

Indometacin (Indomethacin)

Newborn use only

2021

Alert	From April 2016, the international spelling for Indomethacin has been changed to Indometacin.			
Indication	Closure of patent ductus arteriosus (PDA) Prevention of severe intra-ventricular haemorrhage.			
Action	Prostaglandin inhibitor. Prostaglandins are important in maintaining ductal patency in utero.			
Drug type	Non-steroidal anti-inflammatory drug (NSAID).			
Trade name	Indocid PDA, Indomethacin Agila			
Presentation	1 mg powder for reconstitution.			
Dose	IV			
	Single daily dose as follows:			
	Postnatal age (days of life) at the commencement	Day 1	Day 2	Day 3
	<48 hours	0.2 mg/kg/dose	0.1 mg/kg/dose	0.1 mg/kg/dose
≥48 hours	0.2 mg/kg/dose	0.2 mg/kg/dose	0.2 mg/kg/dose	
Dose adjustment	Not applicable			
Therapeutic hypothermia	Insufficient data to suggest dose adjustments.			
ECMO	Refer to contraindications section.			
Renal impairment	Insufficient data to suggest dose adjustments.			
Hepatic impairment				
Maximum dose	0.2 mg/kg			
Total cumulative dose	0.6 mg/kg			
Route	IV			
Preparation	Add 1 mL of WFI to the 1 mg powder for reconstitution. Then draw up 1 mL (1 mg) and add 9 mL WFI to make a final volume of 10 mL with a concentration of 0.1 mg/mL.			
Administration	IV: Over 20--30 minutes. Inspect visually for particulate matter and discolouration prior to administration.			
Monitoring	Monitor urine output, cardiovascular status, serum biochemistry, renal function and for signs of bleeding.			
Contraindications	Renal impairment: urine output <1 mL/kg/hour during the preceding 8 hours; serum creatinine ≥140 µmol/L; blood urea nitrogen >14 mmol/L. (17) Serious infection, active bleeding, thrombocytopenia or coagulopathy, necrotising enterocolitis (NEC) or intestinal perforation, significant renal dysfunction, ductal dependent congenital heart disease and pulmonary hypertension.			
Precautions	Indomethacin is associated with transient renal impairment. Late and prolonged treatment of the ductus arteriosus with indomethacin may increase the incidence of NEC.			
Drug interactions	Aminoglycosides: Dose may need to be modified if indomethacin affects renal function. Digoxin: Reduces indomethacin volume of distribution – increased dose may be required. Diuretics: Use of frusemide in combination with indomethacin may increase the incidence of renal impairment. Systemic corticosteroids: Intestinal perforation has been described in infants treated with early dexamethasone and indomethacin.			
Adverse reactions	Prophylactic indomethacin is associated with oliguria/anuria. Treatment of the ductus arteriosus with indomethacin and prolonged courses of indomethacin are associated with NEC. Gastrointestinal perforation and possibly bleeding. Extravasation.			
Compatibility	Fluids: Sodium chloride 0.9%, water for injection. Y site: Atropine, Cephazolin, cefotaxime, ceftazidime, clindamycin, dexamethasone, digoxin, fentanyl, fluconazole, frusemide, heparin, hydrocortisone, benzylpenicillin, potassium chloride, sodium bicarbonate.			
Incompatibility	Fluids: Glucose 7.5%, Glucose 10% Y-site: Amino acid solutions, adrenaline, amikacin, atracurium, aztreonam, benztropine, buprenorphine, calcium chloride, calcium gluconate, chlorpromazine, dobutamine, dopamine, erythromycin, esmolol, gentamicin, glycopyrrolate, haloperidol lactate, hydralazine, labetalol, magnesium sulfate, metaraminol, midazolam, morphine sulfate, noradrenaline, ondansetron,			

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	pentamidine, pethidine, phenylephrine, promethazine, protamine, suxamethonium, tobramycin, vancomycin, vasopressin, verapamil.
Stability	Discard unused portion. Diluted solution is stable for 6 hours at room temperature.
Storage	Store unopened vials at room temperature (20–25°C)
Excipients	
Special comments	
Evidence	<p>Effectiveness:</p> <p>Prophylactic intravenous indomethacin in preterm infants has short-term benefits including a reduction in the incidence of symptomatic PDA, PDA surgical ligation and severe intraventricular haemorrhage (IVH). However, there is no evidence of effect on mortality or neurodevelopment (5) (LOE I GOR C). Safety: Prophylactic indomethacin is associated with oliguria but not an increased creatinine or gastrointestinal side effects.</p> <p>Indomethacin for asymptomatic patent ductus arteriosus: Treatment of an asymptomatic PDA with indomethacin reduced the incidence of symptomatic PDA, duration of supplemental oxygen, with no effect on mortality, IVH, retinopathy of prematurity, length of ventilation, or NEC. Safety: Renal and gastrointestinal toxicities and long term neurodevelopment were not reported (10) (LOE I, GOR C).</p> <p>Indomethacin versus ibuprofen for the treatment of patent ductus arteriosus in preterm or low birth weight infants: Indomethacin is as effective as ibuprofen in closing a PDA (6). Safety: Indomethacin increases the risk of NEC and transient renal insufficiency compared to ibuprofen.</p> <p>Summary recommendation: Ibuprofen is as effective as indomethacin in closing a PDA and currently appears to be the drug of choice. Ibuprofen reduces the risk of NEC and transient renal insufficiency compared to indomethacin⁶ (LOE I GOR B).</p> <p>Dose: Indomethacin given in total amounts for the prolonged course (6–8 doses) of 0.6–1.6 mg/kg compared with the short course 0.3–0.6 mg/kg (2–3 doses): There was no difference in efficacy between a short or prolonged course of indomethacin (LOE 1, GOR C). Safety: A prolonged course is associated with an increased risk of NEC but a decreased incidence of renal function impairment (oliguria and increased serum creatinine) 7 (LOE I, GOR B). Pharmacokinetic studies reported substantial interpatient variability (11, 12) in clearance related to postnatal age. (2, 12) Bolus infusions of indomethacin are associated with alterations in renal, mesenteric and cerebral blood flow (13). Ductus arteriosus closure rates are related to dose and indomethacin concentrations.(11,14).</p>
Practice points	
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