Aspirin (Acetylsalicylic Acid) 2023

Newborn use only

Alert	
Indication	Prophylaxis against thrombotic occlusion of a systemic-to-pulmonary shunt or endovascular stents in infants with congenital heart disease.
Action	Inhibits thromboxane synthesis and prostacyclin formation, thereby inhibiting platelet aggregation.
Drug type	Antiplatelet
Trade name	Aspro clear
Presentation	300 mg effervescent tablet
Dose	Oral: 5 mg/kg/dose once daily (Range: 1-5mg/kg/dose)[2]
Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – No information. Renal impairment [3] GFR ≥10 mL/minute/1.73 m^2 : No dosage adjustment necessary GFR <10 mL/minute/1.73 m^2 : Avoid use Hepatic impairment – Avoid in severe liver impairment
Maximum dose	5 mg/kg/dose
Total cumulative dose	
Route	Oral
Preparation	Dissolve a 300 mg effervescent tablet in 30 mL of water for injection to make a final volume of 30 mL with a final concentration of 10 mg/mL. Shake or stir until a clear solution is formed. Make a fresh batch for each dose, discard any remaining solution
Administration	Given orally or via intra-gastric/gastrostomy tube with or after feed immediately after dispersion.
Monitoring	N/A
Contraindications	Allergy to aspirin or NSAIDs. Aspirin-sensitive asthma. Severe active bleeding or disease states with an increased risk of severe bleeding, e.g., bleeding disorders, erosive gastritis or peptic ulcer disease, severe hepatic disease.
Precautions	Use with caution in severe renal impairment because of increased risk of bleeding and of further deterioration of renal function. Other drugs that can affect the clotting process may increase the risk of bleeding. Other antiplatelet or anticoagulant drugs may be used with low-dose aspirin where indicated Consider prophylaxis of gastrointestinal bleeding with a proton pump inhibitor
Drug interactions	Aspirin displaces warfarin, phenytoin and methotrexate from binding sites on plasma proteins and hence can increase the toxicity of these drugs. Its antiplatelet action increases the risk of bleeding in patients on oral anticoagulants.[4,5] The concomitant use of ibuprofen antagonizes the irreversible platelet inhibition that is induced by aspirin; thus ibuprofen should be avoided in children with coronary aneurysms taking aspirin for its antiplatelet effects
Adverse reactions	Common (>1%): GI irritation, asymptomatic blood loss, increased bleeding time Infrequent (0.1–1%): Stevens-Johnson syndrome, toxic epidermal necrolysis, iron deficiency anaemia, GI haemorrhage Rare (<0.1%): intracranial haemorrhage, GI ulcer Allergy: bronchospasm, angioedema, urticaria and rhinitis have been precipitated by aspirin; there is cross-reactivity with other NSAIDs.
Compatibility	N/A
Incompatibility	N/A
Stability	Once prepared, solution should be used immediately. Discard remaining solution
Storage	Store at room temperature in original packaging, protect from moisture
Excipients	Sodium, saccharin, sulfites, sorbates
Special comments	
Evidence	**Efficacy** Adequate neonatal studies have not been performed. Neonatal dosage is derived from clinical experience.[2] The dose of aspirin for optimal inhibition of platelet aggregation is not known. Empirical doses of 1 to 5 mg/kg per day have been proposed.[6]

	A retrospective series of 546 modified B-T shunt (MBTS) procedures reported no significant differences between heparin and no heparin in early failure rate (1.4% vs 3.4%, P= .29), in later failure rate (9.1% vs 13.6%, P =.17), or between aspirin and no aspirin (11.0% vs 6.7%, P=.18).[7] Li et al reported reduced thrombosis in a large cohort of patients treated with aspirin for 12 months after shunt surgery.[8] In another small case study, aspirin was reported to decrease the incidence of stent thrombosis after MBTS surgery.[9] Post discharge occlusion of shunt has been reported.[10, 11] In a study of 146 infants[11] aged <60 days who underwent MBTS and were discharged from the hospital alive, the mortality of patients discharged on aspirin (11%) was almost identical to that of patients discharged on no antithrombotic therapy (12.3%). No published RCTs guide the antithrombotic medical management of patients with MBTSs. American college of chest physicians recommends intraoperative unfractionated heparin for MBTS and either aspirin or no antithrombotic therapy as compared with prolonged low molecular weight heparin or vitamin K antagonists in neonates and children. **Safety** In children, aspirin rarely causes important haemorrhage, except in the presence of an underlying haemostatic defect or in children also treated with anticoagulants or thrombolytic therapy. The relatively low doses of aspirin used as antiplatelet therapy, compared with the much higher doses used for anti-inflammatory therapy, seldom cause other side effects. **Pharmacokinetics** Pharmacokinetics of anti-platelet drugs in children is mostly extrapolated from adult studies. Aspirin is absorbed from the stomach and small intestines and rapidly deacetylated in the gut wall, liver, and plasma, to release salicylic acid, the major circulating and active form. Metabolism of salicylate occurs primarily by hepatic conjugation. Excretion is through urine (75% as salicyluric acid, 10% as salicylic acid). Half-life elimination of salicylate is dose dependent from 3 hours at lower doses to up to 10 hours in higher doses. Aspirin acts by irreversible inhibition of thromboxane synthase. As platelets have no nuclei, after acetylation by aspirin, fresh enzyme cannot be synthesized. Thus, aspirin mediated platelet inhibitory effect lasts for the lifetime of platelet (5-7 days).
Practice points	
References	1. Undas A, Brummel-Ziedins KE, Mann KG. Antithrombotic properties of aspirin and resistance to aspirin: Beyond strictly antiplatelet actions. Blood. 2007; 109:2285–92. 2. Monagle P, Chan A, Goldenberg NA, et al. Antithrombotic Therapy in Neonates and Children: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (9th Edition). Chest. 2012; 141(2) (suppl):e737-e801. 3. Aronoff GR, Bennett WM, Berns JS, et al. Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children, 5th ed. Philadelphia, PA: American College of Physicians; 2007;20-136 4. Tripathi KD. Essentials of Medical Pharmacology. 6th ed. India: Jaypee Brothers Medical Publishers Ltd; 2008. Drugs affecting coagulation, bleeding and thrombosis; pp. 608–11. 5. Schneider DJ, Sobel BE. Conundrums in the combined use of anticoagulants and antiplatelet drugs. Circulation. 2007; 116:305–15. 6. Israels SJ, Michelson AD. Antiplatelet therapy in children. Thromb Res. 2006; 118 (1): 75 - 83.) 7. Al Jubair KA, Al Fagih MR, Al Jarallah AS, et al. Results of 546 Blalock-Tausig shunts performed in 478 patients. Cardiol Young. 1998; 8 (4): 486 - 490.) 8. Li JS, Yow E, Berezny KY, and et al. Clinical outcomes of palliative surgery including a systemic-to-pulmonary artery shunt in infants with cyanotic congenital heart disease: does aspirin make a difference? Circulation. 2007; 116 (3): 293 - 297.) 9. Motz R, Wessel A, Ruschewski W, Bürsch J. Reduced frequency of occlusion of aorta-pulmonary shunts in infants receiving aspirin . Cardiol Young. 1999; 9 (5): 474 - 477.) 10. Ahmad U, Fatimi S H, N aqvi I, e t al. Modified Blalock-Tausig shunt: immediate and short-term follow-up results in neonates. Heart Lung Circ. 2008; 17 (1): 54 - 58.) 11. Fenton KN, Siewers RD, Rebovich B, Pigula FA. Interim mortality in infants with systemic-to-pulmonary artery shunts. Ann Thorac Surg. 2003; 76 (1): 152 - 156, discussion 156-157.

VERSION/NUMBER	DATE
Original 1.0	**6/04/2023**
REVIEW (5 years)	**6/04/2028**

Authors Contribution

Original author/s	Kirsty Minter, Mohammad Irfan Azeem, Bhavesh Mehta
Evidence Review	Bhavesh Mehta
Expert review	
Nursing Review	Eszter Jozsa, Renae Gengaroli
Pharmacy Review	Mohammad Irfan Azeem, Rebecca O'Grady
ANMF Group contributors	Nilkant Phad, Srinivas Bolisetty, Cindy Chen, Rebecca Barzegar, Thao Tran, Helen Huynh, Martin Kluckow, Michelle Jenkins, Stephanie Halena, Allegaert K.
Final editing	Mohammad Irfan Azeem
Electronic version	Cindy Chen, Ian Callander
Facilitator	Nilkant Phad

Citation

Minter K, Azeem MI, Mehta B, Jozsa E, Gengaroli R, O'Grady R, Phad N, Bolisetty S, Barzegar R, Huynh H, Jenkins M, Chen C, Kluckow M, Halena S, Allegaert K, Callander I. Aspirin. Consensus formulary by the Australasian Neonatal Medicines Formulary group. Version 1, dated 6 April 2023. www.anmfonline.org