Naloxone infusion for treatment of Opioid Overdose

***Initial immediate bolus**: 0.04 mg, rapidly repeated as necessary up to a total dose of 0.4 mg*
***Subsequent maintenance infusion**: two-thirds the total bolus dose of naloxone that resulted in reversal, infused over an hour and then continued at that rate.*

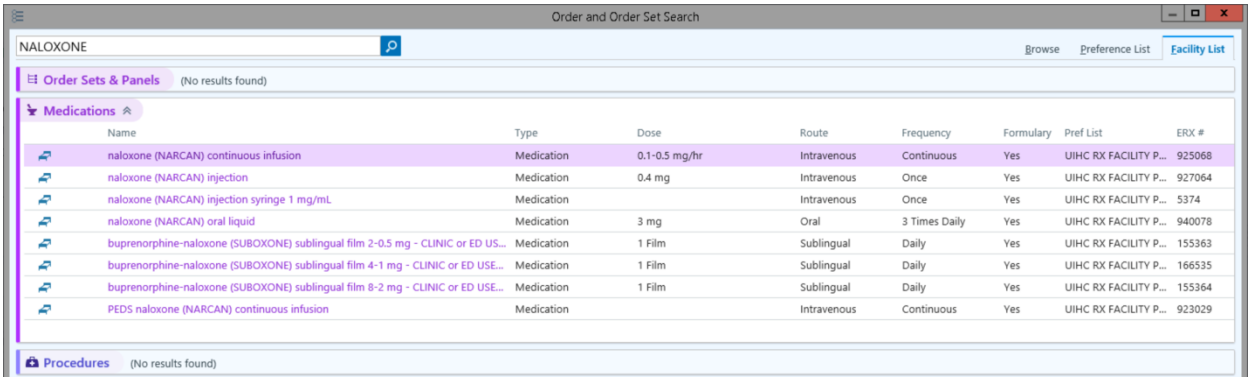
Naloxone is a competitive antagonist (antidote) to opioid drugs and is used in the treatment of opioid overdose. Its duration of action is shorter than most opioid drugs, so close patient monitoring and repeated doses or an infusion may be required to maintain clinical effect. Single-dose naloxone for reversal of opioid effect without a continuous infusion may lead to renarcotization of the patient in the PACU, as the elimination of naloxone is faster than the elimination of opioids. Conversely, repeated doses without clinical effect should prompt the search for an alternative diagnosis.

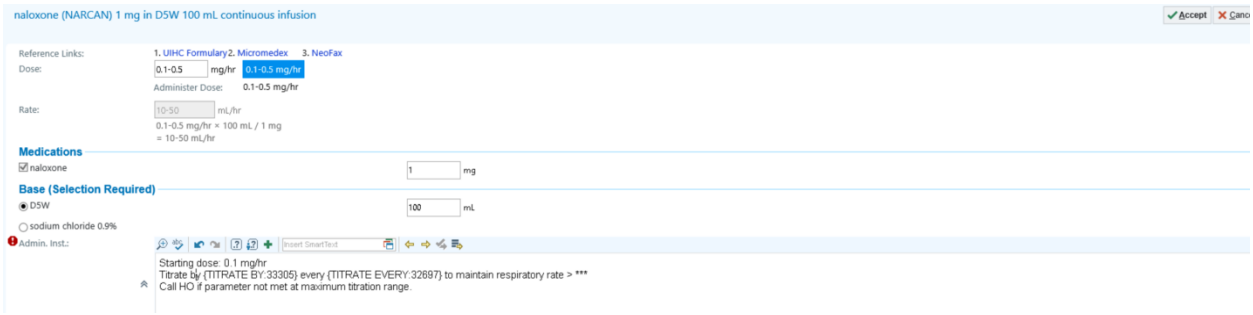
Naloxone will almost immediately reverse opioid induced respiratory depression, however, it will also antagonize the analgesic effect. This rapid reversal can have significant adverse effects including intense pain, arrhythmias, pulmonary edema, and even death, so its use in anything other than a life-threatening emergency (respiratory arrest on profound unconsciousness) should be cautious. Slow titration instead of a big bolus dose is recommended.

For titration of naloxone – Small titrated doses of 0.04 mg (40 mcg) (i.e., $1/10^{th}$ of the concentration in a standard vial), up to a total dose of 0.4 mg. If clinical improvement appears but the patient is still obtunded, continue titration to a total dose of 0.8 mg (2 vials), after which other causes of the clinical state should be investigated.

Continuous Infusion Dose - ***Based on a literature review, a continuous infusion of two-thirds of the bolus dose that resulted in reversal each hour, will maintain the plasma naloxone levels equal to or greater than the naloxone levels that would have existed 30 minutes following the bolus dose.***
For example, if the initial dose of Naloxone that was required to reverse the opioid respiratory depression was 0.4 mg, then the continuous infusion rate can be calculated at 2/3 x 0.4 = 0.27 mg/hour. For convenience, round off to the nearest higher whole number, for example, 0.3 mg/hour.

Ordering in EPIC – Order Naloxone infusion through the order sets and prescribe the calculated dose.





Reconstitution – In the rare event of a pharmacy downtime, to reconstitute a naloxone infusion, mix 1 mg (2.5 vials of 0.4 mg naloxone) in a 100 mL 0.9% NaCL or a D5W bag to achieve a final concentration of a 100 mcg/mL. In the above example, the infusion will need to be run at 0.27 mcg/hour (or 27 mL/hour of the said concentration).

Of note, these are starting recommendations and the infusion should be titrated to clinical effect and the patient should be monitored closely in the PACU, with all hemodynamic monitors such as BP, pulse oximetry and EKG monitoring. The infusion should be clearly labelled and the nurse taking care of the patient and the responsible physician should be promptly informed, so that they can continue to monitor the patient.

Follow-up – strong consideration should be given to admitting the patient to the ICU for monitoring. The patient should remain in a monitored setting (PACU or ICU) until the infusion is discontinued and concerns for renarcotization are resolved

References

Goldfrank, Lewis, et al. "A dosing nomogram for continuous infusion intravenous naloxone." *Annals of emergency medicine* 15.5 (1986): 566-570.

Lewis, J. M., Klein-Schwartz, W., Benson, B. E., Oderda, G. M., & Takai, S. (1984). Continuous naloxone infusion in pediatric narcotic overdose. *American Journal of Diseases of Children*, *138*(10), 944-946.