CLINICAL PRACTICE GUIDELINE
Guideline coverage includes NICU KEMH, NICU PMH and NETS WA

Nitric Oxide Therapy (iNO)

This document should be read in conjunction with the Disclaimer

Indications

- Hypoxic respiratory failure despite "maximal medical therapy" i.e. Surfactant, sedation, conventional or HFOV/ HFJV with lung recruitment optimised, and therapy directed to maintenance of mean arterial blood pressure within the normal range commenced. An Oxygenation index of more than 20 in term infants may also indicate a trial of iNO should be considered.
- Presence of persistent pulmonary hypertension of the newborn (PPHN). Ideally a cardiac echo should be performed before starting iNO, if this is not possible then one should be arranged after iNO commences

A cranial ultrasound should be performed if possible prior to commencing iNO therapy. A recent CXR may aid in assessing lung recruitment is optimised.

Caution

There is little trial evidence to support iNO use in preterm infants <34 weeks. Although the sub group of infants <34 weeks with prolonged rupture of membranes and pulmonary hypoplasia have been reported to show improvement with iNO therapy. iNO is used internationally in these infants as a"rescue" therapy in infants failing to improve oxygenation despite maximal medical therapy.

In addition care should be taken in infants with severe IVH or hypoxic ischemic encephalopathy or in infants with coagulopathy.

Prior to starting

Discuss the use of iNO with parents prior to starting wherever possible.

Starting Dosage of iNO

- **All neonates**: Start with 20 parts per million (ppm).

Assessment of response to iNO

After iNO use of 30-60 minutes medical staff to assess for response:

Positive response:

- Increase in PaO_2 of ≥ 20mmHg.
- Or increase in $Sp0_2$ by 10%.
- Or able to drop $Fi0_2$ by 0.2.

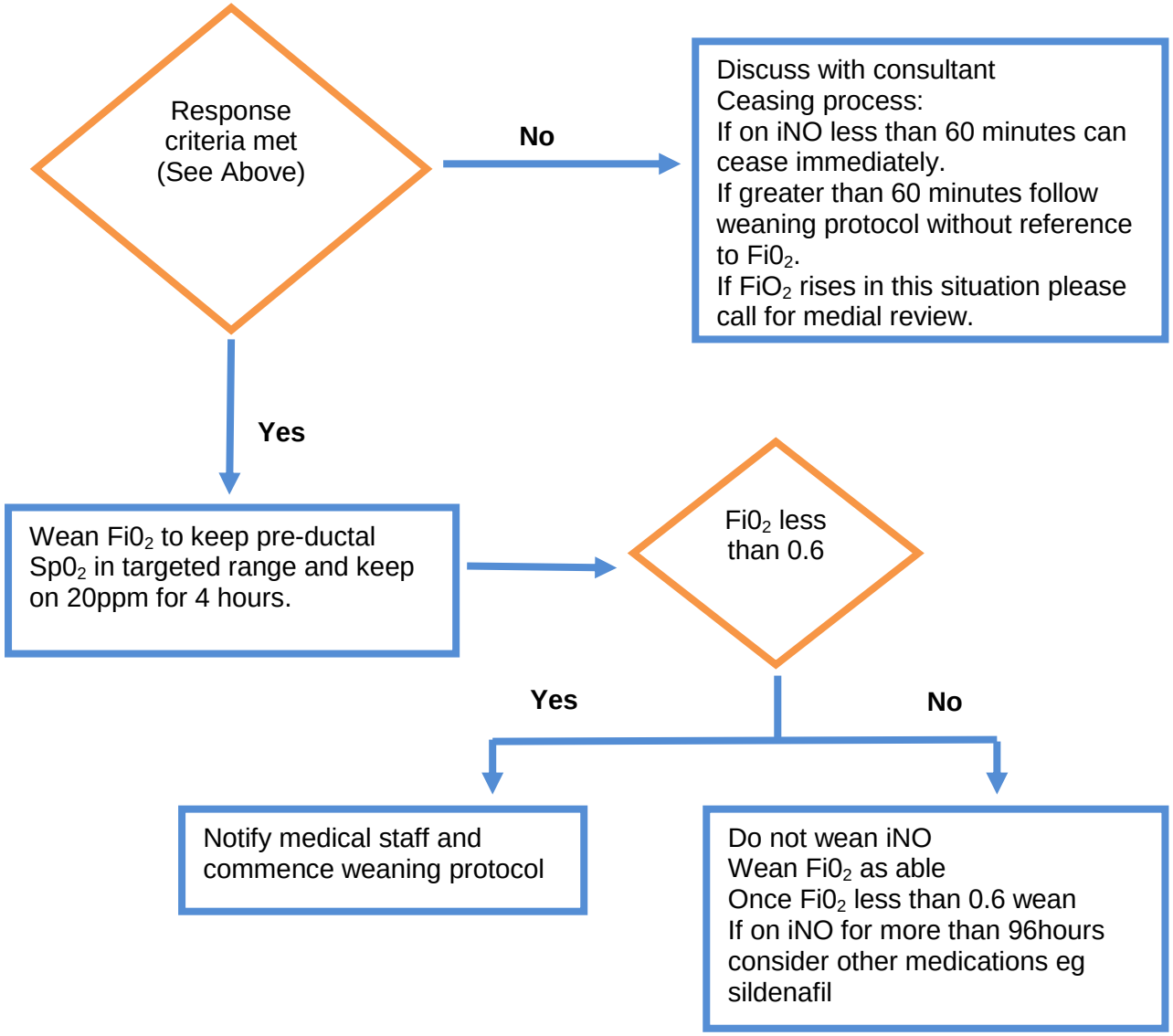
Partial response:

- Increase in PaO_2 of 15-20 mmHg.
- Or Increase in $Sp0_2$ by 5-10%.
- Or able to drop $Fi0_2$ by at least 0.1-0.2.

If does not meet partial or positive response criteria discuss with consultant and in general iNO should be ceased. Consultant discretion however is available to continue. If have been on iNO for less than 60 minutes can cease immediately.

If have been on iNO for over an hour can follow weaning protocol without reference to $Fi0_2$. If the FiO_2 rises in this situation please call for medical review.

Ongoing iNO



Monitoring Met Hb

- Met Hb levels available via blood gas.
- Met Hb less than 2.5% is safe.
- MetHb 5-10% decrease iNO by 50%.
- MetHb more than 10% cease iNO.

Weaning

After 4 hours of iNO assess for weaning. If $Fi0_2$ is less than 0.6 can start weaning. In certain other circumstances a consultant may choose to wean even if $Fi0_2$ is more than 0.6 is stability in $Fi0_2$ is achieved.

In most circumstances iNO will be weaned first and then MAP. Discuss MAP weaning strategy with consultant.

The weaning process involves a step wise process with repeated assessments for weaning failure.

Weaning failure is defined as:

- Increase in $Fi0_2$ by more than 0.2.
- Or Fall in $Sp0_2$ by more than 5%.
- Or pre/post ductal $Sp0_2$ gradient of more than 10% returns.

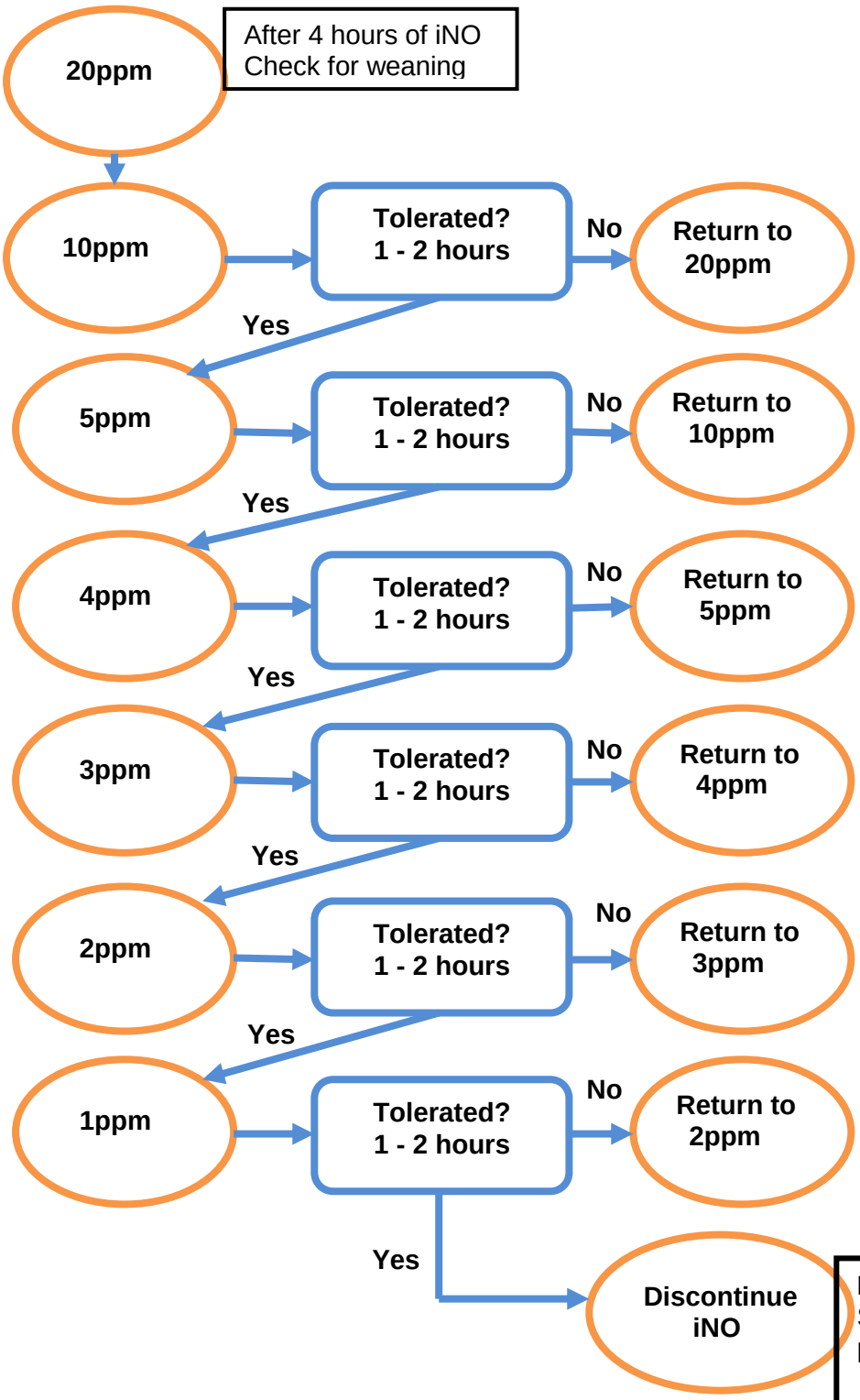
If weaning failure occurs return iNO to previous dose then wait 4 hours before re-attempting to wean.

Each weaning step should be considered 1-2 hours after the prior step if weaning criteria are met. If weaning a step is not successful, notify medical staff.

The step wise weaning process is:

- Decision by medical staff to commence weaning. Medical staff to document in the notes to wean as per protocol. Nursing staff can then follow protocol to wean each step without medical review. Nurses to notify medical staff if weaning failure occurs.
- 20ppm decreased to 10ppm.
- Assess for weaning failure.
- If none then after 2 hours reduce to 5ppm.
- Assess for weaning failure.
- If none then after 1-2 hours reduce to 4ppm.
- Thereafter reduce every 1-2 hours by 1ppm if no evidence of weaning failure at each step, until iNO ceased. Turn tank off.

Consider increasing $Fi0_2$ by 0.1-0.2, 10 minutes prior to ceasing iNO.



Failure to wean:
Stop wean and return to previous dose if:

- Increase in FiO_2 by 0.2
- Fall in SpO_2 by more than 5%
- Increase in pre/postductal SpO_2 gradient of more than 10% returns

Wait more than **4 hours** before reattempting to wean
If on iNO **for more than 96 hours** consider adding in medications such as sildenafil.

References

1. Elmekkawi A, More K, Shea J, Sperling C, Da Silva Z, Finelli M, et al. Impact of Stewardship on Inhaled Nitric Oxide Utilization in a Neonatal ICU. Hospital pediatrics. 2016;6(10):607-15.
2. Soraisham AS, Harabor A, Shivananda S, Alvaro R, Ye XY, Lee SK, et al. Trends and Variations in the Use of Inhaled Nitric Oxide in Preterm Infants in Canadian Neonatal Intensive Care Units. Am J Perinatol. 2016;33(7):715-22.
3. Ellsworth MA, Harris MN, Carey WA, Spitzer AR, Clark RH. Off-label use of inhaled nitric oxide after release of NIH consensus statement. Pediatrics. 2015;135(4):643-8.
4. Finer NN, Barrington KJ. Nitric oxide for respiratory failure in infants born at or near term. Cochrane database of systematic reviews (Online). 2006(4):CD000399.
5. Donohue PK, Gilmore MM, Cristofalo E, Wilson RF, Weiner JZ, Lau BD, et al. Inhaled nitric oxide in preterm infants: a systematic review. Pediatrics. 2011;127(2):e414-22.

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