MIL

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Naloxone for the Management of Opioid Toxicity in Adults

OPIOID TOXICITY

Features

In someone who was prescribed opioids OR has evidence of opioid use

- Sedation – reduced ACVPU – non-responsive to voice
- Respiratory Rate (RR) of 8 or less
- SaO_2 less than 94% on room air
- If on supplemental oxygen, consider raised $PaCO_2$

Risk Factors

- Opioids:
  - New prescription
  - Recent increase in daily dosage (by 50 - 100%)
  - Opioid transdermal patch in place
  - Long-acting agents (especially if renal impairment)
- Renal impairment (AKI or eGFR less than 30ml/min)
- Fever or infection
- Recreational drug use

Assessment

Assess airway, breathing (Maintain SaO_2 at target for patient)

REMOVE ANY OPIOID-CONTAINING TRANSDERMAL PATCHES (E.g. Fentanyl, Buprenorphine)

Do you require a resuscitation team (call 2222)?

NO

NON-RESUSCITATION

- Escalate to senior doctor/nurse
- Dilute naloxone as **40micrograms/ml**
- Give "**non-resuscitation**" naloxone IV & observe response:
  - Initial dose: 80micrograms
  - Observe response
  - If no response, repeat with 40micrograms doses every 5 minutes until clinical response or up to 400micrograms has been given.

Naloxone infusion is required if more than 3 repeat doses of 400micrograms naloxone are given. (Appendix)

YES

RESUSCITATION

- Call the resuscitation team
- Escalate to senior doctor/nurse
- Give "**resuscitation**" doses of naloxone:
  - IV/Intraosseous (undiluted): 400micrograms, then 800micrograms, then 800micrograms, then 2mg
  - IM/SC (undiluted): 800 micrograms then 400 micrograms every 2-3 minutes as needed
- Monitor for response for 1 minute between doses
- **Doses up to 4mg may be required in severe poisoning. Consider naloxone infusion (Appendix)**

Clinical response?

- Improvement in RR, SaO_2, CO_2 normalised
- Improvement in GCS/ACVPU (NB: do not aim for full reversal of unconsciousness)

YES

- Ensure good hydration
- Review opioid prescription; consider
  - Dose reduction (~25%)
  - Switching long-acting opioids to short-acting

Consider referral to ITU if high naloxone requirements /infusion required.

NO

*Consider alternative diagnoses:

- Respiratory failure
- Hypoglycaemia
- Septic shock
- Medication (CNS depressants)
- Delirium
- End of Life (NB: It is rare for these patients to need naloxone)

Preparation / Administration for non-resuscitation dose

- Dilute 400micrograms (1ml ampoule) with 9ml with sodium chloride 0.9% → 40 micrograms in 1mL solution

Monitoring response

- Repeat doses will likely be required as naloxone has a shorter half-life than all opioids.
- Once an adequate response has occurred, monitor SaO_2, RR, GCS/ACVPU:
  - 1st hour: every 15 minutes
  - Hours 2-4: every 30 minutes
- Avoid sudden opioid withdrawal:
  - Increases sympathetic stimulation, cytokine release, hyperalgesia
  - Leads to acute pain, hypertension, arrhythmia, pulmonary oedema, cardiac arrest.
- Naloxone is unlikely to be needed beyond 24 hours after the last opioid stopped, unless the patient is receiving a transdermal opioid preparation. If patient is still sedated, seek advice (as below) and consider alternative diagnoses.
- Consider completing a Ulysses form when naloxone is administered in an inpatient setting.

Seeking advice

In-hours Mon-Fri	Adult pain service: 0800 - 1600 • **John Radcliffe:** Bleep 1362, Ext. 20284 • **Churchill**: Bleep 4375, Ext. 25403 • **NOC:** Bleep 7175 or 7106, Ext. 38229 • **Horton**: Bleep 4375 via Churchill switch, Ext. 25403 Palliative care service: 0830 – 1700 NB: For patients known to palliative care OR likely to be in last 6-12m of life Extension 21741
Out of hours (all other times)	On-call site medical registrar or anaesthetist (JR Bleep 4321, otherwise via switchboard) **Palliative care patients:** Consultant on call (via switchboard)

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Further information	• Naloxone injection monograph on Medusa (available via Eolas app) • Naloxone entry TOXBASE.org. • Resuscitation Council (UK) (2021). Advanced Life Support (8th Edition), Resuscitation Council (UK), London. • Naloxone entry, Palliative Care Formulary, Medicines Complete. • NHS England, Patient Safety Alert (20/11/2014). • Boland J, Boland E & Brooks D. (2013). DOI: 10.7861/clinmedicine.13-2-149. • Facey C, Brooks D & Boland JW (2016). DOI: 10.1080/21548331.2016.1149016.
Review date	December 2027

Appendix: Naloxone Infusion

<table>
<tr><td>Indication</td><td>

Naloxone infusion is required if more than 3 repeat doses of 400micrograms naloxone are given.
Seek help from anaesthetics, intensive care or palliative care team.
Consider transfer to a high dependency area.

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<tr><td>Preparation</td><td>

Mix 4mg (10 x 400micrograms ampoules) of naloxone in 30mL sodium chloride 0.9% or glucose 5% to provide a final 40 mL volume.
Final concentration 100 micrograms/mL; infuse via infusion pump.

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<tr><td>Starting the infusion</td><td>

Prescribe Naloxone Infusion using the Adult Naloxone PowerPlan on ePMA.
The initial hourly rate for infusion should be 60% of the total bolus doses required to obtain a response.
e.g. If the initial response required 200 micrograms, start the infusion at 120 micrograms per hour.

<table>
<tr><th>Total initial bolus dose required for response (micrograms)</th><th>Starting infusion rate (microgram/h)</th><th>Starting infusion rate (mL/h)</th></tr>
<tr><td>200 micrograms</td><td>120 microgram/h</td><td>1.2 mL/h</td></tr>
<tr><td>400 micrograms</td><td>240 microgram/h</td><td>2.4 mL/h</td></tr>
<tr><td>600 micrograms</td><td>360 microgram/h</td><td>3.6 mL/h</td></tr>
<tr><td>800 micrograms</td><td>480 microgram/h</td><td>4.8 mL/h</td></tr>
<tr><td>1000 micrograms</td><td>600 microgram/h</td><td>6.0 mL/h</td></tr>
<tr><td>1200 micrograms</td><td>720 microgram/h</td><td>7.2 mL/h</td></tr>
<tr><td>1400 micrograms</td><td>840 microgram/h</td><td>8.4 mL/h</td></tr>
<tr><td>1600 micrograms</td><td>960 microgram/h</td><td>9.6 mL/h</td></tr>
<tr><td>1800 micrograms</td><td>1080 microgram/h</td><td>10.8 mL/h</td></tr>
<tr><td>2000 micrograms</td><td>1200 microgram/h</td><td>12.0 mL/h</td></tr>
</table>

Titrate infusion to clinical effect.

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<tr><td>Weaning/stopping infusion</td><td>

In most circumstances, infusion can be discontinued at 24 hours.
Continue for 4 hours at same rate initially; then wean by 25% every 1-2 hours until stopped.
In general, do not stop a naloxone infusion between midnight and 0600 as it is harder to detect recurrence of acute toxicity while the patient is asleep.

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<tr><td>Managing complications</td><td>
<u>If Further Ventilatory Impairment Occurs</u>

Consider alternative diagnoses
Give additional IV boluses of 100-200 micrograms every minute until response.
Then increase infusion’s hourly rate by 60% of the total bolus dose of naloxone that was required.
E.g. If additional IV 200 micrograms bolus dose is required, infusion rate should increase by 120 micrograms per hour.

<u>Opioid withdrawal</u>
Use Opioid Withdrawal Scale (EPR →Interactive View → Pain Management)

Mild (5-24): Decrease infusion rate by 50%
Severe (over 25): Pause infusion; restart after 30-60 minutes at 50% of the previous rate.

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