

**MTF Formulary Management for Narcotic Antagonists
Products Approved for Bystander-Administration**
Defense Health Agency Pharmacy Operations Division

Bottom Line

- Narcan Nasal Spray is designated with Basic Core Formulary (BCF) status. Evzio is nonformulary (NF) due to the lack of head-to-head trials in the setting of opioid overdose and lack of cost effectiveness.
- Consider recapturing patients currently receiving Evzio at the Retail Pharmacy Network by encouraging their transition to Narcan Nasal Spray prescriptions through the MTF.
- Evzio autoinjectors currently in circulation are nearing their expiration date/shelf life of 24 months. When patients come in for Evzio refills, consider appropriateness of dispensing a Narcan Nasal Spray prescription in place of Evzio.
- Quantity limits apply for both products and no refills are allowed; a new prescription is required for each fill.
 - Narcan Nasal Spray: 2 cartons per fill (each carton contains 2 single-use spray devices)
 - Evzio: 1 carton per fill (each carton has 2 Evzio autoinjectors and 1 trainer device)
 - There is no limit on the number of prescriptions a patient can have in one year.

Uniform Formulary Decision: The Director, DHA, approved the recommendations from the August 2016 DoD P&T Committee meeting on November 8, 2016, with an implementation date of January 11, 2017.

Uniform Formulary (UF)		Nonformulary (NF) Agents
MTFs <u>must</u> have on formulary	MTFs <u>may</u> have on formulary	MTFs <u>must not</u> have on formulary
<ul style="list-style-type: none"> • naloxone nasal 4 mg/0.1 mL (Narcan Nasal Spray) 	N/A	<ul style="list-style-type: none"> • naloxone autoinjector 0.4 mg/0.4 mL (Evzio)

Formulary Management Issues

- The DoD P&T Committee recommendations pertain only to the formulary decision for the bystander-approved products as part of the TRICARE outpatient pharmacy benefit (Narcan Nasal Spray and Evzio). Naloxone use in the MTF clinic setting or by MTF first responders is NOT affected by this formulary decision.
- The formulary status of other naloxone formulations (e.g., vials, ampules, pre-filled syringes, luer-lock syringes) is also not affected by the DoD P&T Committee decision.
- The DoD P&T Committee did not make recommendations as to the most appropriate candidates to receive a bystander-approved naloxone product. Therefore, there are no requirements to limit dispensing based on a minimum number of morphine equivalent daily dosage [MEDD] or concomitant medications, such as benzodiazepines or sedative hypnotics, or based on the Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD) score. Current, local MTF, and national prescribing guidelines should be followed. For additional information, consult recommendations from other Military Health System groups (e.g., Tri-Service Pain Working Group) and the March 2016 CDC guidelines for prescribing opioids for chronic pain.
- Evzio pricing at the Retail Pharmacy Network is extraordinarily expensive (\$3,750/carton at Retail versus ~\$420/carton at the MTFs as of August 2016). MTFs are strongly encouraged to consider recapture of patients in their catchment area who are currently receiving Evzio at the Retail Network and transition those patients to Narcan Nasal Spray (~\$75.00–\$150.00/box at the MTFs as of August 2016).
- Evzio may be an appropriate substitute over Narcan Nasal Spray in patients with significant nasal malformations or obstructions. Additionally, Evzio may be preferred in patients where the bystander most likely to administer a naloxone reversal in response to an opioid overdose is a juvenile family member or caregiver (since the Evzio autoinjector provides a voice prompt to call 911). Consider patient-specific factors when selecting a naloxone product.

Clinical Effectiveness Summary

- The FDA has approved two formulations of naloxone specifically labeled for bystander use in the outpatient, non-medical setting: Evzio autoinjector (0.4 mg/0.4 mL) and Narcan Nasal Spray (4 mg/0.1 mL). If opioid overdose is suspected, these products must be administered by someone other than the patient, including a family member or caregiver. These products are not a substitute for emergency medical care. Patients/caregivers should be

reminded to seek emergency medical care immediately after administering naloxone. A repeat dose may be necessary.

- Evzio and Narcan Nasal Spray were both approved by showing bioequivalence to generic intramuscular/subcutaneous naloxone formulations. The manufacturer of Evzio also conducted a human factors validation study, which has been published. Narcan Nasal Spray appears easy-to-use based on unpublished data that the manufacturer submitted to the FDA.
- Data from studies using intranasal or intramuscular naloxone “kits” in the community setting to reverse heroin overdose has shown that these products can successfully reverse opioid-induced respiratory depression.
- **Narcan Nasal Spray**
 - Advantages include that it is a smaller; more portable device than Evzio. Additionally, it is a needle-free alternative to injectable formulations. The volume of liquid (0.1 mL) is lower than that provided in intranasal kits using nasal atomizers. The product appears easy for bystander/first responder/family member administration; however, there is only unpublished data showing the usability of this product.
 - Disadvantages include the need for the patient to be in supine position and then turned to the side (“recovery position”). It is unknown whether drug efficacy will adversely be affected by nasal malformations or blockage.
- **Evzio**
 - Advantages include that it provides audio and visual cues for administration. The device is easy to use, with even non-English-speaking adults averaging only 60 seconds to administer. The device reminds the bystander to call 911. The retractable needle decreases the risk of accidental exposure. The product can be injected through pants, including denim jeans.
 - Disadvantages to the device include the long needle, which for children under one year requires the skin to be pinched on the thigh. There is no data in patients/bystanders with an aversion to needles. The autoinjector device was used in another marketed product (epinephrine [Auvi-Q]), but there have been no reports of malfunction with Evzio.

Summary

- The FDA approval of Evzio and Narcan Nasal Spray provide new, easy-to-administer formulations to reverse opioid adverse effects, but neither product has data showing outcomes in the real word setting or data in patients receiving prescriptions for opioids.

References

- DoD P&T Committee minutes: <http://www.health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee <http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-PT-Committee>
- TRICARE Formulary Search Tool: <http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents and Executive Summaries available at: <http://www.health.mil/DoDPTResources>
- Point of contact for additional information: dha.jbsa.pharmacy.list.poduf@mail.mil
- CDC Guidelines for prescribing opioids for chronic pain. Morbidity and Mortality Weekly Report (MMWR). March 18, 2016;65(1):1-49. <http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>

Narcotic Antagonists MTF Dose/Price Comparison	
Drug	MTFAvg Cost/Day (Aug 2016)
Basic Core Formulary	
• Narcan Nasal Spray	\$ = Most Cost-Effective
Nonformulary	
• Evzio	\$\$\$\$ = Least Cost Effective
Legend: \$ = “Most Cost-Effective” represents Rx’s with the <u>lowest cost</u> and best clinical efficacy \$\$ = “Less Cost-Effective” represents <u>higher cost</u> Rx’s with similar clinical efficacy \$\$\$ = “Less Cost-Effective” represents <u>next higher cost</u> Rx’s with similar clinical efficacy \$\$\$\$ = “Least Cost-Effective” represents Rx’s with the <u>highest cost</u> with similar clinical efficacy	