1 NAME OF THE MEDICINAL PRODUCT

NAGLAZYME 1 mg/mL concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 1 mg galsulfase. One vial of 5 mL contains 5 mg galsulfase.

Galsulfase is a recombinant form of human N-acetylgalactosamine-4-sulfatase and is produced by recombinant DNA technology using mammalian Chinese Hamster Ovary (CHO) cell culture.

3 PHARMACEUTICAL FORM

NAGLAZYME is intended for intravenous infusion and is supplied as a sterile, nonpyrogenic, colorless to pale yellow, clear to slightly opalescent solution. Do not use if the solution is discolored or if there is particulate matter in the solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

NAGLAZYME is indicated for long-term enzyme replacement therapy in patients with Mucopolysaccharidosis VI (MPS VI, N-acetylgalactosamine 4-sulfatase deficiency, Maroteaux-Lamy syndrome).

4.2 Posology and Method of Administration

As for all lysosomal genetic disorders, it is of primary importance, especially in severe forms, to initiate treatment as early as possible, before appearance of non-reversible clinical manifestations of the disease.

Naglazyme treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Naglazyme should be administered by a healthcare professional in an appropriate clinical setting where resuscitation equipment to manage medical emergencies would be readily available.

4.2.1 Posology

The recommended dosage regimen of NAGLAZYME is 1 mg/kg body weight administered once weekly as an intravenous infusion over a period of no less than 4 hours.

4.2.1.1 Special Populations

Renal and Hepatic Impairment
The safety and efficacy of NAGLAZYME in patients with renal or hepatic insufficiency have not been evaluated and no alternative dose regimen can be recommended in these patients

Elderly (Geriatric Use)
The safety and efficacy of NAGLAZYME in patients older than 65 years has not been established, and no alternative dosage regimen can be recommended in these patients. It is not known whether older patients respond differently from younger patients.

Pediatric Use
There is no evidence for special considerations when NAGLAZYME is administered to the pediatric population. However, data from patients ≤ 1 year of age are limited *[see Adverse Reactions (4.8) and Mechanism of Action (5.1)]*.

4.2.2 Method of Administration

NAGLAZYME must be diluted with 0.9% Sodium Chloride Injection, USP to a total volume of 100 mL or 250 mL based on the patient's weight, prior to infusion *[see Dilution and Administration Instructions (6.2.1)]*. Patients who are susceptible to fluid overload or with a body weight of 20 kg or less should receive a total volume of 100 mL. Patients with a body weight greater than 20 kg should receive a total volume of 250 mL.

Adjust the initial infusion rate to allow approximately 2.5% of the total solution to be infused within the first hour. The remaining solution (approximately 97.5%) should be infused over the next three hours.

4.3 Contraindications

Severe or life-threatening hypersensitivity to the active substance or to any of the excipients, if hypersensitivity is not controllable.

4.4 Warnings and Precautions

4.4.1 Spinal or Cervical Cord Compression

Spinal/cervical cord compression (SCC) with resultant myelopathy is a known and serious complication of MPS VI. SCC is expected to occur in the natural history of the disease, including in patients on NAGLAZYME. There have been post-marketing reports of patients treated with NAGLAZYME who experienced the onset or worsening of SCC requiring decompression surgery. Patients with MPS VI should be monitored for signs and symptoms of spinal/cervical cord compression (including back pain, paralysis of limbs below the level of compression, urinary and fecal incontinence) and given appropriate clinical care.

4.4.2 Anaphylaxis and Allergic Reactions

Anaphylaxis and severe allergic reactions have been observed in patients during and up to 24 hours after NAGLAZYME infusion. Some of the reactions were life-threatening and included anaphylaxis, shock, respiratory distress, dyspnea, bronchospasm, laryngeal edema, and hypotension. If anaphylaxis or other severe allergic reactions occur, NAGLAZYME should be immediately discontinued, and appropriate medical treatment should be initiated. 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 infusion.

4.4.3 Immune-mediated Reactions

Type III immune complex-mediated reactions including membranous glomerulonephritis have been observed with NAGLAZYME, as with other enzyme replacement therapies. If immune-mediated reactions occur, discontinuation of the administration of NAGLAZYME should be considered, and appropriate medical treatment initiated. The risks and benefits of re-administering NAGLAZYME following an immune-mediated reaction should be considered. Some patients have successfully been re-challenged and have continued to receive NAGLAZYME under close clinical supervision.

4.4.4 Risk of Acute Cardio-respiratory Failure

Caution should be exercised when administering NAGLAZYME to patients susceptible to fluid volume overload such as in patients weighing 20 kg or less, patients with acute underlying respiratory illness, or patients with compromised cardiac and/or respiratory function, because congestive heart failure may result. Appropriate medical support and monitoring measures should be readily available during NAGLAZYME infusion, and some patients may require prolonged observation times that should be based on the individual needs of the patient.

4.4.5 Acute Respiratory Complications Associated with Administration

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 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.

Consider delaying NAGLAZYME infusions in patients who present with an acute febrile or respiratory illness because of the possibility of acute respiratory compromise during infusion of NAGLAZYME.

4.4.6 Infusion Reactions

Because of the potential for infusion reactions, patients should receive antihistamines with or without antipyretics prior to infusion. Despite routine pretreatment with antihistamines, infusion reactions, some severe, occurred in 33 of 59 (56%) patients treated with NAGLAZYME. Serious adverse reactions during infusion included laryngeal edema, apnea, pyrexia, urticaria, respiratory distress, angioedema, and anaphylactoid reaction. Severe adverse reactions included urticaria, chest pain, rash, dyspnea, apnea, laryngeal edema, and conjunctivitis.

The most common symptoms of drug-related infusion reactions were pyrexia, chills/rigors, rash, urticaria, dyspnea, nausea, vomiting, pruritis, erythema, abdominal pain, hypertension, and headache. Respiratory distress, chest pain, hypotension, angioedema, conjunctivitis, tremor, and cough were also reported. Infusion reactions began as early as Week 1 and as late as Week 146 of NAGLAZYME treatment. Twenty-three of 33 patients (70%) experienced recurrent infusion reactions during multiple infusions though not always in consecutive weeks.

Symptoms typically abated with slowing or temporary interruption of the infusion and administration of additional antihistamines, antipyretics, and occasionally corticosteroids. Most patients were able to complete their infusions. Subsequent infusions were managed with a slower rate of NAGLAZYME administration, treatment with additional prophylactic antihistamines, and, in the event of a more severe reaction, treatment with prophylactic corticosteroids.

If severe infusion reactions occur, immediately discontinue the infusion of NAGLAZYME and initiate appropriate treatment. The risks and benefits of re-administering NAGLAZYME following a severe reaction should be considered.

No factors were identified that predisposed patients to infusion reactions. There was no association between severity of infusion reactions and titer of anti-galsulfase antibodies.

4.5 Interactions with Other Medicinal Products and Other Forms of Interactions

No interaction studies have been performed.

4.6 Fertility, Pregnancy, Lactation, Carcinogenesis, Mutagenesis

4.6.1 Fertility

Reproduction studies have been performed in rats and rabbits at doses up to 3 mg/kg/day and have revealed no evidence of impaired fertility or harm to the embryo or fetus due to NAGLAZYME. *[see Pre-clinical Safety (5.4)]*

4.6.2 Pregnancy

Studies have not been conducted with NAGLAZYME in pregnant women. NAGLAZYME should be used during pregnancy only if clearly needed.

Reproduction studies have been performed in rats at intravenous doses up to 3 mg/kg/day (about 0.5 times the recommended human dose of 1 mg/kg based on the body surface area) and in rabbits at intravenous doses up to 3 mg/kg/day (about 0.97 times the recommended human dose of 1 mg/kg based on the body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to NAGLAZYME.

4.6.3 Lactation

It is not known whether NAGLAZYME is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when NAGLAZYME is administered to a nursing mother.

4.6.4 Carcinogenesis, Mutagenesis

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with NAGLAZYME.

4.7 Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Adverse Reactions

NAGLAZYME was studied in a randomized, double-blind, placebo-controlled trial in which 19 patients received weekly infusions of 1 mg/kg NAGLAZYME and 20 patients received placebo; of the 39 patients, 66% were female, and 62% were white, non-Hispanic. Patients were aged 5 years to 29 years. NAGLAZYME-treated patients were approximately 3 years older than placebo-treated patients (mean age 13.7 years versus 10.7 years, respectively).

Serious adverse reactions experienced in this trial included apnea, pyrexia and respiratory distress. Severe adverse reactions included chest pain, dyspnea, laryngeal edema, and conjunctivitis.

The most common adverse reactions requiring interventions were infusion reactions.

Table 1 summarizes the adverse reactions that occurred in the placebo-controlled trial in at least 2 patients more in the NAGLAZYME treated group than in the placebo-treated group.

Table 1: Adverse Reactions that Occurred in the Placebo-Controlled Trial in at least 2 Patients More in the NAGLAZYME Group than in the Placebo Group

MedDRA Preferred Term	NAGLAZYME (n = 19)	Placebo (n = 20*)
	No. Patients (%)	No. Patients (%)
All	19 (100)	20 (100)
Abdominal Pain	9 (47)	7 (35)
Ear Pain	8 (42)	4 (20)

Arthralgia	8 (42)	5 (25)
Pain	6 (32)	1 (5)
Conjunctivitis	4 (21)	0
Dyspnoea	4 (21)	2 (10)
Rash	4 (21)	2 (10)
Chills/Rigors	4 (21)	0
Chest Pain	3 (16)	1 (5)
Pharyngitis	2 (11)	0
Areflexia	2 (11)	0
Corneal Opacity	2 (11)	0
Gastroenteritis	2 (11)	0
Hypertension	2 (11)	0
Malaise	2 (11)	0
Nasal Congestion	2 (11)	0
Umbilical Hernia	2 (11)	0
Hearing Impairment	2 (11)	0
[*]One of the 20 patients in the placebo group dropped out after Week 4 infusion		

Four open-label clinical trials were conducted in MPS VI patients aged 3 months to 29 years with NAGLAZYME administered at doses of 0.2 mg/kg (n = 2), 1 mg/kg (n = 55), and 2 mg/kg (n = 2). The mean exposure to the recommended dose of NAGLAZYME (1 mg/kg) was 138 weeks (range = 54 to 261 weeks). Two infants (12.1 months and 12.7 months) were exposed to 2 mg/kg of NAGLAZYME for 105 and 81 weeks, respectively.

In addition to those listed in Table 1, common adverse reactions observed in the open-label trials include pruritus, urticaria, pyrexia, headache, nausea, and vomiting. The most common adverse reactions requiring interventions were infusion reactions. Serious adverse reactions included laryngeal edema, urticaria, angioedema, and other allergic reactions. Severe adverse reactions included urticaria, rash, and abdominal pain.

Observed adverse events in four open-label studies (up to 261 weeks treatment) were not different in nature or severity to those observed in the placebo-controlled study. No patients discontinued during open-label treatment with NAGLAZYME due to adverse events.

4.8.1 Immunogenicity

Ninety-eight percent (53/54) of patients treated with NAGLAZYME and evaluable for the presence of antibodies to galsulfase developed anti-galsulfase IgG antibodies within 4 to 8 weeks of treatment (in four clinical studies). In 19 patients treated with NAGLAZYME from the placebo-controlled study, serum samples were evaluated for a potential relationship of anti-galsulfase antibody development to clinical outcome measures. All 19 patients treated with NAGLAZYME developed antibodies specific to galsulfase; 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. Antibodies were assessed for the ability to inhibit enzymatic activity but not cellular uptake.

In some patients higher antibody levels were associated with decreases in complement parameters (C3, C4, and CH50). While this association was observed, there was no association with an increase in adverse events or alteration of the safety profile. Higher antibody levels and decreases in complement parameters were not associated with the development of anaphylactoid reactions during infusion. Decreases in complement parameters were observed intermittently, primarily in the first 24 weeks of treatment, in all 3 clinical studies and in all dose groups, including placebo.

The data reflect the percentage of patients whose test results were considered positive for antibodies to galsulfase using specific assays and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibodies in an assay may be influenced by several factors including sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to galsulfase with the incidence of antibodies to other products may be misleading.

4.8.3. Post-marketing Experience

The following adverse reactions have been identified during post-approval use of NAGLAZYME. *[Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure]*.

In addition to infusion reactions reported in clinical trials, serious reactions that occurred during NAGLAZYME infusion in the worldwide marketing experience include anaphylaxis, shock, hypotension, bronchospasm, and respiratory failure.

Additional infusion reactions included pyrexia, erythema, pallor, bradycardia, tachycardia, hypoxia, cyanosis, tachypnea, and paresthesia.

During postmarketing surveillance, there has been a single report of membranous nephropathy and a small number of thrombocytopenia reports. In a case of membranous nephropathy, renal biopsy revealed galsulfase-immunoglobulin complexes in the glomeruli. With both membranous nephropathy and thrombocytopenia, patients have been successfully re-challenged and have continued to receive NAGLAZYME.

4.9 Overdose

Several patients have received their total dose of Naglazyme at approximately twice the recommended infusion rate without apparent adverse events.

5 PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Mucopolysaccharide storage disorders are caused by the deficiency of specific lysosomal enzymes required for the catabolism of glycosaminoglycan (GAG). MPS VI is characterized by the absence or marked reduction in N–acetylgalactosamine 4-sulfatase. The sulfatase activity deficiency results in the accumulation of the GAG substrate, dermatan sulfate, throughout the body. This accumulation leads to widespread cellular, tissue, and organ dysfunction. NAGLAZYME is intended to provide an exogenous enzyme that will be taken up into lysosomes and increase the catabolism of GAG. Galsulfase uptake by cells into lysosomes is most likely mediated by the binding of mannose-6-phosphate-terminated oligosaccharide chains of galsulfase to specific mannose-6-phosphate receptors.

Clinical efficacy

A total of 56 patients with MPS VI, ages 5 years to 29 years, were enrolled in three clinical studies. The majority of patients had severe manifestations of the disease as evidenced by poor performance on a test of physical endurance.

Study ASB-03-05

In the randomized, double-blind, multicenter, placebo-controlled Phase III clinical study, 39 patients, aged 5 years to 29 years, with MPS VI received 1 mg/kg NAGLAZYME or placebo, once-weekly for 24 weeks. The primary efficacy endpoint was the number of meters walked in 12 minutes at Week 24 compared to the number of meters walked at baseline. Enrollment was restricted to patients who could walk more than 5 meters but less than 250 meters in 6 minutes of a 12-minute walk test (12-MWT) or no more than 400 meters at the 12-minute time point at baseline, (Table 2). All patients were treated with antihistamines prior to each infusion. The secondary efficacy endpoints were the rate of stairs climbed in three minutes and the urinary glycosaminoglycan (GAG) excretion of treated patients compared to placebo at Week 24 (Table 2).

The NAGLAZYME-treated group showed greater mean increase in the distance walked in 12 minutes (12-MWT) compared with the placebo group. Treated patients experienced a 5.7 stair per minute improvement in the 3 Minute Stair Climb relative to placebo-treated patients (Table 2). Treated patients also experienced a mean decrease in urinary GAG excretion of 238 ± 17.8 μg/mg creatinine (± Standard Error [SE]) following 24 weeks of treatment relative to placebo-treated patients. GAG results approached the normal range for age in the NAGLAZYME-treated group.

Table 2: Results from Placebo-Controlled Clinical Study (Study ASB-03-05)

	NAGLAZYME			Placebo			NAGLAZYME vs. Placebo
	Baseline	**Week 24**	**Change**	**Baseline**	**Week 24**	**Change**	**Difference in Changes**
N	19	19	19	20	19*	19	
Results from the 12-Minute Walk Test (Meters)							
Mean ± SD	227 ± 170	336 ± 227	109 ± 154	381 ± 202	399 ± 217	26 ± 122	83 ± 45† 92 ± 40‡ (p = 0.025)‡,§
Median Percentiles (25th, 75th)	210 90, 330	316 125, 483	48 7, 183	365 256, 560	373 204, 573	34 –3, 89	
Results from 3-Minute Stair Climb Test (Stairs/Minute)							
Mean ± SD	19.4 ± 12.9	26.9 ± 16.8	7.4 ± 9.9	31.0 ± 18.1	32.6 ± 19.6	2.7 ± 6.9	4.7 ± 2.8† 5.7 ± 2.9‡ (p = 0.053)‡,§
Median Percentiles (25th, 75th)	16.7 10.0, 26.3	22.8 14.8, 33.0	5.2 2.2, 9.9	24.7 18.1, 51.5	29.0 14.2, 57.9	4.3 1.0, 6.2	

* One patient in the placebo group dropped out after 4 weeks of infusion
† Observed mean of NAGLAZYME - Placebo ± SE
‡ Model-based mean of NAGLAZYME - Placebo ± SE, adjusted for baseline
§ p-value based on the model-based mean difference

Study ASB-03-06

Following the 24-week placebo-controlled study period, 38 patients from study ASB-03-05 received open-label NAGLAZYME for 72 weeks. Among the 19 patients who were initially randomized to NAGLAZYME and who continued to receive treatment for 72 weeks (total of 96 weeks), increases in the 12-MWT distance and in the rate of stair climbing were observed, compared to the start of the open-label period (mean [± SD] change): 72 ± 116 meters and 5.6 ± 10.6 stairs/minute, respectively). Among the 19 patients who were randomized initially to placebo for 24 weeks, and then crossed over to treatment with NAGLAZYME, the increases after 72 weeks of NAGLAZYME treatment compared to the start of the open-label period, (mean [± SD] change): were 118 ± 127 meters and 11.1 ± 10.0 stairs/minute, for the 12-MWT and the rate of stair climbing, respectively.

Bioactivity was evaluated with urinary GAG concentration. Overall, 95% of patients showed at least a 50% reduction in urinary GAG levels after 72 weeks of treatment with NAGLAZYME. No patient receiving NAGLAZYME reached the normal range for urinary GAG levels.

Study ASB-008

In an additional Phase 4, randomized, two-dose level study, four MPS VI patients <1 year of age were treated at 1 or 2 mg/kg/week for 53 to 153 weeks. Safety results in infants were consistent with results observed in patients 5 to 29 years old *(see Adverse Reactions 4.8).*

5.2 Pharmacodynamic Properties

The responsiveness of urinary GAG to dosage alterations of NAGLAZYME is unknown, and the relationship of urinary GAG to other measures of clinical response has not been established. No association was observed between antibody development and urinary GAG levels.

5.3 Pharmacokinetic Properties

The pharmacokinetic parameters of NAGLAZYME were evaluated in 13 patients with MPS VI who received 1 mg/kg of NAGLAZYME as a weekly 4-hour infusion for 24 weeks. The pharmacokinetic parameters at Week 1 and Week 24 are shown in Table 3.

Table 3: Pharmacokinetic Parameters (Median, Range)

Pharmacokinetic Parameter	Week 1	Week 24
C_{max} (mcg/mL)	0.8 (0.4 to 1.3)	1.5 (0.2 to 5.5)
AUC_{0-t} (hr•mcg/mL)*	2.3 (1.0 to 3.5)	4.3 (0.3 to 14.2)
Vz (mL/kg)	103 (56 to 323)	69 (59 to 2,799)
CL (mL/kg/min)	7.2 (4.7 to 10.5)	3.7 (1.1 to 55.9)
Half-life (min)	9 (6 to 21)	26 (8 to 40)
* Area under the plasma galsulfase concentration-time curve from start of infusion to 60 minutes post infusion.		

Galsulfase pharmacokinetic parameters listed in Table 3 require cautious interpretation because of large variability. Development of anti-galsulfase antibodies appears to affect galsulfase pharmacokinetics, however, the data are limited.

Nearly all patients who receive treatment with NAGLAZYME develop antibodies to galsulfase. Of 30 patients with MPS VI who received weekly NAGLAZYME infusions and had pharmacokinetics evaluated, 29 developed antibodies to galsulfase. Four patients with high antibody titres had decreases in plasma AUC between Weeks 1 and 24. One patient with high antibody titres had an increase in plasma AUC between Weeks 1 and 24.

5.4 Preclinical Safety

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, single-dose toxicity, repeated-dose toxicity or on general reproductive performance or embryo-fetal development in rats or rabbits. Peri- and post-natal toxicity have not been investigated. Genotoxic and carcinogenic potential are not expected.

The clinical relevance of the hepatic toxicity (bile duct hyperplasia / periportal inflammation) seen at clinically relevant doses in the repeated dose monkey toxicity study is not known.

6 PHARMACEUTICAL PARTICULARS

6.1 Shelf Life and Storage Conditions

Unopened vials: 3 years.

Diluted solutions:

From a microbiological safety point of view, Naglazyme should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and should normally not be longer than 24 hours at 2°C - 8°C followed by up to 24 hours at room temperature (23°C - 27°C) including administration.

Store in a refrigerator (2°C - 8°C).

Do not freeze or shake.

6.2 Handling and Use

6.2.1 Dilution and Administration Instructions

Each vial of Naglazyme is intended for single use only.
Naglazyme must be diluted with sodium chloride 9 mg/mL (0.9%) solution prior to administration. The number of Naglazyme vials to be diluted is based on the individual patient's weight. The recommended dose of Naglazyme is 1 mg/kg.

<u>Prepare Naglazyme using aseptic technique according to the following steps.</u>

1. Remove vials from the refrigerator approximately 20 minutes in advance in order to allow them to reach room temperature.
2. Obtain an infusion bag containing 9 mg/mL (0.9%) sodium chloride solution suitable for IV administration. The total volume of the infusion is determined by the patient's body weight.
    1. Patients who are susceptible to fluid overload or with a body weight of 20kg or less should receive a total volume of 100 mL.
    2. Patients with a body weight greater than 20 kg should receive a total volume of 250 mL.
    3. Determine the number of vials to be diluted based on the individual patient's weight and the recommended dose of 1 mg/kg, using the following equation:
        - Patient's weight (kg) x 1 mg/kg /(1 mg/mL concentrate of Naglazyme) = Total # mL of Naglazyme, then
        - Total # of mL of Naglazyme ÷ 5 mL per Vial = Total # of vials.

3. Before withdrawing Naglazyme from the vial, visually inspect each vial for particulate matter and discoloration. The Naglazyme solution should be clear to slightly opalescent and colorless to pale yellow. Do not use if the solution is discolored or if there is particulate matter in the solution.
4. Withdraw and discard a volume of the 9 mg/mL (0.9%) sodium chloride solution from the infusion bag, equal to the volume of Naglazyme concentrate to be added. When using 100 mL infusion bags, the volume of Naglazyme may be added directly to the infusion bag.
5. Slowly withdraw the calculated volume of Naglazyme from the appropriate number of vials using caution to avoid excessive agitation. Do not use a filter needle, as this may cause agitation. Agitation may denature Naglazyme, rendering it biologically inactive.
6. Slowly add Naglazyme to the 9 mg/mL (0.9%) sodium chloride solution using care to avoid agitation.
7. Gently rotate the infusion bag to ensure proper distribution of Naglazyme. Do not shake the solution.

6.2.2 Special Precautions for Disposal and Other Handling

Any unused product or waste material is to be disposed of in accordance with local requirements.

6.3 List of Excipients

Sodium chloride
Sodium phosphate monobasic, monohydrate
Sodium phosphate dibasic, heptahydrate
Polysorbate 80
Water for injection

6.4 Incompatibilities

This medicinal product must not be mixed with other medicinal products except with sodium chloride solution 9 mg/mL (0.9%).

6.5 Nature and Contents of Container

Vial (type I glass) with a stopper (siliconized chlorobutyl rubber) and a seal (aluminium) with a flip-off cap (polypropylene).

Pack sizes: 1 and 6 vials.
Not all package sizes may be marketed.

7. PRODUCT OWNER

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