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<tr><td>Alert</td><td>From April 2016, the international spelling for Indomethacin has been changed to Indometacin.</td></tr>
<tr><td>Indication</td><td>Closure of patent ductus arteriosus (PDA)
Prevention of severe intra-ventricular haemorrhage.</td></tr>
<tr><td>Action</td><td>Prostaglandin inhibitor. Prostaglandins are important in maintaining ductal patency in utero.</td></tr>
<tr><td>Drug Type</td><td>Non-steroidal anti-inflammatory drug (NSAID).</td></tr>
<tr><td>Trade Name</td><td>Indocid PDA, Indomethacin Agila</td></tr>
<tr><td>Presentation</td><td>1 mg powder for reconstitution.</td></tr>
<tr><td>Dosage/Interval</td><td>
<table>
<tr><td>Post-natal Age</td><td>Day 1</td><td>Day 2</td><td>Day 3</td></tr>
<tr><td>≤ 48 hours</td><td>0.2 mg/kg/dose</td><td>0.1 mg/kg/dose</td><td>0.1 mg/kg/dose</td></tr>
<tr><td>> 48 hours</td><td>0.2 mg/kg/dose</td><td>0.2 mg/kg/dose</td><td>0.2 mg/kg/dose</td></tr>
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</td></tr>
<tr><td>Maximum daily dose</td><td>0.2 mg/kg</td></tr>
<tr><td>Total cumulative dose</td><td>0.6 mg/kg</td></tr>
<tr><td>Route</td><td>IV</td></tr>
<tr><td>Preparation/Dilution</td><td>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.</td></tr>
<tr><td>Administration</td><td>IV: Over 20–-30 minutes.

Inspect visually for particulate matter and discolouration prior to administration.</td></tr>
<tr><td>Monitoring</td><td>Monitor urine output, cardiovascular status, serum biochemistry, renal function and for signs of bleeding.</td></tr>
<tr><td>Contraindications</td><td>Serious infection, active bleeding, thrombocytopenia or coagulopathy, necrotising enterocolitis (NEC) or intestinal perforation, significant renal dysfunction, ductal dependent congenital heart disease and pulmonary hypertension.</td></tr>
<tr><td>Precautions</td><td>Indomethacin is associated with transient renal impairment. Late and prolonged treatment of the ductus arteriosus with indomethacin may increase the incidence of NEC.</td></tr>
<tr><td>Drug Interactions</td><td>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.</td></tr>
<tr><td>Adverse Reactions</td><td>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.</td></tr>
<tr><td>Compatibility</td><td>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.</td></tr>
<tr><td>Incompatibility</td><td>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, pentamidine, pethidine, phenylephrine, promethazine, protamine, suxamethonium, tobramycin, vancomycin, vasopressin, verapamil.</td></tr>
<tr><td>Stability</td><td>Discard unused portion. Diluted solution is stable for 6 hours at room temperature.</td></tr>
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Storage	Store unopened vials at room temperature (20−25°C)
Special Comments	Nil
Evidence summary	Effectiveness: 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. 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). 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. 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 indomethacin[6] (LOE I GOR B). 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].
References	1. Allegaert K. The impact of ibuprofen or indomethacin on renal drug clearance in neonates. The journal of maternal-fetal & neonatal medicine. 2009;22;88–91. 2. Smyth JM, Collier PS, Darwish M, Millership JS, Halliday HL, Petersen S, McElnay JC. Intravenous indomethacin in preterm infants with symptomatic patent ductus arteriosus. A population pharmacokinetic study. British journal of clinical pharmacology. 2004;58:249–58. 3. Lee BS, Byun SY, Chung ML, Chang JY, Kim HY, Kim EA, Kim KS, Pi SY. Effect of furosemide on ductal closure and renal function in indomethacin-treated preterm infants during the early neonatal period. Neonatology. 2010;98:191–9. 4. Brion LP, Campbell DE. Furosemide for symptomatic patent ductus arteriosus in indomethacin-treated infants. The Cochrane database of systematic reviews. 2001:CD001148. 5. Fowlie PW, Davis PG, McGuire W. Prophylactic intravenous indomethacin for preventing mortality and morbidity in preterm infants. The Cochrane database of systematic reviews. 2010:CD000174. 6. Ohlsson A, Walia R, Shah SS. Ibuprofen for the treatment of patent ductus arteriosus in preterm or low birth weight (or both) infants. The Cochrane database of systematic reviews. 2015;2:CD003481. 7. Herrera C, Holberton J, Davis P. Prolonged versus short course of indomethacin for the treatment of patent ductus arteriosus in preterm infants. The Cochrane database of systematic reviews. 2007:CD003480. 8. Stark AR, Carlo WA, Tyson JE, Papile LA, Wright LL, Shankaran S, Donovan EF, Oh W, Bauer CR, Saha S, Poole WK, Stoll BJ, National Institute of Child H, Human Development Neonatal Research N. Adverse effects of early dexamethasone in extremely-low-birth-weight infants. National Institute of Child Health and Human Development Neonatal Research Network. The New England journal of medicine. 2001;344:95–101. 9. Walker SE, Gray S, Schmidt B. Stability of reconstituted indomethacin sodium trihydrate in original vials and polypropylene syringes. American journal of health-system pharmacy : AJHP :

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