Clinical Policy: Naloxone (Evzio)
Reference Number: CP.PMN.139
Effective Date: 11.16.16
Last Review Date: 08.20
Line of Business: Commercial, Medicaid

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. Medical justification supports inability to use naloxone (Narcan®) nasal spray and naloxone solution for injection (e.g., contraindications to excipients in these agents);
      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
      1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Opioid Overdose (must meet all):
      1. Previously received medication via Centene benefit 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:
   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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narcan® nasal spray</td>
<td>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</td>
<td>Not applicable</td>
</tr>
<tr>
<td>(naloxone)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>naloxone 0.4 mg/mL</td>
<td>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</td>
<td>Not applicable</td>
</tr>
<tr>
<td>solution</td>
<td>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</td>
<td></td>
</tr>
</tbody>
</table>

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.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known or suspected opioid overdose</td>
<td>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.</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

VI. Product Availability

Auto-injector containing a single dose of naloxone 0.4 mg/0.4 mL or 2 mg/0.4 mL; each carton contains two auto-injectors

VII. References

2. FDA’s Summary Review for Regulatory Action for Evzio accessed at: [http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205787Orig1s000SumR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205787Orig1s000SumR.pdf).

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.11.17</td>
<td>8.17</td>
</tr>
<tr>
<td>05.21.18</td>
<td>08.18</td>
</tr>
</tbody>
</table>

Converted to new template; minor changes to verbiage and grammar. References updated.

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.
## 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.

### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>05.20.19</td>
<td>08.19</td>
</tr>
<tr>
<td>05.11.20</td>
<td>08.20</td>
</tr>
</tbody>
</table>

3Q 2019 annual review: no significant changes; references reviewed and updated.

3Q 2020 annual review: no significant changes; references reviewed and updated.
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.

©2018 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.