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IN BRIEF

A New OTC Naloxone Nasal Spray (*RiVive*)

The FDA has approved *RiVive* (Harm Reduction Therapeutics), a 3-mg naloxone nasal spray, as an over-the-counter (OTC) product for emergency treatment of opioid overdose.¹ Two 4-mg naloxone nasal spray formulations, *Narcan* and one of its generics, were approved for OTC sale in 2023.^{1,2}

NALOXONE – Naloxone is the drug of choice for reversal of opioid overdose. Every state in the US now has a naloxone access law; in most states, these laws grant both civil and criminal immunity to laypersons who administer the drug.³ The US Department of Health and Human Services has recommended that certain individuals who are prescribed opioids or are at high risk for an opioid overdose, their caregivers, and other persons who are likely to respond to an overdose event carry naloxone nasal spray (see Table 1).⁴

CLINICAL STUDIES – No new clinical trials were required for approval of *RiVive*. Approval was based on pharmacokinetic data (summarized in the FDA review documents) showing that systemic naloxone exposure is about 3-fold higher and early naloxone absorption is similar with a 3-mg intranasal dose of the new formulation compared to a 0.4-mg IM dose of naloxone.^{1,5} *RiVive* has not been compared directly with other naloxone nasal sprays.

DOSAGE, ADMINISTRATION, AND COST – *RiVive* is supplied in packages containing two single-use nasal spray devices, each of which delivers 3 mg of naloxone. The recommended initial dose is one spray in one nostril; if necessary, additional doses can be administered every 2-3 minutes until emergency medical personnel arrive.

RiVive is being marketed primarily to US harm reduction organizations and government entities, many of which provide intranasal naloxone to residents at no cost.^{6,7} A box containing two doses costs \$36,⁸ which is less than the OTC cost of two doses of *Narcan* (\$45) or its generic (\$40).⁹ ■

Table 1. Persons Who Should Carry Naloxone^{1,2}

Patients prescribed opioids who:

- ▶ Are taking ≥ 50 morphine milligram equivalents (MME) per day.
- ▶ Have respiratory conditions such as chronic obstructive pulmonary disease (COPD) or obstructive sleep apnea (regardless of opioid dose), renal failure, liver failure, or advanced age/frailty.
- ▶ Have been prescribed a benzodiazepine.
- ▶ Have a non-opioid substance use disorder, report excessive alcohol use, or have a mental health disorder.

Patients at high risk for an opioid overdose, including those:

- ▶ Using heroin or illicit synthetic opioids or misusing prescription opioids.
- ▶ Using other illicit drugs such as methamphetamine or cocaine that could potentially be contaminated with illicit synthetic opioids like fentanyl.
- ▶ Receiving treatment for opioid use disorder, including medication-assisted treatment (MAT) with buprenorphine, methadone, or naltrexone.
- ▶ With a history of opioid misuse who were recently released from incarceration or other controlled settings and are no longer tolerant to opioids.
- ▶ Living with or spending time with people who use drugs.
- ▶ With children in the same household as prescription opioids.

1. HHS. Naloxone: the opioid reversal drug that saves lives. Available at: <https://bit.ly/3k68NiV>. Accessed February 29, 2024.
2. Includes at-risk individuals, their caregivers, and those likely to respond to an overdose event.

1. FDA News Release. FDA approves second over-the-counter naloxone nasal spray product. July 28, 2023. Available at: <https://bit.ly/49BGLxq>. Accessed February 29, 2024.
2. In brief: Over-the-counter Narcan nasal spray. *Med Lett Drugs Ther* 2023; 65:72.
3. Legislative Analysis and Public Policy Association. Naloxone: summary of state laws. July 2022. Available at: <https://bit.ly/3ZNK1H9>. Accessed February 29, 2024.
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5. Center for Drug Evaluation and Research. Integrated review. *RiVive* (naloxone hydrochloride) 3 mg/0.1 mL nasal spray. July 21, 2023. Available at: <https://bit.ly/4bVG0I8>. Accessed February 29, 2024.
6. NEXT Distro. Available at: <https://nextdistro.org>. Accessed February 29, 2024.
7. National Harm Reduction Coalition. Find harm reduction resources near you. Available at: <https://bit.ly/49JceEI>. Accessed February 29, 2024.
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9. Cost at www.walgreens.com. Accessed February 29, 2024.

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