

Alert	Oral dose: Hydrocortisone is not soluble in water and the dose is not evenly distributed in the solution. Refer to preparation section for specific instructions on the oral preparation.
Indication	<ol style="list-style-type: none"> 1. Treatment of cortisol deficiency (hypoadrenalism). 2. Treatment of hypotension NOT responding to inotrope. 3. Short term adjunctive therapy for persistent hypoglycaemia. 4. Prevention of bronchopulmonary dysplasia (not routinely recommended)
Action	<ol style="list-style-type: none"> 1. Adrenal corticosteroid with primarily glucocorticoid effects. 2. Enhances vascular reactivity to other vasoactive substances by increasing expression of adrenergic receptors in the vascular wall and increasing calcium concentrations in myocardial cells. 3. Decreases breakdown of catecholamines. 4. Stimulates the liver to produce glucose from amino acids and glycerol, and stimulates the deposition of glucose as glycogen.
Drug Type	Corticosteroid.
Trade Name	IV: Solu-Cortef. Oral: Hysone.
Presentation	100 mg vial, 4 mg tablet, 20mg tablet
Dosage / Interval	<p>For oral dosing round dose off to the nearest whole milligram (ie round dose off to the nearest half or quarter tablet).</p> <p>Hypotension ≥ 35 weeks CGA/PMA: 1 mg/kg/dose 6–8 hourly (range 1–2 mg/kg/dose). < 35 weeks CGA/PMA: 1 mg/kg/dose 6–12 hourly (range 1–2 mg/kg/dose).</p> <p>Hypoglycaemia: 1–2.5 mg/kg/dose every 6 hours.</p> <p>Physiologic replacement (hypoadrenalism): 8-20 mg/m²/day in 3-4 divided doses. [2] Dosing and dose adjustment should be done in consultation with a Paediatric Endocrinologist.</p> <p>Stress dose: 50 mg/m²/day in 4 divided doses [up to 100 mg/m²/day]. [If length not available use hypoglycaemia dose].</p> <p>Body Surface Area (BSA) calculation:</p> $BSA (m^2) = \sqrt{\frac{height (cm) \times weight (kg)}{3600}}$ <p>Low dose for prevention of bronchopulmonary dysplasia (not routinely recommended) [1-3]: 0.5 mg/kg/dose every 12 hours for 7 days; then 0.5 mg/kg/dose every 24 hours for 3 days.</p>
Route	IV, oral.
Preparation	<p>IV Add 2 mL of water for injection to the 100 mg vial (50 mg/mL). Draw up 1 mL (50 mg) of reconstituted solution and add 4 mL sodium chloride 0.9% to make a final volume of 5 mL with a concentration of 10 mg/mL.</p> <p>Oral Hydrocortisone is not soluble in water. Underdosing or inaccurate dosing can occur when a whole 4mg tablet is dispersed in water, and a proportion of the final volume administered. Doses of hydrocortisone for oral administration should be rounded off to the nearest whole milligram (ie round dose off to the nearest half or quarter tablet).</p> <p>Instructions to prepare an oral dose: Using a tablet cutter, cut a 4mg tablet in halves or quarters (depending on the dose required). Crush the portion of tablet required for the dose</p>

	<p>and disperse it in 1-2mL of sterile water or milk for administration to patient. Discard remaining portion of tablet.</p> <p>Refer to Appendix 1 for instruction sheet for staff and parents.</p>
Administration	<p>IV: Slow IV injection over at least 1 minute.</p> <p>Oral: With feeds.</p>
Monitoring	<p>Measure blood pressure and blood glucose frequently during acute illness.</p> <p>In infants with primary adrenal insufficiency, monitor glucocorticoid replacement by clinical assessment, including growth velocity, body weight, blood pressure and energy levels.</p>
Contraindications	<p>Hydrocortisone is contraindicated in systemic fungal infections and patients with known hypersensitivity to the product and its constituents.</p>
Precautions	<p>Use of hydrocortisone in preterm infants in the first week is associated with intestinal perforation, particularly when treating concurrently with indomethacin.</p> <p>Untreated systemic bacterial infections.</p> <p>Use with caution in patients with renal impairment, hypothyroidism or cardiac disease.</p> <p>Prolonged use of corticosteroids (> 14 days) may cause prolonged adrenal suppression requiring a tapering dose of hydrocortisone.[4-6]</p> <p>Caution should be used when using hydrocortisone for treatment of hyperinsulinaemic hypoglycaemia given the lack of evidence, potential for adrenal suppression and side effects.</p>
Drug Interactions	<p>Drugs that induce hepatic enzymes such as phenobarbitone, phenytoin may increase the clearance of corticosteroids and may require increases in corticosteroid dose to achieve the desired response.</p> <p>Ketoconazole may inhibit the metabolism of corticosteroids and thus decrease their clearance. Therefore, the dose of corticosteroid should be titrated to avoid steroid toxicity.</p> <p>Increased GI toxicity with concurrent use of indomethacin.</p>
Adverse effects	<p>Hyperglycaemia, glycosuria.</p> <p>Hypertension after 24–48 hours.</p> <p>Vomiting, diarrhoea, gastric irritation, gastrointestinal ulceration and bleeding.</p> <p>Use of hydrocortisone in preterm infants in the first week is associated with intestinal perforation, particularly when treating concurrently with indomethacin.</p> <p>Salt and water retention.</p> <p>Hypokalaemia.</p> <p>Hypocalcaemia and long-term exposure increases the risk of osteopenia.</p> <p>Inhibits immune function and decreases resistance to infection. May mask symptoms of infection.</p> <p>Neutrophilia, thrombocytopenia.</p> <p>Irritability.</p> <p>Acute withdrawal after use > 14 days can lead to acute adrenal insufficiency with fever, hypotension, hypoglycaemia and shock.</p> <p>Long-term use can adversely affect somatic growth.</p>
Compatibility	<p>Fluids: Glucose 5%, glucose 10%, Hartmann's, sodium chloride 0.9%</p> <p>Y-site: Amino acid solutions. Aciclovir, amifostine, aminophylline, anidulafungin, atracurium, atropine, aztreonam, bivalirudin, calcium gluconate, caspofungin, chlorpromazine, cisatracurium, dexamethasone, digoxin, dopamine, doripenem, droperidol, fentanyl, filgrastim, foscarnet, frusemide, granisetron, hyoscine hydrobromide, lignocaine, linezolid, magnesium sulfate, morphine sulfate, neostigmine, noradrenaline, oxytocin, pancuronium, pethidine, piperacillin-tazobactam (EDTA-free), remifentanyl, sodium bicarbonate, suxamethonium, vecuronium.</p>
Incompatibility	<p>Fluids: No information.</p> <p>Y-site: Adrenaline hydrochloride, azathioprine, calcium chloride, ciprofloxacin, colistin, dobutamine, dolasetron, ephedrine, ganciclovir, haloperidol lactate, labetalol, midazolam, mycophenolate mofetil, pentamidine, phenobarbitone, promethazine, protamine, rocuronium.</p>

Stability	<p>IV: Reconstituted solution: Stable for 24 hours at 2–8 °C. Protect from light. Diluted solution: Stable for 4 hours below 25 °C or 24 hours at 2–8°C.</p> <p>Oral: Discard remaining pieces of tablet after dose administration.</p>
Storage	Ampoules and tablets: Store below 25°C. Protect from light.
Special Comments	<p>Serum cortisol is recommended prior to commencing treatment with hydrocortisone. Caution – Increased risk of GI perforation particularly with simultaneous treatment with indomethacin. If hydrocortisone is required, delay treatment with indomethacin for at least 72 hours if possible. For management of cortisol deficiency, change to oral preparation when possible.</p>
Evidence summary	<p>Efficacy:</p> <p>Treatment of hypotension: For primary treatment of hypotension: Hydrocortisone has not been shown to change clinical outcome and may not be as effective as dopamine. (LOE II, GOR D). [7] For treatment of refractory hypotension: Hydrocortisone was effective in preventing persistent hypotension. (LOE I, GOR C). Dose range used in trials: 1 to 2.5 mg/kg every 6 to 12 hours weaned over 48 hours to 6 days. [7] There were no statistically significant effects on any other short or long-term outcome but analyses are underpowered to detect differences in clinical and safety outcomes.</p> <p>Prevention of bronchopulmonary dysplasia: Trials in ventilated preterm infants at risk of BPD started hydrocortisone from 2 hours to < 7 days, used various regimens ranging from 0.5 mg/kg/dose 12 hourly for 7 days and 24 hourly for 3 days [1, 2], 1 to 2 mg/kg every 8 to 24 hours for a duration 2 to 6 days [3, 8], up to 15 mg/kg x 2 doses [3, 8]. Subgroup analysis of trials of hydrocortisone found hydrocortisone was associated with reduced rates of patent ductus arteriosus, mortality, and the combined outcome of mortality or chronic lung disease, but with increased occurrence of intestinal perforation. Results showed that hydrocortisone was not associated with obvious longer-term problems [3]. Conclusion: Short-term and longer-term effects of early hydrocortisone to prevent bronchopulmonary dysplasia require further evaluation. (LOE I, GOR B)</p> <p>Endocrine Society Clinical Practice Guidelines recommend treatment of primary adrenal insufficiency: [9] Maintenance treatment of primary adrenal insufficiency in children: Hydrocortisone 8 mg/m²/day in 3 or 4 divided doses. Management of adrenal crisis: Hydrocortisone 50–100 mg/m² IV or IM, then 50–100 mg/m² every 24 hours. Home management of illness with fever: Hydrocortisone replacement doses doubled (> 38°C) or tripled (> 39°C) until recovery. Unable to tolerate oral medication due to gastroenteritis or trauma: Hydrocortisone 50 mg/m² IM. Minor to moderate surgical stress: Hydrocortisone 50 mg/m² IM or hydrocortisone replacement doses doubled or tripled. Major surgery: Hydrocortisone 50 mg/m² IV followed by hydrocortisone 50–100 mg/m²/day divided 6 hourly. Acute adrenal crisis: Rapid bolus of normal saline 0.9% 20 mL/kg. Can repeat up to a total of 60 mL/kg within 1 hour for shock. Hydrocortisone 50–100 mg/m² bolus followed by hydrocortisone 50–100 mg/m²/day divided 6 hourly.</p> <p>Treatment of neonatal hypoglycaemia: There are case reports of short term use of hydrocortisone for neonatal hyperinsulinaemic hypoglycaemia.[10, 11] Use of corticosteroids is not addressed in guidelines for management.</p> <p>Safety: Use of hydrocortisone in preterm infants in the first week is associated with intestinal perforation. [3, 8] (LOE I) The risk may be increased with concomitant treatment with</p>

	<p>indomethacin.[12, 13] (LOE II) Use of hydrocortisone increased risk of hyperglycaemia in hypotensive preterm infants treated with adrenaline. (LOE II) [14] Pharmacokinetics and pharmacodynamics: The half-life of hydrocortisone is reported to be < 3 hours in newborn and premature infants. An increase in unbound hydrocortisone clearance was observed at 35 weeks postmenstrual age. [15, 16] The pharmacodynamics effect of hydrocortisone on blood pressure in hypotensive preterm infants has been reported to have an onset by 2 hours and persist for at least 12 hours. [17, 18]</p>
<p>References</p>	<ol style="list-style-type: none"> 1. Baud O, Maury L, Lebail F, Ramful D, El Moussawi F, Nicaise C, Zupan-Simunek V, Coursol A, Beuchee A, Bolot P, Andrini P, Mohamed D, Alberti C, group Pts. Effect of early low-dose hydrocortisone on survival without bronchopulmonary dysplasia in extremely preterm infants (PREMILOC): a double-blind, placebo-controlled, multicentre, randomised trial. <i>Lancet</i>. 2016;387:1827-36. 2. Baud O, Trousson C, Biran V, Leroy E, Mohamed D, Alberti C, Group PT. Association Between Early Low-Dose Hydrocortisone Therapy in Extremely Preterm Neonates and Neurodevelopmental Outcomes at 2 Years of Age. <i>JAMA</i>. 2017;317:1329-37. 3. Doyle LW, Cheong JL, Ehrenkranz RA, Halliday HL. Early (< 8 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. <i>The Cochrane database of systematic reviews</i>. 2017;10:CD001146. 4. Ng PC, Lam CW, Lee CH, Chan IH, Wong SP, Fok TF. Suppression and recovery of the hypothalamic function after high-dose corticosteroid treatment in preterm infants. <i>Neonatology</i>. 2008;94:170-5. 5. Ng PC, Lee CH, Bnur FL, Chan IH, Lee AW, Wong E, Chan HB, Lam CW, Lee BS, Fok TF. A double-blind, randomized, controlled study of a "stress dose" of hydrocortisone for rescue treatment of refractory hypotension in preterm infants. <i>Pediatrics</i>. 2006;117:367-75. 6. Walther FJ, Findlay RD, Durand M. Adrenal suppression and extubation rate after moderately early low-dose dexamethasone therapy in very preterm infants. <i>Early Human Development</i>. 2003;74:37-45. 7. Ibrahim H, Sinha IP, Subhedar NV. Corticosteroids for treating hypotension in preterm infants. <i>The Cochrane database of systematic reviews</i>. 2011:CD003662. 8. Doyle LW, Ehrenkranz RA, Halliday HL. Postnatal hydrocortisone for preventing or treating bronchopulmonary dysplasia in preterm infants: a systematic review. <i>Neonatology</i>. 2010;98:111-7. 9. Bornstein SR, Allolio B, Arlt W, Barthel A, Don-Wauchope A, Hammer GD, Husebye ES, Merke DP, Murad MH, Stratakis CA, Torpy DJ. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. <i>The Journal of clinical endocrinology and metabolism</i>. 2016;101:364-89. 10. Rahmah R, Hayati AR, Kuhnle U. Management and short-term outcome of persistent hyperinsulinaemic hypoglycaemia of infancy (nesidioblastosis). <i>Singapore Medical Journal</i>. 1999;40:151-6. 11. Sotelo-Cruz N, Cordero-Olivares A, Ramirez-Rodriguez C, Lopez-Cervantes G, Hurtado-Valenzuela J, Lopez-Cervantes BM. [Persistent hyperinsulinemic hypoglycemia. Two case reports]. <i>Cirugia y Cirujanos</i>. 2004;72:409-14. 12. Peltoniemi O, Kari MA, Heinonen K, Saarela T, Nikolajev K, Andersson S, Voutilainen R, Hallman M. Pretreatment cortisol values may predict responses to hydrocortisone administration for the prevention of bronchopulmonary dysplasia in high-risk infants. <i>The Journal of pediatrics</i>. 2005;146:632-7. 13. Watterberg KL, Gerdes JS, Cole CH, Aucott SW, Thilo EH, Mammel MC, Couser RJ, Garland JS, Rozycki HJ, Leach CL, Backstrom C, Shaffer ML. Prophylaxis of early adrenal insufficiency to prevent bronchopulmonary dysplasia: a multicenter trial. <i>Pediatrics</i>. 2004;114:1649-57. 14. Salas G, Travaglianti M, Leone A, Couceiro C, Rodriguez S, Farina D. [Hydrocortisone for the treatment of refractory hypotension: a randomized controlled trial]. <i>Anales de pediatria</i>.

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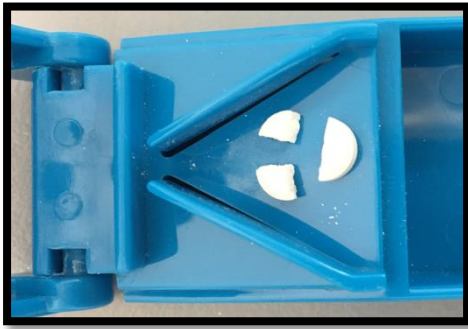
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Appendix 1– Guide to Parents on preparation of Hydrocortisone tablets – See next page

Appendix 1
Guide to parents on preparation of Hydrocortisone dose

Hydrocortisone is available as a 4 mg tablet. Always check the tablet's expiry date before administering. The tablet is not soluble in water or milk.

1. Using a tablet cutter, cut a 4mg tablet in halves or quarters (depending on the dose required).



2. Crush the required piece/s of tablet and mix with 1-2 mL of freshly boiled and cooled water, or milk on a spoon.
3. Administer down the side of the mouth while the baby is sucking a dummy or administer through sucking dummy.

Please NOTE: DO NOT ADD THIS TO THE BOTTLE OF FEED

4. If tablet is cut, discard the remaining pieces of tablet, do not keep and use later.
5. If vomiting occurs within 15 minutes after giving the medication the dose should be repeated. This does not include "possits".
6. If persistent vomiting occurs you need to contact your doctor or go to the Emergency department.

NOTE: If giving only $\frac{1}{2}$ or $\frac{1}{4}$ tablets, do not dissolve the whole tablet in water and give a proportion of the solution. First cut the tablet in halves or quarters, then disperse the required dose in water/milk as above.