University Hospitals of Derby and Burton NHS Foundation Trust

Document control sheet

GUIDELINE NUMBER	
AREA IN WHICH THIS MONOGRAPH APPLIES	NEONATAL UNIT

DIVISIONAL AUTHORISATION	
GROUP	**DATE**
Paediatric monograph review group	13.04.2022
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Reviewed by: Name		
Checked by: Name		

Change history:

Changes Reference	Change details	Date

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NICU: Intravenous Paracetamol

<table>
<tr><td>Presentation:</td><td>Paracetamol 500mg/50mL (10mg/mL) solution for infusion</td></tr>
<tr><td>Indication:</td><td>Pain/Pyrexia where oral route not tolerated/appropriate, Closure of PDA</td></tr>
<tr><td>Dose:</td><td>For dosing, use corrected gestational age (CGA)

Indication: Pain/Pyrexia where oral route not tolerated/appropriate
<table>
<tr><td rowspan="2">Preterm</td><td><32 weeks CGA</td><td rowspan="3">7.5mg/kg</td><td>12 hourly</td><td>Max daily dose: 15mg/kg/day</td></tr>
<tr><td>32^{+0} – 36^{+6} CGA</td><td>8 hourly</td><td>Max daily dose: 22.5mg/kg/day</td></tr>
<tr><td>Term</td><td>≥ 37 weeks to 44 weeks*</td><td>6 hourly</td><td>Max daily dose: 30mg/kg/day</td></tr>
</table>
**Higher doses of 10mg/kg can be given in term babies, but the 24-hour daily maximum dose remains the same.*

Indication: Closure of PDA [see additional comments]
<table>
<tr><td>23^{+0} – 25^{+6} weeks CGA
AND ≤ 7 days old</td><td>LOAD</td><td>20mg/kg</td><td>Maintenance</td><td>12.5mg/kg</td><td>6 hourly</td></tr>
<tr><td>23^{+0} – 25^{+6} weeks CGA
AND > 7 days old</td><td>LOAD</td><td>20mg/kg</td><td>Maintenance</td><td>15mg/kg</td><td>6 hourly</td></tr>
<tr><td>≥ 26 weeks CGA</td><td>LOAD</td><td>20mg/kg</td><td>Maintenance</td><td>15mg/kg</td><td>6 hourly</td></tr>
</table>
PDA closure: Course length range between 2-7 days, typically in practice 3 days.

Monitoring: Check paracetamol [red-top bottle] level immediately <u>before giving the third maintenance dose</u>. Desired level 15-25 mg/mL. Where levels are within range, continue with regimen. If course > 3 days, recheck levels on alternate days. Check LFT's daily. If liver toxicity suspected (INR>1.5 or LFTs > 3 x baseline) withhold the dose and check paracetamol level 4 hours after the dose was administered. Where paracetamol level is ≥25mg/dL, stop therapy.</td></tr>
<tr><td>Route of administration:</td><td>Intravenous
Infusion time: Give over 15 minutes</td></tr>
<tr><td>Instructions for preparation:</td><td>Order a 500mg/50mL solution for infusion from Pharmacy

Withdraw the required dose from a 500mg in 50mL preparation into a syringe and administer using a Syramed infusion pump.

E.g. If you have a 2.5kg 36^{+1} week gestation baby
7.5mg x 2.5kg = 18.75mg (dose prescribed = 18mg)

You have a 500mg/50mL (10mg/mL) solution; therefore withdraw the dose 18mg [1.8mL] + overage from the solution.

If needed, to aid administration consider withdrawing the volume to be administered and further diluting with sodium chloride 0.9% or glucose 5% to a minimum concentration of 1mg in 1mL.
The diluted solution should be used immediately but if this is not possible the expiry time of the diluted solution should be limited to one hour (including infusion time).</td></tr>
<tr><td>Prescribing</td><td>Prescribe on paper drug chart as per Trust prescribing policy</td></tr>
<tr><td>SMART pump directions</td><td>Use emergency drug setting</td></tr>
</table>

Known compatibility issues	Compatible: Fentanyl, Morphine, Hydrocortisone, Potassium Chloride, Vancomycin, Midazolam. Incompatible: Aciclovir
Additional Comments:	NB. IV paracetamol is not licensed in pre-term neonates Avoid large doses in liver impairment. Use with care in babies on other drugs affecting the liver. Neonates may be more susceptible to paracetamol induced liver toxicity, therefore treatment with N-acetylcysteine should be considered in all paracetamol overdoses. NB. Caution where babies are dependent on maintaining patency of ductus arteriosus, as paracetamol may close PDA. Paracetamol clearance is lower in neonates than in children and adults. After metabolic conversion, paracetamol is subsequently eliminated by the renal route. Paracetamol appears to be a promising alternative to indomethacin and ibuprofen for the closure of a PDA with possibly fewer adverse effects. Additional studies testing this intervention and including longer-term follow-up are needed before paracetamol can be recommended as standard treatment for a PDA in preterm infants.

Note: The contents of this monograph should be read in conjunction with information available in the BNFC and Medusa

References:

NUH NICU Pharmacopoeia Paracetamol monograph, accessed via www.nuh.nhs.uk on 12.11.20
British National Formulary for Children, accessed via www.medicinescomplete.com on 16.06.21
Medusa Injectable Medicines Guide, accessed via http://medusa.wales.nhs.uk on 12.11.20
Trissel LA (Ed), Handbook on Injectable Drugs, accessed via www.medicinescomplete.com on 12.11.20
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Ohlsson A, Shah PS. Paracetamol (acetaminophen) for patent ductus arteriosus in preterm or low birth weight infants. Cochrane Database of Systematic Reviews 2020, Issue 1. Art. No.: CD010061. DOI: 10.1002/14651858.CD010061.pub4
Mitra S, Florez ID, Tamayo ME, et al: Association of placebo, indomethacin, ibuprofen, and acetaminophen with closure of hemodynamically significant patent ductus arteriosus in preterm infants: a systematic review and meta-analysis. JAMA 2018; 319(12):1221-1238.
Tekgündüz, K., Ceviz, N., Caner, İ, Olgun, H., Demirelli, Y., Yolcu, C., . . . Kara, M. (2015). Intravenous paracetamol with a lower dose is also effective for the treatment of patent ductus arteriosus in pre-term infants. *Cardiology in the Young, 25*(6), 1060-1064. doi:10.1017/S1047951114001577
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