Sodium Phenylbutyrate
Newborn use only

2025

Alert	Available through Special Access Scheme only. Repeated boluses or very high doses of phenylbutyrate can saturate the scavenger-converting systems, increasing the risk of drug accumulation and toxicity.[1] Overdose can be fatal in children.
Indication	Urea cycle defects
Action	Sodium phenylbutyrate (NaPBA) is a precursor of sodium phenylacetate (NaPA). NaPBA is first oxidised to phenylacetate and then conjugated with glutamine to form phenylacetylglutamine (PAGA). This pathway lowers serum ammonia by diverting blood urea nitrogen to phenylacetylglutamine (PAGA) conjugation pathway.[1-3]
Drug Type	Ammonia Scavenger
Trade Name	Ambutyrate, Pheburane, Ammonaps
Presentation	**IV:** Sodium Phenylbutyrate (Ambutyrate) 2g/10mL injection **ORAL:** Sodium Phenylbutyrate (Ambutyrate) 250mg/mL powder for oral **solution** Sodium Phenylbutyrate (Pheburane) 483mg/g **granule** Sodium Phenylbutyrate (Ammonaps) 940mg/g **granule**
Dose	**To be prescribed only on the advice of paediatric metabolic specialists/paediatrician specialised in metabolic disorders.** **Note: Sodium benzoate, sodium phenylbutyrate and L- arginine and can be infused together. A combined infusion preparation is available (see preparation section)** **IV for acute hyperammonaemia (ANMF consensus)[1,2]** Commence loading dose at 250 mg/kg over 90–120 minutes, followed by maintenance dose at 250 mg/kg daily given as a continuous infusion over 24 hours (preferred) or rarely, on the advice of paediatric metabolic specialist, as intermittent infusions in 4 divided doses. Adjust dose according to response - Maximum 500 mg/kg daily. Change to oral route when stable. **ORAL Maintenance treatment[1,2]** 250 mg/kg daily in 3 or 4 doses. Adjust dose according to response - Maximum 600 mg/kg daily.
Dose adjustment	Therapeutic hypothermia - No information. ECMO – No information. Renal impairment – use with caution. Hepatic impairment – Use with caution.
Maximum Dose	Oral: 600mg/kg/day in 3 to 6 divided doses.
Route	IV ORAL
Preparation	**IV** **Load / maintenance** Sodium phenylbutyrate single infusion preparation Draw up 12.5 mL (2500mg) of sodium phenylbutyrate and add 37.5 mL of glucose 10% to make a final volume of 50 mL with a concentration of 50 mg/mL. Sodium benzoate, sodium phenylbutyrate and L-arginine combined infusion preparation Draw up 12.5mL (2500mg) of sodium phenylbutyrate, 4.2mL (2500mg) of L-arginine hydrochloride and 12.5mL of sodium benzoate and add 20.8mL of glucose 10% to make a final volume of 50 mL with a concentration of 50 mg/mL of sodium phenylbutyrate, L-arginine and sodium benzoate each. **ORAL:** Sodium Phenylbutyrate (Ambutyrate) 250mg/mL powder for oral solution

	Add 80 mL purified water to powder, shake vigorously and allow to stand until powder completely dissolves.
Administration	**IV** Can be administered via central or peripheral venous routes. **ORAL** Give with meals.
Monitoring	Ammonia, amino acids, electrolytes, urea and creatinine, full blood count, liver function tests – Frequency as per the advice of metabolic physician.
Contraindications	Hypersensitivity to sodium phenylbutyrate or any component of the formulation
Precautions	Fluid retention
Drug Interactions	Corticosteroids, valproate may increase the ammonia concentration, dose increase of Sodium Phenybutyrate may be needed.
Adverse Reactions	May cause sodium and fluid retention. Metabolic acidosis, hypoalbuminaemia, hypernatraemia
Overdose	AUSTRALIA: Contact the Poisons Information Centre on **13 11 26** for information on the management of overdose NEW ZEALAND: Contact the National Poisons Centre on **0800 764 766** for information on the management of overdose.
Compatibility	Fluids: Glucose 10%[4] PN at Y-site: No information.[4] No information on lipid emulsions.[4] Y-site: Arginine and sodium benzoate[4] (in practice as per metabolic experts can be made up in a solution with arginine and sodium benzoate)
Incompatibility	Fluids: No information. No information on lipid emulsions.[4] PN at Y-site: No information. No information on lipid emulsions.[4] Y site: No information.
Stability	IV continuous infusion: In practice, the continuous IV infusion of sodium phenylbutyrate in D10W is changed every 24 hours. Oral: Re-constituted solution has an expiry period of 28 days at room temperature (<25°C)
Storage	Store at room temperature (<25°C)
Excipients	**IV** 2g/10mL vial contains 10.8mmol of Sodium. **ORAL** **Solution:** Sodium Phenylbutyrate (Ambutyrate) powder for 250mg/mL oral solution contains aspartame **Granules:** Each gram of sodium phenylbutyrate contains 124 mg (5.4 mmol) of sodium and 768 mg of sucrose, Other excipients - Ethylcellulose, Hypromellose, macrogol 1500 ,maize starch, povidone.
Special Comments	
Evidence	**Background** Ammonia is the nitrogen waste product from protein catabolism. Ammonia is present in all body fluids and exists primarily as ammonium ion at physiologic pH. Hyperammonemia is defined as a blood ammonia concentration greater than about 100 micromol/L in neonates or 50 micromol/L in children and adults (precise cut-offs vary, depending on individual laboratory normative ranges). A 5- to 10-fold increase in blood ammonia concentration usually is toxic to the nervous system.[2] In urea cycle defects (UCD), nitrogen removal is blocked, and nitrogen accumulates in the form of ammonia, causing acute episodes of hyperammonemia.[5] Hyperammonaemia can be caused by inborn errors of metabolism or acquired conditions such as total parenteral nutrition, liver failure and urinary tract infections due to protease sp.[2] In Australia, sodium phenylacetate (NaPA) is now superseded by sodium phenylbutyrate (NaPBA). Sodium Phenylbutyrate is first oxidised to phenylacetate and then conjugated with glutamine to form phenylacetylglutamine, which is readily excreted in the urine.[3] Phenylbutyrate is usually given as the sodium salt in doses of 250 mg/kg/day but has been given in doses of up to 630 mg/kg/day.[6] It is usually thought that conjugation and excretion are almost complete, but

	recoveries appear to be variable. If conjugation and excretion are complete, the nitrogen removed following 250 mg/kg and 630 mg/kg would be equivalent to 0.24 g and 0.6 g of protein/kg, respectively.[7] **Efficacy** Brusilow and colleagues reported a therapeutic protocol for the treatment of hyperammonemia in UCDs. Protocol included a combination of intravenous sodium benzoate, sodium phenylacetate, and arginine, and nitrogen-free intravenous alimentation. Dialysis was performed if the hyperammonemia was unresponsive to drug therapy. The combined therapy involved 12 episodes of hyperammonemia in 7 children ages 3 to 26 months. The plasma ammonia concentrations decreased to normal or nearly normal levels in all patients, except one.[8] **Guidelines** 2019 European expert panel consensus: In hyperammonemia, IV NaPBA/NaPA to be given as IV in glucose 10% at 250 mg/kg as bolus in 90-120 minutes, then maintenance 250-500 mg/kg/day.[1] British Inherited Metabolic Disease Group: The standard dose is 250 mg/kg/d in divided doses. This may be increased to 600 mg/kg/d in an emergency.[3] **Pharmacokinetics** After an intravenous load, phenylbutyrate is quickly converted to phenylacetate with saturable nonlinear kinetics. The subsequent conjugation to phenylacetylglutamine is rapid, so that the concentrations of phenylacetate remains low. The peak concentration of phenylacetate is between 1 and 2 hours and that of phenylacetylglutamine after 1 to 3.5 hours.[7] When it is given orally, phenylbutyrate peak concentration is between 1- and 2-hours post dose and the concentrations of phenylacetate and phenylacetylglutamine peak simultaneously at 3 hours. When repeated doses are given, the concentration of phenylacetate increase during the day, only returning to baseline overnight.[7] **Safety** Adverse effects that can be extrapolated from other population to neonates include poor weight gain, acidosis and alkalosis, hypoalbuminemia, hyper- and hypophosphataemia, mucositis (ORAL route). The sided effects are not easy to distinguish between the effects of the disease and of the medication.[7]
Practice points	
References	1. Häberle J, Burlina A, Chakrapani A, Dixon M, Karall D, Lindner M, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: first revision. Journal of inherited metabolic disease. 2019;42(6):1192-230. 2. Niemi A-K, Enns GM. Pharmacology review: sodium phenylacetate and sodium benzoate in the treatment of neonatal hyperammonemia. NeoReviews. 2006;7(9):e486-e95. 3. British Inherited Metabolic Disease Group. Medicines used for the tretament of hyperammonaemia. https://bimdg.org.uk/wp-content/uploads/2024/12/Paeds_NH3_meds_NEW-DEC-VERSION.pdf. Downladed on 26 February 2025. 4. MerativeTM Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: Feb/26/2025). 5. Husson M-C, Schiff M, Fouilhoux A, Cano A, Dobbelaere D, Brassier A, et al. Efficacy and safety of iv sodium benzoate in urea cycle disorders: a multicentre retrospective study. Orphanet journal of rare diseases. 2016;11:1-8. 6. Brusilow SW. Phenylacetylglutamine may replace urea as a vehicle for waste nitrogen excretion. Pediatric research. 1991;29(2):147-50. 7. Feillet F, Leonard J. Alternative pathway therapy for urea cycle disorders. Journal of inherited metabolic disease. 1998;21(Suppl 1):101-11. 8. Brusilow SW, Danney M, Waber LJ, Batshaw M, Burton B, Levitsky L, et al. Treatment of episodic hyperammonemia in children with inborn errors of urea synthesis. New England Journal of Medicine. 1984;310(25):1630-4.

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