Pharmacy Drug Policy

SUBJECT: Genglycos (pariglasgene brecaparvovec-opnr) – Medical Benefit
POLICY NUMBER: PHARMACY-147
EFFECTIVE DATE: 11/2026
LAST REVIEW DATE: 11/24/2026

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Glycogen Storage Disease Type Ia, or Von Gierke Disease, is a subtype of autosomal recessive disorders caused by an inactivating mutation in G6PC, the gene that codes the glucose-6-phosphatase-a enzyme (G6Pase-a). Between meals, blood glucose homeostasis is maintained by G6PT and G6Pase-a that hydrolyzes G6P to glucose in the final step of gluconeogenesis and glycogenolysis in the liver, kidneys, and intestines. The G6PT transports G6P from the cytoplasm to the endoplasmic reticulum, where it should be hydrolyzed to glucose and inorganic phosphates by G6Pase-a. The detrimental mutation in G6Pase-a causes metabolic imbalance, primarily seen as severe hypoglycemia alongside increased G6P levels following a short period of not eating. This causes overactivation of other metabolic pathways causing ailments including hepatomegaly, hypercholesterolemia, lactic acidemia, osteoporosis, hepatocellular adenomas, and more.

GSD-1a affects around 6,000 people in commercially accessible geographies (areas where a sponsor can legally and operationally deliver investigational/approved products), with a disease prevalence of around 1 in 100,000, with around 80% of cases being type 1a. The mutation is genetically inherited, with the strongest risk factor being familial history of GSD-1a or other related GSD1 disorder. There are no known racial or ethnic risk factors for this disease. GSD-1a is often diagnosed early in life as a neonate or an infant. Some patients present with hypoglycemia and lactic acidosis in the neonatal period. However, most do not show clinical symptoms until they are a few months old, with symptomatic hypoglycemia or hepatomegaly often being the first symptom. Guidelines from the European Study on GSD-1 (eSGSD-1) recommend that diagnosis is initially made based on clinical presentation and biochemical abnormalities. Genetic testing for identification of pathogenic variants of the G6PC1 gene confirms diagnosis. If inconclusive, liver biopsies are often performed to assess the presence of mutation. This test is not part of the Recommended Uniform Screening Panel (RUSP) of newborn genetic screening. This is a lifelong diagnosis, and early intervention is critical to prevent complications of the disease.

Prior to Genglycos (pariglasgene brecaparvovec), patients with GSD-1a have had few strategies for management of the disease - the most common being strict dietary changes. The core goals of management of the disease is to maximize time in euglycemia, avoid fasting, and limit disease related metabolic complications. Children under 3 years old typically receive a nocturnal nasogastric infusion of glucose to avoid hypoglycemia. Patients over 3 years of age are prescribed uncooked

cornstarch, which is a slow-releasing carbohydrate that prolongs euglycemia between meals. Dietary interventions are often effective with very few deaths or developmental effects, however, are disruptive to daily life and prone to error. About 95% of patients reported hypoglycemia despite their best efforts to manage it. Adjunct therapies have also been used to manage complications of the disease such as ACE-I for renal dysfunction and lipid lowering agents for hypercholesterolemia. Liver transplantation is considered for patients with unresectable hepatocellular adenomas that are not responsive to dietary therapy. If left untreated, adenomas can progress to severe compression, hemorrhage, and hepatocellular carcinomas.
Genglycos is an AAV8 vector-based gene therapy manufactured using recombinant DNA technology. Genglycos delivers a functional copy of glucose-6-phosphatase catalytic subunit 1 (G6PC) gene to hepatocytes, resulting in production of normal functioning glucose-6-phosphatase enzyme (G6Pase) which cam respond to usual hormonal signals like insulin or cortisol. Accelerated approval was based on the Phase 3 GlucoGene Study (NCT05139316). The effectiveness of Genglycos was evaluated in a randomized, double-blind, placebo-controlled study in patients with GSDIa followed over 48 weeks after dosing. Patients treated with Genglycos demonstrated a statistically significant mean reduction from baseline in daily cornstarch intake of 31% compared to placebo, the study's primary endpoint. A mean reduction from baseline of one cornstarch dose per day was seen in the Genglycos group compared to placebo, the study's secondary endpoint. Genglycos-treated patients experienced a numerical (mean 3%) increase in the percentage of glucose values in the hypoglycemic range (< 70 mg/dL) compared to placebo.
Across two clinical studies of Genglycos, including the randomized clinical study, serious adverse reactions reported in Genglycos-treated patients included anaphylaxis, adrenal insufficiency (a condition where the adrenal glands do not produce enough stress hormones), high lactate levels, and hypoglycemia. The most commonly reported adverse reactions included increased transaminases (elevation of liver enzymes), nausea, headache, constipation, and hyperglycemia. Genglycos-treated patients had a higher rate of hypertriglyceridemia (high blood triglyceride levels), a metabolic marker of GSDIa, compared to placebo-treated patients (29% vs 8%). The prescribing information contains warnings about the risks of anaphylaxis, liver toxicity, adrenal insufficiency, and risk of tumorigenicity (development of tumors). Genglycos should not be used during pregnancy.

POLICY:

Genglycos (pariglasgene brecaparvovec-opnr) - Medical
Commercial/Essential/Exchange: Based on a review of the available peer-reviewed evidence, pariglasgene brecaparvovec (Genglycos) is considered not medically necessary for the treatment of Glycogen Storage Disease Type 1a. (Von Gierke Disease) In the 48 week, randomized, double-blind, placebo-controlled, phase 3 "GlucoGene" trial (NCT05139316), pariglasgene brecaparvovec demonstrated a statistically significant reduction in total daily cornstarch intake and frequency of cornstarch dosing. The study showed a 41.3% daily cornstarch dose reduction in the treatment group compared to 10.3% in the placebo group. It also showed a mean reduction of 1.1 cornstarch doses per day in the treatment group as compared to 0.2 in the placebo group. Secondary endpoints included a non-statistically significant reduction in the number of night-time cornstarch doses as well as the percent of patients that were able to eliminate the need for nighttime dosing. However, there is **insufficient evidence to conclude that these improvements translate into clinically meaningful patient outcomes**. As stated in the Genglycos package insert, FDA approval was based on reduction in daily cornstarch intake, not based on clinical benefit from confirmatory trials.

Additional clinical data from the phase 3 trial "GlucoGene" is limited. A secondary endpoint of maintenance of glucose control at week 48 in the treatment group (glucose values at or above 70 mg/dL) was shown to be noninferior to placebo. The phase 1/2 trial (NCT03517085) assessed clinical endpoints, including the mean time in minutes/g of carbohydrates to hypoglycemia and average monthly time in euglycemia with cornstarch dosing. The study revealed that the mean percent increase of normalized time to hypoglycemia during baseline to week 51 was 46%. This endpoint was not proven to be statistically significant and did not demonstrate clinical benefit. Average monthly time in euglycemia with cornstarch dosing was seen to have increased despite reductions in daily cornstarch intake. This datapoint was not proven to be statistically significant.

GSD-Ia is a rare and heavily burdensome disease. The frequency and quantity of cornstarch dosing, including nocturnal administration, are inhibitory to patients' quality of life. While treatment with Genglycos reduced daily cornstarch requirements, **uncertainty remains regarding whether the magnitude of this reduction translates into clinically meaningful improvements in patient outcomes beyond treatment burden itself.** Therefore, disease rarity, first-in-indication status, and unmet need were not considered sufficient to resolve the uncertainty surrounding the clinical impacts of the observed benefit.

Reconsideration of Medical Necessity
This determination will be reconsidered if new evidence addresses the uncertainty regarding the clinical and statistical significance of pariglasgene brecaparvovec (Genglycos) treatment-attributable benefit. Evidence that may support reconsideration includes:

- A prespecified, statistically controlled responder analysis demonstrating a clinically meaningful incremental benefit versus placebo or an appropriate active comparator;
- Replication or confirmation of clinically meaningful responder benefit in an additional adequately designed study;
- Demonstration of sustained benefit beyond the currently established 48-week controlled treatment period;
- Statistically and clinically meaningful between-group improvement in patient-centered outcomes such as reductions in life-threatening GSD-related events, glycemic control, metabolic control, etc.;
- Longer-term evidence that more broadly characterizes the benefit-risk profile.
- Evidence demonstrating a clinically meaningful reduction in treatment burden, including frequency of cornstarch dosing, overnight feeding requirements, or caregiver impacts
- Results from confirmatory studies verifying that reductions in cornstarch requirements translate into clinically meaningful benefits

Medicare Advantage/Medicaid/HARP:

1. Must be at least 8 years of age **AND**
2. Prescribed by or in consultation with a geneticist, metabolic disease specialist, endocrinologist, hepatologist experienced and/or specializes in the treatment of GSD-1a **AND**
3. Must have documentation of a diagnosis of GSD-1a based on one of the following:
    a. Identification of biallelic pathogenic variants in G6PC1 (GSD-1a) **OR**
    b. Liver biopsy with enzymatic confirmation **AND**
4. Prescriber must attest that the patient is clinically stable on current disease management interventions, such as the use of uncooked cornstarch (adequate nutrition, stable glucose control, no recent hospitalizations within the last 3 months due to GSD-1a related hypoglycemia) **AND**
5. Patient must **NOT** have detectable, pre-existing AAV8 antibodies prior to therapy **AND**
6. Patient must **NOT** have any of the following:
    a. Liver cirrhosis or fibrosis of any stage **OR**
    b. Present liver adenoma measuring >5 cm (*Medicaid ONLY*) **OR**

c. Present liver adenoma measuring between 3-5 cm with a documented annual growth rate of ≥ 0.5 cm (*Medicaid ONLY*) **OR**
d. History of liver transplantation (*Medicaid ONLY*) **OR**
e. Current pregnancy (*Medicaid ONLY*) **AND**

7. Must continue dietary adjustments and/or cornstarch as deemed fit in collaboration with prescriber **AND**
8. Must have scheduled access to corticosteroid therapy beginning 2 weeks post-infusion for a minimum of 8 weeks with monitoring of hepatic enzymes and adrenal function
9. Recommended dosage for GSD-1a is a single lifetime infusion of 1.0×10^{13} gc/kg of body weight
10. Genglycos (pariglasgene brecaparvovec) is indicated for one-time single-dose intravenous use only and therefore will not be authorized for retreatment. Retreatment will be considered experimental/investigational.
11. Genglycos (pariglasgene brecaparvovec) is considered experimental/investigational when the above criteria are not met.
12. Genglycos (pariglasgene brecaparvovec) to treat other indications will be considered experimental/investigational.
13. Approval will be for 6 months to allow one-time administration

POLICY GUIDELINES:

1. Utilization Management are contract dependent. Refer to specific contract/benefit language for exclusions.
   a. Coverage criteria may be dependent on the contract renewal date.
   b. Coverage of drugs listed in this policy are contract dependent.
   c. Not all contracts/benefits allow coverage of healthcare professional administered drugs as part of their pharmacy benefit
   d. Not all contracts/benefits cover all medical infusible drugs.
   e. Not all policy criteria may apply if treatment of specific disease states or conditions is not a covered benefit.
2. Clinical documentation must be submitted for each request (initial and recertification [if applicable]) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments and treatment history, diagnostic testing, laboratory test results, genetic testing or biomarker results, imaging and other objective or subjective measures of benefit. Requested dosing must remain consistent with FDA-approved dosing recommendations.
3. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
4. Unless otherwise indicated within drug specific criteria, the drugs listed in this policy are administered by a healthcare professional and therefore are covered under the medical benefit.
5. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
6. For commercial contracts, medical necessity determinations align with the Certificate of Coverage issued by the Health Plan, which states that covered services must be clinically appropriate and not primarily for the convenience of the member, the member's family, or the provider.
7. This policy is based on available evidence as of the last review date. Coverage determinations are subject to applicable plan documents, state and federal regulations, and individual patient circumstances. This policy does not constitute medical advice.

8. This policy is subject to ongoing revision. Newly marketed drugs and existing drugs with new indications may be subject to prior authorization until formal coverage criteria are established. Inclusion of a drug in this policy does not guarantee its current availability on the market, as some agents may be discontinued, withdrawn, or otherwise unavailable. As product status changes, drugs may be removed from the policy.
9. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS permits a Medicare Advantage Organization (MAO) to establish its own coverage determinations in accordance with 42 CFR § 422.101(b)(6). Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan. Step therapy requirements may be imposed in addition to LCD/NCD requirements.
10. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html
11. The requested site of care may impact approval timeframe and is subject to review.
12. Approval timeframes may be extended to align authorization periods for drugs administered as part of a multidrug regimen, including when regimen components are administered across different benefits. This provision does not apply when the approval timeframe reflects a drug-specific limitation on duration of therapy
13. The following applies to all gene and cellular therapies unless otherwise specified within the drug-specific coverage criteria:
    a. Administration, Retreatment, and Treatment with Additional or Other Gene/Cellular Therapies
        i. One-Time Administration
            1. Most gene and cellular therapies, whether autologous, allogeneic (“off-the-shelf”), or in vivo gene-transfer therapies, are designed and studied as one-time treatments.
            2. Repeat dosing, reinfusion, or sequential therapy with other gene or cellular products has not been established as safe, effective, or clinically appropriate.
        ii. Retreatment/Repeat Administration
            1. Retreatment with the same gene or cellular therapy product is considered experimental and investigational because:
                a. Clinical trials evaluated these therapies as single-administration interventions
                b. Safety, efficacy, and durability of a second administration have not been established
                c. Risks of immune activation, insertional mutagenesis, or vector immunity may be increased with repeat dosing
        iii. Treatment with an Additional or Other Gene/Cellular Therapy
            1. Treatment with an additional or different gene or cellular therapy after prior exposure to any gene or cellular therapy is also considered experimental and investigational, unless supported by evidence demonstrating (a-c):
                a. Anticipated clinical benefit beyond available standard therapies
                b. Safety of sequential administration

c. Justification for selecting a second gene/cellular intervention after a prior one
2. This includes, but is not limited to:
a. Switching between CAR-T products (e.g., CD19 → CD19 or CD19 → BCMA)
b. Switching between autologous and allogeneic cellular therapies
c. Sequential use of CAR-T, TCR-T, NK-cell therapies, or other genetically engineered cell therapies
d. Receiving a gene therapy after previous gene or cellular therapy exposure
e. Receiving an in vivo gene therapy following any prior vector-based therapy

iv. Prior Gene/Cell Therapy Exposure
1. An individual is generally not eligible for additional gene or cellular therapy if they have previously received:
a. Any autologous cellular therapy (e.g., CAR-T, TCR-T, TIL),
b. Any allogeneic genetically modified cellular therapy,
c. Any in vivo gene therapy (e.g., AAV, lentiviral vector)
d. Any ex vivo gene-modified cell product
e. Are being considered for any other gene or cellular therapy without documented evidence supporting safety and anticipated benefit.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.
Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).
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HCPCS: J3590 (NOC)

UPDATES:

Date	Revision
11/24/2026	Created
11/12/2026	P&T Committee Approval of Criteria

REFERENCES:

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4. GENGLYCOS™ (pariglasgene brecaparvovec-opnr) [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical Inc; 2026.