Effective Date **3/15/2024**
Next Review Date **3/15/2025**
Coverage Policy Number **IP0039**

Glucagon Products

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following glucagon products:

- **GlucaGen® HypoKit®** (glucagon for injection)
- **Glucagon Emergency Kit** (glucagon for injection)
- **Gvoke™** (glucagon for injection)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Non-Covered Product	Criteria
GlucaGen HypoKit (glucagon for injection)	**Standard/Performance/Legacy Drug List Plans:** Covered as Preferred Brand

Non-Covered Product	Criteria
	<u>Value/Advantage/Cigna Total Savings Drug List Plans:</u> **GlucaGen HypoKit** is considered medically necessary when there is documentation of failure, contraindication, or intolerance to **ONE** of the following: 1. Baqsimi (glucagon nasal powder) 2. Generic glucagon, human recombinant (glucagon for injection) 3. Zegalogue (dasiglucagon)
Glucagon Emergency Kit (glucagon for injection)	**<u>Standard/Performance/Legacy Drug List Plans:</u>** Covered as Preferred Brand **<u>Value/Advantage/Cigna Total Savings Drug List Plans:</u>** **Glucagon Emergency Kit** is considered medically necessary when there is trial of **<u>generic glucagon, human recombinant (glucagon for injection)</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction.
Gvoke Hypopen Auto-Injector, Kit or Prefilled Syringe (glucagon for injection)	**<u>Standard/Performance/Legacy Drug List Plans:</u>** Covered as Preferred Brand **<u>Value/Advantage/Cigna Total Savings Drug List Plans:</u>** **GlucaGen HypoKit** is considered medically necessary when there is documentation of **EITHER** of the following: 1. Less than 4 years of age 2. Failure, contraindication, or intolerance to **ONE** of the following: A. Baqsimi (glucagon nasal powder) B. Generic glucagon, human recombinant (glucagon for injection) C. Zegalogue (dasiglucagon)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of glucagon products are considered medically necessary when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
All of the glucagon products are indicated for the treatment of **severe hypoglycemia** in adults and pediatric patients.[1-5] Of note, glucagon vials (GlucaGen diagnostic vial, glucagon 1 mg vial) are also available for use as a diagnostic aid in imaging procedures; these products are not targeted in this policy.

GUIDELINES

The ADA Standards of Care (2023) address the use of glucagon.[6] Glucose is the preferred treatment for conscious individuals with blood glucose < 70 mg/dL, although any form of carbohydrate may be used. Glucagon is indicated for treatment of hypoglycemia if carbohydrates cannot be consumed by mouth. Glucagon should be prescribed for all individuals at increased risk of level 2 hypoglycemia (blood glucose < 54 mg/dL) or level 3 hypoglycemia (altered mental and/or physical functioning that requires assistance from another person for recovery) so it is available if needed. Those in close contact with, or having custodial care of, people with hypoglycemia-prone diabetes (family members, roommates, school personnel, coworkers, etc.) should be instructed on the use of glucagon, including where the product is kept and how to administer it. It is noted that, in addition to traditional glucagon injection powder that requires reconstitution before injection, intranasal glucagon (Baqsimi) and ready-to-inject glucagon preparations are available, and may be beneficial in view of safety, efficacy, and ease of use.

The Endocrine Society guidelines for the management of individuals at high risk for hypoglycemia (2022) recommend glucagon preparations that do not have to be reconstituted over glucagon preparations that do have to be reconstituted be used for outpatients with severe hypoglycemia.[7] The guidelines note that all of the available glucagon formulations have roughly equivalent efficacy (if properly administered). However, non-inferiority between forms of glucagon requiring reconstitution and those not requiring reconstitution, is relevant only once the glucagon is given in full dosage which may be less likely to occur with products requiring reconstitution. They recommend that glucagon preparations that do not have to be reconstituted be prescribed for all patients with diabetes who use insulin or insulin secretagogues (sulfonlyureas, meglitinides). Ready-to-use glucagon formulations should be available for use by emergency medical services and in medical offices, schools, airports, and other pertinent locations.

References

1. Baqsimi™ nasal powder [prescribing information]. Indianapolis, IN: Lilly; October 2020.
2. Glucagon injection [prescribing information]. Indianapolis, IN: Lilly; January 2021.
3. GlucaGen® injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2021.
4. Gvoke™ injection [prescribing information]. Chicago, IL: Xeris; May 2023.
5. Zegalogue® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; January 2023.
6. ElSayed NA, Aleppo G, Aroda VR. American Diabetes Association. Standards of medical care in diabetes – 2023. *Diabetes Care*. 2023;46(Suppl 1):S1-S290.
7. McCall AL, Lieb DL, Gianchandani R, et al. Management of individuals with diabetes at high risk for hypoglycemia: An Endocrine Society Clinical Practice Guideline. *J Clin Endocr Met.* 2023;108:529-562.