Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Dasiglucagon (ZP4207)

Reference Number: CP.PHAR.642
Effective Date: FDA Approval Date
Last Review Date: 11.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Dasiglucagon (ZP4207®/™) is a glucagon receptor agonist.

FDA Approved Indication(s) [Pending]

ZP4207* is indicated for the treatment of congenital hyperinsulinism (CHI) in patients 7 days of age and older.

Limitation(s) of use: [XXX]*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that [ZP4207]* is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Congenital Hyperinsulinism (must meet all)**:**

1. Diagnosis of CHI as evidence by any one of the following (a, b, c, or d, *see Appendix D*):*
   a. Plasma insulin detection during an event of hypoglycemia;
   b. Plasma free fatty acid < 1.7 mmol/L;
   c. Beta-hydroxybutyrate < 1.8 mmol/L;
   d. Plasma glucose > 30 mg/dL after one administration of glucagon administration;
2. Prescribed by or in consultation with an endocrinologist or geneticist;*
3. Age ≥ 7 days;*
4. Body weight ≥ 2 kg;*
5. Documentation of number of hypoglycemic events per week (*see Appendix D*);*
6. Failure of diazoxide, unless member has a mutation in the *ABCC8* or *KCNJ11* genes or contraindicated or clinically significant adverse effects are experienced (*see Appendix D*);* †
   †For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395
7. Member has previously undergone near-total pancreatectomy or is not eligible for pancreatic surgery;*

8. Prescriber attestation that member is concurrently receiving standard of care for CHI intensive medical therapy (e.g., continuous dextrose administration, somatotstatin analog);*
9. Dose does not exceed FDA maximum dose.*

Approval duration:
HIM/Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Congenital Hyperinsulinism (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters (a or b, *see Appendix D*):
   a. Decrease in number of hypoglycemic events per week;
   b. Reduction of time in hypoglycemic events;
3. If request is for a dose increase, new dose does not exceed FDA maximum dose.*

Approval duration:
HIM/Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CHI: congenital hyperinsulinism
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
diazoxide (Proglycem®)†	*Neonates and infants:* 8 mg/kg/day PO divided into 3 equal doses every 8 hours or 2 equal doses every 12 hours *Children, Adolescents, and Adults:* 3 mg/kg/day PO divided into 3 equal doses every 8 hours or 2 equal doses every 12 hours	*Neonates and infants:* 20 mg/kg/day *Children, Adolescents, and Adults:* 8 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
†off-label

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General Information

- Laboratory evidence of CHI includes detectable insulin and/or C-peptide, beta-hydroxybutyrate (BOHB), free fatty acids (FFA), and glycemic response to glucagon at time of hypoglycemia:
  - Hyperinsulinemia:
    - Plasma glucose is < 50mg/dL with detectable amounts of insulin
    - C-peptide concentration ≥ 0.5 ng/mL
  - Hypofattyacidemia: plasma FFA < 1.7 mmol/L
  - Hypoketonemia: BOHB < 1.8 mmol/L
  - Glycemic response: increase in glucose of ≥ 30 mg/dL after administration of glucagon
- Hypoglycemia in both phase 3 studies were defined as plasma glucose < 70 mg/dL
- CHI intensive medical therapy includes:
  - Continuous dextrose administration via gastrostomy tube
  - Somatostatin analog (e.g., octreotide, lanreotide)
- Diazoxide treatment and responsiveness are starting points to distinguish CHI phenotypes since patients that do not respond to diazoxide will often require surgery or intensive medical therapy. For patients that do not respond to diazoxide, gene analysis for *ABCC8* and *KCNJ11* genes should be done. Genetic testing is necessary for patients that do not respond to diazoxide since approximately 90% of patients with diazoxide-unresponsive CHI carry a mutation in the *ABCC8* or *KCNJ11* gene. Patients who do not respond to diazoxide may have focal CHI, which is curative with surgery. For patients who do not respond to diazoxide and have diffuse CHI, the next step is either near-total pancreatectomy or intensive medical therapy.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
CHI*	10 µg/hr SC infusion*	Pending*

VI. Product Availability [Pending]

Pending*

VII. References

1. ClinicalTrials.gov. Trial evaluating efficacy and safety of dasiglucagon in children with congenital hyperinsulinism. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04172441. Accessed July 10, 2025.
2. ClinicalTrials.gov. A two-period open-label trial evaluating and safety of dasiglucagon in children with congenital hyperinsulinism. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03777176. Accessed July 10, 2025.

3. ClinicalTrials.gov. Extension trial evaluating the long-term safety and efficacy of dasiglucagon in children with congenital hyperinsulinism. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03941236. Accessed July 10, 2025.
4. Rosenfeld E, Ganguly A, De Leon DD. Congenital hyperinsulinism disorders: Genetic and clinical characteristics. Am J Med Genet C Semin Med Genet. 2019 Dec;181(4):682-692. doi: 10.1002/ajmg.c.31737.
5. Thornton PS, Stanley CA, De Leon DD, et al; Pediatric Endocrine Society. Recommendations from the Pediatric Endocrine Society for evaluation and management of persistent hypoglycemia in neonates, infants, and children. J Pediatr. 2015 Aug;167(2):238-45. doi: 10.1016/j.jpeds.2015.03.057.
6. Yorifuji T, Horikawa R, Hasegawa T, et al; (on behalf of The Japanese Society for Pediatric Endocrinology and The Japanese Society of Pediatric Surgeons). Clinical practice guidelines for congenital hyperinsulinism. Clin Pediatr Endocrinol. 2017;26(3):127-152. doi: 10.1297/cpe.26.127.
7. Demirbilek H, Hussain K. Congenital hyperinsulinism: Diagnosis and treatment update. J Clin Res Pediatr Endocrinol. 2017 Dec 30;9(Suppl 2):69-87. doi: 10.4274/jcrpe.2017.S007.
8. De Leon DD, Arnoux JB, Banerjee I, et al. International Guidelines for the Diagnosis and Management of Hyperinsulinism. Horm Res Paediatr. 2024;97(3):279-298. doi: 10.1159/000531766.
9. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed July 29, 2025.

Coding Implications [Pending]

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively.	08.29.23	11.23
4Q 2024 annual review: no significant changes as drug is still not FDA approved; for initial approval criteria, changed approval duration from 3 months to 6 months; for Appendix B, updated diazoxide dosing; references reviewed and updated.	07.22.24	11.24
4Q 2025 annual review: no significant changes; added step therapy bypass for IL HIM per IL HB 5395; extended approval duration from 6 months to 12 months for HIM and Medicaid and revised commercial duration from 6 months to "6 months or to the member's renewal date, whichever is longer"; references reviewed and updated.	07.10.25	11.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.