Statement Regarding High Dose Naloxone and
Long Acting Nalmefene Opioid Overdose Reversal Formulations

We, the undersigned, make the following statement regarding high-dose naloxone ("Klaxxado" 8 mg, "Zimhi" 5 mg) or long-acting nalmefene ("Opvee" 2.7 mg) formulations for the treatment of a suspected opioid overdose:

First, we support the practice of using 4 milligram or lower dose naloxone to reverse the effects of an opioid overdose. It is extremely effective even in the case of overdoses involving prescription or illicitly manufactured fentanyl. Additionally, accessing 911 emergency medical services is always recommended. When needed, subsequent doses may be administered. Overdose prevention, recognition, and response training using naloxone can be accessed anywhere in New Mexico by contacting 505-270-5943. These trainings may also include instruction about how to administer a lower dose, intramuscular naloxone (.4mg), and supportive ventilation via mouth to mouth rescue breathing.

At this time, we do not recommend the use of any high-dose or long acting overdose reversal agents in New Mexico. Use of powerful (e.g. greater than 4 mg) and long-acting opioid antagonists will likely produce unintended consequences that are counterproductive to efforts to prevent opioid-related overdose deaths.[1] Consequences such as precipitated opioid withdrawal, a known risk of naloxone for opioid-tolerant individuals, can produce symptoms such as hyperalgesia, diarrhea, and vomiting, particularly at higher doses.[2,3] This may lead some people who use opioids to avoid carrying or using it.

The Viewpoint article from the International Journal of Drug Policy concludes that the "development and marketing of more powerful opioid antagonists should be viewed with great skepticism."[1] In fact, new research suggests that a low dose of naloxone should be administered initially and additional doses titrated until adequate reversal of respiratory depression is achieved, as long as ventilation can be supported, in order to avoid precipitating opioid withdrawal.[2,4]

For further research evidence and clinical views informing this statement, please see the following:

1. Hill LG, Zagorski CM, Loera LJ. Increasingly powerful opioid antagonists are not necessary. *Int J Drug Policy*. 2022;99:103457. doi:10.1016/j.drugpo.2021.103457
2. Purssell R, Godwin J, Moe J, Buxton J, Crabtree A, Kestler A, DeWitt C, Scheuermeyer F, Erdelyi S, Balshaw R, Rowe A, Cochrane CK, Ng B, Jiang A, Risi A, Ho V, Brubacher JR. Comparison of rates of opioid withdrawal symptoms and reversal of opioid toxicity in patients treated with two naloxone dosing regimens: a retrospective cohort study. Clin Toxicol (Phila). 2021 Jan;59(1):38-46. doi: 10.1080/15563650.2020.1758325. Epub 2020 May 13. PMID: 32401548.
3. Higher-Dose Naloxone Nasal Spray (Kloxxado) for Opioid Overdose. JAMA. 2021 Nov 9;326(18):1853-1854. doi: 10.1001/jama.2021.15948. PMID: 34751711.
4. Moustaqim-Barrette A, Papamihali K, Williams S, Ferguson M, Moe J, Purssell R, Buxton JA. Adverse events related to bystander naloxone administration in cases of suspected opioid overdose in British Columbia: An observational study. PLoS One. 2021 Oct 29;16(10):e0259126. doi: 10.1371/journal.pone.0259126. PMID: 34714854; PMCID: PMC8555799.

Snehal Bhatt — Digitally signed by Snehal Bhatt Date: 2023.06.22 16:17:24 -06'00' — Snehal Bhatt, MD

Julie G. Salvador — Digitally signed by Julie G. Salvador Date: 2023.06.16 12:02:22 -06'00' — Julie G. Salvador, PhD

Caroline Bonham — Digitally signed by Caroline Bonham Date: 2023.06.22 16:29:26 -06'00' — Caroline Bonham, MD

HUMAN SERVICES DEPARTMENT

SCHOOL OF MEDICINE
DEPARTMENT OF PSYCHIATRY & BEHAVIORAL SCIENCES