Clinical Policy: Nalmefene (Opvee, Zurnai)

Reference Number: CP.PHAR.638
Effective Date: 09.01.23
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Nalmefene (Opvee®, Zurnai®) is an opioid antagonist.

FDA Approved Indication(s)

Opvee and Zurnai are indicated for the emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years and older, as manifested by respiratory and/or central nervous system depression.

Opvee and Zurnai are intended for immediate administration as emergency therapy in settings where opioids may be present. Opvee and Zurnai are not a substitute for emergency medical care.

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 Opvee and Zurnai are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

*For members in **Nevada**, medical management techniques, including quantity management, beyond step therapy is not allowed.

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

1. Member may have access to opioids;
2. Age ≥ 12 years;
3. Medical justification supports inability to use generic naloxone nasal spray or naloxone solution for injection (e.g., contraindications or clinically adverse effects to naloxone, member is prescribed a long-acting opioid)*;
   ** For Illinois HIM requests, the step therapy requirements above do not apply to formulary agents as of 1/1/2026 per IL HB 5395*
4. Requested quantity does not exceed any of the following (a or b):
   a. Opvee: two boxes (4 nasal spray devices) per prescription;
   b. Zurnai: 4 autoinjectors per prescription.

Approval duration: 12 months

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, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

*For members in **Nevada**, medical management techniques, including quantity management, beyond step therapy is not allowed.

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 any of the following (a or b):
   a. Opvee: two boxes (4 nasal spray devices) per prescription;
   b. Zurnai: 4 autoinjectors per prescription.

Approval duration: 12 months

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, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to nalmefene or to any of the other ingredients
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Nalmefene (Opvee)	The recommended initial dose of Opvee is one spray delivered by intranasal administration, which delivers 2.7 mg of nalmefene. If desired response is not obtained after 2 to 5 minutes, administer an additional dose of Opvee using a new Opvee nasal spray device. If there is still no response and additional doses are available, administer additional doses of Opvee nasal spray every 2 to 5 minutes using a new Opvee nasal spray device with each dose until emergency medical assistance arrives.	Not applicable
Nalmefene (Zurnai)	The recommended initial dose of Zurnai is 1.5 mg administered IM or SC into the anterolateral aspect of the thigh, through clothing if necessary. If the desired response is not obtained after 2 to 5 minutes, administer an additional dose of Zurnai using a new auto-injector. If there is still no response and additional doses are available, administer additional doses of Zurnai every 2 to 5 minutes using a new Zurnai	Not applicable

Drug Name	Dosing Regimen	Maximum Dose
	auto-injector for each dose until emergency medical assistance arrives.	

VI. Product Availability

Drug Name	Availability
Nalmefene (Opvee)	Nasal spray: 2.7 mg/0.1 mL
Nalmefene (Zurnai)	Pre-filled, single-dose autoinjector: 1.5 mg/0.5 mL

VII. References

1. Opvee Prescribing Information. Santa Monica, CA: Opiant Pharmaceuticals; June 2023. Available at: www.opvee.com. Accessed April 23, 2025.
2. Zurnai Prescribing Information. Stamford, CT: Purdue Pharma L.P.; August 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218590s000lbl.pdf. Accessed April 23, 2025.
3. Dowell D, Ragan KR, Jones CM, Baldwin GT, and Chou R. CDC clinical practice guideline for prescribing opioids for pain – United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1-95.
4. Kampman K and Jarvis M. American Society of Addiction Medicine (ASAM): National practice guideline for the use of medications in the treatment of addiction involving opioid use. J Addict Med. 2015 Oct; 9(5):358-367. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4605275/. Accessed April 23, 2025.
5. Cunningham C, Edlund MJ, Gordon AJ et al. The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. Available from: https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline. Accessed April 23, 2025.

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
G0532	Take-home supply of nasal nalmefene hydrochloride; one carton of two, 2.7 mg per 0.1 ml nasal sprays (provision of the services by a medicare-enrolled opioid treatment program); (list separately in addition to each primary code).

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.20.23	08.23
3Q 2024 annual review: no significant changes; references reviewed and updated.	07.23.24	08.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added disclaimer that medical management techniques, including quantity management, beyond step therapy is not allowed for members in NV per SB 43; Added reference to the American Society of Addiction Medicine clinical practice guideline per compliance request.		
RT4: added newly approved Zurnai to the policy.	08.19.24	
HCPCS code added [G0532]	11.19.24	
3Q 2025 annual review: added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	04.23.25	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.

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.