Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 10/08/2026

Genglycos™ (pariglasgene brecaparvovec-opnr)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Coverage of the requested drug is considered investigational/experimental for all indications due to insufficient evidence of a clinical benefit
      i. BCBSM and BCN are awaiting the results of ongoing clinical trials to provide evidence of a clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Glycogen storage disease type Ia (GSD1a) is a rare, autosomal recessive disorder caused by a mutation on the glucose-6 phosphatase (G6PC) gene. It is characterized by a dysfunctional glucose-6-phosphatase enzyme which is responsible for the production of free glucose that can enter the bloodstream. When the enzyme is not functional, glycogen and fat accumulate in the liver and kidneys.

- The primary symptom of GSD1a in infancy is hypoglycemia. Symptoms usually begin at three to four months of age and include hepatomegaly, nephromegaly, elevated levels of lactate, uric acid, and lipids, and possible seizures due to repeated episodes of hypoglycemia. Continued low blood sugar can lead to delayed growth and development and muscle weakness. Affected children typically have doll-like faces with fat cheeks, relatively thin extremities, short stature, and protuberant abdomen. Other conditions associated with untreated GSD1a include xanthomas, osteoporosis, delayed puberty, gout, kidney disease, pulmonary hypertension, hepatic adenoma, polycystic ovaries, pancreatitis, diarrhea, and changes in brain function.

- The 2014 American College of Medical Genetics and Genomics Diagnosis and Management of Glycogen Storage Disease Type 1 Practice Guidelines state presence of hepatomegaly with hypoglycemia should prompt a workup that

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includes measurement of blood glucose, lactate, uric acid, liver function tests, cholesterol, triglycerides, a basic chemistry panel, creatine kinase, and a complete blood cell count. The combination of hypoglycemia, lactic acidosis, hypercholesterolemia, hypertriglyceridemia, and hyperuricemia is strongly suggestive of the diagnosis of GSD1a. Diagnosis should be confirmed via genetic testing showing a genetic mutation in the G6PC gene.

- The primary goal of treatment is maintenance of physiologic glucose levels. Guidelines recommend keeping blood glucose greater than or equal to 70 mg/dL as other clinical and biochemical parameters, such as somatic growth, lactic acidosis, and hypertriglyceridemia, improve in parallel with improved glucose control. Between meals, glucose concentrations can be maintained with oral administration of uncooked cornstarch. In many cases, a dose of cornstarch is also needed during the night. Guidelines recommend a dose of uncooked cornstarch of 1.6 g/kg every 3 to 4 hours for young children and 1.7 to 2.5 g/kg every 4 to 6 hours for older children, adolescents, and adults.

- Genglycos is a disease modifying therapy approved to reduce daily cornstarch intake as an adjunct to nutritional management in adult and pediatric patients 8 years of age and older with GSD1a. It is an adeno-associated virus (AAV) vector-based gene therapy that replaces the disfunction G6PC gene in GSD1a patients with a functional copy. This indication is approved under accelerated approval based on reduction in daily cornstarch intake. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

- Safety and efficacy were evaluated in the GlucoGene trial, a phase III, randomized, double-blind, placebo-controlled study of 46 patients 8 years and older with GSD1a. Patients were included in the trial if they had disease confirmed via genetic testing or decreased glucose 6-phosphatase activity on liver biopsy. Participants must have been on a cornstarch regimen resulting in stable nutritional, glycemic, and clinical status. Subjects were excluded from the trial if they had detectable pre-existing antibodies to the AAV8 capsid, history of liver transplant, liver disease, non-fasting triglycerides greater than or equal to 1000 mg/dL, and/or significant hepatic inflammation or cirrhosis as evidenced by imaging or any of the following: alanine aminotransferase (ALT) or aspartate aminotransferase (AST) greater than the upper limit of normal (ULN), total bilirubin greater than 1.5 times the ULN, alkaline phosphatase greater than 2.5 times the ULN. The primary endpoint was the reduction in oral glucose replacement with cornstarch while maintaining glucose control. Patients treated with Genglycos demonstrated a statistically significant mean reduction from baseline in daily cornstarch intake of 31% compared to placebo (p-value < 0.0001).

- The commercial plan considers cellular and gene therapies to be proven effective to treat a condition if the following are true: the drug has full Food and Drug Administration approval that was not obtained under the FDA's accelerated approval pathway and the drug met all of its primary endpoint(s) in its pivotal trials, or if confirmatory trials were required, the drug met its primary endpoint(s) in its confirmatory trial(s). Cellular and gene therapies that haven't been proven effective (do not meet the listed criteria) are considered a benefit contract exclusion for most commercial plans.

- Genglycos was approved under the FDA's accelerated approval pathway, and therefore, is considered experimental/investigational for the commercial plan until further confirmatory trials are complete and the medication gets full FDA approval.

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References:

1. Genglycos [prescribing information]. Novato, CA: Ultragenyx Pharmaceutical Inc.; August 2026.
2. Clinicaltrials.gov. A study of adeno-associated virus serotype 8-mediated gene transfer of glucose-6-phosphatase in patients with glycogen storage disease type Ia (GSDIa) (NCT05139316). Available at: https://clinicaltrials.gov/study/NCT05139316. Accessed on August 20, 2026.
3. Weinstein DA, Derks TG, Rodriguez-Buritica DF, et al. Safety and efficacy of DTX401, an AAV8-mediated liver-directed gene therapy, in adults with glycogen storage disease type Ia (GSDIa). J Inherit Metab Dis. 2025 Mar; 48 (2): e70014.
4. National Organization of Rare Disorders. Glycogen storage disease type I. 2019 Dec 23. Available at: https://rarediseases.org/rare-diseases/glycogen-storage-disease-type-i/. Accessed on August 20, 2026.
5. Kishnani PS, Austin SL, Abdenur JE, et al. Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics. Genet Med. 2014; 16: e1.

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.2</td><td>Effective Date: 10/08/2026</td><td>New Policy - This criteria replaces previously approved preliminary criteria</td></tr>
<tr><td>1.1</td><td>Effective Date: 08/31/2026</td><td>UM medical management system update for BCBS and BCN
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
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<tr><td>1.0</td><td>Effective Date: 12/04/2025</td><td>Preliminary Drug Review
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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