CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Glycogen Storage Disease – Gene Therapy – Genglycos Utilization Management Medical Policy

- Genglycos™ (pariglasgene brecaparvovec-opnr intravenous infusion – Ultragenyx)

REVIEW DATE: 09/02/2026; selected revision 09/09/2026

OVERVIEW

Genglycos, an adeno-associated virus (AAV) vector-based gene therapy, is indicated to reduce daily cornstarch intake as an adjunct to nutritional management in adults and pediatric patients ≥ 8 years of age with **glycogen storage disease type 1a** (GSD1a).[1]

Genglycos was approved under accelerated approval based on reduction in daily cornstarch intake.[1] Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Genglycos is given at a dose of 1.0×10^{13} genome copies per kg of body weight, as a single intravenous (IV) infusion.[1]

Disease Overview

GSD1a, also known as Von Gierke disease, is an ultra-rare, autosomal recessive disorder with a prevalence of one in 100,000.[2] GSD1a is caused by biallelic pathogenic variants in the glucose-6-phosphatase C (*G6PC*) gene, which results in a deficiency in the enzyme glucose-6-phosphatase (G6Pase).[2,3] Deficiency in G6Pase affects carbohydrate homeostasis and results in accumulation of glucose-6-phosphate and glycogen in tissues. Clinical manifestations include hepatomegaly and hypoglycemia, especially in-between meals. Long-term consequences include hepatic adenocarcinoma and chronic renal disease. First-line management of GSD1a is dietary management to provide a continuous exogenous source of glucose. Raw cornstarch remains the cornerstone of treatment of GSD1a. The cornstarch dose needs to be individualized; undertreatment may result in hypoglycemia events, seizures, and death. Overtreatment can lead to obesity, hyperlipidemia and metabolic instability, worsening hepatomegaly, hyperinsulinemia, and lactic acidosis.

Clinical Efficacy

Genglycos was studied in one randomized, double-blind, multicenter, placebo-controlled (Week 1 to Week 48), crossover (Week 48 to Week 96) study (unpublished) [n = 46].[1,4,5] Eligible patients were ≥ 8 years of age with documented GSD1a with confirmation by molecular testing or enzymatic activity on liver biopsy.[4] Patients with detectable anti-AAV8 total antibodies at baseline were excluded.[1,4] In addition, patients with a history of liver transplant or significant liver disease could not participate.[4] Before randomization, patients completed a 16-week period of nutritional optimization and stabilization, during which cornstarch dosing and dietary intake were adjusted.[1,4] Patients were randomized to receive a single IV infusion of either Genglycos at a dose of 1.0×10^{13} genome copies per kg of body weight or placebo. The mean patient age was 20.5 years.[1] At baseline, the mean daily cornstarch intake was 294 g in the Genglycos group and 272 g in the placebo group, and the mean number of daily cornstarch doses in each group was 5.8 and 5.1, respectively. In addition, at baseline, in the Genglycos group, 2.5% of glucose values were in the hypoglycemic range (< 70 mg/dL); in the placebo group, 1.9% of glycemic values were in the hypoglycemic range. The primary efficacy endpoint was the percent change in total daily cornstarch intake from baseline to Week 48. The secondary efficacy endpoints included the change in the number of daily cornstarch doses

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from baseline and the proportion of glucose values in the hypoglycemia range (< 70 mg/dL) averaged over a 4-week period. At Week 48, the mean daily cornstarch dose was reduced by 41.1% in the Genglycos group and by 10.2% in the placebo group (treatment difference of 30.9%; P < 0.0001).[1,5] The mean number of daily cornstarch doses in the Genglycos group was decreased by 1.2 at Week 48; in the placebo group, the reduction was 0.2 (treatment difference of 1.0 doses).[1] Compared with placebo group, patients in the Genglycos group experienced a 3.1% increase in the percentage of glucose values in the hypoglycemia range. However at Week 48, the time to a hypoglycemia event after a dose of cornstarch was increased by 1.1 hours in the Genglycos group and by 0.5 hours in the placebo group.[5]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Genglycos. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Genglycos as well as the specialized training required for administration of Genglycos, approval requires Genglycos to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one-time (per lifetime) as a single dose. The approval duration is 90 days to allow for an adequate timeframe to administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for use of Genglycos as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Genglycos is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Glycogen Storage Disease Type 1a.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, and J):
   Note: Glycogen Storage Disease Type 1a is also known as Von Gierke disease.
   - **A)** Patient is ≥ 8 years of age; AND
   - **B)** Patient has not received Genglycos in the past **[verification in claims history required]**; AND
     Note: If no claims for Genglycos is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Genglycos.
   - **C)** Diagnosis of glycogen storage disease type 1a is confirmed by ONE of the following (i or ii):
     - **i.** Molecular testing showing variants in the glucose-6-phosphatase C (*G6PC*) gene **[documentation required]**; OR
     - **ii.** Liver biopsy showing reduced or absent glucose-6-phosphatase activity **[documentation required]**; AND
   - **D)** Patient does not have detectable preexisting antibodies to the adeno-associated virus serotype 8 (AAV8) capsid **[documentation required]**; AND
   - **E)** Patient has not had a liver transplant in the past; AND

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F) According to the prescribing physician, patient does not have severe liver disease; AND
Note: Examples of severe liver disease include severe hepatic fibrosis or cirrhosis.

G) The medication will be used in conjunction with nutritional management **[documentation required]**; AND
Note: Nutritional management includes use of cornstarch.

H) The medication is prescribed by an endocrinologist, hepatologist, gastroenterologist, medical geneticist, or metabolic disease specialist.

I) Current patient body weight has been obtained within the past 30 days **[documentation required]**; AND

J) If criteria A through I are met, approve one dose of Genglycos to provide a one-time (per lifetime) single dose of 1 x 10^{13} genome copies per kg of body weight by intravenous infusion **[verification required]**. Genglycos is provided as a customized kit to meet dosing requirements for each patient per their weight (in kilograms). Genglycos kit sizes (per the cited NDC) are in Table 1.

Dosing. The recommended dose of Genglycos is a one-time (per lifetime) single-dose intravenous infusion of 1.0 x 10^{13} genome copies per kg of body weight. Genglycos is provided as a customized kit to meet dosing requirements for each patient per their weight (in kilogarams). Refer to the appropriate NDC number below for approval.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Genglycos is not recommended in the following situations:

1. **Prior Receipt of Gene Therapy**. Genglycos has not been studied in patients who have undergone prior gene therapy.[1,4,5]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Table 1. Genglycos Kits.

Patient Body Weight Range (kg)	Total Dose Volume (mL)	Number of Vials	NDC Number
15 to < 21	6	3	69794-333-03
21 to < 27	8	4	69794-334-04
27 to < 33	10	5	69794-335-05
33 to < 39	12	6	69794-336-06
39 to < 45	14	7	69794-337-07
45 to < 51	16	8	69794-338-08
51 to < 57	18	9	69794-339-09
57 to < 63	20	10	69794-340-10
63 to < 69	22	11	69794-341-11
69 to < 75	24	12	69794-342-12
75 to < 81	26	13	69794-343-13
81 to < 87	28	14	69794-344-14
≥ 87	30	15	69794-345-15

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REFERENCES

1. Genglycos™ intravenous infusion [prescribing information]. Novato, CA; Ultragenyx: August 2026.
2. Derks TGJ, Rodrigues-Buritica, Ahmad A, et al. Glycogen storage disease type 1a: current management options, burden and unmet needs. *Nutrients*. 2021;11:3282.
3. Nana M, Anastasopoulou C, Parikh NS, et al. Glycogen Storage Disease Type I. [Updated 2025 Apr 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534196/. Accessed on August 20, 2026.
4. Genglycos – Data on File, Pre-Approval. From Ultragenyx, received 07.24.2026.
5. Genglycos – Data on File, Post-Approval. From Ultragenyx, received 08.25.2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	09/02/2026
Selected Revision	**Policy Statement:** Regarding specialist physician, the phrase "or in consultation with" was removed; Genglycos must be prescribed by a physician who specialized in the condition being treated. Statements regarding verification were added: If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. It was added that all reviews (approvals and denials) will be forwarded to the Medical Director for evaluation. **Documentation Section:** This was added to the policy. **Glycogen Storage Disease Type 1a:** The following changes were made to the policy: **1.** Added a requirement that patient has <u>not</u> received Genglycos in the past and a Note that if there is no claim or if claims history is not available, the prescribing physician confirms that patient has not previously received Genglycos. **2.** "Documentation required" was added to the following requirements: diagnosis (either by molecular testing or liver biopsy) and patient does not have detectable preexisting antibodies to the adeno-associated virus serotype 8 (AAV8) capsid. **3.** The phrase "According to the prescribing physician" was added to the requirement that patient does not have severe liver disease. **4.** Regarding the requirement that the medication is used with nutritional management, the example of cornstarch was moved to a Note. It was added that documentation is required for this requirement. **5.** For the requirement that the medication is prescribed by or in consultation with a specialist, the wording "or in consultation with" was deleted; the requirement now reads: The medication is prescribed by an endocrinologist, hepatologist, gastroenterologist, medical geneticist, or metabolic disease specialist. **6.** Added a requirement that body weight was obtained within the past 30 days, with documentation required. **7.** Added a requirement that if criteria A through J are met, approve one dose of Genglycos to provide a one-time (per lifetime) single dose of 1 x 10^{13} genome copies per kg of body weight by intravenous infusion **[verification required]**. Genglycos is provided as a customized kit to meet dosing requirements for each patient per their weight (in kilograms). Genglycos kit sizes (per the cited NDC) were added in a table (Table 1). **8.** The Dosing section was slightly reworded to the standardized form. It was noted in this section that Genglycos is provided in kits.	09/09/2026

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