Clinical Policy: Naloxone (Evzio)

Reference Number: CP.PMN.139
Effective Date: 11.16.16
Last Review Date: 08.22
Line of Business: Commercial, Medicaid

Coding Implications
Revision Log

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

Description

Naloxone (Evzio®) is an opioid antagonist.

FDA Approved Indication(s)

Evzio is indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression in adults and pediatric patients.

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 Evzio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Opioid Overdose (must meet all)**:**

1. Member may have access to opioids;
2. Member must use generic naloxone nasal spray and naloxone solution for injection, unless contraindicated or clinically significant adverse effects are experienced;
3. Requested quantity does not exceed two boxes (4 autoinjectors) per prescription.

Approval duration:
Medicaid – 6 months
Commercial – 6 months or to member's renewal period, 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 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 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 and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Opioid Overdose (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. If request is for a dose increase, the requested quantity does not exceed two boxes (4 autoinjectors) per prescription.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or to member's renewal period, 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 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 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 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 and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviations/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
naloxone nasal spray (Narcan®)	4 mg intranasally as a single spray in one nostril. Repeat as needed every 2 to 3 minutes with a new nasal spray in alternate nostrils. Additional doses may be administered every 2 to 3 minutes until emergency medical assistance arrives	Not applicable
naloxone 0.4 mg/mL solution	Adults: 0.4 to 2 mg IV, repeat every 2 to 3 minutes as needed; if no response after 10 mg, reconsider diagnosis of opioid toxicity; may administer IM or SC if IV route is unavailable Pediatrics: 0.01 mg/kg IV followed by 0.1 mg/kg IV if desired clinical response has not been achieved; divided doses may be given via IM or SC route if IV route is not available	Not applicable

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

- Contraindication(s): hypersensitivity to naloxone hydrochloride
- Boxed warning(s): none reported

Appendix D: General Information

- Evzio is intended for immediate administration as emergency therapy in settings where opioids may be present.
- Evzio is not a substitute for emergency medical care. If the desired response is not obtained after 2 or 3 minutes, another Evzio dose may be administered. If there is still no response and additional doses are available, additional Evzio doses may be administered every 2 to 3 minutes until emergency medical assistance arrives. If no response is observed after 10 mg of naloxone hydrochloride have been administered, the diagnosis of narcotic-induced or partial narcotic induced toxicity should be questioned. Additional supportive and/or resuscitative measures may be helpful while awaiting emergency medical assistance.
- As of November 2020, Kaléo, the makers of Evzio, have recently discontinued the production of the Evzio naloxone auto-injector and its generic equivalent. The reason for discontinuation of the auto-injectors are unknown; however, the existing product will remain in pharmacies and Kaleo did not express concerns regarding continued use of the product through the expiration date.

Subject: production discontinued for Evzio naloxone auto-injector and its generic equivalent. Clinical Bulletin. November 18, 2020. Available at
https://www.coventrywcs.com/sites/default/files/pdf/CLINICAL_BULLETIN-Production-discontinued-for-Evzio-naloxone-auto-injector-and-its-generic-equivalent-20201118.pdf.
Accessed April 13, 2022.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Known or suspected opioid overdose	0.4 mg or 2 mg IM or SC. Repeat doses of Evzio may be required depending upon the amount, type, and route of administration of the opioid being antagonized. If there is still no response and additional doses are available, additional Evzio doses may be administered every 2 to 3 minutes until emergency medical assistance arrives.	Not applicable

VI. Product Availability

Pre-filled autoinjector: 0.4 mg/0.4 mL or 2 mg/0.4 mL; each carton contains two auto-injectors

VII. References

1. Evzio Prescribing Information. Richmond, VA: Kaleo Inc.; October 2016. Available at: www.evzio.com. Accessed April 13, 2022.
2. FDA's Summary Review for Regulatory Action for Evzio accessed at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205787Orig1s000SumR.pdf.
3. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed April 13, 2022.
4. Subject: production discontinued for Evzio naloxone auto-injector and its generic equivalent. Clinical Bulletin. November 18, 2020. Available at: https://www.coventrywcs.com/sites/default/files/pdf/CLINICAL_BULLETIN-Production-discontinued-for-Evzio-naloxone-auto-injector-and-its-generic-equivalent-20201118.pdf. Accessed April 13, 2022.

Coding Implications

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
J3490	EVZIO 2MG/0.4ML Solution Auto-injector, unclassified drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: combined policy for Medicaid (new) and commercial; removed Narcan from the policy as Narcan is formulary without PA for both Medicaid and Commercial; references reviewed and updated.	05.21.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.20.19	08.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.11.20	08.20
3Q 2021 annual review: no significant changes; added Legacy WCG LOB with initial auth duration of 12 months, retired WCG.CP.PMN.139 Naloxone (Evzio) 12.10.20; updated "Medical justification" language to "Member must use"; added HCPCS code; references reviewed and updated.	05.12.21	08.21
3Q 2022 annual review: no significant changes; approval duration for Legacy WCG consolidated to 6/12 months; redirection to generic naloxone nasal spray; references reviewed and updated.	04.13.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.04.22	

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.