Clinical Policy: Epinephrine (EpiPen, EpiPen Jr, Auvi-Q, Neffy)

Reference Number: CP.PCH.55
Effective Date: 06.01.25
Last Review Date: 08.25
Line of Business: Commercial, HIM

Revision Log

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

Description

Epinephrine (EpiPen®, EpiPen Jr®, Auvi-Q®, Neffy®) is a non-selective alpha and beta-adrenergic receptor agonist.

FDA Approved Indication(s)

EpiPen and EpiPen Jr are indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis.

Auvi-Q is indicated for the emergency treatment of type 1 allergic reactions, including anaphylaxis, in adult and pediatric patients who weigh 7.5 kg or greater.

Neffy is indicated for emergency treatment of type I allergic reactions, including anaphylaxis, in adult and pediatric patients 4 years of age and older who weigh 15 kg or greater.

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 EpiPen, EpiPen Jr, Auvi-Q, and Neffy are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Allergic Reactions (must meet all)**:**

1. Diagnosis of an allergy that may require emergency treatment;
2. For Neffy requests: Member weighs ≥ 15 kg;
3. For Auvi-Q: Member weighs ≥ 7.5 kg;
4. Member experienced clinically significant adverse effects to generic epinephrine auto-injector, has contraindication(s) to its excipients, or for Neffy requests only, has limitations (e.g., manual dexterity, needle phobia) that preclude use of an auto-injector.†

   †For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395

Approval duration:
HIM – 6 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 and HIM.PA.33 for health insurance marketplace; 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 and HIM.PA.103 for health insurance marketplace; 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 and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Allergic Reactions (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.

Approval duration:
HIM – 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 and HIM.PA.33 for health insurance marketplace; 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 and HIM.PA.103 for health insurance marketplace; 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 and HIM.PA.154 for health insurance marketplace.

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 and HIM.PA.154 for health insurance marketplace or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
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
epinephrine auto-injector	0.15-0.3 mg IM/SC; if anaphylactic symptoms persist, dose may be repeated once	2 sequential doses (0.3-0.6 mg)

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.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Epinephrine (EpiPen)	≥ 30 kg (66 lbs): 0.3 mg IM/SC into the anterolateral aspect of the thigh	2 sequential doses (0.6 mg)
Epinephrine (EpiPen Jr)	15 to 30 kg (33 lbs to 66 lbs): 0.15 mg IM/SC into the anterolateral aspect of the thigh	2 sequential doses (0.3 mg)
Epinephrine (Auvi-Q)	IM/SC into the anterolateral aspect of the thigh: • 7.5 to 15 kg (16.5 to 33 lbs): 0.1 mg • 15 to 30 kg (33 to 66 lbs): 0.15 mg • ≥ 30 kg (66 lbs): 0.3 mg	2 sequential doses
Epinephrine (Neffy)	15 to < 30 (33 to < 66 lbs): One spray of Neffy 1 mg into one nostril ≥ 30 kg (66 lbs): One spray of Neffy 2 mg into one nostril In the absence of clinical improvement or if symptoms worsen after initial treatment, a second dose of Neffy may be administered in the same nostril with a new nasal spray starting 5 minutes after the first dose.	2 sequential doses

VI. Product Availability

Drug Name	Availability
Epinephrine (EpiPen)	Pre-filled auto-injector: 0.3 mg/0.3 mL (2 pens per package)
Epinephrine (EpiPen Jr)	Pre-filled auto-injector: 0.15 mg/0.3 mL (2 pens per package)
Epinephrine (Auvi-Q)	Pre-filled auto-injector: 0.1 mg/0.1 mL, 0.15 mg/0.15 mL, 0.3 mg/0.3 mL (2 auto-injectors per package)
Epinephrine (Neffy)	Nasal spray: 1 mg/0.1 mL per spray, 2 mg/0.1 mL per spray (2 nasal spray devices per carton)

VII. References

1. EpiPen and EpiPen Jr Prescribing Information. Morgantown, WV; Mylan Specialty L.P.: February 2023. Available at: https://www.epipen.com/en. Accessed April 10, 2025.
2. Neffy Prescribing Information. San Diego, CA: ARS Pharmaceuticals Operations, Inc.; March 2025. Available at: https://www.ars-pharma.com/wp-content/uploads/pdf/Prescribing_Information.pdf. Accessed April 10, 2025.
3. Auvi-Q Prescribing Information. Richmond, VA: Kaleo, Inc.; April 2025. Available at: https://www.auvi-q.com. Accessed May 25, 2025.
4. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier; 2025. Available at: www.clinicalkey.com/pharmacology. Accessed May 25, 2025.
5. Golden DBK, Wang J, Waserman S, et al. Anaphylaxis: a 2023 practice parameter update. Ann Allergy Asthma Immunol. 2024;132:124−76.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created per March SDC and prior clinical guidance (adapted from CP.CPA.256): added HIM line of business, added Auvi-Q to criteria. RT4: updated Neffy indication and weight minimum and added new 1 mg strength to Section VI per updated prescribing information.	03.11.25	05.25
3Q 2025 annual review: updated Auvi-Q indication and added weight minimum in initial criteria per FDA labeled indication; updated criteria from "for Neffy requests only, has manual dexterity limitations that preclude use of an auto-injector" to "for Neffy requests only, has limitations (e.g., manual dexterity, needle phobia) that preclude use of an auto-injector"; for section VI, updated Auvi-Q dose from 0.15 mg/0.3 mL to 0.15 mg/0.15 mL per prescribing information; added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	04.10.25	08.25

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.