosidase deficiency).[1] MYOZYME is indicated for both Infantile-Onset Pompe Disease (IOPD) and Late-Onset Pompe Disease (LOPD), diagnosed at any age. The recommended dose regimen of MYOZYME is 20 mg/kg of body weight administered once every 2 weeks.[1]

Description of the identified risks

The following important identified risks associated with MYOZYME administration have been identified (refer to section 1):

1	2	3
INFUSION ASSOCIATED REACTIONS including hypersensitivity and anaphylactic reactions, with or without development of IgG and IgE antibodies.	IMMUNE-MEDIATED REACTIONS.	IMMUNOGENICITY leading to loss of response (High sustained IgG antibody titres and or neutralising antibodies).

The SIP provides a full description of identified risks associated with MYOZYME infusion and guidance on the clinical management of adverse reactions (refer to section 2).

Immunological testing & Recommendations

Sanofi has established a post-marketing immunosurveillance program for MYOZYME to determine the extent of antibody formation against MYOZYME and its clinical impact, if any (refer to section 3). The below summary is fully detailed in sections 1 & 3.

1. Collect baseline serum sample collection prior to the first infusion.
2. Monitor patients for IgG antibody formation periodically and based on their clinical phenotype.
    a. For Infantile Onset Pompe Disease (IOPD) patients, regular monitoring during first year of treatment (example: every 3 months) and subsequent monitoring dependent on clinical outcomes and antibody titre levels.
    b. For Late Onset Pompe Disease (LOPD) patients, antibody development should be assessed within 6 months after treatment start and subsequent monitoring as clinically warranted based on safety and efficacy considerations.
3. Collect samples for testing of inhibition of enzyme uptake or activity if patients experience a decrease in clinical benefit despite continued treatment with Myozyme.
4. Collect samples for **testing of IgG and IgE antibodies, complement activation and tryptase** for patients who experience moderate to severe or recurrent IARs suggestive of hypersensitivity reactions.

The SIP provides information on Sanofi's Rare Disease Specialty Testing Program (RDSTP). This Program provides antidrug IgG antibody and adverse event related immunogenicity testing services. These services are free of charge (refer to section 3).

Please contact Sanofi Medical Information for questions on how to access Sanofi's RDSTP or other test-related questions for MYOZYME. Contact details are provided in **KEY CONTACTS.**

The processes presented in this document serve as overall guidance but are subject to local medical practice and national rules and regulations.

KEY CONTACTS

To report adverse event(s) and/or pregnancy occurring in association with the use of MYOZYME:

Please contact Medical Information:

Phone: 1800 818 806 (Australia) **OR** 0800 283 684 (New Zealand)

Fax: 1800 053 105 (Australia) **OR** 09 523 6716 (New Zealand)

E-mail: medInfo.australia@sanofi.com

Alternately, you may report adverse events and/or pregnancy directly to the Therapeutic Goods Administration (TGA) or Centre for Adverse Reactions Monitoring (CARM).

TGA (Australia) Phone: 1800 044 114

Fax: +61 2 6232 8392

E-mail: adr.reports@tga.gov.au

Online reporting at: https://aems.tga.gov.au

CARM (New Zealand) Phone: +64 (03) 479 7247

Fax: +64 (03) 479 7150

E-mail: carmnz@otago.ac.nz

Online reporting at: https://nzphvc.otago.ac.nz/report/

For medical information regarding Pompe Disease or Myozyme:

Phone: 1800 818 806 (Australia) OR 0800 283 6848 (New Zealand)

E-mail: medinfo.australia@sanofi.com

Or visit: http://www.sanofi.com.au/l/au/en/contact-us

1. DESCRIPTION OF RISKS ASSOCIATED WITH MYOZYME[1]

Identified safety risks of MYOZYME (alglucosidase alfa) treatment include:

- infusion-associated reactions (IARs) including hypersensitivity and anaphylactic reactions, with or without development of IgG and IgE antibodies
- immune- mediated reactions
- immunogenicity leading to loss of response (High sustained IgG antibody titres and/or neutralising antibodies)

1.1. Infusion-associated reactions including hypersensitivity and anaphylactic reactions with or without development of IgG and IgE antibodies

An IAR is defined as any adverse event (AE) occurring during the infusion or during the hours following infusion and assessed as potentially causally related to the administration of the product (MYOZYME). Related events occurring after the post-infusion period may be considered IARs at the discretion of the reporter. The exact mechanism for IARs is not fully understood but knowledge has improved over the years. Table 1 shows a list of potential mechanisms[2,3]:

Table 1. Potential mechanisms of IARs, including hypersensitivity and anaphylactic reactions

- IgE-mediated
- IgG-mediated with complement activation
- Cytokine release with unclear mechanism
- Non-specific immunogenic mechanism which is not understood to date
- Direct stimulation of mast cells by drug with release of histamine
- Higher infusion rate, i.e. protein load in a shorter period

In clinical trials, the occurrence of IARs was approximately 50% in infantile-onset patients treated with MYOZYME (over a period of 52 weeks) and 28% in late-onset patients (over a period of 18 months)[4,5,6,7]. The occurrence of IARs is not unexpected given the clinical presentation of immunogenic responses to recombinant human proteins. While the majority of reactions were assessed as mild to moderate, some were severe. A small number of patients (<1%) in clinical trials and in the commercial setting developed anaphylactic shock and/or cardiac arrest during MYOZYME infusion that required life-support measures.

Reactions generally occurred shortly after initiation of the infusion of MYOZYME. Patients presented with a constellation of signs and symptoms, primarily respiratory, cardiovascular, oedematous and/or cutaneous in nature (Table 2).

Table 2. Observed signs and symptoms of hypersensitivity/anaphylactic reactions	
System organ class	**Sign/Symptom***
Musculoskeletal	Arthralgia Muscle spasms Myalgia
Respiratory	Apnoea Bronchospasm Cough Dyspnoea Hypoxia Pharyngeal oedema Reduced/decreased oxygen saturation Respiratory arrest Respiratory distress Stridor Tachypnoea Throat irritation Throat tightness Wheezing
Cardiovascular	Bradycardia Cardiac arrest Cyanosis Flushing Hypertension Hypotension Paleness Palpitations Tachycardia Vasoconstriction
Cutaneous	Blister Erythema Hyperhidrosis Livedo reticularis Pruritus Rash Transient skin discoloration Urticaria
Nervous system	Agitation Dizziness Headache Pain Paraesthesia Restlessness Somnolence Tremor

Table 2. continued. Observed signs and symptoms of hypersensitivity / anaphylactic reactions	
System organ class	**Sign/Symptom***
Gastrointestinal	Abdominal pain Diarrhoea Dyspepsia Dysphagia Nausea Retching Vomiting
Eye	Conjunctivitis Lacrimation increased Periorbital oedema
General disorders and administration site conditions	Angioedema Asthenia Chest discomfort/pain Chills Facial oedema Fatigue Feeling hot/cold Infusion site reactions (including pain, swelling, induration, extravasation, erythema, urticaria, and pruritus) Irritability Malaise Peripheral oedema Peripheral coldness Pyrexia

*Signs and symptoms are in alphabetical order and not in order of frequency.

Additionally, recurrent reactions consisting of flu-like illness or a combination of events such as fever, chills, myalgia, arthralgia, pain, or fatigue occurring post-infusion and lasting usually for a few days, have been observed in some patients treated with MYOZYME.

IARs and immunogenicity

In clinical trials, the majority of the Pompe disease patients (approximately 90%) developed IgG antibodies to MYOZYME, generally within 3 months of initiation of treatment[4,5,6,7]. Similar proportions of patients treated in the commercial setting have developed IgG antibodies to MYOZYME. A trend toward decreasing IgG antibody titres over time was observed in the majority of patients.

A correlation was not observed between the onset of IARs and the time of IgG antibody formation. IARs can occur across all levels of antibody titres, however a trend was observed for more frequent IARs with higher titres of IgG antibody[4,5,8]. A tendency was observed for IOPD patients treated with a higher dose (40 mg/kg) to develop higher titres of IgG antibodies. Infantile-onset patients who develop high antibody titres appear to be at higher risk for developing more frequent IARs[6]. In the LOPD study however, there was no apparent association between higher IgG titres and occurrence of IARs[4,5].

Patients who develop IgE antibodies to MYOZYME appear to be at a higher risk for the

occurrence of IARs and/or anaphylactic reactions when MYOZYME is readministered. Therefore, these patients should be monitored more closely during administration of MYOZYME. Some IgE positive patients were successfully rechallenged with MYOZYME using a slower infusion rate at lower initial doses (or desensitisation procedures) and have continued to receive MYOZYME under close clinical supervision[9,10].

Patients with moderate to severe and recurrent IARs should be evaluated for specific IgG and IgE antibodies, as well as skin testing, a more sensitive measure to detect IgE antibodies, which is recommended for patients who experienced significant hypersensitivity reactions (see section 3). It is unknown who will develop immediate hypersensitivity reactions (IgE positive) to MYOZYME.

Patients who have experienced severe hypersensitivity reactions (and in particular anaphylactic reactions) should be treated with caution when re-administering MYOZYME. For more information and guidance on infusion management, please refer to section 2. For more information on MYOZYME preparation, administration and storage, please refer to Appendix 1, 2 and 3, respectively.

Table 3. Patients at increased risk of complications associated with IARs

- Patients with any acute underlying febrile illness.
- Patients with severe Pompe disease (may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARS).
- Patients who develop IgE antibodies to MYOZYME (are at a higher risk for occurrence of anaphylaxis and severe hypersensitivity reactions).
- Patients receiving MYOZYME at higher infusion rates or higher doses.
- Patients who developed high and sustained IgG antibody titres, especially patients with IOPD
- Patients who have experienced previous IARs.
- Patients who have temporarily interrupted MYOZYME treatment (e.g., during pregnancy).

1.2. Immune-mediated reactions

Severe cutaneous and systemic immune-mediated reactions have been reported in a small number of patients treated with MYOZYME. The potential mechanism for immune-mediated reactions consists of the deposition of intermediate-sized circulating immune complexes in tissues and vascular endothelium leading to inflammation and resulting in a heterogeneous array of clinical signs and symptoms such as glomerulonephritis, haematuria, proteinuria, papular rash, purpura-like eruptions, arthritis, serositis, and vasculitis[11,12.]

Reactions are self-limiting and usually develop within 7 to 10 days of antigen infusion, starting with some constitutional flu-like symptoms: fever, myalgia, arthralgia and rash. Clinical recovery is usually apparent after 7 to 28 days.

Severe cutaneous reactions, including ulcerative and necrotising skin lesions, possibly immune-mediated, have been reported with MYOZYME. Skin biopsy in one patient demonstrated deposition of anti-rhGAA antibodies in the lesion.

Systemic immune-mediated reactions, including possible type III immune complex-mediated reactions, have been observed with MYOZYME. These reactions occurred several weeks to 3

years after initiation of MYOZYME infusions.

Nephrotic syndrome was observed in a few patients with Pompe disease treated with MYOZYME and who had high IgG antibody titres (≥102,400). In these patients, renal biopsy showed immune complex deposition. Patients improved following treatment interruption.

RECOMMENDATION: IT IS RECOMMENDED TO PERFORM PERIODIC URINALYSIS AMONG PATIENTS WITH HIGH IgG ANTIBODY TITRES

Patients should be monitored for the development of systemic immune-mediated reactions. If immune- mediated reactions occur, discontinuation of the administration of MYOZYME should be considered, and appropriate medical treatment initiated. The risks and benefits of readministering MYOZYME following an immune-mediated reaction should be considered. Some patients have been successfully re-challenged and continued to receive MYOZYME under close clinical supervision.

1.3. Immunogenicity leading to loss of response (high sustained IgG antibody titres and/or neutralising antibodies)

As a therapeutic protein, MYOZYME has the potential to trigger an immunologic response, involving the formation of antibodies against recombinant human acid α-glucosidase (anti-rhGAA IgG antibodies and anti- rhGAA IgE antibodies)[13].

1.3.1. Anti-rhGAA IgG antibodies including neutralising antibodies.

The effect of IgG antibody formation on MYOZYME efficacy has been evaluated in clinical trials and over years of post-marketing experience. In clinical studies, the majority of patients developed IgG antibodies to MYOZYME, and seroconversion typically occurred within 3 months of treatment.

The clinical impact of IgG antibodies on MYOZYME efficacy is multifactorial, however the development of high and sustained IgG titres (HSAT) is a contributing factor.

1. With regards to IOPD, a tendency was observed for patients treated with a higher dose (40 mg/kg) to develop higher titres of IgG antibodies[6]. The development of HSAT has been shown in MYOZYME treated patients to have poor outcome. HSAT is defined as titres ≥51 200 at 2 or more timepoints after 6 months on MYOZYME treatment that were at least 12 weeks apart. Furthermore, CRIM status (Cross Reactive Immunologic Material: endogenous GAA protein) is a risk factor for HSAT development. This risk is higher among CRIM negative patients versus CRIM-positive patients and is a contributing factor to a poor outcome. Such prolonged HSAT could result in suboptimal dosing of drug to patients due to immune complex formation. HSAT has also occurred in a limited number of CRIM-positive patients[14,15,16].

2. With respect to LOPD patients, the majority showed either stabilising or decreasing antibody titres over time. Patients with LOPD produce endogenous enzyme and are considered CRIM-positive. These patients are generally not at risk for developing HSAT and very few make high ADA titres which then decrease

over time. Thus, the impact of IgG antibodies is more limited for LOPD patients[4,8].

A small number of the IgG positive patients treated with MYOZYME in clinical trials and/or the post marketing setting were tested positive for inhibition of enzyme activity and/or uptake when tested in-vitro. The clinical relevance of in vitro inhibition is unclear. Patients with positive uptake inhibition generally had higher IgG antibody titres than patients who remained negative for uptake inhibition in infantile-onset and late-onset studies. Neutralising antibodies, particularly those which inhibit drug cellular uptake, have developed in some IOPD patients treated with MYOZYME and generally were associated with high ADA titres. CRIM-negative IOPD patients are at risk for developing HSAT and neutralising antibodies with documented loss of clinical response[14,15,16.]

RECOMMENDATION: IgG ANTIBODY TITRES SHOULD BE MONITORED PERIODICALLY BASED ON CLINICAL PHENOTYPE

1. Collect baseline serum sample collection prior to the first infusion.
2. For IOPD patients, regular monitoring during first year of treatment (example: every 3 months) is suggested and subsequent monitoring depending on clinical outcomes and antibody titers level.
3. For LOPD patients, antibody development should be assessed within 6 months after treatment start and subsequent monitoring as clinically warranted based on efficacy considerations.
4. Collect samples for testing of inhibition of enzyme uptake or activity if patients experience a decrease in clinical benefit despite continued treatment with Myozyme.

   Please refer to section 3.1.1 for IgG and neutralising antibody testing.

1.3.2 Immunomodulation in patients with IOPD: benefits and risks

Immunogenicity data from clinical trials and published literature in CRIM-negative infantile-onset patients (IOPD) suggests that the administration of immune tolerance induction (ITI) regimens given to MYOZYME naive patients (prophylactic ITI) may be effective in preventing or reducing the development of High Sustained Antibody Titre (HSAT) against MYOZYME. Data from a small number of patients who developed HSAT with or without neutralising activity following treatment with MYOZYME showed limited treatment effect of ITI when commenced after HSAT development. Better treatment responses were observed in younger patients with less advanced disease who received prophylactic ITI before development of HSAT, which suggests that early initiation of ITI can result in improved clinical outcomes[14,15,16.] ITI regimens may need to be tailored to individual patient needs.

Patients with Pompe disease are at risk of respiratory infections due to the progressive effects of the disease on the respiratory muscles. Patients with Pompe disease treated with immunosuppressive agents maybe at further increased risk of developing severe infections and vigilance is recommended. Fatal and life-threatening respiratory infections have been observed in some of these patients.

KEY POINTS

- As MYOZYME is a therapeutic protein there is the potential for an immunologic response. IgG antibodies to alglucosidase alfa generally develop within 3 months of treatment initiation. IARs, with or without the development of IgG or IgE antibodies, may occur during the infusion or during the hours following infusion. Hypersensitivity/ anaphylactic reactions, some of which are IgE-mediated, have been reported and generally occurred during or shortly after initiation of MYOZYMEMYOZYME infusion.
- Patients who develop IgE antibodies should be monitored more closely during administration of MYOZYME since they appear to be at a higher risk for the occurrence of IARs and/or anaphylactic reactions.
- Patients treated with MYOZYME should be monitored for IgG antibody formation periodically based on clinical phenotype and in case of clinical decline.
- Immune-mediated reactions including severe cutaneous and systemic reactions have been reported in a small number of cases.

2. CLINICAL MANAGEMENT OF IDENTIFIED RISKS[3,17,23]

2.1 Pre-infusion stage

The complex underlying medical problems of Pompe disease must be considered prior to initiating ERT with MYOZYME. Patients with an acute underlying illness at the time of MYOZYME infusion appear to be at greater risk for IARs. Careful consideration should be given to the patient's clinical status prior to administration of MYOZYME. All patients should be clinically evaluated prior to each MYOZYME infusion to rule out any acute or underlying illness.

Careful consideration should be given to the potential short- and long-term effects of repeated use of corticosteroids, antihistamines, and antipyretics, especially in paediatric patients. Dosing recommendations for such treatments should be in line with individual Product Information (PI) or Data Sheet (DS).

Pre-treatment in patients with previous IgE-mediated hypersensitivity reactions

- **The use of antihistamines for pre-treatment is not recommended in patients with previous IgE-mediated hypersensitivity reaction.** Antihistamines can mask early symptoms of a hypersensitivity reaction (skin reaction) making it difficult for the infusion staff to recognise the initial signs of distress and the need to decrease the infusion rate and/or otherwise intervene. Additionally, in cases where significant histamine is released, antihistamine administration after release or as a premedication will not be fully effective in managing anaphylactic reactions[22.]
- **Exposure to beta-blockers may exacerbate anaphylactic reactions and is a relative contraindicatio**n when a patient is at a risk of anaphylaxis. Beta-blockers are also a relative contraindication for adrenaline (epinephrine) administration[19,20,23.]

2.2 MYOZYME infusion stage

Any recommendations should be used as guidelines only. Final decisions concerning the management of individual patients reside with the treating physician.

2.2.1 Recommended infusion rate

- It is recommended that the initial infusion rate of MYOZYME be no more than 1 mg/kg/hr. The infusion rate may be increased by 2 mg/kg/hr every 30 minutes, after patient tolerance to the infusion rate is established, until the recommended maximum infusion rate of 7 mg/kg/hr is reached. Patients who have experienced IARs should be treated with caution when re-administering MYOZYME.
- If the IAR appears rate-related, the following modification(s) to the infusion rate ramp schedule are suggested:
    - decrease maximum infusion rate and/or
    - prolong each infusion rate ramp step by 15-30 minutes.

2.2.2 Mild or moderate reactions[3,17,18,*]

Slow infusion to half the rate or temporarily stop the infusion until symptoms improve or subside.

- If symptoms subside, resume infusion rate at half the rate at which the IAR(s) occurred for 30 minutes, followed by an increase in infusion rate by 50% for 15 to 30 minutes.
- If symptoms do not recur, increase the infusion rate to the rate at which the IAR(s) occurred and consider continuing to increase the rate in a stepwise manner until the maximum rate is achieved.
- If symptoms persist despite temporarily stopping the infusion, it is suggested that the treating physician wait at least 30 minutes more for symptoms of the IAR to clear prior to deciding to halt the infusion for the remainder of the day.

Example:

If the patient experiences mild or moderate IAR(s) at an infusion rate of 5 mg/kg/hr, reduce the infusion rate to 2.5 mg/kg/hr, or temporarily stop the infusion and wait for the symptoms to subside.

If symptoms subside, administer infusion at a rate of 2.5 mg/kg/hr for 30 minutes. If well tolerated, increase the infusion rate to 3.75 mg/kg/hr for at least 15 to 30 minutes.

If well tolerated, increase the infusion rate to 5 mg/kg/hr and administer for 15 to 30 minutes.

If well tolerated, increase the infusion rate to the maximum recommended infusion rate of 7 mg/kg/hr and administer at this rate for the remainder of the infusion as tolerated.

Vital signs should be obtained at the end of each step.

---

* These definitions serve as guidelines only based on CDSIC SDTM standard terminology v3.1.1. Overall severity assessment is at the discretion of the treating physician.

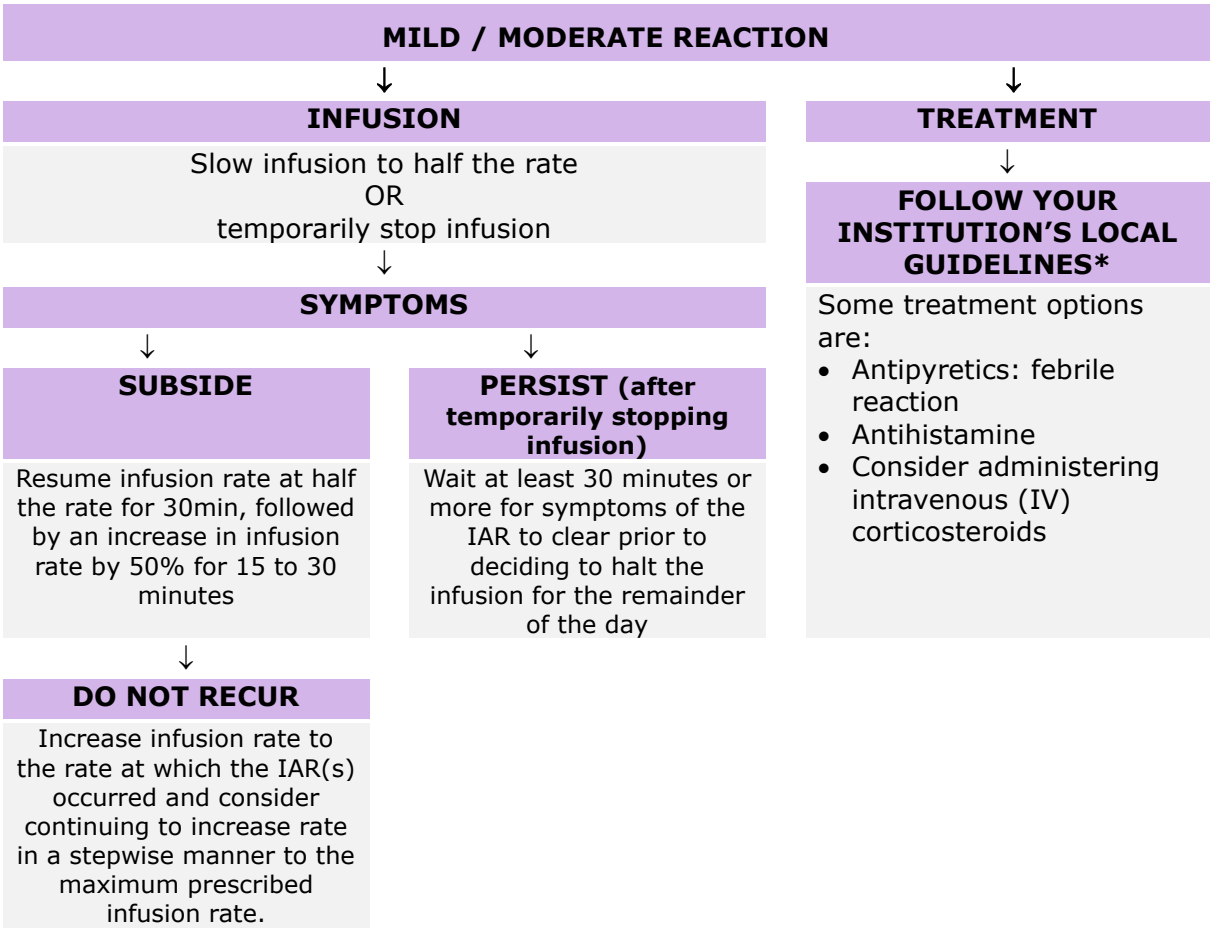
Mild: A type of AE that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living.

Moderate: A type of AE that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort, but poses no significant or permanent risk of harm to the research participant.

Treatment recommendations for mild to moderate reactions

- Administer antipyretics for febrile reactions.
- Administer age-appropriate dose of antihistamine, H1-antagonist.
- Consider administering intravenous (IV) corticosteroids.
- Administer IV fluids as necessary to maintain normal vital signs (e.g., blood pressure).

Figure 1. Clinical management of mild to moderate reactions



2.2.3 Severe reactions^: hypersensitivity / anaphylactic reactions including anaphylactic shock and IgE-mediated hypersensitivity reaction[18,19,23]

WARNING

Serious hypersensitivity reactions, including life-threatening anaphylactic reactions, have been observed in patients during MYOZYME infusion, some of which were IgE-mediated.

A small number of patients developed anaphylactic shock and/or cardiac arrest during MYOZYME infusion that required life-support measures. Medical support measures, including **cardiopulmonary resuscitation equipment**, should be readily available when MYOZYME is administered.

- Anaphylactic reactions are often life-threatening, with acute onset within minutes to several hours following infusion initiation. Even when there are mild symptoms initially, the potential for progression to a severe and even irreversible outcome must be recognised. Because of the potential for severe hypersensitivity or anaphylactic reactions, appropriate medical support, including cardiopulmonary resuscitation equipment, should be readily available when MYOZYME is administered.
- Early detection of signs and symptoms of hypersensitivity or anaphylactic reactions may assist in effective management of patients and prevent possible significant or irreversible outcomes.
- It is important to recognise the allergic phenomenon early so the infusion can be interrupted, the rate can be reduced and/or other corrective intervention can take place.

The risks and benefits of re-administering MYOZYME following an anaphylactic or severe hypersensitivity reaction should be considered. Some patients have been re-challenged and have continued to receive MYOZYME under close clinical supervision. Extreme care should be exercised, with appropriate resuscitation measures available, if the decision is made to re-administer the product.

---

^ This definition serves as guideline only based on CDSIC SDTM standard terminology v3.1.1. Overall severity assessment is at the discretion of the treating physician:

Severe: A type of AE that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.

Treatment recommendations for severe reactions

- The administration of MYOZYME should be immediately discontinued, and appropriate medical treatment should be initiated, as described below.
  - Administration of adrenaline (epinephrine) IM in upper extremity or thigh is generally indicated for life-threatening anaphylactic reactions. Although in general, careful consideration should be given to the contraindications to the use of adrenaline (epinephrine). Contraindications should always be weighed against the benefit or need to use adrenaline (epinephrine) as a life-saving measure in case of life-threatening anaphylactic reactions. For detailed information please consult the PI of adrenaline (epinephrine).
  - For significant symptoms such as bronchospasm, oxygen desaturation, cyanosis, dyspnoea, or wheezing, consider administering moderate to high-flow oxygen by mask or nasal catheter or a beta agonist (e.g., salbutamol) via metered dose inhaler or nebuliser.
  - Administer IV fluids as necessary to maintain normal vital signs (e.g., blood pressure). Consider administering IV corticosteroids. Alpha-adrenergic agents and pressors with non-existent or minimal beta-adrenergic action should be considered to maximise inotropy and minimise chronotropy in patients with hypertrophic cardiomyopathy.
  - Institute advanced cardiopulmonary resuscitation measures if appropriate.
- If deemed appropriate, subsequent infusions should be initiated with a desensitisation procedure, typically without pre-treatment, in patients with previous IgE-mediated hypersensitivity reaction.
- Please contact Sanofi Medical Information for desensitisation guidelines. Contact details are provided in KEY CONTACTS.
- Recommendations for management of IgE-positive patients provided herein are to be used as guidelines only. Final decisions concerning management of individual patients reside with the treating physician.

Figure 2. Clinical management of severe reactions

SEVERE REACTION e.g. hypersensitivity / anaphylactic reactions

↓

INFUSION

Discontinuation of administration

↓

If subsequent infusion:

Consider desensitisation

↓

TREATMENT

↓

FOLLOW YOUR INSTITUTION'S LOCAL GUIDELINES*

Warning: institute advanced cardiopulmonary resuscitation measures if appropriate

- Some treatment options are:
- Adrenaline (epinephrine) IM: anaphylactic reaction
- For significant symptoms such as bronchospasm, oxygen desaturation, cyanosis, dyspnoea, or wheezing, consider administering moderate to high-flow oxygen by mask or nasal catheter or a beta agonist (e.g., salbutamol) via metered dose inhaler or nebuliser. If respiratory symptoms persist
- or severity warrants, consider subcutaneous administration of adrenaline (epinephrine) in upper extremity or thigh. The use of adrenaline (epinephrine) must be carefully weighed in patients with underlying cardiovascular disease.
- Administer IV fluids as necessary to maintain normal vital signs (e.g., blood pressure).

*Contraindications should always be weighed against the benefit or need to use adrenaline (epinephrine) as a life-saving measure in case of life-threatening anaphylactic reactions.

2.3 Post-infusion observation

It is recommended that patients be observed for safety purposes both during and after the completion of each intravenous MYOZYME infusion by appropriate medical personnel familiar with Pompe disease and potential reactions to MYOZYME. In clinical trials, patients were monitored for 2 hours at the end of the MYOZYME infusion. The appropriate length of post-infusion monitoring is to be determined by the treating physician based on the patient's clinical status and infusion history.

3. IMMUNOLOGY TESTING

3.1 Description

As part of the general post-approval safety surveillance, Sanofi has initiated an immunosurveillance program for MYOZYME to determine the extent of antibody formation against MYOZYME to understand the clinical impact, if any. There are currently no marketed tests for antibodies against MYOZYME; however, a free testing service is provided by Sanofi (see Table 4). Please contact your local Sanofi- representative or Sanofi Medical Information via e-mail at medinfo.australia@sanofi.com for information how to access Sanofi's RDSTP.

3.1.1 Immunosurveillance program: IgG antibody testing including neutralising antibodies

As described in section 1, development of IgG may be linked to IARs in some patients and development of HSAT has been associated to poor efficacy outcomes, especially for the patients with infantile onset. Thus, the below recommendations for IgG testing are suggested.

RECOMMENDATION

1. Collect baseline serum sample collection prior to the first infusion.
2. Periodically monitor for IgG antibody formation based on patients' clinical phenotype.
    a. For IOPD patients, regular monitoring during first year of treatment (example: every 3 months) and subsequent monitoring dependent on clinical outcomes and antibody titer levels.
    b. For LOPD patients, antibody development within 6 months after treatment start and subsequent monitoring as clinically warranted based on safety and efficacy considerations.
3. Test for inhibition of enzyme uptake or activity if patients experience a decrease in clinical benefit despite continued treatment with MYOZYME.

3.1.2. Immunological testing for moderate/severe infusion associated reactions: IgG, IgE, complement activation and serum tryptase testing

Testing for IgG and IgE antibodies is typically performed for moderate or severe or recurrent IARs suggestive of hypersensitivity reactions. A small number of patients who were evaluated tested positive for MYOZYME-specific IgE antibodies, some of whom experienced anaphylactic reactions.

Some patients have been successfully re-challenged using slower rates and/or lower initial doses, and continued to receive treatment with MYOZYME under close clinical supervision.

RECOMMENDATION

- To further characterise the potential mechanism of IARs, collect samples for testing for IG and IgE antibodies, complement activation and tryptase for patients who experience moderate to severe or recurrent IARs suggestive of hypersensitivity reactions.
- Samples for complement activation and serum tryptase testing must be drawn 1-3 hours after the onset of the infusion reaction. Samples for IgE testing must be drawn at least 72 hours after the infusion ends. Samples for IgG should ideally be collected at trough, before the next infusion.

3.1.3 Skin Testing[20,21]

Skin testing may be performed at the discretion of the treating physician in patients who experience an IAR that meets the following criteria (Table 4):

- IAR is suggestive of an IgE-mediated reaction, with persistent symptoms such as bronchospasm, hypotension and/or urticaria requiring intervention OR any other signs or symptoms which the treating physician considers (as) relevant.

- Skin testing may be another predictor of IgE-mediated reactions and may be suggested for confirmation of the IgE results.

If the decision to perform skin testing is made, it is recommended to postpone MYOZYME infusions until skin testing has been performed and the results reviewed by the treating physician.

Note: Certain medications (e.g., antihistamines, adrenergic drugs) may interfere with test results. Prior to skin testing, patient's medications should be reviewed to assess whether or not they may interfere with test results.

It is recommended that skin testing is performed by a trained allergist or a medical person trained in allergy skin testing and that the testing is performed at minimum 48 hours after MYOZYME infusion, and preferably >3 weeks after an anaphylactic episode because of transient desensitisation.

The procedure only involves prick/puncture testing. If prick/puncture testing is negative, intradermal testing may be warranted. Testing includes MYOZYME and positive and negative controls.

3.1.4 Circulating immune complex testing

If a patient exhibits signs or symptoms suggestive of systemic immune-mediated reactions involving skin and other organs while receiving MYOZYME, serum samples are obtained for the evaluation of circulating immune complexes. Patients should be monitored for continuing immune complex symptomatology, and additional serum samples obtained for evaluation, as appropriate.

Consideration for further evaluation of possible immune complex disease, including biopsy of suspected organs involved (e.g., skin to assess for vasculitis and kidney biopsy to assess for immune complex deposition in the glomerular basement membrane) is left to the discretion of the treating physician.

Table 4. Clinical immunology and skin testing characteristics

TEST[a]	INDICATION FOR TESTING	SAMPLE TYPE	FREQUENCY	COLLECTION TIME[b]
Skin testing	IARs suggestive of IgE- mediated reaction with persistent symptoms or for confirmation of IgE results	Prick / puncture testing	Ad hoc (after IAR)	Min. of 48h after infusion and preferably >3 weeks after anaphylactic episode
IgG[c]	Routine monitoring	Serum-Frozen Whole blood (received within 24 hours of collection)	Routine monitoring	Sample should be pre-infusion or ≥3 days post-infusion
IgG/neutralising antibody	Decreased response to treatment or lack of effect	Serum-Frozen Whole blood (received within 24 hours of collection)	Ad hoc (as needed)	Sample should be pre- infusion ≥3 days post-infusion

IgG/IgE antibody	Moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions	Serum-Frozen Whole blood (received within 24 hours of collection)	Ad hoc (as needed)	Pre-infusion or at least ≥3 days post-infusion
Serum tryptase	Moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions	Serum-Frozen	Ad hoc (as needed)	1-3 hours post-infusion reaction
Complement activation	Moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions	EDTA Plasma-Frozen	Ad hoc (as needed)	1-3 hours post-infusion reaction
Circulating immune complex & IgG antibodies	Reactions suggestive of systemic immune-mediated reactions	Serum-Frozen	Ad hoc (as needed)	1-3 hours post-infusion (Testing done on IgG sample)

[a] Sanofi Rare Disease Specialty Testing Program offers a service free of charge for collection, , packaging and shipping of blood samples to the Labcorp central laboratory. This service applies to all tests performed as part of an IAR investigation (including IgG antibody, IgE antibody, neutralising antibody, complement activation, and serum tryptase) and to all clinical samples for routine IgG monitoring.

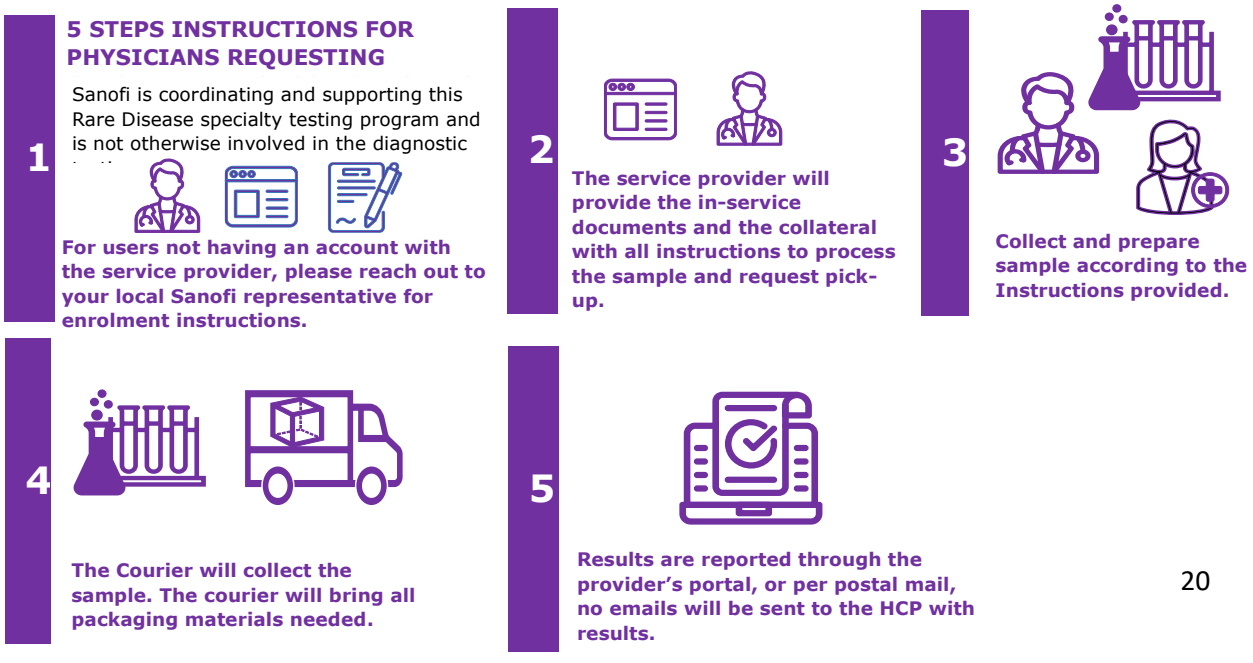
[b] Skin testing is usually performed locally. Document the time and date when the sample was taken.

[c] If results show high IgG antibody titres, periodic urinalysis is recommended.

3.2. Procedure for testing

This procedure applies to all tests performed as part of an IAR investigation (including IgG antibody, IgE antibody, neutralising antibody, complement activation, and serum tryptase) and to all clinical samples for routine post-marketing analysis and reporting (Figure 3).

Figure 3. Procedure for Testing



Please contact Sanofi Medical Information for collection, packaging, and shipping of blood samples. Contact details are provided in KEY CONTACTS.

4. REPORTING ADVERSE EVENTS

Reporting adverse events after administration of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the TGA (Australia) or CARM (New Zealand), or by contacting Sanofi Patient Safety & Pharmacovigilance department at ae@sanofi.com. For full contact details on reporting adverse reactions, please refer to **KEY CONTACTS**.

5. PREGNANCY & BREASTFEEDING

There is limited data from the use of MYOZYME in pregnant women. Studies in animals have not shown reproductive toxicity (section 4.6 PI or Datasheet). MYOZYME should not be used during pregnancy unless the clinical condition of the woman requires treatment with MYOZYME (section 4.6 PI or Datasheet).

Limited data suggest that MYOZYME is excreted in breast milk in very low concentrations. No clinical effect is expected in a breastfed infant due to low breast milk transfer and poor bioavailability. Breastfeeding during treatment with MYOZYME may therefore be considered. As a precautionary measure, breastfeeding interruption for the first 24 hours after treatment may be considered.

Reporting information on drug exposure in pregnancy to Sanofi Patient Safety & Pharmacovigilance is necessary to identify agents harmful to the developing fetus. Conversely, data on pregnancy exposure can also establish that the fetal toxicity of a product is limited. In order to collect, review and communicate information on safety in pregnancy, to dispose of more accurate information Sanofi will follow-up on all reported pregnancy cases.

Sanofi strongly encourages physicians and other HCPs to report all pregnancies and pregnancy outcomes in patients exposed to MYOZYME, regardless of whether the exposure is associated with an adverse event or not. For full contact details on reporting pregnancies, please refer to **KEY CONTACTS.**

6. POMPE REGISTRY

Medical or healthcare professionals are encouraged to register patients who are diagnosed with Pompe disease at https://www.registrynxt.com. Patient data will be anonymously collected in this Registry. The objectives of the Pompe Registry are to enhance the understanding of Pompe disease and to monitor patients and their response to enzyme replacement therapy over time, with the ultimate goal of improving clinical outcomes for these patients. Please contact the Sanofi Medical Information Department for more information.

For more information on how to enrol your patient at a participating Registry site and/or to contact the Sanofi Registries staff, please visit the Registry website at www.registrynxt.com/Home/Contact-Us and complete the Contact Us form.

7. REFERENCES

1. MYOZYME Australian Product Information,
2. Luskin AT, Luskin SS. Anaphylaxis and Anaphylactoid Reactions: Diagnosis and Management. Am J Ther. 1996 Jul;3(7):515–20.
3. Lenz H-J. Management and preparedness for infusion and hypersensitivity reactions. Oncologist. 2007 May;12(5):601–9.
4. Van der Ploeg AT, Clemens PR, Corzo D, et al. A randomized study of alglucosidase alfa in late-onset Pompe's disease. N Engl J Med. 2010;362(15):1396-1406.
5. Van der Ploeg AT, Barohn R, Carlson L, et al. Open-label extension study following the Late-Onset Treatment Study (LOTS) of alglucosidase alfa. Mol Genet Metab. 2012;107(3):456-461.
6. Kishnani PS, Corzo D, Nicolino M, Byrne B, Mandel H, Hwu WL, et al. Recombinant human acid [alpha]-glucosidase: major clinical benefits in infantile-onset Pompe disease. Neurology. 2007 Jan 9;68(2):99–109.
7. Nicolino M, Byrne B, Wraith JE, Leslie N, Mandel H, Freyer DR, et al. Clinical outcomes after long-term treatment with alglucosidase alfa in infants and children with advanced Pompe disease. Genet Med. 2009 Mar;11(3):210–9.
8. De Vries JM, Kuperus E, Hoogeveen-Westerveld M, et al. Pompe disease in adulthood: effects of antibody formation on enzyme replacement therapy. Genet Med. 2017;19(1):90-97.
9. Ertoy Karagol HI, Inci A, Terece SP, et al. Long-Term Experience with Anaphylaxis and Desensitisation to Alglucosidase Alfa in Pompe Disease [published online ahead of print, 2023 Jan 9]. Int Arch Allergy Immunol. 2023;1-6.
10. Gallay L, Petiot P, Durieu I, Streichenberger N, Berard F. SWORD: A simplified desensitisation protocol for enzyme replacement therapy in adult Pompe disease. Neuromuscul Disord. 2016;26(11):801-804.
11. Crespo MS. Immune Complex Processing: A Phagocytosis-Based Mechanism with Proinflammatory Potential. Transfus Med Hemotherapy. Karger Publishers; 2005;32(6):355–62.
12. Hiltz RE, Cupps TR. Cutaneous vasculitis. Curr Opin Rheumatol. 1994 Jan;6(1):20–4.
13. Frost H. Antibody-mediated side effects of recombinant proteins. Toxicology. 2005 Apr 15;209(2):155–60.
14. Banugaria SG, Prater SN, Patel TT, DeArmey SM, Milleson C, et al. Algorithm for the Early Diagnosis and Treatment of Patients with Cross Reactive Immunologic Material-Negative Classic Infantile Pompe Disease: A Step towards Improving the Efficacy of ERT. PLOS ONE. 2013;8(6): e67052.
15. Berrier KL, Kazi ZB, Prater SN, et al. CRIM-negative infantile Pompe disease: characterization of immune responses in patients treated with ERT monotherapy [published correction appears in Genet Med. 2015 Jul;17(7):596. Rosenburg, Amy S [corrected to Rosenberg, Amy S]]. Genet Med. 2015;17(11):912-918.
16. Kazi ZB, Desai AK, Berrier KL, et al. Sustained immune tolerance induction in enzyme replacement therapy-treated CRIM-negative patients with infantile Pompe disease. JCI Insight. 2017 Aug;2(16):94328
17. Miebach E. Management of infusion-related reactions to enzyme replacement therapy in a cohort of patients with mucopolysaccharidosis disorders. Int J Clin Pharmacol Ther. 2009 Jan;47 Suppl 1:S100–6.
18. Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF, Bock SA, Branum A, *et.al.* Second symposium on the definition and management of anaphylaxis: summary report-Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006 Feb;117(2):391–7.
19. Lieberman P, Nicklas RA, Oppenheimer J, Kemp SF, Lang DM, Bernstein DI. *et.al.* The diagnosis and management of anaphylaxis practice parameter: 2010 update. J Allergy Clin Immunol. 2010 Sep;126(3):477–80.e1–42.
20. Lockey R. Academy position statement: adrenergic blockers, allergen immunotherapy and skin testing. AAAAI Position Statement and Work Group Reports. November 2002.
21. Bernstein IL, Storms WW. Practice parameters for allergy diagnostic testing. Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma. The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol. 1995 Dec;75(6 Pt 2):543–625.
22. Vervloet D, Durham S. ABC of allergies: Adverse reactions to drugs. BMJ. 1998 May 16;316(7143):1511–4.
23. Bernstein L, *et.al.* Disease management of drug hypersensitivity: a practice parameter. Ann Allergy, Asthma Immunol Off Publ Am Coll Allergy, Asthma, Immunol. 1999;83(6):665–700.
24. de Vries JM, Kuperus E, Hoogeveen-Westerveld M, Kroos MA, Wens SC, Stok M. *et al.* Pompe disease in adulthood: effects of antibody formation on enzyme replacement therapy. Genet Med. 2016; doi:10.1038/gim.2016.70.
25. Masat E, Laforêt P, De Antonio M, Corre G, Perniconi B, Taouagh N. *et al.* Long-term exposure to MYOZYME results in a decrease of anti-drug antibodies in late-onset Pompe disease patients. Sci Rep. 2016;6:36182. doi: 10.1038/srep36182.

8. APPENDICES

Appendix 1. Preparation of MYOZYME[1]

Use aseptic technique during preparation

The following items are required for the preparation and administration of MYOZYME.

- Required quantity of MYOZYME vials based on the patient's dose.
- Intravenous administration set with 0.2 µm low protein-binding in-line filter.
- Sterile water for injection, for reconstitution
- 0.9% sodium chloride for injection, for dilution
- Syringes for reconstitution and dilution
- Needles with diameter not larger than 20G for reconstitution and dilution
- Additional supplies required per institution protocol

Note: Filter needles should not be used during preparation of MYOZYME.

1. Determine the number of vials to be reconstituted based on the individual patient's weight and the recommended dose of 20 mg/kg. Round up to the nearest whole vial.

   Remove the required number of vials from the refrigerator and allow them to reach room temperature prior to reconstitution.

   Vials should reach room temperature in approximately 30 minutes.

Dose calculation:

Patient weight (kg) x Dose (mg/kg) = Patient dose (in mg)

Patient dose (in mg) ÷ 50 mg/vial = Number of vials to reconstitute.
If the number of vials includes a fraction, round up to the next whole number.

Examples:

A. **Infantile-onset:** Patient weight (9 kg) x Dose (20 mg/kg) = Patient dose (180 mg) 180 mg ÷ 50 mg/vial = 3.6 vials; therefore, 4 vials should be reconstituted

B. **Adult-onset:** Patient weight (68 kg) x Dose (20 mg/kg) = Patient dose (1360 mg) 1360 mg ÷ 50 mg/vial = 27.2 vials; therefore, 28 vials should be reconstituted.

2. Reconstitute each 50 mg vial of MYOZYME by slowly injecting 10.3 mL of sterile water for injection to the inside wall of each vial using a syringe with a needle diameter not larger than 20G. Each vial will yield 5 mg/mL.

   The total extractable dose per vial is 50 mg in 10 mL. Avoid forceful impact of the water for injection on the powder and avoid foaming. This is done by slow drop-wise addition of the water for injection down the inside of the vial and not directly onto the lyophilised cake. Tilt and roll each vial gently. Do not invert, swirl or shake. The reconstituted MYOZYME solution should be protected from light.

3. Perform an immediate visual inspection of the reconstituted vials for particulate matter and discolouration. If upon immediate inspection opaque particles are observed or if the solution is discoloured, do not use and contact Medical Information. Contact details are provided in **KEY CONTACTS.**

   The reconstituted solution may occasionally contain some alglucosidase alfa particles (typically less than 10 in a vial) in the form of thin white strands or translucent fibres subsequent to the initial inspection. This may also happen following dilution for infusion. These particles have been shown to contain alglucosidase alfa and may appear after the initial reconstitution step and increase over time. Studies have shown that these particles are removed via in-line filtration using a 0.2 µm low protein-binding filter without having a detectable effect on the purity or strength.

4. Withdraw the calculated volume of MYOZYME from the appropriate number of vials.

5. MYOZYME should be diluted in 0.9% sodium chloride for injection, immediately after reconstitution, to a final MYOZYME concentration of 0.5 to 4 mg/mL. See Table 1 for the recommended total infusion volume based on patient weight. Discard any vial with unused reconstituted solution.

   Patient dose (in mg) ÷ 5 mg/mL = number of mL of reconstituted MYOZYME required for patient dose.

Example

Patient dose = 320 mg
320 mg ÷ 5 mg/mL = 64 mL of MYOZYME

PATIENT WEIGHT RANGE (KG)	TOTAL INFUSION VOLUME	INFUSION RATES			
		Step 1 1 mg/kg/hr (mL/hr)	Step 2 3 mg/kg/hr (mL/hr)	Step 3 5 mg/kg/hr (mL/hr)	Step 4 7 mg/kg/hr (mL/hr) (until total volume has been infused)
1.25-10	50	3	8	13	18
10.1-20	100	5	15	25	35
20.1-30	150	8	23	38	53
30.1-35	200	10	30	50	70
35.1-50	250	13	38	63	88
50.1-60	300	15	45	75	105
60.1-100	500	25	75	125	175
100.1-120	600	30	90	150	210
120.1-140	700	35	105	175	245
140.1-160	800	40	120	200	280
160.1-180	900	45	135	225	315
180.1-200	1000	50	150	250	350

6. Slowly withdraw the reconstituted solution from each vial using a syringe with a needle diameter not larger than 20G. Avoid foaming in the syringe.

7. Remove airspace from the infusion bag to minimise particle formation due to the sensitivity of MYOZYME to air-liquid interfaces.

8. Also remove an equal volume of sodium chloride 0.9% solution for injection that will be replaced with reconstituted MYOZYME.

9. Add the reconstituted MYOZYME solution slowly and directly into the sodium chloride solution. Do not add directly into airspace that may remain within the infusion bag. Avoid foaming in the infusion bag.

10. Gently invert or massage the infusion bag to mix. Do not shake. To reduce microbial hazard, use as soon as practicable after dilution. If storage is necessary, hold at 2°C-8°C for no more than 24 hours. Protect from light.

11. Vials are single-use in one patient only. Discard any unused product.

Appendix 2. Administration of MYOZYME[1]

Note: MYOZYME should not be infused in the same intravenous line with other products. The diluted solution should be filtered through a 0.2 µm, low protein-binding, in-line filter during administration to remove any visible particles. Visible particles (aggregated enzyme and degradants) are removed by the in-line filter without any detectable effect on the purity or strength of MYOZYME.

Patients with an acute underlying illness at the time of MYOZYME infusion appear to be at greater risk for infusion reactions. Careful consideration should be given to the patient's clinical status prior to administration of MYOZYME.

1. Explain the administration procedure to the patient.
2. Obtain vital signs, including blood pressure, pulse, respiratory rate, and temperature prior to the infusion.
3. Obtain IV access. Antecubital, wrist, or hand veins may be used for access. Central access is also an option.
4. Draw any required blood work if applicable and flush line with 0.9% sodium chloride for injection.
5. It is recommended that a primary infusion line of 0.9% sodium chloride for injection be initiated at a rate specified by the physician, in order to maintain the patency of the IV access. If possible, use a programmable intravenous infusion pump to control this infusion rate.
6. Set up and prime the administration set with the MYOZYME infusion solution. Use care to prevent the appearance of air bubbles in the tubing. In order to ensure precise control of the infusion rate, it is recommended that this infusion be performed with the use of a programmable intravenous infusion pump.
7. Connect the MYOZYME solution administration set to the 0.2 µm in-line low protein-binding filter set and prime the line.
8. Connect the MYOZYME solution line to the lowest additive port on the patient's primary administration set.
9. Infusions should be administered in a step-wise manner using an infusion pump.
10. When the infusion is complete, flush the tubing with 0.9% sodium chloride for injection (at the last infusion rate) to ensure that the entire dose of MYOZYME is administered to the patient.
11. Remove the administration set, and along with any unused product or waste material, discard and dispose of in accordance with local requirements.

Appendix 3. Storage of MYOZYME[1]

Unreconstituted MYOZYME vials should be stored under refrigeration between 2°-8°C. Do not use MYOZYME after the expiration date on the vial.

After dilution, an immediate use is recommended. However, chemical and physical in-use stability has been demonstrated for 24 hours at 2°-8°C when stored under protection from light. Storage of the reconstituted and diluted solution at room temperature is not recommended. DO NOT FREEZE OR SHAKE.

Please see PI or Datasheet for full prescribing

AUSTRALIA

PBS information: This product is not listed on the PBS.
This product is funded under the Life Saving Drugs Program

Please review full Product Information before prescribing. Full Product Information is available from sanofi-aventis australia pty ltd at https://bit.ly/myoz-pi or 1800 818 806.

Scan for more information

NEW ZEALAND

Myozyme (alglucosidase alfa 50mg/ 10ml) is a Prescription Medicine. Myozyme is fully reimbursed for patients that meet Special Authority Criteria for Subsidy outlined in Section B of the Pharmaceutical Schedule (SA1986). Please review Product Data Sheet before prescribing, available at www.medsafe.govt.nz or call 0800 283 684, option 2 (Sanofi's Medical Communications service in New Zealand).

Before prescribing MYOZYME, please refer to the data sheet (available at https://bit.ly/myoz-pi) for information on dosage, contraindications, precautions, interactions, and adverse effects.