Pharmacode

Cerezyme® 400 U

Imiglucerase for Injection
Powder for concentrate for solution for infusion

genzyme A SANOFI COMPANY sanofi

1. NAME OF THE MEDICINAL PRODUCT

Cerezyme 400 U Powder for concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 400 units* of imiglucerase**.
After reconstitution, the solution contains 40 units (approximately 1.0 mg) of imiglucerase per ml (400 U/10 ml).

* An enzyme unit (U) is defined as the amount of enzyme that catalyses the hydrolysis of one micromole of the synthetic substrate para-nitrophenyl ß-D-glucopyranoside (pNP-Glc) per minute at 37°C.
** Imiglucerase is a modified form of human acid ß-glucosidase and is produced by recombinant DNA technology using a mammalian Chinese Hamster Ovary (CHO) cell culture, with mannose modification for targeting macrophages.

Excipients:
For a full list of excipients, see section 6.1.
This medicinal product contains sodium and is administered in 0.9% sodium chloride intravenous solution (see section 6.6). After reconstitution, the solution contains 1.24 mmol sodium (400 U/10 mL). To be taken into consideration by patients on a controlled sodium diet.

3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion.
Cerezyme is a white to off-white powder.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that result in one or more of the following conditions:
a. Anaemia after exclusion of other causes, such as iron deficiency
b. Thrombocytopenia
c. Bone disease after exclusion of other causes such as Vitamin D deficiency
d. Hepatomegaly or splenomegaly

4.2 Posology and method of administration

Disease management should be directed by physicians knowledgeable in the treatment of Gaucher disease.

Posology
Due to the heterogeneity and the multi-systemic nature of Gaucher disease, dosage should be individualised for each patient based on a comprehensive evaluation of all clinical manifestations of the disease. Once individual patient response for all relevant clinical manifestations is well-established, dosages and frequency of administration may be adjusted with the goal to either maintain already reached optimal parameters for all clinical manifestations or further improve those clinical parameters which have not yet been normalised.

A range of dosage regimens has proven effective towards some or all of the non-neurological manifestations of the disease. Initial doses of 60 U/kg of body weight once every 2 weeks have shown improvement in haematological and visceral parameters within 6 months of therapy and continued use has either stopped progression of or improved bone disease. Administration of doses as low as 15 U/kg of body weight once every 2 weeks has been shown to improve haematological parameters and organomegaly, but not bone parameters. The usual frequency of infusion is once every 2 weeks; this is the frequency of infusion for which the most data are available.

Paediatric population
No dose adjustment is necessary for the paediatric population.

The efficacy of Cerezyme on neurological symptoms of chronic neuronopathic Gaucher patients has not been established and no special dosage regimen can be recommended for these manifestations (see section 5.1).

Method of Administration
After reconstitution and dilution, the preparation is administered by intravenous infusion. At initial infusions, Cerezyme should be administered at a rate not exceeding 0.5 unit per kg body weight per minute. At subsequent administrations, infusion rate may be increased but should not exceed 1 unit per kg body weight per minute. Infusion rate increases should occur under supervision of a health care professional.

Infusion of Cerezyme at home may be considered for patients who are tolerating their infusions well for several months. Decision to have patient move to home infusion should be made after evaluation and recommendation by the treating physician. Infusion of Cerezyme by the patient or caregiver at home requires training by a health care professional in a clinical setting. The patient or caregiver will be instructed in infusion technique and the keeping of a treatment diary. Patients experiencing adverse events during the infusion need to immediately **stop the infusion process and** seek the attention of a healthcare professional. Subsequent infusions may need to occur in a clinical setting. Dose and infusion rate should remain constant while at home, and not be changed without supervision of a health care professional.
For instructions on reconstitution and dilution of the medicinal product before administration, see section 6.6.
Medical or healthcare professionals are encouraged to register Gaucher patients, including those with chronic neuronopathic manifestations of the disease, in the "ICGG Gaucher Registry" (see section 5.1).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients (see section 4.4).

4.4 Special warnings and precautions for use

Hypersensitivity
Current data using a screening ELISA followed by a confirmatory radioimmunoprecipitation assay, suggest that, during the first year of therapy, IgG antibodies to imiglucerase are formed in approximately 15% of the treated patients. It appears that patients who will develop IgG antibody are most likely to do so within 6 months of treatment and will rarely develop antibodies to Cerezyme after 12 months of therapy.

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It is suggested that patients suspected of a decreased response to the treatment be monitored periodically for IgG antibody formation to imiglucerase.

Patients with antibody to imiglucerase have a higher risk of hypersensitivity reactions (see section 4.8). If a patient experiences a reaction suggestive of hypersensitivity, subsequent testing for imiglucerase antibodies is advised. As with any intravenous protein product, severe allergic-type hypersensitivity reactions are possible, but occur uncommonly. If these reactions occur, immediate discontinuation of the Cerezyme infusion is recommended and appropriate medical treatment should be initiated. The current medical standards for emergency treatment are to be observed.

Patients who have developed antibodies or symptoms of hypersensitivity to Ceredase (alglucerase) should be treated with caution when administering Cerezyme (imiglucerase).

Excipients
This medicinal product contains sodium and is administered in 0.9% sodium chloride intravenous solution (see section 6.6). To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Limited experience from 150 pregnancy outcomes (primarily based on spontaneous reporting and literature review) is available suggesting that use of Cerezyme is beneficial to control the underlying Gaucher disease in pregnancy. Furthermore, these data indicate no malformative toxicity for the foetus by Cerezyme, although the statistical evidence is low. Foetal demise has been reported rarely, although it is not clear whether this related to the use of Cerezyme or to the underlying Gaucher disease.

No animal studies have been carried out with respect to assessing the effects of Cerezyme on pregnancy, embryonal/foetal development, parturition and postnatal development. It is not known whether Cerezyme passes via the placenta to the developing foetus.

In pregnant Gaucher patients and those intending to become pregnant, a risk-benefit treatment assessment is required for each pregnancy. Patients who have Gaucher disease and become pregnant may experience a period of increased disease activity during pregnancy and the puerperium. This includes an increased risk of skeletal manifestations, exacerbation of cytopenia, haemorrhage, and an increased need for transfusion. Both pregnancy and lactation are known to stress maternal calcium homeostasis and to accelerate bone turnover. This may contribute to skeletal disease burden in Gaucher disease.

Treatment naïve women should be advised to consider commencing therapy prior to conception in order to attain optimal health. In women receiving Cerezyme treatment continuation throughout pregnancy should be considered. Close monitoring of the pregnancy and clinical manifestations of Gaucher disease is necessary for the individualization of dose according to the patient's needs and therapeutic response.

Breast-feeding
It is not known whether this active substance is excreted in human milk, however, the enzyme is likely to be digested in the child's gastrointestinal tract

4.7 Effects on ability to drive and use machines

Cerezyme has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse drug reactions are listed by system organ class and frequency (common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and rare (≥1/10,000 to <1/1,000)) in the table below. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness.

Nervous system disorders	Uncommon:	Dizziness, headache, paraesthesia*
Cardiac disorders	Uncommon:	Tachycardia*, cyanosis*
Vascular disorders	Uncommon:	Flushing*, hypotension*
Respiratory, thoracic and mediastinal disorders	Common:	Dyspnoea*, coughing*
Gastrointestinal disorders	Uncommon:	Vomiting, nausea, abdominal cramping, diarrhoea
Immune system disorders	Common: Rare:	Hypersensitivity reactions Anaphylactoid reactions
Skin and subcutaneous tissue disorders	Common:	Urticaria/angioedema*, pruritus*, rash*
Musculoskeletal and connective tissue disorders	Uncommon:	Arthralgia, backache*
General disorders and administration site conditions	Uncommon:	Infusion site discomfort, infusion site burning, infusion site swelling, injection site sterile abscess, chest discomfort*, fever, rigors, fatigue

Symptoms suggestive of hypersensitivity (* marked in the table above) have been noted, overall in approximately 3% of the patients. Onset of such symptoms has occurred during or shortly after infusions. These symptoms generally respond to treatment with antihistamines and/or corticosteroids. Patients should be advised to discontinue infusion of the product and contact their physician if these symptoms occur.

4.9 Overdose

No case of overdose has been reported. In patients dosages up to 240 U/kg body weight once every two weeks have been used.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Enzymes-Imiglucerase (recombinant macrophage targeted ß-glucocerebrosidase), ATC code: A16AB02.

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Cerezyme® 400 U

Imiglucerase untuk Injeksi Serbuk untuk larutan konsentrat untuk infus

genzyme A SANOFI COMPANY sanofi

Bacalah seluruh leaflet ini dengan seksama sebelum Anda mulai menggunakan obat ini karena mengandung informasi penting untuk Anda.
- Simpan leaflet ini. Anda mungkin perlu untuk membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker Anda.
- Obat ini telah diresepkan untuk Anda. Jangan diberikan kepada orang lain. Hal ini dapat membahayakan mereka, meskipun gejala yang mereka dan Anda alami sama.
- Jika salah satu efek samping menjadi semakin serius, atau jika Anda menyadari efek samping apapun yang tidak tercantum dalam leaflet ini, hubungi dokter atau apoteker Anda.

Apa saja informasi dalam lembaran ini:
1. Apa itu Cerezyme dan apa kegunaannya.
2. Sebelum Anda menggunakan Cerezyme.
3. Aturan pakai Cerezyme.
4. Efek samping yang mungkin timbul.
5. Cara menyimpan Cerezyme.
6. Informasi lebih lanjut

1. APA ITU CEREZYME DAN APA KEGUNAANNYA

Cerezyme digunakan untuk mengobati pasien yang telah dipastikan menderita penyakit Gaucher Type I, yang mengalami gejala penyakit tersebut, misalnya:
- anemia (rendahnya jumlah sel darah merah) setelah menyingkirkan penyebab lain misalnya kekurangan besi,
- kekurangan keping darah / trombosit yang mengakibatkan kecenderungan mudah berdarah
- kelainan tulang, setelah menyingkirkan penyebab lain seperti kekurangan vitamin D
- pembesaran limpa atau hati atau pembesaran hati.

Penderita penyakit Gaucher memiliki kekurangan enzim yang disebut *acid ß-glucosidase*. Enzim ini membantu tubuh mengendalikan tingkat glucosylceramide. Glucosylceramide adalah zat alami dalam tubuh, terbuat dari gula dan lemak. Pada penyakit Gaucher tingkat glucosylceramide dapat menjadi sangat tinggi.

Cerezyme adalah enzim buatan yang disebut imiglucerase –yang dapat menggantikan enzim alami acid ß-glucosidase yang kurang atau tidak cukup aktif pada pasien yang menderita penyakit Gaucher.

Informasi dalam leaflet ini berlaku untuk seluruh kelompok pasien termasuk anak-anak, remaja, dewasa dan orang tua.

2. SEBELUM ANDA MENGGUNAKAN CEREZYME
Jangan gunakan Cerezyme
- Jika Anda alergi (hipersensitif) terhadap imiglucerase, atau
- Jika Anda alergi terhadap salah satu bahan lain dari Cerezyme.

Perhatian khusus menggunakan Cerezyme
- Jika Anda sedang menjalani pengobatan dengan Cerezyme, Anda mungkin mengalami reaksi alergi saat Anda diberi obat atau tidak lama sesudahnya. Jika Anda mengalami reaksi seperti ini, **segera hubungi dokter Anda.** Dokter mungkin akan memeriksa apakah Anda memiliki reaksi alergi terhadap imiglucerase.
- Beberapa pasien yang menderita penyakit Gaucher memiliki tekanan darah tinggi di paru-paru (hipertensi pulmonal). Penyebabnya dapat tidak diketahui, atau dapat disebabkan masalah jantung, paru-paru atau hati. Hal ini dapat terjadi terlepas dari apakah pasien sedang menjalani pengobatan dengan Cerezyme atau tidak. Tetapi jika Anda menderita **sesak napas**, Anda harus menghubungi dokter Anda.

Menggunakan obat-obatan lain
Hubungi dokter atau apoteker Anda jika Anda akan atau belum lama ini menggunakan obat lain, termasuk obat-obatan yang diperoleh tanpa resep.

Cerezyme tidak boleh diberikan sebagai campuran dengan produk obat lainnya dalam infus yang sama (tetes).

Kehamilan dan menyusui
Konsultasikan dengan dokter atau apoteker Anda sebelum menggunakan obat ini jika Anda sedang hamil atau berpikir Anda mungkin sedang hamil. Disarankan agar berhati-hati dalam menggunakan Cerezyme selama kehamilan dan menyusui.

Informasi penting tentang beberapa bahan Cerezyme
Produk obat ini mengandung natrium dan diberikan dalam larutan intravena natrium klorida 0,9%. Untuk dipertimbangkan oleh pasien yang sedang menjalani diet natrium terkontrol.

3. CARA MENGGUNAKAN CEREZYME

Petunjuk penggunaan yang benar
Cerezyme diberikan melalui infus ke dalam pembuluh darah (melalui infus intravena).

Tersedia dalam bentuk serbuk yang akan dicampur dengan cairan steril sebelum diberikan.

Cerezyme hanya boleh digunakan dalam pengawasan dokter yang memiliki pengetahuan luas dalam pengobatan penyakit Gaucher. Dokter Anda mungkin akan mengijinkan Anda menjalani rawat jalan jika Anda memenuhi beberapa kriteria tertentu. Hubungi dokter Anda jika Anda ingin menjalani rawat jalan.

Dosis Anda akan dibuat khusus untuk Anda. Dokter akan meresepkan dosis Anda berdasarkan seberapa parah gejala Anda, dan faktor-faktor lainnya. Dosis Cerezyme yang dianjurkan adalah 60 unit/kg berat badan diberikan setiap 2 minggu sekali.

Dokter Anda akan memantau ketat respon tubuh Anda terhadap pengobatan yang dijalani, dan dapat merubah dosis (menaikkan atau menurunkan) sampai dokter menemukan dosis terbaik untuk mengendalikan gejala yang Anda alami.

Setelah menemukan dosis yang tepat, dokter tetap akan memeriksa respon tubuh Anda untuk memastikan Anda menggunakan dosis yang tepat. Ini mungkin perlu dilakukan setiap 6 sampai 12 bulan.

Tidak ada informasi mengenai pengaruh Cerezyme pada gejala-gejala terhadap otak pada pasien yang menderita penyakit Gaucher neuronopathic kronis. Oleh karena itu tidak ada regimen dosis tertentu yang dapat direkomendasikan.

ICGG Gaucher Registry
Anda dapat meminta dokter Anda untuk mendaftarkan informasi pasien ke "ICGG Gaucher Registry". Tujuan dari Registry ini adalah untuk meningkatkan pemahaman tentang penyakit Gaucher dan untuk memeriksa seberapa baik terapi penggantian enzim itu bekerja, seperti Cerezyme. Hal ini tentunya akan meningkatkan keamanan dan efektivitas Cerezyme. Data Anda sebagai pasien akan didaftarkan secara anonim - tidak seorang pun akan tahu itu adalah informasi tentang Anda.

Jika Anda menggunakan Cerezyme lebih dari yang seharusnya

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Tidak ada laporan kasus overdosis Cerezyme.

Jika Anda lupa menggunakan Cerezyme
Jika Anda telah melewatkan jadwal infus, hubungi dokter Anda.

Jika Anda memiliki pertanyaan lebih lanjut mengenai penggunaan produk ini, hubungi dokter atau apoteker Anda.

4. KEMUNGKINAN EFEK SAMPING

Sebagaimana halnya dengan semua obat-obatan, Cerezyme dapat menyebabkan efek samping, namun tidak semua orang mengalaminya.

Jika Anda mengalami efek samping yang serius atau efek samping yang tidak tercantum di bawah ini, **segera hubungi dokter Anda.**

Efek samping yang lazim (terjadi pada lebih dari 1 dalam 100 pasien) adalah:
- Sesak napas
- Batuk
- Gatal-gatal/pembengkakan lokal dari kulit atau selaput mulut atau tenggorokan
- Gatal
- Ruam

Efek samping yang jarang (terjadi pada lebih dari 1 dalam 1000 pasien) adalah:
- Pusing
- Sakit kepala
- Sensasi kesemutan, seperti ditusuk-tusuk, seperti terbakar atau mati rasa pada kulit
- Peningkatan denyut jantung
- Kulit kebiruan
- Kulit memerah
- Penurunan tekanan darah
- Muntah
- Mual
- Kram perut
- Diare
- Nyeri pada sendi
- Ketidaknyamanan pada lokasi infus
- Sensasi seperti terbakar pada lokasi infus
- Pembengkakan pada lokasi infus
- Abses steril pada lokasi infus
- Dada terasa nyeri
- Demam
- Kaku
- Kelelahan
- Sakit punggung

Beberapa efek samping terlihat terutama ketika pasien diberi obat tersebut atau tidak lama sesudahnya. Hal ini termasuk gatal, kemerahan, gatal-gatal/pembengkakan lokal pada kulit atau selaput mulut atau tenggorokan, dada terasa nyeri, peningkatan denyut jantung, kulit kebiruan, sesak napas, sensasi kesemutan, seperti ditusuk-tusuk, seperti terbakar atau mati rasa pada kulit, penurunan tekanan darah dan sakit punggung. Jika Anda mengalami gejala-gejala tersebut, **segera hubungi dokter Anda.** Anda mungkin perlu diberi obat tambahan untuk mencegah reaksi alergi (misalnya antihistamin dan/atau kortikosteroid).

Jika salah satu efek samping tersebut menjadi serius, atau jika Anda menyadari ada efek samping yang tidak tercantum dalam leaflet ini, hubungi dokter atau apoteker Anda.

5. CARA MENYIMPAN CEREZYME

Jauhkan dari jangkauan dan penglihatan anak-anak.

Jangan gunakan Cerezyme setelah tanggal kadaluwarsa yang tercetak pada label setelah huruf "EXP". Tanggal kadaluwarsa mengacu pada tanggal terakhir dari bulan itu.

Vial yang belum dibuka:
Simpan di lemari pendingin (2°C - 8°C)

Larutan yang diencerkan:
Disarankan agar Cerezyme segera digunakan setelah dicampur dengan cairan steril. Larutan campuran dalam vial tersebut tidak boleh disimpan dan harus segera diencerkan dalam kantong infus; hanya larutan yang telah diencerkan dapat bertahan hingga 24 jam jika disimpan di tempat yang dingin (2°C - 8°C) dan dalam gelap.

Obat tidak boleh dibuang melalui air limbah atau sampah rumah tangga. Konsultasikan kepada apoteker Anda bagaimana cara
membuang obat-obatan yang tidak diperlukan lagi. Langkah-langkah ini dapat melestarikan lingkungan.

6. INFORMASI LEBIH LANJUT

Apa yang terkandung dalam Cerezyme
- Zat aktif imiglucerase. Imiglucerase adalah bentuk modifikasi dari enzim manusia acid ß-glucosidase yang dihasilkan oleh teknologi DNA rekombinan. Satu vial mengandung 400 unit imiglucerase. Setelah dilarutkan, larutan tersebut mengandung 40 unit imiglucerase per ml.
- Bahan-bahan lain:
- Mannitol, Natrium sitrat, asam sitrat monohydrate, Polysorbate 80

Seperti apa bentuk Cerezyme dan isi kemasannya
Cerezyme, 400 U, tersedia dalam bentuk serbuk sebagai konsentrat untuk larutan infus (dalam vial- ukuran kemasan 1, 5 atau 25). Tidak semua ukuran kemasan dapat dipasarkan.

Cerezyme tersedia dalam bentuk serbuk yang berwarna putih hingga putih pudar. Setelah dilarutkan menjadi jernih, cairan yang tidak berwarna, bebas dari partikel asing. Larutan yang telah direkonstitusi tersebut harus diencerkan lebih lanjut.

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

Diproduksi Oleh:
Genzyme Irlandia Limited,
Waterford - Irlandia

Dikemas & Dirilis Oleh:
Genzyme Corporation
Northborough - MA 01532 USA

Didaftarkan Oleh:
PT Kalventis Sinergi Farma,
Jakarta-Indonesia

PRESENTASI
Cerezyme® 400 unit
Box, 1 vial @ 424 unit imiglucerase
Reg.No .: DKI1745300280A1

Cerezyme® adalah merek dagang terdaftar dari Genzyme Corporation.

Gaucher disease is a rare recessively inherited metabolic disorder that results from a deficiency of the lysosomal enzyme acid ß-glucosidase. This enzyme breaks down glucosylceramide, a key component of the lipid structure of cell membranes, into glucose and ceramide. In individuals with Gaucher disease, glucosylceramide degradation is insufficient, leading to accumulation of large quantities of this substrate within the lysosomes of macrophages (termed 'Gaucher cells'), leading to widespread secondary pathology.

Gaucher cells are typically found in liver, spleen and bone marrow and occasionally in lung, kidney and intestine. Clinically, Gaucher disease is a heterogeneous phenotypic spectrum. The most frequent disease manifestations are hepatosplenomegaly, thrombocytopenia, anaemia, and skeletal pathology. The skeletal abnormalities are frequently the most debilitating and disabling features of Gaucher disease. These skeletal manifestations include bone marrow infiltration, osteonecrosis, bone pain and bone crises, osteopenia and osteoporosis, pathological fractures, and growth impairment. Gaucher disease is associated with increased glucose production and increased resting energy expenditure rate, which may contribute to fatigue and cachexia. Patients with Gaucher disease may also have a low grade inflammatory profile. In addition, Gaucher disease has been associated with an increased risk of immunoglobulin abnormalities such as hyperimmunoglobulinemia, polyclonal gammopathy, monoclonal gammopathy of undetermined significance (MGUS) and multiple myeloma. The natural history of Gaucher disease usually shows progression, with the risk of irreversible complications arising in various organs over time. The clinical manifestations of Gaucher disease can adversely affect quality of life. Gaucher disease is associated with increased morbidity and early mortality.
Signs and symptoms presenting in childhood typically represent more severe Gaucher disease. In children, Gaucher disease can lead to growth retardation and delayed puberty.

Pulmonary hypertension is a known complication of Gaucher disease. Patients who have undergone a splenectomy have an increased risk of pulmonary hypertension. Cerezyme therapy reduces the requirement for splenectomy in most cases and early treatment with Cerezyme has been associated with a reduced risk of pulmonary hypertension. Routine evaluation to detect the presence of pulmonary hypertension after diagnosis of Gaucher disease and over time is recommended. Patients diagnosed with pulmonary hypertension, in particular, should receive adequate doses of Cerezyme to ensure control of underlying Gaucher disease as well as be evaluated for the need of additional pulmonary hypertension specific treatments.

Imiglucerase (recombinant macrophage targeted acid ß-glucosidase) replaces the deficient enzyme activity, hydrolysing glucosylceramide, thus correcting initial pathophysiology and preventing secondary pathology. Cerezyme reduces spleen and liver size, improves or normalises thrombocytopenia and anaemia, improves or normalises bone mineral density and bone marrow burden, and reduces or eliminates bone pain and bone crises. Cerezyme reduces resting energy expenditure rate. Cerezyme has been shown to improve both mental and physical aspects in the quality of life of Gaucher disease. Cerezyme decreases chitotriosidase, a biomarker for glucosylceramide accumulation in macrophages and response to treatment. In children, Cerezyme has been shown to enable normal pubertal development, and to induce catch-up growth, leading to normal height and bone mineral density in adulthood.

The rate and extent of response to Cerezyme treatment is dose-dependent. Generally, improvements in organ systems with a faster turnover rate, such as the haematological, can be noted far more rapidly than in those with a slower turnover, such as the bone.
In an ICGG Gaucher Registry analysis of a large cohort of patients (n=528) with Gaucher disease type 1, a time- and dose-dependent effect for Cerezyme was observed for haematological and visceral parameters (platelet count, haemoglobin concentration, spleen and liver volume) within the dose range of 15, 30 and 60 U/kg body weight once every 2 weeks. Patients treated with 60 U/kg body weight every 2 weeks showed a faster improvement and a greater maximum treatment effect as compared to patients receiving the lower doses.

Similarly, in an ICGG Gaucher Registry analysis of bone mineral density using dual-energy X-ray absorptiometry (DXA) in 342 patients, after 8 years of treatment normal bone mineral density was achieved with a Cerezyme dose of 60 U/kg body weight once every 2 weeks, but not with lower doses of 15 and 30 U/kg body weight once every 2 weeks (Wenstrup et al, 2007).

In a study investigating 2 cohorts of patients treated with a median dose of 80 U/kg body weight every 4 weeks and a median dose of 30 U/kg body weight every 4 weeks, among the patients with bone marrow burden score ≥ 6, more patients in the higher dose cohort (33%; n=22) achieved a decrease in the score of 2 points after 24 months of Cerezyme treatment compared with patients in the lower dose cohort (10%; n=13) (de Fost, 2006).

Treatment with Cerezyme at a dose of 60 U/kg body weight once every 2 weeks, showed improvement in bone pain as early as 3 months, decrease in bone crises within 12 months, and improvement in bone mineral density after 24 months of treatment (Sims et al, 2008).

The usual frequency of infusion is once every 2 weeks (see section 4.2). Maintenance therapy every 4 weeks (Q4) at the same cumulative dose as the bi-weekly (Q2) dose has been studied in adult patients with stable residual Gaucher disease type 1. Changes from baseline in hemoglobin, platelets, liver and spleen volumes, bone crisis, and bone disease comprised a predefined composite endpoint; achievement or maintenance of established Gaucher disease therapeutic goals for the hematologic and visceral parameters comprised an additional endpoint. Sixty-three percent of Q4- and 81% of Q2-treated patients met the composite endpoint at Month 24; the difference was not statistically significant based on the 95% CI (-0.357, 0.058). Eighty-nine percent of Q4- and 100% of Q2-treated patients met the therapeutic goals-based endpoint; the difference was not statistically significant based on the 95% CI (-0.231, 0.060). A Q4 infusion regimen may be a therapeutic option for some adult patients with stable residual Gaucher disease type 1, but clinical data are limited.

No controlled clinical studies have been conducted on the efficacy of Cerezyme on neurological manifestations of the disease. Therefore no conclusions on the effect of enzyme replacement therapy on the neurological manifestations of the disease can be drawn.

Medical or healthcare professionals are encouraged to register Gaucher patients, including those with chronic neuronopathic manifestations of the disease, in the "ICGG Gaucher Registry". Patient data will be anonymously collected in this Registry. The objectives of the "ICGG Gaucher Registry" are to enhance the understanding of Gaucher disease and to evaluate the effectiveness of enzyme replacement therapy, ultimately leading to improvement in the safe and efficacious use of Cerezyme.

5.2 Pharmacokinetic properties

During 1 hour intravenous infusions of 4 doses (7.5, 15, 30, 60 U/kg) of imiglucerase, steady-state enzymatic activity was achieved by 30 minutes. Following infusion, plasma enzymatic activity declined rapidly with a half-life ranging from 3.6 to 10.4 minutes. Plasma clearance ranged from 9.8 to 20.3 ml/min/kg, (mean ± S.D, 14.5 ± 4.0 ml/min/kg). The volume of distribution corrected for weight ranged from 0.09 to 0.15 l/kg (mean ± S.D 0.12 ± 0.02 l/kg). These variables do not appear to be influenced by dose or duration of infusion, however, only 1 or 2 patients were studied at each dose level and infusion rate.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, single and repeated dose toxicity, and genotoxicicty.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients

Mannitol, Sodium citrate (to adjust pH), Citric acid monohydrate (to adjust pH), Polysorbate 80

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened vials:
3 years.

Diluted solution:
From a microbiological safety point of view, the product should be used immediately. If not used immediately, in-use storage and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2ºC - 8ºC under protection from light.

6.4 Special precautions for storage

Store in a refrigerator (2ºC – 8ºC).
For storage conditions of the diluted medicinal product, see section 6.3

6.5 Nature and contents of container

Cerezyme is supplied in type I borosilicate (clear) glass 20 ml vials. The closure consists of a siliconised butyl stopper with a tamper proof flip-off cap.

To provide sufficient volume to allow accurate dispensing, each vial is formulated to contain an overfill of 0.6 ml.

Package sizes: 1, 5 or 25 vials per carton.
Not all package sizes may be marketed.

6.6 Special precautions for disposal and other handling

Each vial of Cerezyme is for single use only.

The powder for concentrate for solution for infusion has to be reconstituted with water for injections, diluted with 0.9% sodium chloride intravenous solution and then administered by intravenous infusion.

Determine the number of vials to be reconstituted based on the individual patient's dosage regimen and remove the vials from the refrigerator.

Occasionally, small dosage adjustments may be made to avoid discarding partially used vials. Dosages may be rounded to the nearest full vial, as long as the monthly administered dosage remains substantially unaltered.

Use Aseptic Technique
Reconstitution
Reconstitute each vial with 10.2 ml water for injections; avoid forceful impact of water for injections on the powder and, by mixing gently, avoid foaming of the solution. The reconstituted volume is 10.6 ml. The pH of the reconstituted solution is approximately 6.1.

After reconstitution it is a clear, colourless liquid, free from foreign matter. The reconstituted solution must be further diluted. Before further dilution, visually inspect the reconstituted solution in each vial for foreign particles and discoloration. Do not use vials exhibiting foreign particles or discoloration. After reconstitution, promptly dilute vials and do not store for subsequent use.

Dilution
The reconstituted solution contains 40 units imiglucerase per ml. The reconstituted volume allows accurate withdrawal of 10.0 ml (equal to 400 units) from each vial. Withdraw 10.0 ml reconstituted solution from each vial and combine the withdrawn volumes. Then dilute the combined volumes with 0.9% sodium chloride intravenous solution to a total volume of 100 to 200 ml. Mix the infusion solution gently.

It is recommended to administer the diluted solution through an in-line low protein-binding 0.2 µm filter to remove any protein particles. This will not lead to any loss of imiglucerase activity. It is recommended that the diluted solution be administered within 3 hours. The product diluted in 0.9% sodium chloride intravenous solution will retain chemical stability if stored up to 24 hours at 2°C and 8°C under protection from light; but microbiological safety will depend on the reconstitution and dilution having been performed aseptically.
Cerezyme contains no preservatives. Any unused product or waste material should be disposed of in accordance with local requirements.

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

Manufactured By:
Genzyme Ireland Limited,
Waterford - Ireland

Packed & Released By:
Genzyme Corporation,
Northborough - MA 01532 USA

Registered By:
PT Kalventis Sinergi Farma,
Jakarta-Indonesia

PRESENTATION
Cerezyme® 400 units
Box, 1 vial @ 424 units of imiglucerase
Reg.No.: DKI1745300280A1

Cerezyme® is a registered trademark of Genzyme Corporation.

SAP / ID. number : PI-PIL Cerezyme-1 / XXXXXX		Film code : KSF/XXXXXX	
Country	: INDONESIA	Min. point size of text	: 6,5 pt
Version number	: 3	Type of text	: Ocean Sans Pro Family
Date	: 17.07.2023	Dimensions	: 240 x 300 mm
Material	: HVS 60 g/m²	Type of prefold	: 4x Horizontal - 2x Vertical
Pharmacode	: XXXXX	Dimension after folded	: 60 x 18.75 mm (± 2 mm)
Prepared by	: Rahmat Hafid		

Printing Colour
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Technical Information
outline

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