Title:	**Guideline for the management of Patent Ductus Arteriosus (PDA).**
Reference Number	GL-ODN-09
Main Author (s)	North West, North Wales & Isle of Man Children's Heart Network with comments from all NW neonatal clinical leads
Target Audience	NWNODN clinicians
Network Responsible for document control	NWNODN
Ratified by:	SMT Shared with all locality NSG
Date Ratified:	7th Sept 2023
Review Date:	7th Sept 2026
Version:	Final
Document status:	Ratified

Document History:			
Date	**Version**	**Author**	**Notes**
2019	V1	Various	Original document produced and agreed by NW Cardiac Network. Responsibility for document control now falls with NWNODN
Nov 2019	V2	NVS	Circulated for comments and updated
May 2020	V3	NVS/KH	Updated with NW Clinical Lead comments and document formatted.
July 2020	V4	CN	Word versions of forms inserted. Awaiting new referral process
Jan 2021	V5	CN	New referral process inserted & document linked to Cardiac NW guideline. No other amendments

Nov 2025	V6	RH	Removal of out-of-date LWH drug monographs (prev appendix 3 and 4). Ibuprofen and paracetamol dosing recommendations added in tables.

Contents

Management of Patent Ductus Arteriosus

Background

The ductus arteriosus closes spontaneously in many preterm infants but prolonged ductal patency is a complication of extreme preterm birth [1]. A persistently patent ductus with a large ductal shunt (a 'haemodynamically significant', hsPDA) is associated with pulmonary hyper-perfusion, systemic hypo-perfusion and adverse clinical outcomes including pulmonary haemorrhage, NEC, CLD and mortality [2].

Which babies should undergo echocardiography?

An echocardiogram should be performed in any preterm baby in whom the clinical signs and/or radiological features suggest the presence of a hsPDA. These include murmur, tachycardia, full pulses, an active precordium, hypotension, cardiomegaly, worsening respiratory status and dependence on respiratory support.

Diagnosis of hsPDA

Diagnosis of PDA can only be made using 2D and Doppler echocardiography; clinical signs are unreliable and should not be used in isolation to make the diagnosis. Early echocardiographic 'screening' for PDA is not routinely performed. Diagnostic echocardiography should include an initial assessment to exclude structural heart disease and, specifically, duct-dependent cardiac defects.

Assessment of hsPDA should include measures of ductal size and the magnitude and impact of the ductal shunt. The following echocardiographic indices and thresholds should be used to define a hsPDA [3]:

1. PDA diameter $\geq$ 2.0 mm (either using 2D or colour Doppler)
2. Ductal flow pattern ('growing' pattern or pulsatile with Vmax < 2 m/s and Vmax/Vmin $\geq$ 2)
3. Retrograde post ductal aortic/coeliac/SMA diastolic flow
4. La/Ao $\geq$ 2
5. LVO > 300 mL/kg/min
6. Mitral valve E/A ratio > 1

The diagnosis of hsPDA should be made in the presence of supportive clinical signs and at least 3 of the above echo indices.

Management of babies with PDA

a. **Babies with PDA and a small ductal shunt** (i.e. not haemodynamically significant) should be managed expectantly. A repeat echo should be performed if the baby has a cardiorespiratory deterioration or if a murmur is still present prior to discharge home. Refer to cardiology if PDA is still present at discharge.

b. **Asymptomatic babies with echocardiographic criteria of hsPDA** should also be managed expectantly, but with a low threshold for repeating the echo if the baby develops any symptoms of hsPDA. Subsequently, management should follow (a) or (c), as appropriate.

c. **Symptomatic babies* with a hsPDA** may be treated with diuretics, ibuprofen and/or paracetamol (see below).

**Clinical features include persistent hypotension, pulmonary haemorrhage, prolonged dependence (or increase in) invasive or non-invasive respiratory support, feed intolerance.*

Management strategies/therapeutic interventions (see appendix 1)

Expectant management

This approach is used when uncomplicated spontaneous closure of the ductus arteriosus is anticipated. Management is the same as in a baby in whom the PDA is closed.

Non-pharmacological intervention

Although there is no clear evidence of clinical efficacy, various approaches including fluid restriction, increasing PEEP, permissive hypercapnia, maintaining a high haematocrit and higher target SpO_2 (89-94%) have all been used as part of a 'conservative' approach to managing a hsPDA [4].

Action:
- Follow current unit guidelines for fluid, blood transfusion and oxygen and respiratory support;
- Give information leaflet on PDA to parents.

Diuretic therapy

There is some evidence that furosemide stimulates renal synthesis of prostaglandin E2 (a dilator of the ductus arteriosus) and delays ductal closure. The risk of PDA is greater with furosemide compared with chlorothiazide. Furosemide is associated with nephro- and ototoxicity.

Action:
- Use chlorothiazide (and not furosemide) for management of PDA-associated left heart volume overload and pulmonary oedema.

Pharmacological closure

Although pharmacological closure of the DA is associated with decreased severe IVH and pulmonary haemorrhage, there is no convincing evidence of longer-term benefit from randomised controlled trials [5]. A conservative management approach might also be superior to early routine treatment in babies dependent on respiratory support [6].

a. Ibuprofen

Ibuprofen is effective in achieving ductal closure in around 70-80% of cases [7, 8]. There is some evidence that oral therapy and higher dosage regimens are associated with higher closure rates [7-9].

Action:
- Use standard dose ibuprofen as routine first-line pharmacological treatment of hsPDA in babies < 21 days of age;
- Use oral (rather than IV) ibuprofen if baby is receiving full enteral feeds;
- Re-assess the ductus arteriosus and ductal shunt after 3 days;
- A second course of high dose ibuprofen can be considered if baby is still under 21 days of age after waiting at least 48 hours from completion of primary course.

NWNODN Ibuprofen dosing regimen (oral or IV) for treatment of haemodynamically significant patent ductus arteriosis (PDA)

Day of treatment	Standard Regimen (primary course)	High dose regimen (secondary course)
Day 1	10 mg / Kg	20 mg / Kg
Day 2	5 mg / Kg	10 mg / Kg
Day 3	5 mg / Kg	10 mg / Kg

Please consult BNFC and product literature for side effects, cautions and information on interactions. Medusa provides up to date information on administration.

b. Paracetamol (acetaminophen)

Paracetamol has comparable efficacy to ibuprofen in ductal closure but there is limited information on long-term safety [10]. There is some evidence to support the use of paracetamol in late treatment of PDA after failure of previous NSAID therapy, although the efficacy in achieving ductal closure was only 15% [11].

Action:
- Consider using paracetamol to treat hsPDA in babies ≥ 21 days of age, or in babies < 21 days in whom there are contraindications to using ibuprofen
  Reassess the ductus arteriosus and ductal shunt after 3 days.

NWNODN paracetamol dosing regimen (IV) for treatment of haemodynamically significant patent ductus arteriosis (PDA) In babies greater than 21 days of age, or in babies less than 21 days in whom there are contraindications to using ibuprofen

Route of admin	Loading dose	Maintenance dose	Frequency
IV	20 mg / kg	10 mg / kg	Every 6 hours for a total of **12** doses. i.e. 3-day course
ORAL	Not required	15 mg / kg	Every 6 hours for a total of **12** doses. i.e. 3-day course

Please consult BNFC and product literature for side effects, cautions and information on interactions. Medusa provides up to date information on administration.

Surgical closure

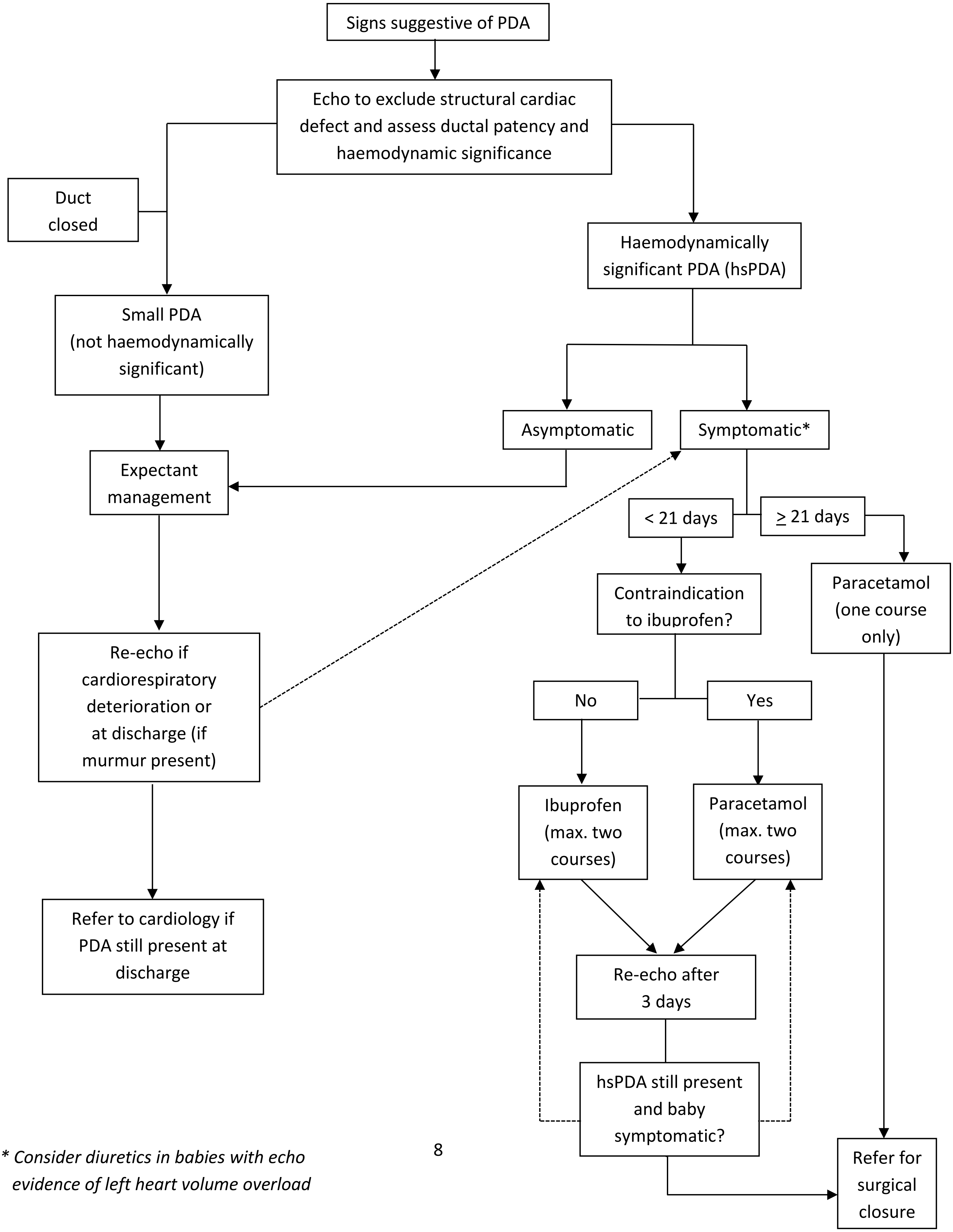
Surgical closure should be considered in babies with hsPDA despite pharmacological therapy (or in whom pharmacological therapy is contraindicated) who remain dependent on high levels of respiratory support (ventilation, CPAP or HFNC). Duct ligation carries significant risks associated with transfer, surgery and post-operative complications (such as post-ligation cardiac syndrome) [12]. Catheter closure might be appropriate in selected larger babies (> 6 kg) at the discretion of the cardiologists.

If after the above sequential assessment, the baby is felt to require consideration for surgical or interventional closure of a haemodynamically significant Persistent Ductus Arteriosus (hsPDA) please refer to the *Congenital Heart Network Guidance 'Referral for management of patent ductus arteriosus (PDA) in premature babies'.*

Action:

- Consider duct ligation in babies with hsPDA who are dependent on high levels of respiratory support (ventilation, CPAP or HFNC).
- A consultant-to-consultant referral should be made to the cardiology team verbally and using the referral process outlined in the Congenital Cardiac *Congenital Heart Network Guidance 'Referral for management of patent ductus arteriosus (PDA) in premature babies'.* See Appendix 2 for flow chart of process.
- A pre-op echo should be performed within 3 days of transfer to confirm that a hsPDA is still present.

Appendix 1



** Consider diuretics in babies with echo evidence of left heart volume overload*

Appendix 2: Summary of PDA Referral Pathway

hsPDA confirmed on assessment
Neonatal guidance suggests intervention
Patient should be fully assessed and be free of inter-current infection

Referring team to complete MDT Form

MDT Coordinators
Megan Johnson
megan.johnson23@nhs.net
0151 282 4514
Tracy Oakes
tracy.oakes@nhs.net
0151 282 4515

Neonatal team contacts Alder Hey Paediatric Cardiology ST or consultant of the week

Via Switchboard on 0151 228 4811

Directly on Consultant of the week phone 0151 252 5220

Via SpR on Call 0151 228 4811 Bleep 369

Echo images/CXR to be sent via PACS where possible
MDT discussion form to be sent to cardiology ST on call
Ahc-tr.cardreg@nhs.net for review and telephone discussion
Referral accepted
MDT coordinator will liaise with referrer to agree date for MDT discussion via MS Teams

****

Please note any **changes to clinical condition** following referral should be discussed with the cardiology on call team e.g

****Escalation of respiratory support***
****New vasoactive support***
****Infection concerns***

Patient discussed at regional cardiac MDT
If suitable patient listed for surgery or intervention
On call team to feedback meeting outcome and plan to referring team

Provisional date arranged (listing meeting)
Cardiac surgery or interventional PCO to liaise with referring centre regarding date and enter on calendar

Transport to be arranged for date
Please telephone ICU on 0151 252 5242/ 5241 on the morning of transfer and prior to departure to confirm bed available and provide clinical handover

ICU to contact referring centre and transport team when patient ready for transport back to neonatal care

General References

1. Semberova J, Sirc J, Miletin J, Kucera J, Berka I, Sebkova S, O'Sullivan S, Franklin O, Stranak Z. Spontaneous Closure of Patent Ductus Arteriosus in Infants ≤1500 g. Pediatrics 2017 Aug;140(2).
2. Sellmer A, Bjerre JV, Schmidt MR, McNamara PJ, Hjortdal VE, Høst B, Bech BH, Henriksen TB. Morbidity and mortality in preterm neonates with patent ductus arteriosus on day 3. Arch Dis Child Fetal Neonatal Ed. 2013 Nov;98(6):F505-10.
3. Van Laere D, Van Overmeire B, Gupta S, El Khuffash A, Savoia M, McNamara PJ, Schwarz CE, de Boode WP; European Special Interest Group “Neonatologist Performed Echocardiography” (NPE). Application of NPE in the assessment of a patent ductus arteriosus. Pediatr Res. 2018 Jul;84(Suppl 1):46-56.
4. Smith A, McNamara PJ, El-Khuffash AF. Non-pharmacological management of a hemodynamically significant patent ductus arteriosus. Semin Fetal Neonatal Med. 2018 Aug;23(4):245-249.
5. Benitz WE, Bhombal S. The use of non-steroidal anti-inflammatory drugs for patent ductus arteriosus closure in preterm infants. Semin Fetal Neonatal Med. 2017 Oct;22(5):302-307.
6. Clyman RI, Liebowitz M, Kaempf J et al. PDA-TOLERATE (PDA: TO LEave it alone or Respond And Treat Early) Trial Investigators. PDA-TOLERATE Trial: An Exploratory Randomized Controlled Trial of Treatment of Moderate-to-Large Patent Ductus Arteriosus at 1 Week of Age. J Pediatr. 2018 Oct 16. pii: S0022-3476(18)31283-6.
7. Ohlsson A, Walia R, Shah SS. Ibuprofen for the treatment of patent ductus arteriosus in preterm or low birth weight (or both) infants. Cochrane Database Syst Rev. 2018 Sep 28;9:CD003481.
8. Dani et al. High-dose ibuprofen for patent ductus arteriosus in extremely preterm infants: a randomized controlled study. Clin Pharmacol Ther. 2012 Apr;91(4):590-6.
9. 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.
10. Jain A, Shah PS. Diagnosis, Evaluation, and Management of Patent Ductus Arteriosus in Preterm Neonates. JAMA Pediatr. 2015 Sep;169(9):863-72.
11. Kluckow M, Carlisle H, Broom M, Woods P, Jeffery M, Desai D, Chen Y, Evans N. A pilot randomised blinded placebo-controlled trial of paracetamol for later treatment of a patent ductus arteriosus. J Perinatol 2019 Jan;39(1):102-107.
12. Weisz DE, Giesinger RE.Surgical management of a patent ductus arteriosus: Is this still an option? Semin Fetal Neonatal Med. 2018 Aug;23(4):255-266.