

NITRIC OXIDE • 1/2

INDICATIONS

- Persistent pulmonary hypertension of the newborn in term and near term (>34 weeks) babies, proven on clinical grounds or by echocardiography [see **Persistent pulmonary hypertension of the newborn (PPHN)** guideline]
- Oxygen index >20
- Pre and post ductal SpO₂ difference >10%
- Initiate treatment with nitric oxide (NO) only after discussion with **on-call consultant**
- Babies requiring NO should be referred to a **NICU** for ongoing management, in accordance with Toolkit principles

CAUTIONS

- Preterm baby
- no evidence of benefit for preterm babies needing ventilation for RDS and some evidence of harm
- may be some survival benefit for preterm babies with pulmonary hypoplasia and PPHN – discuss with consultant
- Platelets <50 × 10⁹/L
- Known or suspected major haemorrhage
- Congenital diaphragmatic hernia

CONTRAINDICATIONS

- Congenital heart disease (especially circulations dependent on right-to-left shunting)

DOSE AND ADMINISTRATION

Starting NO

Preparation

- Ensure ventilation optimal and that other aspects of the **Persistent pulmonary hypertension of the newborn (PPHN)** guideline have been followed
- Echocardiogram (if available) to exclude cyanotic congenital heart disease
- A sustained inflation immediately before starting NO can enhance response

Administration

- Document FiO₂ and SpO₂ immediately before starting NO
- Start NO at 20 ppm
- NO displaces oxygen so expect inspired oxygen displayed on INOvent to read lower than that on ventilator. Ensure consistency of documentation on charts
- Assess response after 30–60 min. If no response (see below) stop NO
- NO can be stopped abruptly without weaning if given for <4 hr

Definition of response to NO

- An increase in SpO₂ or PaO₂ whilst on the same ventilator settings or an ability to wean FiO₂ whilst maintaining SpO₂ occurring within 60 min of starting NO
- Approximately 30% of babies with PPHN do not respond to NO

Table 1: Definition of a response to NO

Response	Increase in SpO ₂	Increase in PaO ₂	Fall in FiO ₂
Full	>20%	>3 kPa	>0.2
Partial	10–20%	2–3 kPa	≥0.1

Weaning

- If no response to NO after 60 min stop NO without weaning
- If NO has been administered for ≥4 hr, wean gradually to prevent rebound (as below)
- If full or partial response to NO when preductal SpO₂ can be maintained in target range with FiO₂ <0.6 and after at least 4 hr treatment weaning can be attempted
- reduce NO to 10 ppm
- in 1–2 hr reduce NO to 5 ppm
- in 1–2 hr reduce NO to 4 ppm and continue to reduce NO by 1 ppm every 1–2 hr
- after 1–2 hr at 1 ppm increase FiO₂ by 0.1–0.2 10 min before stopping NO
- some babies will require low dose (<0.5 ppm) for some time (up to 24 hr) during weaning
 - may be necessary to temporarily increase FiO₂ by 0.1–0.2 to facilitate weaning
- Failure of weaning is defined as either
- >5% reduction in SpO₂ or

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- need to increase FiO_2 by >0.2 to maintain SpO_2 or
- development of $>10\%$ difference between pre- and postductal SpO_2
- If weaning fails at any stage increase NO to previous dose and wait ≥ 4 hr before trying again
- Once discontinued, wait ≥ 6 hr before removing NO circuit from ventilator

MONITORING

- Use SpO_2 to monitor response
- Blood gases 4-hrly
- Monitor methaemoglobin before starting NO, 1 hr after starting and then 12-hrly. Maximum proportion of total haemoglobin is reached after 8 hr
 - normal $<1\%$
 - 2–3% is acceptable
 - 4% requires action: reduce NO and repeat in 1 hr
 - if still $>4\%$, stop NO
 - if $>6\%$, treat with methylthioninium chloride (methylene blue) 1 mg/kg IV over 1 hr
- NO inhibits platelet function and can trigger bleeding if baby has bleeding problem or thrombocytopenia. Check FBC daily while baby receiving NO
- If $\text{NO}_2 > 1$ ppm reduce NO dose