Wyoming Drug Utilization Review

Over-The-Counter Narcan® Approval

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The opioid crisis has plagued our nation for many years. Tragically, as many as 187 people die each day from prescription and illicit opioid-related overdoses (1). While naloxone, a potentially life-saving medication, is available to dispense to patients and those who care for patients at high risk of opioid overdose, only an average of 1.5 naloxone prescriptions is given for every 100 high-dose opioid prescriptions (1). Additionally, rural counties are three times more likely to be considered a "low dispensing" region compared to metropolitan areas, who may have as much as 25 times higher naloxone dispensing rates (1). In an effort to combat the ever reigning opioid crisis, the Food and Drug Administration (FDA) has recently approved Narcan® intranasal 4 mg spray for over-the-counter (OTC) use (2).

Naloxone exerts its action as a pure opioid antagonist that competes for and displaces opioids directly at the receptor site (3). In addition to the intranasal dose form, it is also available as an intravenous, intramuscular, and subcutaneous medication. It does not require any renal or hepatic dosing adjustments, and for the intranasal dose form, adult dosing is appropriate for use in pediatrics as well. Adverse effects of naloxone are largely associated with symptoms of acute opioid withdrawal (tachycardia, confusion, nausea/vomiting, abdominal pain, etc.), and while they may cause discomfort to patients, these symptoms are unlikely to be harmful (3).

The OTC product is manufactured by Emergent BioSolutions, the current manufacturer of brand name prescription Narcan® (2,4). The new OTC product is the same formulation and dosing with identical device design as the current prescription product (4). It is currently packaged as two, single-use nasal sprays per box and is available both in stores and through online retailers.

The Centers for Disease Control and Prevention have guidelines on who naloxone should be dispensed to. It includes a patient or someone they know who takes ≥50 morphine equivalents per day, takes concurrent opioids and benzodiazepines, uses illicit opioids, or if someone is at increased risk of overdose or opioid use disorder (5). Under naloxone prescription-only conditions, prescribers and pharmacists are able to write prescriptions for naloxone for anyone at risk of overdose and to those who may know someone at risk (6). First responders can also obtain naloxone through grant programs and other avenues that provide the medication at no cost (7). Under the new OTC conditions, the FDA is aiming to remove the 'middleman' prescriber and sell directly to consumers to improve access (2). Proposed locations to sell OTC Narcan® include pharmacies, gas stations, convenience stores, grocery stores, and through online retailers (2).

A potential barrier in OTC Narcan® is the lack of training that may now be present. In an effort to combat this, the FDA has tested a new Drug Facts Label (DFL) with detailed pictograms on the

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administration of Narcan® (2). Eggleston et al. (8) studied naloxone administration in simulated overdose environments by untrained community members (8). The 207 adult participants received no instructions on administration and were randomly assigned to administer naloxone via nasal spray, intramuscular injection, or an improvised nasal atomizer (8). The primary outcome was successful administration which was defined as administration within 7 minutes and without critical errors (8). Below is a table of study results.

Table 1: Findings from Eggleston, *et al*[8]

Dose Form	Successful Administration (p<0.001)	Median Time to Successful Administration (p<0.001)	Critical Errors Found
Intranasal	66.7%	16 seconds	• Failure to place device tip into a nostril • Failure to depress the device and release the naloxone into the nostril
Intramuscular Kit	51.5%	58 seconds	• Failure to attach needle to syringe • Failure to remove the cap from naloxone • Failure to draw up >90% of naloxone • Failure to puncture the simulated flesh pad with the needle • Failure to push the naloxone into the simulated flesh pad
Nasal Atomizer	2.9%	113 seconds	• Failure to remove both caps from the device • Failure to remove cap from the naloxone • Failure to attach atomizer to device • Failure to attach naloxone the device • Drug leakage before administration • Administration of the total volume in a single nostril

This study concluded that even with no training, the most simple device to use (nasal spray) was successfully administered by the majority of particpants (8). This data translates well to potential safety of Narcan® as an OTC product and how well untrained community members can administer this product in the event of an overdose.

The prospective cost of OTC Narcan® is also a topic of concern. The current cash price of prescription Narcan® nasal spray is $75.00 (3). Wyoming Medicaid currently prefers brand name Narcan®, and it can be dispensed to patients with a co-pay of $3.65 (9). FDA has encouraged the manufacturer to make it a priority to be "available as soon as possible and at an affordable price" (2).

There are many pros and cons regarding OTC naloxone. By removing the need for a prescription, Narcan® will be more accessible to the public, especially those in low-dispensing rural counties. There is also minimal harm with administration although it may cause discomfort. Additionally, increased availability could reduce the stigma that is associated with Narcan®. Patients, families, and caregivers may feel less judgement being able to obtain Narcan®more discretely over-the-counter and thus may be more inclined to purchase this life-saving medication. A 2018 article by McClellan et al. (12) demonstrated benefits associated with expansion of naloxone availability. Using statistics from 2000-2014, they evaluated the association between expanded naloxone and Good Samaritan laws with a change in opioid overdose deaths. In states that had expanded access and laws, there was a 14% decrease in opioid overdose fatalities. There was also a 16% reduction in death in those aged 35-44 years and a 23% lower incidence among the Black non-Hispanic sub-group. Even in early stages of naloxone expansion, this study concluded that increased access can significantly decrease fatalities (12).

There are several challenges to consider. It is still unknown if there will be a cost barrier for patients. It is possible that expanded access will decrease affordability especially for those with Medicaid where the program denies coverage of over-the-counter products (9). Many private insurance companies and Medicare handle OTC product coverage the same way. In addition to a reduction in training on the use of Narcan®, there is also the potential that many patients with opioid use disorder could fall through the cracks by being able to obtain Narcan® more readily without anyone being able to see the frequent use. This leads to the inability to provide help and resources to these patients and their friends and families. Furthermore, with the use of more potent opioids such as fentanyl, two 4 mg single-use nasal sprays may not be enough for complete opioid reversal and could fail when patients need it most.

In the midst of the opioid crisis, increasing access to a life-saving medication has the potential to make a great impact in saving members of the community. McClellan et al. demonstrated the impact increased naloxone access can have on reduction of opioid-related fatalities, and this expansion of Narcan® to an OTC product may prove to have the same benefit. Additionally, while there is concern for lack of training among members of the community who no longer need pharmacist counseling to obtain naloxone, another study showed that even with no instruction provided, participants were able to successfully administer intranasal naloxone a majority of the time. This approval has the potential to save numerous lives and help to combat the fatalities associated with the opioid crisis.

While there are many pros and cons to consider, making decisions on what is best for patients is of the utmost priority. Further information on the product, the FDA approval, and naloxone itself can be found in the links of the references listed below.

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The P&T Committee met for its quarterly business meeting on November 9, 2023

Highlights of this meeting include:

The upper dose limit on long-acting opioids will be reduced from 120 morphine equivalent dose (MED) to 90 MED. Patients who are currently on more than 90 MED will be grandfathered.

Xdemvy, Lodoco, Sohonos, Ilaris, and Elevidys were reviewed. All were limited to indication. Miebo, Brenzavvy, Jesduvroq, Vyvgart and Rystiggo were reviewed with no evidence of a significant difference in safety or efficacy versus the existing classes of products. All were referred to the Department of Health for cost analysis and Preferred Drug List placement.

The 2024 draft Preferred Drug List was reviewed. This document will be posted at www.uwyo.edu/DUR for public comment. Comments should be sent by email to alewis13@uwyo.edu by December 15, 2023.

The next P&T Committee meeting will be held February 8, 2024 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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