

## **BNF for Children dose review: use of naloxone for the reversal of respiratory and CNS depression resulting from opioid administration to mother during labour**

### **Context**

The BNF for Children currently provides naloxone dosing for neonates for a number of indications - these are overdose with opioids, reversal of postoperative respiratory depression, and reversal of respiratory depression and CNS depression resulting from opioid administration to mother during labour. This dosing is being reviewed, following a review of naloxone dosing for children aged 1 month and over, and adults.

We did an initial review of this dosing and consulted with expert advisers from the National Poisons Information Service. They proposed that the dosing of naloxone for opioid overdose in TOXBASE for children under 12 years would also be suitable for use in neonates. TOXBASE provides both high-dose and low-dose regimens of naloxone for use in overdose (with the latter regimen used for patients at risk of acute withdrawal). The advisers also suggested that we remove the indication of reversal of respiratory depression and CNS depression resulting from opioid administration to mother during labour from the BNF for Children. Their reasoning was that this was not used in routine clinical practice, and if a neonate did require naloxone, the proposed dosing for opioid overdose would be suitable for use.

We presented the proposed dosing amendments to the governance committee for the BNF for Children – the Paediatric Formulary Committee (PFC) – last year. The PFC agreed with including the TOXBASE opioid overdose regimens for neonates but asked us to further review the use of naloxone for the reversal of respiratory depression and CNS depression resulting from opioid administration to mother during labour. There was discussion amongst committee members that the current dosing was still used in clinical practice, and that a single intramuscular dose of naloxone may be more practical in some circumstances as it provides a longer duration of action, so avoiding the need for repeat injections. Furthermore, intravenous access may also not be readily available in some newborns.

We are therefore reaching out to you for your expert advice on the use of naloxone for the reversal of respiratory depression and CNS depression resulting from opioid administration to mother during labour.

### **Background**

There are four Summaries of Product Characteristics (SPCs) on emc that include the indication of reversal of respiratory and other CNS depression in the new-born resulting from the administration of analgesics to the mother during childbirth. Their recommendations for dosing and routes of administration are as follows:

Two SPCs<sup>1,2</sup> recommend a dose of 10 micrograms/kg, given intravenously, intramuscularly or subcutaneously, which can be repeated at 2-to-3-minute intervals; alternatively 200 micrograms, or approx. 60 micrograms/kg, can be given as a single intramuscular dose. These dosing options are reflected in current BNF for Children content.

Two SPCs<sup>3,4</sup> recommend a dose of 10 micrograms/kg, given intravenously, repeated at 2-to-3-minute intervals; this dose can also be given intramuscularly if intravenous access is not possible.

A literature search found limited evidence for this use of naloxone in neonates. One dated paper from 2003<sup>5</sup> concluded that there is a need for a randomised control trial to determine if there are benefits from the use of naloxone in new-born infants with respiratory depression due to administration of opioids to their mothers during labour. This remained the conclusion of a Cochrane review published in 2018<sup>6</sup>.

The Evelina Formulary (app accessed 1.3.22)<sup>7</sup> states that the preferred dose for neonates with respiration depressed by maternal opioids is 200 micrograms (60 micrograms/kg) given intramuscularly for a prolonged effect within 4 hours of delivery.

### Current BNF for Children text (February 2022 monthly update)

Reversal of respiratory and CNS depression resulting from opioid administration to mother during labour

By intramuscular injection

Neonate

200 micrograms, alternatively 60 micrograms/kg, to be given as a single dose at birth.

By intravenous injection, or by subcutaneous injection

Neonate

10 micrograms/kg, repeated every 2–3 minutes if required.

### Questions to advisers

**Note:** As mentioned above, the intention is for the BNF for Children to include high- and low-dose regimens of naloxone for opioid overdose in neonates, to reflect the recommendations in TOXBASE. These regimens will be in line with the dosing regimens currently included in the BNF and BNF for Children for opioid overdose in children aged 1 month to 11 years, as agreed by the PFC.

1. Should the use of naloxone for the reversal of respiratory depression and CNS depression resulting from opioid administration to mother during labour be included as a stand-alone indication and dose statement in the naloxone monograph in the BNF for Children?

a. If yes, is the preferred dosing regimen reflective of the licensed dosing shown in references 1 and 2, or references 3 and 4 (details provided in background above, references listed below)?

2. Are there any other points from practice that should be considered for this use? Please provide evidence to support additional points if possible

### References

1. SPC Naloxone Hydrochloride 400 micrograms/ml Solution for Injection/Infusion Advanz (Advanz Pharma, revised 30.8.12): <https://www.medicines.org.uk/emc/product/6589/smpc>
2. SPC Naloxone Hydrochloride 1mg/ml Solution for Injection in a pre-filled syringe (Martindale Pharma, revised 12.11.19): <https://www.medicines.org.uk/emc/product/3590/smpc>
3. SPC Naloxone 400 micrograms/ml solution for Injection/Infusion (Hameln Pharma, revised 1.4.20): <https://www.medicines.org.uk/emc/product/6344/smpc>
4. SPC Naloxone 400 microgram/ml solution for injection or infusion (AOP Orphan Pharmaceuticals, revised 4.2019): <https://www.medicines.org.uk/emc/product/8967/smpc>
5. McGuire W, Fowle PW. Naloxone for narcotic exposed newborn infants: systematic review. Arch Dis Child Fetal Neonatal Ed. 2003: <https://fn.bmj.com/content/fetalneonatal/88/4/F308.full.pdf>
6. Moe-Byrne T, Brown JVE, McGuire W: Naloxone for opioid-exposed newborn infants. Cochrane Database Syst Rev. 2018: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6517169/pdf/CD003483.pdf>
7. Evelina Paediatric Formulary Naloxone monograph (accessed online via Clinibee, 1.3.22): see below

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# NALOXONE

Paediatric Formulary  
29 Nov 2021 · 2 min read



Formulary status **RBD** Specialist or hospital prescribing only.

## Preparations

INJECTION 400microgram in 1ml.

PRE-FILLED SYRINGE (Minijet) 400microgram in 1ml.

## Dosage

### REVERSAL OF OPIOID INDUCED RESPIRATORY DEPRESSION

Neonates: *IV injection*, 10microgram/kg, repeated every 2-3 minutes as necessary. Doses up to 100microgram/kg have been used. In neonates with respiration depressed by maternal opioids, it is generally preferred to give an IM injection of 200microgram (60microgram/kg) for a prolonged effect within 4 hours of delivery.

Children: *IV injection*, 4-10microgram/kg. If respiratory improvement is not achieved, a larger