Clinical Policy: Naloxone (Evzio)

Reference Number: ERX.NPA.117
Effective Date: 09.01.19
Last Review Date: 08.22
Line of Business: Commercial, Medicaid

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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: 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Opioid Overdose (must meet all)**:**
1. Previously received medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. If request is for a dose increase, the requested quantity does not exceed two boxes (4 autoinjectors) per prescription.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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.

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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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.01.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.11.20	08.20
3Q 2021 annual review: no significant changes; updated "Medical justification" language to "Member must use"; references reviewed and updated.	05.12.21	08.21
3Q 2022 annual review: no significant changes; modified redirection to Narcan to generic naloxone nasal spray; references reviewed and updated.	04.13.22	08.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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