NHS England

Patient Safety Alert

Stage One: Warning

Risk of distress and death from inappropriate doses of naloxone in patients on long-term opioid/opiate treatment

20 November 2014

Alert reference number:	NHS/PSA/W/2014/016
Alert stage:	One - Warning

Naloxone is an opioid/opiate antagonist licensed for use in:

- complete or partial reversal of central nervous system depression and especially respiratory depression, caused by natural or synthetic opioids; and
- treatment of suspected acute opioid overdose or intoxication.

Naloxone must be given with great caution to patients who have received longer-term opioid/opiate treatment for pain control or who are physically dependent on opioids/opiates. Use of naloxone in patients where it is not indicated, or in larger than recommended doses, can cause a rapid reversal of the physiological effects for pain control, leading to intense pain and distress, and an increase in sympathetic nervous stimulation and cytokine release precipitating an acute withdrawal syndrome. Hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest may result from inappropriate doses of naloxone being used for these types of patients.

The British National Formulary (BNF)[1] recommends a dose range to reverse acute opioid/opiate overdose in adults by intravenous injection of naloxone of 400 micrograms to 2mg. If there is no response, the dose is to be repeated at intervals of two to three minutes to a maximum of 10mg.

The BNF highlights that **doses used in acute opioid/opiate overdose may NOT be appropriate for the management of opioid/opiate-induced respiratory depression and sedation in those receiving palliative care and in chronic opioid/opiate use.** The recommended dose for adults in post-operative respiratory depression and for palliative care and chronic opioid/opiate use by intravenous injection is 100 to 200 micrograms (1.5 to 3 micrograms/kg). If the response is inadequate, give subsequent dose of 100 micrograms every two minutes. The naloxone doses in the BNF may differ from those in product literature. Even where doses are given as recommended, there is still a need for careful monitoring of vital observations and maintaining or restoring pain relief.

NHS England has received details of three patient safety incidents describing failure to follow the BNF guidance, including two incidents that resulted in death. Because this risk appears under-recognised, there may be significant under-reporting.

Additional safeguards that have been locally implemented include raising awareness of the risk of inappropriate doses of naloxone, the use of lower doses of naloxone in clinical protocols and resuscitation drug trays, teaching correct use of naloxone in annual cardiopulmonary resuscitation training sessions, and providing guidance on clinical monitoring and access

Actions

Who: All organisations providing NHS funded care where naloxone is prescribed, dispensed and/or administered.

When: As soon as possible but no later than 22 December 2014.

1. Establish if incidents involving inappropriate use of naloxone have occurred or have the potential to occur in your organisation.
2. Consider if immediate action needs to be taken locally and ensure that an action plan is underway, if required, to reduce the risk of further incidents occurring.
3. Disseminate this Alert to clinical staff who prescribe, dispense or administer naloxone injection.
4. Share any learning from local investigations or locally developed good practice resources by emailing: England.medication-safety@nhs.net

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Technical notes

NRLS search dates and terms
A search of NRLS medication incident involving naloxone for three years data (where incident date fell between 28.2.2011 to 28.2.2014 if reported by 21.05.2014) identified three incidents of wrong dose errors; two of these incidents resulted in fatal outcomes.

Stakeholder engagement
Advice was sought from the Medical Specialities Patient Safety Expert Group, which includes representatives of a range of professional and patient organisations.

Other
Reference [1] British National Formulary, September 2014 edition.

Acknowledgement
Mr Richard von Abendorff, for bringing to the attention to NHS England and the healthcare community the risks of harm from inappropriate dosing of naloxone, after a tragic incident involving the death of his mother, and for sharing with them a useful report by Dr Malcolm VandenBurg www.malcolmvandenburg.co.uk.

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