Molina Clinical Policy
GenGlycos (pariglasgene brecaparvovec): MEDICARE
Policy No. 487b

Initial Approval: 10/21/2026
Next Review Due By: October 2027

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment. Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of the Federal government or CMS for Medicare. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy covers the use of Genglycos (pariglasgene brecaparvovec; DTX401) for the treatment of Glycogen storage disease Type 1a.

Glycogen storage disease type Ia (GSDIa) is a rare, inherited disorder of carbohydrate metabolism caused by biallelic pathogenic variants in the G6PC1 gene (glucose-6-phosphatase catalytic subunit 1), which encodes the enzyme glucose-6-phosphatase (G6Pase). G6Pase catalyzes the final step of glycogenolysis and gluconeogenesis, allowing glucose to be released from the liver into the circulation during fasting. Deficiency of this enzyme impairs endogenous glucose production and results in accumulation of glycogen and metabolic intermediates within affected tissues. GSDIa is generally considered a life-threatening disorder that requires lifelong management (Weinstein et al. 2025)

The primary tissue affected in GSDIa is the liver, although kidneys and intestinal tissues also express G6Pase and may be affected. Deficient enzyme activity leads to excessive glycogen and fat accumulation within hepatocytes, causing hepatomegaly and progressive metabolic dysfunction. Over time, patients may develop hepatic adenomas, hepatic malignancy, nephropathy, nephrolithiasis, osteoporosis, and other long-term complications despite treatment. Clinical manifestations typically begin during infancy, when fasting intolerance becomes apparent after feeding intervals lengthen. Patients commonly present with severe fasting hypoglycemia, lactic acidosis, hypertriglyceridemia, hyperuricemia, growth impairment, hepatomegaly, and feeding difficulties. Although dietary management has substantially improved survival, affected individuals remain at lifelong risk for acute metabolic decompensation and chronic organ complications. Disease burden is driven not only by metabolic abnormalities but also by the need for continuous nutritional intervention, including overnight feeding strategies to prevent hypoglycemia (Bali et al. 2021)

Diagnosis is typically established through a combination of clinical findings, biochemical abnormalities, and molecular genetic testing. Characteristic laboratory findings include fasting hypoglycemia, elevated lactate, hypertriglyceridemia, hyperuricemia, and elevated liver transaminases. Confirmation is generally achieved through identification of pathogenic variants in both alleles of the G6PC1 gene. Liver biopsy and enzyme analysis have historically been used but have largely been replaced by molecular diagnostic testing. There is currently no curative medical therapy for GSDIa. Standard management focuses on prevention of hypoglycemia through strict dietary therapy designed to provide a continuous source of exogenous glucose. Despite adherence to dietary treatment, many patients continue to experience metabolic instability and remain at risk for long-term complications. Liver transplantation may be considered for select patients with severe hepatic disease or malignant transformation but is associated with significant morbidity and lifelong immunosuppression (Bali et al. 2021). The estimated prevalence of GSDIa is approximately 1 in 100,000 individuals, making it an ultra-rare disorder.

Pariglasgene brecaparvovec (Genglycos; DTX401) is a liver-directed gene therapy designed to address the underlying enzyme deficiency in GSDIa. DTX401 utilizes an adeno-associated virus serotype 8 (AAV8) vector to deliver a functional copy of the human G6PC1 gene to hepatocytes, thereby enabling production of glucose-6-phosphatase. Restoration of hepatic G6Pase activity is intended to improve endogenous glucose production during fasting and reduce dependence on daily cornstarch supplementation, (Genglycos FDA prescribing information 2026).

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COVERAGE POLICY

Genglycos (pariglasgene brecaparvovec) may be **considered medically necessary for the treatment of** Glycogen storage disease type Ia (GSDIa) when the following criteria are met:

1. Member is ≥ 8 years of age
2. Documented GSDIa with confirmation via genetic testing or enzymatic activity on liver biopsy
3. Documented history of ≥1 hypoglycemic event with blood glucose <60 mg/dL
4. Member's GSDIa disease is stable, as evidenced by no hospitalizations or severe hypoglycemia episodes 4 weeks prior to administration of therapy
5. Triglyceride level < 1000 mg/dl
6. For members with current liver adenoma(s) > 5 cm in size *or* liver adenoma >3 cm and ≤5 cm in size with documented annual growth rate of ≥0.5 cm per year, definitive adenoma evaluation and treatment must be completed prior to considering DTX401 (documentation required)
7. No significant hepatic inflammation or cirrhosis on imaging
8. No significant laboratory abnormalities, such as:
    a. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > upper limit of normal (ULN)
    b. Total bilirubin > 1.5 x ULN
    c. Alkaline phosphatase > 2.5 x ULN
9. No detectable Anti-AAV8 antibodies
10. No history of liver transplant, including hepatocyte cell therapy/transplant
11. Females of childbearing potential and fertile males must consent to highly effective contraception during treatment. Male members must agree not to father a child or donate sperm.
12. Member is not pregnant or breastfeeding

Limitations and Exclusions

QUANTITY LIMITATIONS: FDA approved dosing with one-time dose per lifetime. Additional infusions of DTX401 will not be authorized.

CONTINUATION OF THERAPY: DTX401 is indicated as a one-time infusion only. Repeat treatment or re-administration of a dose is not supported by labeling or compendia and is not considered medically necessary.

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the Member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

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SUMMARY OF MEDICAL EVIDENCE

Weinstein et al. (2025) reported results from a multicenter, open-label, Phase 1/2 dose-escalation trial (NCT03517085) evaluating pariglasgene brecaparvovec (DTX401), an adeno-associated virus serotype 8 (AAV8) liver-directed gene therapy containing a functional G6PC1 transgene, in adults with genetically confirmed glycogen storage disease type Ia (GSDIa). Twelve adults received a single intravenous infusion of DTX401 and were followed for 52 weeks. Three participants received 2.0 × 10^12 genome copies (GC)/kg and nine participants received 6.0 × 10^12 GC/kg. Corticosteroids were administered prophylactically or reactively to mitigate vector-related immune responses.

The primary endpoint was safety. All participants experienced treatment-emergent adverse events (TEAEs), most commonly transient elevations in liver enzymes, headache, diarrhea, and vomiting. No dose-limiting toxicities, treatment-related serious adverse events, deaths, or discontinuations due to adverse events occurred. Five serious adverse events were reported in four participants (lactic acidosis, metabolic disorder, cellulitis, migraine, and nephrolithiasis); investigators considered all to be unrelated to DTX401 and attributable to underlying disease or pre-existing conditions. Liver enzyme elevations were generally mild to moderate, asymptomatic, and resolved with corticosteroid management.

Efficacy assessments demonstrated improvements in fasting tolerance and reductions in dietary cornstarch requirements. Mean time to hypoglycemia during a controlled fasting challenge increased from 3.4 hours at baseline to 5.2 hours at Week 52. When adjusted for carbohydrate intake, normalized time to hypoglycemia increased by 46% from baseline to Week 52. Mean daily cornstarch consumption decreased from 284 g at baseline to 85 g at Week 52 among evaluable participants, representing a 68% reduction ($p<0.001$). Cornstarch intake decreased in all participants, and one participant completely discontinued cornstarch use by study completion. Continuous glucose monitoring data demonstrated maintained or improved glycemic control despite substantial reductions in cornstarch supplementation.

Patient-reported outcomes suggested clinical benefit, with 89% of participants reporting at least minimal improvement in disease status at Week 52 and no participants reporting worsening. Based on these findings, investigators concluded that DTX401 demonstrated an acceptable safety profile and evidence of clinical efficacy, including sustained reductions in cornstarch requirements and maintenance of glycemic stability through 52 weeks. The dose of 6.0×10^{12} GC/kg was selected for further evaluation in the ongoing Phase 3 trial (NCT05139316).

The FDA used data from study DTX401-CL301 (NCT05139316) in their approval decision. This is a phase 3 study of efficacy and safety of DTX401 in participants 8 years and older with GSD1a. The study was just published as of the writing of this policy. As reported by Mitchell et al (2026), the phase 3 trial is a multicenter, randomized, double-blind, placebo-controlled trial with a crossover extension at 48 weeks. There were 44 participants in the intent to treat population, all underwent nutritional stabilization and optimization prior to DTX401 therapy.

The primary endpoint was reduction in cornstarch intake (a surrogate endpoint). A single intravenous infusion of pariglasgene brecaparvovec resulted in a 41% reduction in daily cornstarch requirements compared with a 10.2% reduction with placebo at Week 48 (treatment difference -30.9%). Reductions in dosing frequency and sustained effects through Week 96 were also observed. Pariglasgene was generally safe and led to meaningful cornstarch reductions.

National and Specialty Organizations

As of August 2026, there are no published guidelines for the use of this therapy.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

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HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Genglycos (pariglasgene brecaparvovec)]
J3590	Unclassified biologics [when specified as Genglycos (pariglasgene brecaparvovec)]

CODING DISCLAIMER: Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

10/21/2026 New policy. IRO review completed on September 16, 2026 by a practicing physician board certified in Pediatrics, Clinical Genetics and Genomics, and Medical Biochemical Genetics.

REFERENCES

1. Bali D. S., El-Gharbawy A., Austin S., Pendyal S., and Kishnani P. S. 2006. “Glycogen Storage Disease Type I,” In GeneReviews® [Internet], edited by Adam M. P., Everman D. B., Mirzaa G. M., et al. University of Washington. Last updated October 14, 2021.
2. ClinicalTrials.gov. Safety and Dose-Finding Study of DTX401 (AAV8G6PC) in Adults with Glycogen Storage Disease Type Ia (GSDIa) [NCT03517085]. National Library of Medicine. Last updated 11/18/2022. https://clinicaltrials.gov/study/NCT03517085
3. 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]. National Library of Medicine. Last updated 3/25/2026. https://clinicaltrials.gov/study/NCT05139316
4. ClinicalTrials.gov. Study of Long-Term Safety and Efficacy on Gene Therapy in Glycogen Storage Disease Type Ia [NCT03970278.]. National Library of Medicine. Last updated March 18, 2026. https://clinicaltrials.gov/study/NCT03970278
5. Mitchell JJ, Abdenur JE, de Boer F, Boyer M, et al. Phase 3 Randomized Trial Results of DTX401 AAV Gene Therapy for the Treatment of GSDIa. J Inherit Metab Dis. 2026 Sep;49(5):e70241. doi: 10.1002/jimd.70241. PMID: 42674977; PMCID: PMC13529436.
6. United States Food and Drug Administration (FDA). Genglycos (pariglasgene brecaparvovec-opnr) prescribing information. Accessed August 2026. https://www.fda.gov/media/194364/download?attachment
7. 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;48:e70014. doi:10.1002/jimd.70014.

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