

## Guidelines for Naloxone Use

### INDICATIONS

- Complete or partial reversal of opioid-induced ventilatory depression

### CRITERIA FOR USE

- Patients should meet both of the following criteria prior to the administration of naloxone:
  - Suspected or documented exposure to an opioid agonist
  - Respiratory rate < 8 breaths/min for adults (<50% age-appropriate rate for children) or clinical signs of hypoventilation/respiratory failure
- Naloxone is not indicated to reverse sedation in patients without ventilatory depression

### THERAPEUTIC CATEGORY

- Opioid Antagonist

### MECHANISM OF ACTION

- Pure opioid antagonist that competitively inhibits binding of opioid agonists to opioid receptor

### PHARMACOKINETICS

- Onset IV: ~2 minutes
- Duration: 20 – 90 minutes [dose/route of naloxone (IN> IM> IV duration)]
  - Be mindful of difference between duration of naloxone and duration of opioid, naloxone is generally shorter acting than the opioid
- Metabolism: primarily hepatic via glucuronidation

### ADVERSE REACTIONS

- Signs of opioid withdrawal syndrome (e.g., yawning, irritability, agitation, lacrimation, diaphoresis, rhinorrhea, piloerection, mydriasis, vomiting, diarrhea, tachycardia, hypertension). Adverse effects are dependent on the dose and route of administration of naloxone and the patient's baseline degree of opioid dependence.
- Agitation, anxiety, and craving may be severe and lead to poor patient decision-making and difficult clinical and interpersonal situations.
- A large increase in catecholamine release occurs and may result in adverse effects such as pulmonary edema, myocardial ischemia, dysrhythmia, heart failure, or cerebrovascular changes.

### PRECAUTIONS

- Use with caution in patient with pre-existing cardiovascular disease
- Excessive doses of naloxone in opioid-dependent patients (e.g. history of chronic opioid analgesic use, methadone maintenance, heroin/fentanyl use) may precipitate opioid withdrawal and/or exacerbate pain
- Duration of action of some opioids may exceed that of naloxone; therefore, patients must be closely observed for at least 2 hours after naloxone for re-emergence of ventilatory depression
- Clinical evaluation should be utilized to rule out other causes of ventilatory depression

### SOURCES

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## Naloxone: Adult Dosing and Administration

Patients should be clinically monitored for at least 2 hours after naloxone is administered. Patients should optimally be monitored with capnometry and pulse oximetry if receiving oxygen or pulse oximetry alone without oxygen.

### **Opioid Induced Ventilatory Depression in Opioid-Dependent or Unknown Patient**

**(RR <8 breaths/min or clinical signs of hypoventilation/respiratory failure)**

- Provide ventilatory support and oxygenation
- Administer **naloxone 0.02-0.04 mg** IVP over 15 seconds, repeat dose in 2 minutes
  - If no response to 0.08 mg, administer 0.2 mg, 0.4mg, 2 mg, and finally 10 mg (rarely) as necessary until therapeutic response\*
    - If no response is seen after the 10 mg dose, opioid is not likely responsible
  - Naloxone 0.4 mg diluted in 9 mL NS in a 10 mL syringe to yield a 0.04 mg/mL solution
- Note that with low-dose naloxone, patient arousal may be slow in onset and more subtle. Provide gentle stimulation before redosing.
- If patient develops withdrawal after bolus, allow effects of bolus to abate (typically about 30 minutes)
- If ventilatory depression recurs, redosing is suggested. If recurrent, see section on *Continuous Infusion*

### **Opioid-Induced Ventilatory Depression in Known Opioid Naïve Patient**

**(RR<8 breaths/minute or clinical signs of hypoventilation or respiratory failure)**

- Provide ventilatory support and oxygenation
- **Naloxone 0.4 mg** undiluted IVP over 15 seconds, repeat dose every 2 to 3 minutes as necessary for therapeutic response\*.
  - If ventilatory depression is not reversed after initial bolus, administer increasing doses of 0.4 mg, 2 mg, and up to 10 mg of naloxone as IV bolus
- If ventilatory depression recurs, redosing is suggested. If recurrent, see section on *Continuous Infusion*

### **Continuous Infusion**

**(If repeated doses do not maintain adequate ventilation, consider a continuous infusion of naloxone)**

- Provide capnometry and pulse oximetry with oxygen, or pulse oximetry alone without oxygen
- **Naloxone 2 mg/ 500 mL** NS or D5W (4 mcg/mL)
  - If naloxone bolus successful, administer 2/3 of the effective bolus dose per hour by IV infusion
    - If patient develops withdrawal during infusion, stop the infusion and allow effects to abate
      - Restart the infusion at half of the initial infusion rate
    - If patient develops ventilatory depression during infusion, re-administer initial effective bolus dose and increase infusion by half (1.5x) the initial rate
      - Assess the patient for continued opioid absorption and other etiologies for ventilatory depression

*\*Therapeutic response defined as adequate ventilation with or without alertness (RASS- Richmond Agitation Sedation scale -1 to 0) without the onset of withdrawal or significant pain. Note that patients die from opioid poisoning primarily through ventilatory depression, and thus this is the endpoint for therapy. Patients may not wake up*