

## Naloxone (Green)\*

### \* Colour code:

**Green** – For medicines routinely initiated and used by generalists

### Introduction

**Description:** Antagonist for use in severe opioid induced respiratory depression.

### Preparations

- 400 micrograms/ml injection (1ml ampoule).

### Indications

- Reversal of life-threatening respiratory depression due to opioid analgesics, indicated by:
  - a low respiratory rate < 8 respirations/minute
  - oxygen saturation <85%, patient cyanosed.
- If less severe opioid toxicity:
  - omit next regular dose of opioid; review analgesia
  - monitor the patient closely; maintain hydration, oxygenation.

### Cautions

- Naloxone is not indicated for opioid-induced drowsiness and/or delirium that are not life threatening.
- Naloxone is not indicated for patients on opioids who are dying.
- Patients on regular opioids for pain and symptom control are physically dependent; naloxone given in too large a dose or too quickly can cause an acute withdrawal reaction and an abrupt return of pain that is difficult to control.
- Patients with pre-existing cardiovascular disease are at more risk of side effects.

### Side effects

Total antagonism will result in severe pain with hyperalgesia and, if physically dependent, severe physical withdrawal symptoms and marked agitation. Opioid withdrawal syndrome: anxiety, irritability, muscle aches; **nausea and vomiting**; can include life-threatening tachycardia and hypertension. Cardiac arrhythmias, pulmonary oedema and cardiac arrest have been described.

## Dose and administration

### Where intravenous administration is possible:

Small doses of naloxone by slow intravenous (IV) injection improve respiratory status without completely blocking the opioid analgesia. Onset of action of IV naloxone is 1-2 minutes.

- Stop the opioid.
- High flow oxygen, if hypoxic.
- Dilute 400 micrograms naloxone (1 ampoule) to 10ml with sodium chloride 0.9% injection in a 10ml syringe. Refer to prolonged, or recurrent, opioid-induced respiratory depression section below.
- Administer a small dose of 80 micrograms (2ml of diluted naloxone) as a slow IV bolus every 2 minutes until the patient's respiratory status is satisfactory (>8 respirations /minute).
- Flush the cannula with sodium chloride 0.9% between the naloxone doses.
- Patients usually respond after 2ml to 4ml of diluted naloxone (=80 micrograms to 160 micrograms) with deeper breathing and an improved conscious level.
- A few patients need 1mg to 2mg of naloxone (this requires between 3 and 5 ampoules). If there is little or no response, consider other causes (for example other sedatives, an intracranial event, acute sepsis, acute renal failure causing opioid accumulation).

Closely monitor respiratory rate and oxygen saturation. Further doses may be needed. The duration of action of many opioids exceeds that of naloxone (15-90 minutes) and impaired liver or renal function will slow clearance of the opioid. Opioid depressant effects may return as the effects of naloxone diminish, and additional naloxone doses (or a continuous IV infusion) may be required.

Note: There is wide variation in the recommended initial bolus dose of naloxone reported in the literature from 20 micrograms (American Pain Society 2008) to 100 micrograms (PCF-4).

### Prolonged, or recurrent, opioid-induced respiratory depression:

- If repeated naloxone doses are required, start a continuous IV infusion of naloxone via an adjustable infusion pump.
  - Add 1mg of naloxone (= 2.5ml of 400 micrograms/ml naloxone injection) to 100ml of sodium chloride 0.9% to give a concentration of 10 micrograms/ml.

- Calculate the dose requirement per hour by totalling the naloxone bolus doses and dividing by the time period over which all the doses have been given.
  - Start the IV infusion of naloxone at half this calculated hourly rate.
  - Adjust the naloxone infusion rate to keep the respiratory rate above 8 (do not titrate to the level of consciousness).
  - Continue to monitor the patient closely.
  - Continue the infusion until the patient's condition has stabilised.
- Additional IV boluses may need to be given using naloxone diluted in sodium chloride 0.9%. Refer to dose and administration section above.
  - Administration should be accompanied by other resuscitative measures such as administration of oxygen, mechanical ventilation, or artificial respiration.

**If in doubt, seek advice.**

- Seek and treat the precipitating cause(s) of the opioid toxicity.
- Review the regular analgesic prescriptions.

**Care settings where there is no immediate access to the IV route, for example community:**

- Naloxone may be administered intramuscular (IM) when IV access is not immediately available.
- Onset of naloxone IM is 2-5 minutes.
- 100 micrograms (0.25ml) naloxone IM should be given and repeated after five minutes if there is no improvement with the first dose.
- An IV line should be sited as soon as possible.

**Practice points**

- Naloxone should be available in all clinical areas where opioids are used (National Patient Safety Agency).
- Naloxone is also available in disposable, pre-filled syringes. These doses may be too high for patients on regular opioid analgesics.
- Reversal of buprenorphine-induced respiratory depression may be incomplete. Larger naloxone doses may be needed.

**Resources**

- Palliative Care Drug Information online <http://www.palliativedrugs.com/>

## References

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