Medication Policy Manual

Policy No: dru002

Topic: Cerezyme®, imiglucerase
VPRIV®, velaglucerase alfa
Elelyso™, taliglucerase alfa

Date of Origin: January 1996

Committee Approval Date: November 11, 2016

Next Review Date: November 2017

Effective Date: April 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), and taliglucerase alfa (Elelyso) are man-made forms of a naturally occurring protein called glucocerebrosidase. A deficiency of glucocerebrosidase is called Gaucher disease. Over time, this deficiency commonly leads to clinical manifestations affecting the skeleton, bone marrow, spleen, liver, and less commonly the lungs.

Policy/Criteria

I. Most contracts require prior authorization approval of imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), and taliglucerase alfa (Elelyso) prior to coverage. Either imiglucerase (Cerezyme) or velaglucerase alfa (VPRIV) may be considered medically necessary in pediatric and adult patients with Gaucher disease, and taliglucerase alfa (Elelyso) may be considered medically necessary in adult patients with Gaucher disease, when criteria A, B, and C below are met.

A. Diagnosis of **type 1 Gaucher disease** confirmed by one of the following:

1. Biochemical assay of glucocerebrosidase activity in white blood cells or skin fibroblasts is less than or equal to 30% of normal activity. (Note: laboratory normals may vary).

OR

2. Genotyping revealing two pathogenic mutations of the glucocerebrosidase gene.

AND

B. Clinically significant symptoms of the disease are present, such as anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly.

AND

C. For imiglucerase (Cerezyme) and velaglucerase alfa (VPRIV), site of care administration requirements are met. [refer to OmedaRx Medication Policy Manual, *Site of Care Review*, dru408]

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx does not consider imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), or taliglucerase alfa (Elelyso) to be self-administered medications.

B. When prior authorization is approved, either imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), or taliglucerase alfa (Elelyso) may be authorized as follows:

1. Initial Authorization

a. Doses up to 30 units/kg every 2 weeks (or other equivalent dose) may be approved when criteria are met.

b. Doses up to 60 units/kg every 2 weeks may be approved when the patient meets high risk dosing guidelines in Appendix 1 for adults or Appendix 2 for children.

2. Continued Authorization

a. Documentation by chart notes of maintenance or improvement in disease must be provided. (This may include, but is not limited to hematologic indices, reduction in spleen or liver volume, MRI of spine/femurs, normalized growth, reduced dependancy on oxygen, quality of life, and/or plain films of skeleton).

b. Doses up to 60 units/kg every 2 weeks may be approved when the physician indicates by chart notes that the patient has not responded to lower doses over a period of 6 months.

C. Initial and continued authorization (after the initial 6 month period) shall be reviewed at least every 12 months to confirm that current medical necessity criteria are met and that the medication is effective.

III. Imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), and taliglucerase alfa (Elelyso) are considered not medically necessary when used in combination with miglustat (Zavesca).

IV. Imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), and taliglucerase alfa (Elelyso) are considered investigational when used for all other conditions and when used in combination eliglustat (Cerdelga) or with each other.

Position Statement

- Imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), and taliglucerase alfa (Elelyso) work by replacing or supplementing the deficient enzyme (i.e. glucocerebrosidase) in order to allow excess material to be degraded.
- Enzyme replacement therapy (ERT) is considered the standard of care in Type 1 (nonneuropathic) Gaucher disease. [1]
- Treatment should be reserved for symptomatic children (including those with malnutrition, growth retardation, impaired psychomotor development, and/or fatigue), and for adults with symptomatic disease (e.g. platelet count < 60,000/mm^3, liver volume > 2.5 times normal size, spleen volume > 15 times normal size, radiological evidence of skeletal disease). [1]
- Treatment goals are elimination or improvement in symptoms, prevention of irreversible complications, and improvement in the overall health and quality of life. [1]
- ERT has not been shown to improve health outcomes in adult patients with Type 1 Gaucher disease without clinical signs or symptoms of the disease. In addition ERT does not provide benefit in reversing or decreasing neurologic symptoms associated with Type 2 (acute neuronopathic) or Type 3 (chronic neuronopathic) Gaucher disease. [2]

- The diagnosis of Gaucher disease is usually confirmed by identifying reduced glucocerebrosidase activity in peripheral leukocytes. Targeted DNA analysis to detect the most common mutations is an effective method for confirming the diagnosis. [1]
- A starting dose of 30 units/kg of body weight every other week is reasonable in the absence of high risk disease. The mean ERT dose used for long-term therapy in the United States is approximately 30 units/kg every other week. [1-4]
- Imiglucerase (Cerezyme) is approved for doses ranging from 2.5 units/kg three times per week up to 60 units/kg every other week. Velaglucerase alfa (VPRIV) and taliglucerase alfa (Elelyso) have been shown to be equivalent to imiglucerase (Cerezyme) on a unit-for-unit basis, and patients switching from imiglucerase (Cerezyme) can be maintained on the same dose. [4,5,6,7,8]
- The addition of miglustat (Zavesca), an oral substrate reduction therapy (SRT) to ERT has not been shown to provide a substantial benefit over ERT alone. [5] However, miglustat (Zavesca) may be an appropriate treatment when ERT is not an option (e.g. allergic hypersensitivity, lack of venous access, patients unwilling to receive intravenous infusions).
- There is no evidence evaluating the addition of eliglustat (Cerdelga), an SRT, to any ERT product. It is unknown if the combination is safe and effective for Gaucher disease.

Clinical Efficacy

- All ERT products used in the treatment of Gaucher disease have demonstrated improvements in some disease-associated parameters (e.g. hemoglobin level, platelet count, spleen and liver volume). [5]
- In studies of patients with Type 1 Gaucher disease switched from imiglucerase (Cerezyme) to the same dose and frequency of either velaglucerase alfa (VPRIV) or taliglucerase alfa (Elelyso), control of disease parameters such as spleen and liver volume, hemoglobin concentration, and platelet counts were maintained. [5]
- ERT with imiglucerase (Cerezyme) improved quality of life in patients with skeletal manifestations of Gaucher disease as measured by The Short Form-36 Health Survey. [6]
- The U.S. Regional Coordinators of the International Collaborative Gaucher Group (ICGG), a panel of physicians who have extensive experience in the care of Gaucher patients, have made recommendations for therapy and dosing based on risk assessment for irreversible morbid complications (see Appendix 1 and 2). [2,3]
    * Initial doses of ERT of 30-60 units/kg of body weight every other week are considered safe and effective in demonstrating improvements in hepatosplenomegaly, anemia, and thrombocytopenia.
    * Dose adjustments should be based on the patient's initial risk and achievement of therapeutic goals based on individual patient characteristics.
    * The time required to achieve therapeutic goals varies by organ system, but usually requires at least 12 to 36 months.

- The ICGG U.S. Regional Coordinators recommend that all children with Gaucher disease be treated with ERT due to high risk for irreversible, morbid complications. [3,4]
    * Diagnosis of Gaucher disease in the first and second decades of life is indicative of a rapidly progressive course.
    * Early intervention is necessary for these children, during the time when the skeleton is immature, to enable them to attain their peak skeletal mass by early adulthood.

Safety [7]

- Anaphylactoid reactions and hypersensitivity reactions, although not common, may occur with imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), or taliglucerase alfa (Elelyso). Management of patients exhibiting signs of hypersensitivity reactions may include reduction in rate of infusion, pretreatment with antihistamines or corticosteroids, or switching products.
- The most common adverse events reported with all three products are infusion-related adverse events such as headache, chest pain/discomfort, asthenia, fatigue, urticaria, erythema, increased blood pressure, back pain, arthralgia, and flushing.

Dosing Considerations [3,8,9]

- Dose adjustments are made on an individual basis and should consider patient-specific factors.
- Increases in dose may be necessary to achieve therapeutic goals or for relapse following dose reduction. An increased dose may also be indicated if visceromegaly, anemia, thrombocytopenia, and biomarkers fail to improve after six months of therapy. However, an increased dose is unlikely to reverse certain types of pathology (e.g. osteonecrosis and fibrosis of the liver, spleen, or lung)
- Dose reductions can be considered in stable patients who have reached all relevant therapeutic goals, but the decision to reduce the dose must take into account patient-specific factors, and may not be appropriate in high-risk adults and children.
- Treatment is continued throughout the patient's life. Prolonged treatment interruptions are not recommended, due to potential for disease progression.

Appendix 1: Adults with Type 1 Gaucher Disease: Risk Assessment and Dosage Recommendations [3]

Initial Dose	Highest Risk: 60 units/kg every 2 weeks	Lowest Risk: 30 units/kg or less every 2 weeks
Risk Criteria	At least one or more of the following: - **Symptomatic skeletal disease:** * Moderate to severe osteopenia defined as reduced bone mineral density (BMD) of > 1 S.D. below the mean (which predicts a relative fracture risk of 2.5 using the World Health Organization criteria). * Chronic bone pain * Bone crises * Avascular necrosis * Pathological fractures * Joint replacement(s) - **Cardiopulmonary disease, including pulmonary hypertension** - **Hematologic symptoms** * Platelet count ≤ 60,000 mm^3 or documented abnormal bleeding episodes * Symptomatic anemia or hemoglobin ≤ 8.0 g/dL * Transfusion dependency - **Significant liver disease** * Severe hepatomegaly defined as liver volume ≥ to 2.5 x norm * Infarcts * Portal hypertension * Hepatitis - **Significant splenic disease** * Severe splenomegaly defined as spleen volume > 15 x normal * Infarcts * Significant renal disease such as evidence of bilaterally reduced (< 8.5 cm) kidney size by imaging studies	- Normal liver, cardiac, lung, and renal function - Skeletal disease limited to mild osteopenia (low bone density) and Erlenmeyer flask deformity - Hemoglobin as follows: **Males:** ≤ 12.5 g/dL and > 11.5 g/dL; **Females:** ≤ 11.5 g/dL and > 10.5 g/dL; or overall < 2.0 g/dL below lower limit of normal for age and sex - Platelet count ≤ 120,000 per mm^3 and > 60,000 mm^3 on three determinations - Liver volume < 2.5 x normal - Spleen volume < 15 x normal

Appendix 2: Children (less than 18 years) with Type 1 Gaucher Disease: Risk Assessment and Dosage Recommendations [3]		
Initial Dose	**Highest Risk: 60 units/kg every 2 weeks**	**Lowest Risk: < 60 units/kg every 2 weeks**
Risk Criteria	One or more of the following in addition to physical signs: – Symptomatic disease (manifestations of abdominal/bone pain, fatigue, exertional limitations, weakness, cachexia) – Growth failure – Evidence of skeletal involvement including Erlenmeyer flask deformity – Platelet count < 60,000 mm^3 and/or documented abnormal bleeding episode(s) – Hemoglobin < 2.0 g/dL below lower limit of normal for age and sex – Impaired quality of life	Children with relevant physical signs without additional criteria described for highest risk patients.

Cross References
Cerdelga™, eliglustat, Medication Policy Manual, Policy dru370
Site of Care Review, Medication Policy Manual, Policy dru408
Zavesca®, miglustat, Medication Policy Manual, Policy dru109

Codes	Number	Description
HCPCS	J1785	Injection, imiglucerase, per unit
HCPCS	J3060	Injection, taliglucerase alfa, 10 units
HCPCS	J3385	Injection, velaglucerase alfa, 100 units

References

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2. Weinreb, NJ, Aggio, MC, Andersson, HC, et al. Gaucher disease type 1: revised recommendations on evaluations and monitoring for adult patients. United States, 2004. p. 15-22.
3. Andersson, HC, Charrow, J, Kaplan, P, et al. Individualization of long-term enzyme replacement therapy for Gaucher disease. United States, 2005. p. 105-10.
4. Charrow, J, Andersson, HC, Kaplan, P, et al. Enzyme replacement therapy and monitoring for children with type 1 Gaucher disease: consensus recommendations. United States, 2004. p. 112-20.
5. Shemesh, E, Deroma, L, Bembi, B, et al. Enzyme replacement and substrate reduction therapy for Gaucher disease. *The Cochrane database of systematic reviews*. 2015;3:CD010324. PMID: 25812601
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7. Micromedex® Healthcare Series [Internet database]. Truven Health Analytics Inc. Updated periodically.
8. Baldellou, A, Andria, G, Campbell, PE, et al. Paediatric non-neuronopathic Gaucher disease: recommendations for treatment and monitoring. *European journal of pediatrics*. 2004 Feb;163(2):67-75. PMID: 14677062
9. Pastores, GM, Weinreb, NJ, Aerts, H, et al. Therapeutic goals in the treatment of Gaucher disease. United States, 2004. p. 4-14.

Revision History

Revision Date	Revision Summary
11/11/2016	– Changed the reauthorization period from 6 months to 12 months. – Effective 4/1/2017, imiglucerase (Cerezyme) and velaglucerase alfa (VPRIV) added to site of care program.