Intravenous Enzyme Replacement Therapy (ERT) for Gaucher Disease

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➲ Instructions for Use

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Related Commercial Policy
- Provider Administered Drugs – Site of Care

Community Plan Policy
- Intravenous Enzyme Replacement Therapy (ERT) for Gaucher Disease

Application

UnitedHealthcare Commercial
This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange
This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

➲ See Benefit Considerations

This policy refers to the following drug products, all of which are intravenous enzyme replacement therapies used in the treatment of Gaucher disease:
- Cerezyme® (imiglucerase)
- Elelyso® (taliglucerase)
- VPRIV® (velaglucerase)

Preferred Product
Medical Necessity Plans
VPRIV is the preferred enzyme replacement therapy for Gaucher Disease. Coverage for VPRIV is contingent on the coverage criteria in the Diagnosis-Specific Criteria section.

Coverage for Cerezyme or Elelyso is contingent on the Preferred Product Criteria in this section and the coverage criteria in the Diagnosis-Specific Criteria section. In order to continue coverage, members already on Cerezyme or Elelyso will be required to change therapy to VPRIV unless they meet the criteria below.

Preferred Product Criteria *(For Medicare reviews, refer to the CMS section.*)*

Treatment with Cerezyme or Elelyso is medically necessary for the indications specified in this policy when one the criteria below are met:

- **Both** of the following:
  - History of a trial of adequate dose and duration of VPRIV, resulting in a failure to meet clinical goals (e.g., persistent anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly); **and**
  - Physician attests that, in their clinical opinion, the clinical response would be expected to be superior than experienced with VPRIV

  or
- **Both** of the following:
  - History of contraindication, intolerance, or adverse event(s) to VPRIV; **and**
  - Physician attests that, in their clinical opinion, the same contraindication, intolerance, or adverse event(s) would not be expected to occur with Cerezyme or Elelyso

Non-Medical Necessity Plans

Cerezyme, Elelyso, or VPRIV is to be approved contingent on the coverage criteria in the Diagnosis-Specific Criteria section.

Diagnosis-Specific Criteria

Cerezyme, Elelyso, and VPRIV are proven for the treatment of Gaucher disease when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - **One** of the following:
    - For Elelyso, diagnosis of type 1 Gaucher disease; **or**
    - For Cerezyme or VPRIV, diagnosis of type 1 or type 3 Gaucher disease

    and
  - Dosing is in accordance with United States Food and Drug Administration (FDA) approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Documentation of positive clinical response to therapy (e.g., reduced severity or resolution of anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly); **and**
  - Dosing is in accordance with FDA approved labeling; **and**
  - Continuation authorization will be for no more than 12 months

Cerezyme, Elelyso, or VPRIV are medically necessary for the treatment of type 1 Gaucher disease when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of type 1 Gaucher disease; **and**
  - Patient has symptomatic disease (e.g., moderate to severe anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly); **and**
  - Dosing is in accordance with FDA approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - **One** of the following:
    - Patient is on Cerezyme or Elelyso and meets the criteria in the Preferred Product Criteria section; **or**
    - Patient is on VPRIV

    and
  - Documentation of positive clinical response to therapy (e.g., reduced severity or resolution of anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly); **and**
  - Dosing is in accordance with FDA approved labeling; **and**
  - Continuation authorization will be for no more than 12 months

Cerezyme or VPRIV is medically necessary for the treatment of type 3 Gaucher disease when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - **One** of the following:
    - **Both** of the following:
      - Diagnosis of type **3** Gaucher disease; **and**

        - Patient has symptomatic chronic neuronopathic disease (e.g., growth retardation, impaired development, moderate to severe anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly)

      or

      - **One** of the following:
        - Patient has suspected type **3** Gaucher Disease and a sibling with chronic neuronopathic Gaucher Disease (type 3); **or**
        - Patient has **one** of the following high-risk genotypes for type 3 Gaucher Disease:
          - L444P/L444P (c.1448T > C homozygote); or
          - D409H/D409H (c.1342G > C homozygote); or
          - L444P/D409H (c.1448T > C/c.1342G > C heterozygote)

      and

    - Dose for the requested product does not exceed 60 units/kg every 2 weeks; **and**
    - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
    - **One** of the following:
      - Patient is on Cerezyme and meets the criteria in the Preferred Product Criteria section; **or**
      - Patient is on VPRIV

      and

    - Documentation of positive clinical response to therapy (e.g., reduced severity or resolution of anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly); **and**
    - Dose does not exceed 60 units/kg every 2 weeks; **and**
    - Continuation authorization will be for no more than 12 months

Cerezyme, Elelyso, and VPRIV are unproven and not medically necessary for type 2 Gaucher Disease.

Elelyso is unproven and not medically necessary for the treatment of type 3 Gaucher disease.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1786	Injection, imiglucerase, 10 units
J3060	Injection, taliglucerase alfa, 10 units
J3385	Injection, velaglucerase alfa, 100 units

Diagnosis Code	Description
E75.22	Gaucher Disease

Background

Gaucher disease is an inherited autosomal recessive disease characterized by deficient glucocerebrosidase and consequent accumulation of glucocerebroside in the reticuloendothelial cells of the liver, spleen, bone marrow, and other tissues. Type 1 Gaucher disease is the most common subtype, accounting for more than 90% of all cases, and is characterized by systemic manifestations without primary central nervous system involvement (non-neuronopathic). Type 2 Gaucher disease is characterized by severe early neurologic manifestations (acute neuronopathic) with death usually occurring before 2 years of age. Type 3 Gaucher disease is characterized by subacute neurologic symptoms (chronic neuronopathic) and systemic manifestations.[4]

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make

coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

Proven

Type 1 Gaucher Disease

Imiglucerase, velaglucerase alfa, and taliglucerase alfa are indicated for long-term enzyme replacement therapy (ERT) in pediatric and adult patients with type 1 Gaucher disease.[1-3]

Hughes et al published the results and the long-term data from a single extension study of two phase III trials for velaglucerase alfa treatment.[18] Fifty-seven patients (25 patients from the TKT032 trial, 32 patients from the HGT-GCB-039 trial), aged 3 to 62 years were enrolled. All patients received their first 3 infusions at the clinical site. If the patient exhibited no signs of adverse events, they were able to receive infusions at an alternative site of care at the direction of the investigator. All patients received velaglucerase alfa, every other week for 1.2 to 4.8 years at 60 U/kg, (some requiring dose reduction) during the extension study. Nineteen of 57 patients completed the extension study. The other patients (34) were discontinued from the trial due to the termination of the trial by the sponsor. Almost all patients in the extension study experienced an adverse event (AE). Sixteen of 57 patients experienced AEs that were deemed possibly or probably related to treatment. Of the 56 drug-related AEs, only events that were experienced by more than one patient were hypertension (infusion related), and headache. Six patients experienced infusion related AEs. Nineteen serious AEs were reported including a spontaneous 1st trimester abortion (patient had history of miscarriages and anti-phospholipid syndrome) and one patient death after a convulsion. No serious AEs were considered to be related to treatment. One patient tested positive for IgG anti-velaglucerase alfa antibodies. The mean increase in hemoglobin concentration was 2.75 g/dL (26%) in the overall velaglucerase alfa group, and there was a 120% mean increase in the platelet count compared with base-line; a 64% mean decrease in spleen volume and a 27% mean decrease in liver volume were also observed. The results of the analysis of efficacy parameters also indicated that there were significant clinical improvements in the first 24 months, which were either maintained or continued at a declining rate over longer term treatment. The authors concluded that Velaglucerase alfa had a good long-term safety and tolerability profile, and patients continued to respond clinically, which is consistent with the results of the extension study to the phase I/II trial of velaglucerase alfa.

A multinational, phase 3 trial was conducted to evaluate the efficacy and safety of two doses of velaglucerase alfa in 25 treatment-naïve anemic patients with type 1 Gaucher disease. Subjects were randomized to intravenous velaglucerase alfa 60 units/kg (n = 12) or 45 units/kg body weight (n = 13) every other week for 12 months.[8] The primary endpoint was change from baseline in hemoglobin concentration in the 60 units/kg arm. At 12 months, mean hemoglobin concentrations increased from baseline [60 units/kg: + 23.3%; + 2.43 g/dL ($p < 0.001$); 45 units/kg: + 23.8%; + 2.44 g/dL ($p < 0.001$)], as did mean platelet counts [60 units/kg: + 65.9%; + 50.9 × 10^9/L ($p = 0.002$); 45 units/kg: + 66.4%; + 40.9 × 10^9/L ($p = 0.01$)]. Mean splenic volume decreased from baseline [60 units/kg: -50.4%, from 14.0 to 5.8 multiples of normal (MN) ($p = 0.003$); 45 units/kg: -39.9%, from 14.5 to 9.5 MN ($p = 0.009$)]. No drug-related serious adverse events or withdrawals were observed. Velaglucerase alfa was generally well tolerated and effective for adults and children with type 1 Gaucher disease in this study. All disease-specific parameters measured demonstrated clinically meaningful improvements after 12 months.

Type 3 Gaucher Disease

The effectiveness of enzyme replacement therapies (ERT) for children with type 1 and type 3 Gaucher disease (GD) were determined in a longitudinal cohort study including prospective and retrospective clinical data.[16] The investigators estimated age- and gender-adjusted treatment effects using generalized linear mixed models. Children (n = 25, aged 1.1 to 15.6 years) with a diagnosis of GD (14 with type 1 and 11 with type 3 GD) who attended a specialist treatment center in England were enrolled in this study. At recruitment, 24 patients were receiving ERT (mean treatment duration, 5.57 years; range 0 to 13.7 years). Children on treatment contributed data before and during treatment, while the child not on treatment contributed natural history data. Platelet count, hemoglobin, and absence/presence of bone pain were the clinical outcomes chosen to reflect disease progression. The investigators found that duration of ERT was associated with statistically significant improvements in platelet count ($p < 0.001$), hemoglobin ($p < 0.001$), and reported bone pain ($p = 0.02$). They noted that the magnitude of effect on hematological parameters was greater in children with GD3 than in those with GD1.

The effectiveness of imiglucerase for treating the non-CNS symptoms of type 1 and type 3 Gaucher disease was evaluated using data from the International Collaborative Gaucher Group (ICGG) Gaucher Disease Registry. The analysis

included individuals with either type 1 or type 3 disease who began therapy with imiglucerase and had an initial clinical assessment followed by at least one additional follow-up assessment. This baseline-controlled study looked at patients with type 1 Gaucher disease ranging from 19 weeks to 87 years old, and patients with type 3 disease ranging from 7 weeks to 54 years old, all of whom started imiglucerase between 1992 and 2021. After roughly two years of treatment (ranging from 1 to 3 years), patients with both type 1 and type 3 disease showed improvements in several clinical measures, including hemoglobin levels, platelet counts, liver and spleen volumes, and height Z-scores. In 1,052 patients with type 1 Gaucher disease, the average hemoglobin level at baseline was 11.8 g/dL, with a mean increase of 1.5 g/dL. Among 1,053 type 1 patients, the baseline platelet count averaged 128 × 10^3/mm^3, increasing by an average of 64 × 10^3/mm^3 during treatment. In 118 patients with type 3 disease, hemoglobin levels started at an average of 10 g/dL and rose by 1.8 g/dL. Among 116 type 3 patients, the baseline platelet count averaged 149 × 10^3/mm^3, with a mean increase of 105 × 10^3/mm^3.

Therapy Change From Imiglucerase to Velaglucerase Alfa

Pastores et al conducted a multicenter open-label study which evaluated the safety of velaglucerase alfa in type 1 Gaucher (GD1) disease patients that were treatment naïve or had been receiving imiglucerase. Patients received intravenous velaglucerase alfa every other week at a dose of 60 U/kg (treatment naïve) or 15-60 U/kg (previously treated).[7] Safety data outcomes included physical examination, vital sign monitoring, clinical laboratory evaluation (hematology and clinical chemistry), assessment for anti–velaglucerase alfa antibodies, and monitoring for adverse events (AEs). A total of 211 (including six treatment-naïve) patients were enrolled. Among the 205 previously treated patients, 35 (17.1%) experienced an AE considered related to study drug. Among the six treatment-naïve patients, one had an AE considered related to study drug. The most frequently reported AE's were headache, nasopharyngitis, nausea, and fatigue. Infusion-related AE's occurred in 28 (13.3%) of the 211 patients and usually occurred during the first 3 infusions. De novo, non-neutralizing, anti-velaglucerase alfa antibodies developed during treatment in one (< 1.0%) previously treated patient and none of the treatment-naïve patients. Researchers concluded that the data supports the safety of initiating treatment with velaglucerase alfa 60 U/kg EOW in patients with GD1 who are naïve to enzyme replacement therapy, in addition to showing the safety of transitioning patients from imiglucerase to velaglucerase alfa at the same dose as their previous imiglucerase dose. The safety profile of velaglucerase alfa observed across a broad range of patient ages is in agreement with that previously observed in controlled trials.

A multicenter, open-label, 12-month study examined the safety and efficacy of velaglucerase alfa in patients with type 1 Gaucher disease who were previously stable on imiglucerase therapy.[9] Eligible patients (n = 40) ≥ 2 years old were switched to velaglucerase alfa at a dose equal to their prior imiglucerase dose. Velaglucerase alfa infused for one hour every other week was generally well tolerated with most adverse events of mild or moderate severity. Hemoglobin concentrations, platelet counts, and spleen and liver volumes remained stable through 12 months. Investigators concluded that adult and pediatric patients with type 1 Gaucher disease may be successfully transitioned to velaglucerase alfa.

The effects of a switch to velaglucerase alfa in a group of adult patients with type 1 Gaucher disease, all of whom had previously had their dose reduced as a consequence of the worldwide imiglucerase shortage, were described in a recent paper.[15] Thirty-two patients from two large European Gaucher centers switched to treatment with velaglucerase alfa after 1 to 8.5 months of dose reduction. The course of important Gaucher disease parameters was studied at four time points: one year before the shortage, just before the shortage, before a switch to velaglucerase and after up to one year of treatment with velaglucerase. These parameters included hemoglobin concentration, platelet count, plasma chitotriosidase activity in all patients, and spleen and liver volumes (as well as bone marrow fat fraction images) in 10 patients. Decreases in platelet counts as a result of reduced treatment with imiglucerase were quickly restored on treatment with velaglucerase alfa. Chitotriosidase activity declined overall after switching. Five out of 10 patients had an increase in liver volume of at least 10% after six months of velaglucerase treatment, which was reversible in 3. Most patients received infusions at home and no important side effects were observed. Velaglucerase alfa appears to be a safe and effective alternative for imiglucerase.

Pregnancy

In order to ascertain pregnancy outcome in women receiving velaglucerase alfa, the medical records of women exposed to this therapy since 2004 were collected from six multinational clinical sites for evaluation.[17] In all, 25 singleton pregnancies (mean gravidity, 2.7; mean parity, 2.0; mean months on ERT, 31.2) were reported in 21 women (mean age, 32.0 years). Two primiparous women suffered three first trimester abortions and one missed abortion occurred in a multigravida female. Live birth rate was 84% (mean gestational age, 39.7 weeks). Mean birthweight was 3234.4 g, with APGAR scores above 9. All but three were vaginal deliveries; elective cesarean sections were performed in two patients with hip arthroplasty and one after previous cesarean. Nine patients received regional analgesia/anesthesia. Post-partum complications were rare, with only one post-partum (placental) bleed which resolved without intervention. Mean

hemoglobin and platelet counts improved during pregnancy (9.45% and 26.0%, respectively). Based upon their evaluation of this post marketing surveillance data collected over an approximate period of 8 years, the evaluators concluded that velglucerase alfa is safe for conception and pregnancy with good maternal and neonatal outcomes.

Cohen et al evaluated the effect of ERT on the pregnancy and obstetric outcome in a unique group of multiparous women with type 1 GD (GD1) who had pregnancies with and without ERT.[24] The Gaucher Unit database (1987-2019) was searched for multiparous women who had pregnancies before and after the institution of ERT. Data were collected from the clinic files and study-specific questionnaires. Descriptive, correlation analysis and generalized estimating equations (GEE) were used to study the effect of ERT and confounding variables on study outcomes. We identified 19 women with 105 pregnancies, among which 26 (24.7%) terminated in first-trimester miscarriage. The risk for miscarriage was associated with the severity of GD1 genotype and phenotype, but not with ERT usage. Early postpartum hemorrhage (PPH) was reported in 16 (84%) women after 25 deliveries (31.6%, 95% CI 21.6%-43.1%). The risks of early PPH and red blood cell (RBC) transfusions were significantly lower when ERT was used during pregnancy, OR (95% CI) 0.13 (0.03-0.54) and 0.27 (0.08-0.94), respectively, compared to pregnancies without the use of ERT. Enzyme replacement therapy during pregnancy is risk reducing for early PPH and RBC transfusions in women with GD1. We suggest considering ERT for the benefit of all pregnant women with GD1, including mild GD1.

Technology Assessments

Gaucher Disease

A 2015 Cochrane review was published to summarize all available randomized controlled study data on the efficacy and safety of enzyme replacement therapies and substrate reduction therapy for treating Gaucher disease.[10] All randomized and quasi-randomized controlled studies (including open-label studies and cross-over studies) assessing enzyme replacement therapy or substrate reduction therapy, or both, in all types of Gaucher disease were included. The authors concluded that the results reflect the limitations of analyzing evidence restricted to prospective randomized controlled trials, especially when dealing with chronic rare diseases. The analysis suggested that, during the first year of treatment, different recombinant glucocerebrosidases are bio-similar and non-inferior in safety and efficacy for surrogate biological response parameters. Enzyme replacement therapy given at 30 to 45 units/kg body weight every two to four weeks was generally as effective as the 60 unit/kg dose for the assessed clinical outcomes. The analysis emphasizes the need to determine whether it is realistic to carry out multi-decade prospective clinical trials for rare diseases such as type 1 Gaucher disease. With large treatment effects on the classical manifestations of the disorder, therapeutic investigations in Gaucher disease mandate innovative trial designs and methodology to secure decisive data concerning long-term efficacy and safety - with the realization that knowledge about disease-modifying actions that are sustained are of crucial importance to people with this chronic condition.

Professional Societies

Gaucher Disease

The Ontario Guidelines for Treatment of Gaucher Disease by Enzyme Replacement with Imiglucerase or Velaglucerase, or Substrate Reduction Therapy (SRT) with Miglustat were last updated in 2011.[12] The guidelines state that ERT and SRT are effective in reversing the visceral manifestations of Gaucher disease. However, data do not suggest that either ERT or SRT is effective in improving central nervous system involvement in patients with type 2 and 3 disease. Treatment with ERT or SRT in patients at risk of neuronopathic disease should therefore be guided by the non-neurological manifestations of their disease but not initiated in asymptomatic patients who have a genotype which increases their risk of neuronopathic involvement.

An update to The Paediatric Gaucher Disease in England: Guidelines for Assessment, Monitoring, and Enzyme Replacement Therapy was released in 2012.[13] All children with types I and III Gaucher disease should commence treatment with enzyme replacement therapy. Visceral disease in type III GD responds well, and so these children should be offered ERT. There is no evidence that the neurological features in patients with type II (neuronopathic Gaucher disease) show any response to ERT and therefore it should not be offered.

Kaplan et al. published Revised Recommendations for the Management of Gaucher disease in Children in 2013.[14] According to the recommendations, every child and adolescent with symptomatic Gaucher disease should be treated with regular intravenous infusions of enzyme replacement therapy. There is no evidence that enzyme replacement therapy, even at high doses, can prevent or slow neurological progression in patients with type 2 or type 3 Gaucher disease. Because enzyme replacement therapy is not recommended for type 2 Gaucher disease, management should be focused on supportive care. For children with type 3 Gaucher disease, enzyme replacement therapy is recommended to ameliorate the severe visceral manifestations.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Cerezyme is a hydrolytic lysosomal glucocerebrosidase-specific enzyme indicated for the treatment of non-central nervous system (CNS) manifestations of type 1 or type 3 Gaucher disease in adults and pediatric patients.[1]

Elelyso is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for the treatment of patients 4 years and older with a confirmed diagnosis of type 1 Gaucher disease.[2]

VPRIV is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease.[3]

Centers for Medicare and Medicaid Services (CMS)

Coverage guidelines for certain Part B drugs may be found in the Medicare Advantage Medical Policy titled Medications/Drugs (Outpatient/Part B). National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. These NCDs/LCDs/LCAs are available at https://www.cms.gov/medicare-coverage-database/new-search/search.aspx.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that certain criteria are met, including that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.

*Preferred therapy criteria does not apply to Medicare Advantage members.

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Policy History/Revision Information

Date	Summary of Changes

06/01/2026	**Template Update**
	• Transferred content to shared policy template that applies to both UnitedHealthcare Commercial and Individual Exchange benefit plans
	• Added *Application* section to indicate this policy applies to:
	  ○ UnitedHealthcare Commercial benefit plans
	  ○ Individual Exchange benefit plans
	Coverage Rationale
	Preferred Product
	• Added language to indicate:
	Medical Necessity Plans
	  ○ VPRIV is the preferred enzyme replacement therapy for Gaucher disease; coverage for VPRIV is contingent on the coverage criteria in the *Diagnosis-Specific Criteria* section [of the policy]
	  ○ Coverage for Cerezyme or Elelyso is contingent on the *Preferred Product Criteria* section [of the policy] and the coverage criteria in the *Diagnosis-Specific Criteria* section [of the policy]
	  ○ In order to continue coverage, members already on Cerezyme or Elelyso will be required to change therapy to VPRIV unless they meet the criteria in the *Preferred Product Criteria* section [of the policy]
	Preferred Product Criteria
	  ○ Treatment with Cerezyme or Elelyso is medically necessary for the indications specified in this policy when one the criteria below are met:
	  ▪ Both of the following:
	  – History of a trial of adequate dose and duration of VPRIV, resulting in a failure to meet clinical goals (e.g., persistent anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly)
	  – Physician attests that, in their clinical opinion, the clinical response would be expected to be superior than experienced with VPRIV
	  ▪ Both of the following:
	  – History of contraindication, intolerance, or adverse event(s) to VPRIV

Date	Summary of Changes
	– Physician attests that, in their clinical opinion, the same contraindication, intolerance, or adverse event(s) would not be expected to occur with Cerezyme or Elelyso Non-Medical Necessity Plans ○ Cerezyme, Elelyso, or VPRIV is to be approved contingent on the coverage criteria in the *Diagnosis-Specific Criteria* section [of the policy] ***Diagnosis-Specific Criteria*** • Added language to indicate: ***Type 2 Gaucher Disease*** ○ Cerezyme, Elelyso, and VPRIV are unproven and not medically necessary for type 2 Gaucher disease ***Type 3 Gaucher Disease*** ○ Cerezyme and VPRIV are proven for the treatment of type 3 Gaucher disease when all of the following criteria are met: Initial Therapy ▪ Diagnosis of type 3 Gaucher disease ▪ Dosing is in accordance with U.S. FDA-approved labeling ▪ Initial authorization will be for no more than 12 months Continuation of Therapy ▪ Documentation of positive clinical response to therapy (e.g., reduced severity or resolution of anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly) ▪ Dosing is in accordance with U.S. FDA-approved labeling ▪ Continuation authorization will be for no more than 12 months ○ Elelyso is unproven and not medically necessary for the treatment of type 3 Gaucher disease • Revised coverage criteria for: ***Type 1 Gaucher Disease*** Proven ○ Removed criterion requiring symptomatic disease (e.g., moderate to severe anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly) Medically Necessary *Initial Therapy* ○ Added criterion requiring the patient has symptomatic disease (e.g., moderate to severe anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly) ○ Removed criterion requiring: ▪ History of failure of VPRIV due to failure to meet clinical goals (e.g., persistent anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly) despite VPRIV therapy ▪ History of failure of VPRIV due to hypersensitivity to VPRIV therapy *Continuation of Therapy* ○ Added criterion requiring one of the following: ▪ Patient is on Cerezyme or Elelyso and meets the criteria in the *Preferred Product Criteria* section [of the policy] ▪ Patient is on VPRIV ***Type 3 Gaucher Disease*** Medically Necessary *Initial Therapy* ○ Added criterion requiring one of the following: ▪ Both of the following: – Diagnosis of type 3 Gaucher disease – Patient has symptomatic chronic neuronopathic disease (e.g., growth retardation, impaired development, moderate to severe anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly) ▪ One of the following: – Patient has suspected type 3 Gaucher disease and a sibling with chronic neuronopathic Gaucher disease (type 3)

Date	Summary of Changes
	– Patient has one of the following high-risk genotypes for type 3 Gaucher disease: L444P/L444P (c.1448T>C homozygote), D409H/D409H (c.1342G>C homozygote), or L444P/D409H (c.1448T>C/c.1342G>C heterozygote) ○ Removed criterion requiring symptomatic disease (e.g., moderate to severe anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly) *Continuation of Therapy* ○ Added criterion requiring one of the following: ▪ Patient is on Cerezyme and meets the criteria in the *Preferred Product Criteria* section [of the policy] ▪ Patient is on VPRIV ○ Removed criterion for treatment with Cerezyme requiring one of the following: ▪ History of failure of VPRIV due to failure to meet clinical goals (e.g., persistent anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly) despite VPRIV therapy ▪ History of failure of VPRIV due to hypersensitivity to VPRIV therapy **Supporting Information** • Added *CMS* section • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy versions 2025D0048P and IEXD0048.09

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.