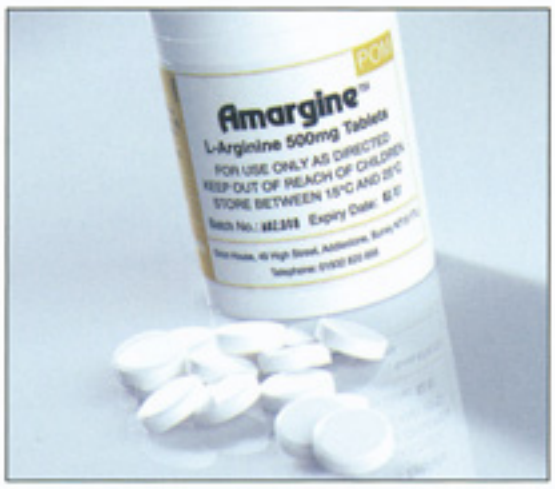
DATA SHEET:

L-ARGININE

500mg Tablet



Dosage and Administration

Indication	Route	Age				Frequency (times daily)	Notes
		Birth-1 month	1 month-2 years	2-12 years	12-18 years		
OTC and CPS deficiencies	Oral	25-35mg/kg				3-4	
Citrullinaemia and ASA	Oral	100-175mg/kg				3-4	Up to 700mg/kg/day

Active Ingredient
L-Arginine (base)

Pack
100 white uncoated tablets with a break-line in a Securitainer. A desiccant is included since L-Arginine is hygroscopic.

Storage
Store in a closed container in a dry place. The tablets disintegrate if left exposed to the atmosphere for 2 days. The shelf life is 2 years.

Therapeutic Indications
1 As a dietary supplement for patients with Carbamoyl Phosphate Synthetase (CPS) and Ornithine Transcarbamylase (OTC) deficiencies. Patients with these diseases cannot produce arginine as part of the urea cycle. They need L-Arginine as a dietary supplement (100mg/kg/day normally, but up to 175mg/kg/day in severe variants). It can also be used with Sodium 4-Phenylbutyrate and Sodium Benzoate.
2 As a medication for patients with: (a) Argininosuccinase (AL) deficiency (400-700mg/kg/day) since they can excrete waste nitrogen as argininosuccinic acid, and (b) Argininosuccinic Acid Synthetase (AS) deficiency (400-700mg/kg/day) since they can excrete waste nitrogen as L-Citrulline.

Pharmacokinetics
Rapidly absorbed after oral administration (T_{MAX}: within 2 hours).

Contraindications
Do not use in Arginase deficiency.

Side Effects and Adverse Reactions
Nausea, vomiting, flushing, hypotension, headache, numbness, hyperchloraemic metabolic acidosis

Interactions in Pregnancy/Breast-Feeding
No information available

Interactions with Other Medicaments
Spironolactone: Potentially fatal hyperkalaemia reported in patients with hepatic disease

Cautions/Special Warnings
Advisable to monitor plasma pH and chloride.

Additional Information
None

Legal Category
L-Arginine 500mg Tablet is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

References
1 Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 42-43
2 Taketomo CK et al, Pediatric Dosage Handbook, 6 ed. USA: Lexi-Comp Inc;1999-2000

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

Special Products Ltd ● Unit 16 Trade City ● Avro Way ● Brooklands Business Park ● Weybridge ● Surrey ● KT13 0YF ● UK

Telephone : +44 (0)1932 690325
Fax : +44 (0)1932 341091
Web : www.specialproducts.biz
Email : info@specialproducts.biz

DATA SHEET

Amargine

L-Arginine 100mg in 1ml Oral Solution

Product Code
A09

Active Ingredient
L-Arginine Ph Eur

Description of Product
Clear, sugar-free, strawberry flavoured oral liquid containing 100mg/1ml L-arginine.

Presentation
L-Arginine 100mg in 1ml Oral Solution is supplied as 200ml of liquid in a plastic amber bottle with a tamper-evident, child-resistant closure.

Storage
Store below 25°C.

Shelf Life
Two Years

Active Excipients
None

Allergenic Information
Lactose free, sugar free, aspartame free, alcohol free.

Therapeutic Indications[1]

A As a dietary supplement for patients with urea cycle disorders: Carbamyl Phosphate Synthetase (CPS) and Ornithine Transcarbamylase (OTC) deficiencies.

Patients with the above diseases cannot produce arginine as part of the urea cycle (see fig. 1).

B For use with sodium 4-phenylbutyrate and sodium benzoate

Patients with Argininosuccinase (AL) deficiency and Argininosuccinic Acid Synthetase (AS) deficiency, as patients with AL defficency can excrete waste nitrogen as argininosuccinic acid and patients with AS deficiency can excrete waste nitrogen as L-Citrulline

C Citrullinaemia (see fig. 1)

Dosage[1]
For CPS and OTC deficiencies:
Neonate- Adult: 100mg/kg/day in divided doses.

For AL and AS deficiencies and Citrullinaemia,
Neonate-Adult: 400-700mg/kg/day in divided doses.

Administration
The liquid may be dissolved in fruit drinks and consumed immediately.
The product is suitable for PEG tube administration.

Contraindications and Precautions
Monitor plasma pH and chloride[1]. Not to be used in the treatment of arginase deficiency[1] or hyperargininaemia[2]

Side-effects and Adverse Reactions[2]
Elevated plasma-potassium concentrations have been reported in uraemic patients and arginine should therefore be used with caution in patients with renal disease or anuria.

Mode of Action
Patients with OTC, CPS, AS and Al deficiencies cannot produce arginine. By supplementing arginine, the urea cycle continues to produce urea and remove nitrogen. For every molecule of arginine two nitrogen atoms are removed from the urea cycle.

Pharmacokinetics
No information available

Interactions with other Medications
Potentially fatal hyperkalaemia reported in patients with hepatic disease taking concomitant Spironolatone.

Pregnancy and Breastfeeding
No information available

Legal Category
L-Arginine 100mg in 1ml Oral Solution is an 'Unlicensed Medicine' within the meaning of the current legislation, governed by the UK Medicines Act 1968.

This publication is solely for the technical guidance of prescribers and dispensers of L-Arginine 100mg in 1ml Oral Solution and must not be considered as a recommendation or endorsement for the clinical use of the product. The information provided in this publication may not be comprehensive.

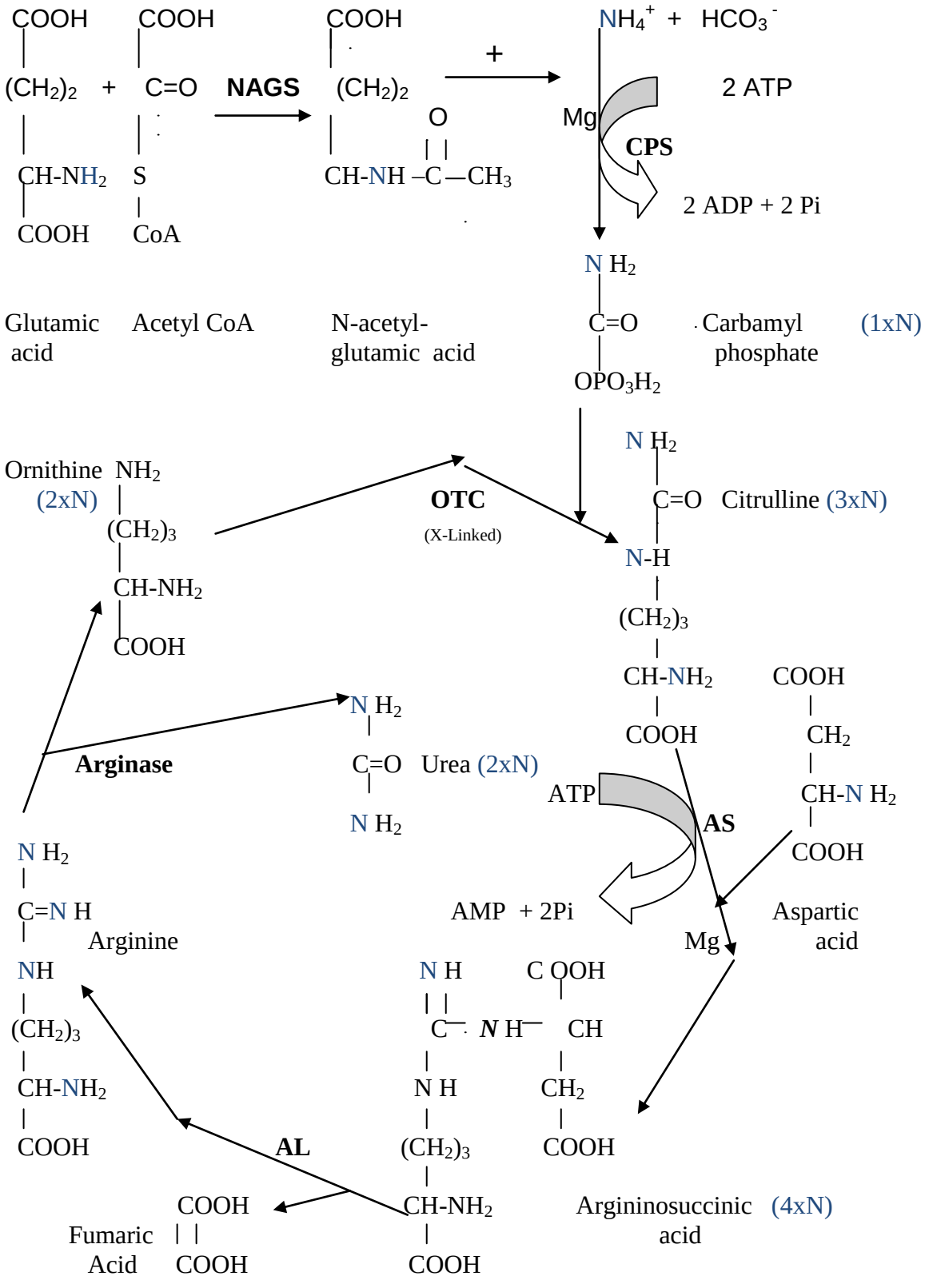
Transmissible Spongiform Encephalopathies
L-Arginine 100mg in 1ml Oral Solution comply with the Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003 [S.I. No.1608].

Approved by: Dr. G. March MRPharmS
Date : 26/04/2011

References:
1) Martin J; British National Formulary for children; BMJ Group, RPS Publishing, 2009
2) S. Sweetman. Martindale the complete Drug Reference. London Pharmaceutical Press. 2009

Fig. 1

EXCRETION OF WASTE NITROGEN VIA THE UREA CYCLE

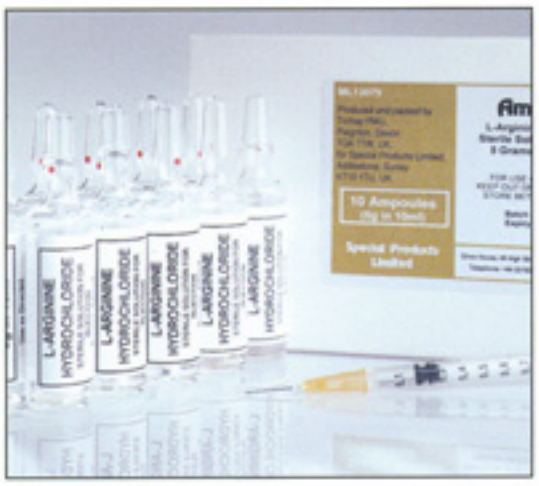


N = waste nitrogen atom **NAGS / CPS / OTC / AS / AL / Arginase** = enzymes

DATA SHEET:

L-ARGININE

5g in 10ml Injection



Active Ingredient
L-Arginine (as the hydrochloride salt)

Pack
10 x 10ml ampoules, each containing 5g L-Arginine Hydrochloride

Storage
Store between 15°C and 25°C. The shelf life is 30 months.

Therapeutic Indications
1 As a dietary supplement for patients with Carbamoyl Phosphate Synthetase (CPS) and Ornithine Transcarbamylase (OTC) deficiencies. Patients with the these diseases cannot produce arginine as part of the urea cycle. They need L-Arginine as a dietary supplement (100mg/kg/day normally, but up to 175mg/kg/day in severe variants). It can also be used with Sodium 4-Phenylbutyrate and Sodium Benzoate.
2 As a medication for patients with: (a) Argininosuccinase (AL) deficiency (400-700mg/kg/day) since they can excrete waste nitrogen as argininosuccinic acid, and (b) Argininosuccinic Acid Synthetase (AS) deficiency (400-700mg/kg/day) since they can excrete waste nitrogen as L-Citrulline.

Dosage and Administration

Indication	Route	Age				Frequency (times daily)	Notes
		Birth-1 month	1 month-2 years	2-12 years	12-18 years		
OTC and CPS deficiencies	IV infusion	200mg/kg				Single dose	Loading dose. Given over 90 minutes
	IV infusion	200mg/kg/day (8.3mg/kg/hour)				Continuous	
Citrullinaemia and ASA	IV infusion	600mg/kg				Single dose	Loading dose. Given over 90 minutes
	IV infusion	600mg/kg/day (25mg/kg/hour)				Continuous	

Dilute to 20mg in 1ml with sterile glucose 10% or 5% infusion. Maximum concentration is 100mg in 1ml. It can be infused at a Y-site with L-Carnitine, Sodium Benzoate and Sodium 4-Phenylbutyrate.

Pharmacokinetics
No information available

Contraindications
Do not use in Arginase deficiency.

Side Effects and Adverse Reactions
Nausea, vomiting, flushing, hypotension, headache, numbness, hyperchloraemic metabolic acidosis, irritation at injection site

Interactions in Pregnancy/Breast-Feeding
No information available

Interactions with Other Medicaments
Spironolactone: Potentially fatal hyperkalaemia reported in patients with hepatic disease

Cautions/Special Warnings
Advisable to monitor plasma pH and chloride.

Additional Information
None

Legal Category
L-Arginine 5g in 10ml Injection is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

References

1 Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 42-43
2 Taketomo CK et al, Pediatric Dosage Handbook, 6 ed. USA: Lexi-Comp Inc;1999-2000

Dr. G. A. March PhD, MRPharmS
Managing Director

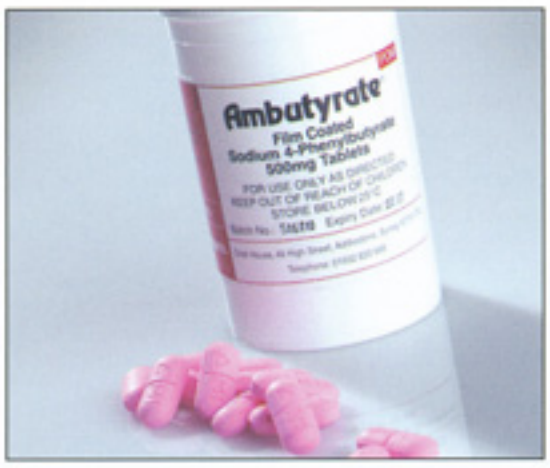
August 2007

DATA SHEET:

SODIUM 4-PHENYLBUTYRATE

500mg Film-Coated Tablet

SPECIAL PRODUCTS



Active Ingredient
Sodium 4-Phenylbutyrate

Pack
100 tablets

Storage
Store below 25°C. The shelf life is 2 years.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)

Dosage and Administration
Birth-18 years: 250-600mg/kg/day in 3 or 4 divided doses (maximum 20g/day)

Pharmacokinetics
Half-life:
i) Sodium 4-Phenylbutyrate - 0.8 hours
ii) Phenylacetate - 1.35 hours
Rate of elimination: 80% of metabolite (phenylacetylglutamine) excreted within 24 hours

Sodium 4-Phenylbutyrate is a pro-drug which is oxidized in vivo to sodium phenylacetate (the active ingredient) within 30 minutes. That compound conjugates with the amino acid glutamine to form phenylacetylglutamine, which is excreted in the urine steadily over 12 hours. The administration of one molecule of Sodium 4-Phenylbutyrate results in the excretion of two atoms of waste nitrogen.

Contraindications
1 Each 500mg dose of Sodium 4-Phenylbutyrate contains 2.7mmol of sodium ions, therefore use with caution in patients with congestive heart failure or severe renal insufficiency.
2 Hypersensitivity to Sodium 4-Phenylbutyrate.

Interactions in Pregnancy/Breast-Feeding
No information available

Cautions/Special Warnings
500mg of Sodium 4-Phenylbutyrate contains 2.7mmol (62.5mg) of sodium ions and caution should be exercised when treating patients with:
i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Treatment for overdose is dialysis.

Legal Category
Sodium 4-Phenylbutyrate 500mg Film-Coated Tablet is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

Additional Information
Patients need to be advised to consume a low protein diet.

References

1 Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 576-577
2 Taketomo CK et al, Pediatric Dosage Handbook, 6 ed. USA: Lexi-Comp Inc;1999-2000

Dr. G. A. March PhD, MRPharmS
Managing Director

August 2007

Side Effects and Adverse Reactions

Cardiovascular	Oedema, arrhythmias, syncope
Central nervous system	Headache, depression
Dermatological	Rash
Endocrine and metabolic	Amenorrhoea, menstrual dysfunction, renal tubular acidosis, hypokalaemia, hypernatraemia, hyperphosphataemia
Gastrointestinal	Anorexia, abnormal taste, gastrointestinal disturbances, nausea, weight gain, gastritis
Haematological	Anaemia, leucopoenia, leukocytosis, thrombocytopoenia, aplastic anaemia
Hepatic	Hepatic insufficiency
Renal	Renal tubular acidosis, renal insufficiency
Other	Body odour

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of phenylacetylglutamine

DATA SHEET:

SODIUM 4-PHENYLBUTYRATE

250mg in 1ml Powder for Oral Solution

SPECIAL PRODUCTS

Active Ingredient
Sodium 4-Phenylbutyrate

Pack
The pack is presented as a sweetened, strawberry flavoured dry powder (25g in a 100ml child-resistant amber glass bottle), which is re-constituted with Purified Water by a pharmacist immediately before dispensing. The patient then dilutes the prescribed dose with ten times as much tap water to produce a long drink.

Storage
1 The dry powder has a shelf-life of 2 years.
2 The re-constituted solution has an expiry period of 28 days at room temperature (<25°C).

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)

Dosage and Administration
Birth-18 years: 250-600mg/kg/day in 3 or 4 divided doses (maximum 20g/day)

Calculate the number of millilitres to be given per dose (250mg in 1ml). Draw up the required dose in an oral syringe. Disperse the contents of the syringe into 8-12 times its volume of cold water according to taste, e.g. disperse a 5ml dose in 50ml of water. Stir for 5 seconds. The sweetened strawberry flavoured drink must be consumed immediately.

Example for a 17kg Child
Prescribed total daily dose is:

17 x 250mg = 4,250mg (17ml per day)

It is advantageous to give the biggest dose at bedtime. Therefore give:

Time	Dose	Volume of Water
7:00 am	4ml	32-48ml
2:00 noon	4ml	32-48ml
5:00 pm	4ml	32-48ml
10:00 pm	5ml	40-60ml

Preparation of Solution
Add 80ml of Purified Water Ph Eur to dissolve the powder. Replace the child resistant closure. Shake the bottle vigorously for one minute to disperse the powder. Annotate the label with the date of preparation of the solution. Allow the powder to dissolve for 5-10 minutes. The solution will not clear completely since a small proportion of the spray dried flavouring agent is insoluble.

Pharmacokinetics
Rapidly absorbed after oral administration (peak serum level: 1 hour).
Half-life:
i) Sodium 4-Phenylbutyrate - 0.8 hours
ii) Phenylacetate - 1.35 hours
Rate of elimination: 80% of metabolite (phenylacetylglutamine) excreted within 24 hours

Sodium 4-Phenylbutyrate is a pro-drug which is oxidized in vivo to sodium phenylacetate (the active ingredient) within 30 minutes. That compound conjugates with the amino acid glutamine to form phenylacetylglutamine, which is excreted in the urine steadily over 12 hours. The administration of one molecule of Sodium 4-Phenylbutyrate results in the excretion of two atoms of waste nitrogen.

Contraindications
1 Each 500mg dose of Sodium 4-Phenylbutyrate contains 2.7mmol of sodium ions, therefore use with caution in patients with congestive heart failure or severe renal insufficiency.
2 Hypersensitivity to Sodium 4-Phenylbutyrate.
3 Patients with Phenylketonuria (PKU) since aspartame is used as a sweetening agent.

Side Effects and Adverse Reactions

Cardiovascular	Oedema, arrhythmias, syncope
Central nervous system	Headache, depression
Dermatological	Rash
Endocrine and metabolic	Amenorrhoea, menstrual dysfunction, renal tubular acidosis, hypokalaemia, hypernatraemia, hyperphosphataemia
Gastrointestinal	Anorexia, abnormal taste, gastrointestinal disturbances, nausea, weight gain, gastritis
Haematological	Anaemia, leucopoenia, leukocytosis, thrombocytopoenia, aplastic anaemia
Hepatic	Hepatic insufficiency
Renal	Renal tubular acidosis, renal insufficiency
Other	Body odour

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of phenylacetylglutamine

Interactions in Pregnancy/Breast-Feeding

No information available

Cautions/Special Warnings

1ml (250mg of Sodium 4-Phenylbutyrate) contains 1.35mmol (31.25mg) of sodium ions and caution should be exercised when treating patients with:

i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Treatment for overdose is dialysis.

Additional Information

Patients need to be advised to consume a low protein diet.

Legal Category

Sodium 4-Phenylbutyrate 250mg in 1ml Powder for Oral Solution is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

References

1 Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 576-577
2 Taketomo CK et al, Pediatric Dosage Handbook, 6 ed. USA: Lexi-Comp Inc;1999-2000

Dr. G. A. March PhD, MRPharmS
Managing Director

August 2007

DATA SHEET:

SODIUM 4-PHENYLBUTYRATE

Powder

Active Ingredient
Sodium 4-Phenylbutyrate. No excipients added.

Pack
100g spray-dried powder

Storage
Store at 15-25°C. The shelf life is 2 years.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)

Dosage and Administration
Birth-18 years: 250-600mg/kg/day in 3 or 4 divided doses (maximum 20g/day)

Pharmacokinetics
Rapidly absorbed after oral administration (peak serum level: 1 hour).
Half-life:
i) Sodium 4-Phenylbutyrate - 0.8 hours
ii) Phenylacetate - 1.35 hours
Rate of elimination: 80% of metabolite (phenylacetylglutamine) excreted within 24 hours

Sodium 4-Phenylbutyrate is a pro-drug which is oxidized in vivo to sodium phenylacetate (the active ingredient) within 30 minutes. That compound conjugates with the amino acid glutamine to form phenylacetylglutamine, which is excreted in the urine steadily over 12 hours. The administration of one molecule of Sodium 4-Phenylbutyrate results in the excretion of two atoms of waste nitrogen.

Contraindications
1 Each 500mg dose of Sodium 4-Phenylbutyrate contains 2.7mmol of sodium ions, therefore use with caution in patients with congestive heart failure or severe renal insufficiency.
2 Hypersensitivity to Sodium 4-Phenylbutyrate.

Interactions, Pregnancy/Breast-Feeding
No information available

Interactions in Pregnancy/Breast-Feeding
No information available

Cautions/Special Warnings
500mg of Sodium 4-Phenylbutyrate contains 2.7mmol (62.5mg) of sodium ions and caution should be exercised when treating patients with:
i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Treatment for overdose is dialysis.

Legal Category
Sodium 4-Phenylbutyrate Powder is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

Additional Information
Patients need to be advised to consume a low protein diet.

References
1 Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 576-577
2 Taketomo CK et al, Pediatric Dosage Handbook, 6 ed. USA: Lexi-Comp Inc;1999-2000

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

Side Effects and Adverse Reactions

Cardiovascular	Oedema, arrhythmias, syncope
Central nervous system	Headache, depression
Dermatological	Rash
Endocrine and metabolic	Amenorrhoea, menstrual dysfunction, renal tubular acidosis, hypokalaemia, hypernatraemia, hyperphosphataemia
Gastrointestinal	Anorexia, abnormal taste, gastrointestinal disturbances, nausea, weight gain, gastritis
Haematological	Anaemia, leucopoenia, leukocytosis, thrombocytopoenia, aplastic anaemia
Hepatic	Hepatic insufficiency
Renal	Renal tubular acidosis, renal insufficiency
Other	Body odour

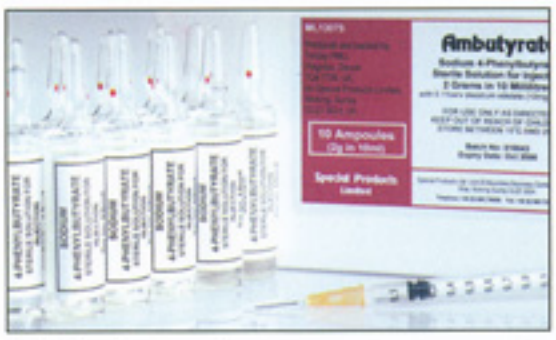
Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of phenylacetylglutamine

DATA SHEET:

SODIUM PHENYLBUTYRATE

2g in 10ml Injection



Active Ingredient
Sodium 4-Phenylbutyrate

Pack
10 x 10ml ampoules, each containing 2g Sodium 4-Phenylbutyrate

Storage
Store at 15-25°C. The shelf life is 2 years.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)

Dosage and Administration
Birth-18 years:

Route	Age				Frequency (times daily)	Notes
	Birth-1 month	1 month-2 years	2-12 years	12-18 years		
IV Infusion	250mg/kg				Single dose	Acute loading dose. IV infusion over 90 minutes
IV Infusion	250-600mg/kg/day (10.4 to 20.8mg/kg/hour)				Continuous	

Dilute to 20mg in 1ml (maximum 50mg in 1ml) with glucose 10% or 5% infusion and infuse via a peripheral vein. Can be infused at a Y-site with L-Arginine, L-Carnitine and Sodium Benzoate.

Pharmacokinetics
Half-life:
i) Sodium 4-Phenylbutyrate - 0.8 hours
ii) Phenylacetate - 1.35 hours
Rate of elimination: 80% of metabolite (phenylacetylglutamine) excreted within 24 hours

Sodium 4-Phenylbutyrate is a pro-drug which is oxidized in vivo to sodium phenylacetate (the active ingredient) within 30 minutes. That compound conjugates with the amino acid glutamine to form phenylacetylglutamine, which is excreted in the urine steadily over 12 hours. The administration of one molecule of Sodium 4-Phenylbutyrate results in the excretion of two atoms of waste nitrogen.

Side Effects and Adverse Reactions

Cardiovascular	Oedema, arrhythmias, syncope
Central nervous system	Headache, depression
Dermatological	Rash
Endocrine and metabolic	Amenorrhoea, menstrual dysfunction, renal tubular acidosis, hypokalaemia, hypernatraemia, hyperphosphataemia
Gastrointestinal	Anorexia, abnormal taste, gastrointestinal disturbances, nausea, weight gain, gastritis
Haematological	Anaemia, leucopoenia, leukocytosis, thrombocytopoenia, aplastic anaemia
Hepatic	Hepatic insufficiency
Renal	Renal tubular acidosis, renal insufficiency
Other	Body odour

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of phenylacetylglutamine

continued...

DATA SHEET:

SODIUM PHENYLBUTYRATE

2g in 10ml Injection

...continued

Contraindications

1 Each 500mg dose of Sodium 4-Phenylbutyrate contains 2.7mmol of sodium ions, therefore use with caution in patients with congestive heart failure or severe renal insufficiency.
2 Hypersensitivity to Sodium 4-Phenylbutyrate.

Interactions in Pregnancy/Breast-Feeding

No information available

Cautions/Special Warnings

500mg of Sodium 4-Phenylbutyrate contains 2.7mmol (62.5mg) of sodium ions and caution should be exercised when treating patients with:

i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Treatment for overdose is dialysis.

Additional Information

Patients need to be advised to consume a low protein diet.

Specifications

Description	Clear, colourless to slightly yellow, odourless liquid
Identification	Sodium 4-Phenylbutyrate present
pH	7.0-9.0
Volume	10.0-11.0ml
Sterility	Conforms to BP
Assay: Sodium 4-Phenylbutyrate	19.0-21.0% (w/v)

Legal Category

Sodium 4-Phenylbutyrate 2g in 10ml Injection is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

References

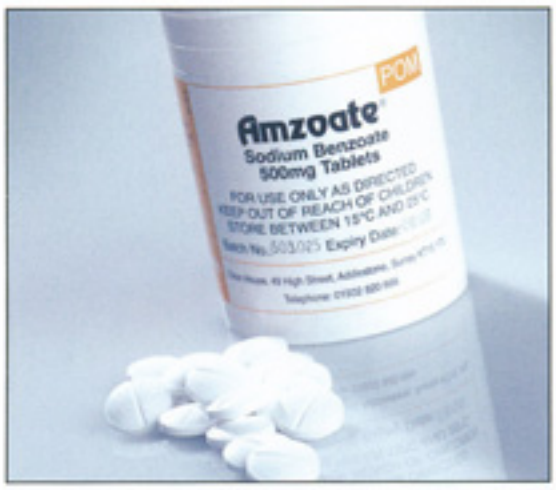
1 Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 576-577
2 Taketomo CK et al, Pediatric Dosage Handbook, 6 ed. USA: Lexi-Comp Inc;1999-2000

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

DATA SHEET:

SODIUM BENZOATE

500mg Tablet



Active Ingredient
Sodium Benzoate Ph Eur

Pack
100 tablets in a Securitainer

Storage
The shelf life is 2 years. Store at 15-25°C.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)
iv) Arginase (ARG)
v) N-Acetylglutamate Synthetase (NAGS)

Dosage and Administration
Birth-18years: 250mg/kg/day to be given in 4-6 divided doses (maximum 20g/day)

Pharmacokinetics
Rapidly absorbed after oral administration (peak plasma level after 30 minutes).

Hippurate is excreted 30 minutes after the administration of Sodium Benzoate and continues for 2-3 hours.

Contraindications
1 Hypersensitivity to Sodium Benzoate
2 Pregnancy (safety not proven)

Side Effects and Adverse Reactions

Common	Vomiting (can be helped by giving smaller doses up to six times daily or giving with food), gastric intolerance, nausea
At higher doses	Anorexia, irritability, hypokalaemia, lethargy, coma & death (at very high doses)

Interactions in Pregnancy/Breast-Feeding
No information available

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of hippurate

Cautions/Special Warnings
500mg of Sodium Benzoate contains 3.5mmol (81mg) of sodium ions and caution should be exercised when treating patients with:
i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Use with caution in neonates with hyperbilirubinaemia (benzoate competes with bilirubin binding sites on albumin).

Additional Information
Sodium Benzoate conjugates with the amino acid glycine to form hippurate, which is excreted in the urine. The administration of one molecule of Sodium Benzoate results in the excretion of one atom of waste nitrogen.

Legal Category
Sodium Benzoate 500mg Tablet is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

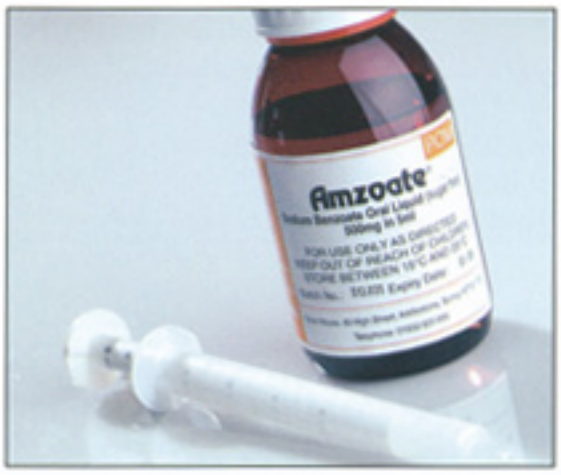
References
Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 566-567

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

DATA SHEET:

SODIUM BENZOATE

500mg in 5ml Oral Liquid



Active Ingredient
Sodium Benzoate Ph Eur

Pack
100ml child-resistant glass bottle containing 100mg in 1ml Sodium Benzoate

Storage
The shelf life is 2 years. Store at 15-25°C.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)
iv) Arginase (ARG)
v) N-Acetylglutamate Synthetase (NAGS)

Dosage and Administration
Birth-18years: 250mg/kg/day to be given in 4-6 divided doses (maximum 20g/day)

Pharmacokinetics
Rapidly absorbed after oral administration (peak blood level after 30 minutes).

Hippurate is excreted 30 minutes after administration of Sodium Benzoate and continues for 2-3 hours.

Contraindications
1 Hypersensitivity to Sodium Benzoate
2 Pregnancy (safety not proven)

Side Effects and Adverse Reactions

Common	Vomiting (can be helped by giving smaller doses up to six times daily or giving with food), gastric intolerance, nausea
At higher doses	Anorexia, irritability, hypokalaemia, lethargy, coma & death (at very high doses)

Interactions in Pregnancy/Breast-Feeding
No information available

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of hippurate

Cautions/Special Warnings
500mg of Sodium Benzoate contains 3.5mmol (81mg) of sodium ions and caution should be exercised when treating patients with:
i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Use with caution in neonates with hyperbilirubinaemia (benzoate competes with bilirubin binding sites on albumin).

Additional Information
Sodium Benzoate conjugates with the amino acid glycine to form hippurate, which is excreted in the urine. The administration of one molecule of Sodium Benzoate results in the excretion of one atom of waste nitrogen.

Flavour
Blackcurrant sweetened with saccharine sodium
Sugar-free
Aspartame-free

Legal Category
Sodium Benzoate 500mg in 5ml Oral Liquid is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

References
Medicines for Children. Great Britain:RCPCH Publications Ltd; 2003, 566-567

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

DATA SHEET:

SODIUM BENZOATE

Powder

Active Ingredient
Sodium Benzoate BP Ph Eur

Pack
250g

Storage
The shelf life is 2 years. Store at 15-25°C.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)
iv) Arginase (ARG)
v) N-Acetylglutamate Synthetase (NAGS)

Dosage and Administration
Birth-18years: 250mg/kg/day to be given in 4-6 divided doses (maximum 20g/day)

Pharmacokinetics
Rapidly absorbed after oral administration (peak blood level after 30 minutes).

Hippurate is excreted 30 minutes after administration of Sodium Benzoate and continues for 2-3 hours.

Contraindications
1 Hypersensitivity to Sodium Benzoate
2 Pregnancy (safety not proven)

Side Effects and Adverse Reactions

Common	Vomiting (can be helped by giving smaller doses up to six times daily or giving with food), gastric intolerance, nausea
At higher doses	Anorexia, irritability, hypokalaemia, lethargy, coma & death (at very high doses)

Interactions in Pregnancy/Breast-Feeding
No information available

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of hippurate

Cautions/Special Warnings
500mg of Sodium Benzoate contains 3.5mmol (81mg) of sodium ions and caution should be exercised when treating patients with:
i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Use with caution in neonates with hyperbilirubinaemia (benzoate competes with bilirubin binding sites on albumin).

Additional Information
Sodium Benzoate conjugates with the amino acid glycine to form hippurate, which is excreted in the urine. The administration of one molecule of Sodium Benzoate results in the excretion of one atom of waste nitrogen.

Legal Category
Sodium Benzoate Powder is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

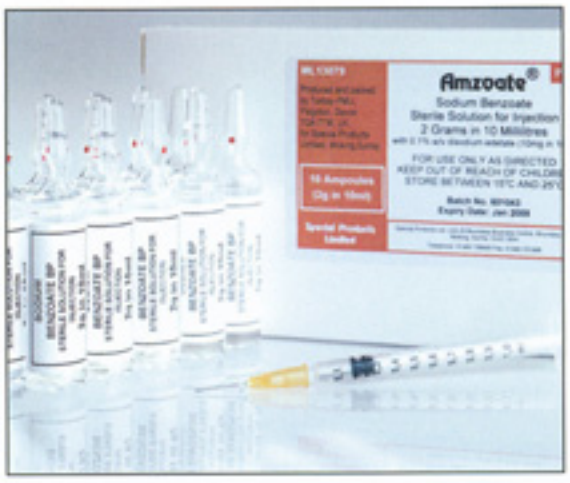
References
Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 566-567

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

DATA SHEET:

SODIUM BENZOATE

2g in 10ml Injection



Active Ingredient
Sodium Benzoate Ph Eur

Pack
10 x 10ml ampoules, each containing 2g Sodium Benzoate in water for injection

Storage
The shelf life is 2 years. Store at 15-25°C.

Therapeutic Indications
The treatment of hyperammonaemia in patients with urea cycle disorders involving deficiencies of the following enzymes:
i) Carbamoyl Phosphate Synthetase (CPS)
ii) Ornithine Transcarbamylase (OTC)
iii) Argininosuccinic Acid Synthetase (AS)
iv) Arginase (ARG)
v) N-Acetylglutamate Synthetase (NAGS)

Dosage and Administration
Birth-18years:
i) Loading dose: 250mg/kg infused IV over 90 minutes as a single dose.
ii) Maintenance dose: 250mg/kg/day as a continuous IV infusion in neonates. Prompt haemodialysis is needed in severe cases.
iii) Maintenance dose up to 500mg/kg/day as a continuous IV infusion in older patients.

The aim is to:
i) Reduce plasma ammonia concentrations below 60 micromol/litre
ii) Reduce plasma glutamine below 800 micromol/litre
iii) Achieve normal plasma concentrations of the essential amino acids

Compatibilities
Can be infused at a Y-site with L-Arginine, L-Carnitine and Sodium 4-Phenylbutyrate.

Preparation for Infusion
Dilute to 20mg in 1ml with 5% or 10% glucose IV solution (max 50mg in 1ml).

Route of Administration
Infuse via a peripheral line.

Pharmacokinetics
Hippurate is excreted within 5 minutes of administration. The half life is about 2 hours.

Contraindications
1 Hypersensitivity to Sodium Benzoate
2 Pregnancy (safety not proven)

Side Effects and Adverse Reactions

Common	Vomiting (can be helped by giving smaller doses up to six times daily or giving with food), gastric intolerance, nausea
At higher doses	Anorexia, irritability, hypokalaemia, lethargy, coma & death (at very high doses)

Interactions with Other Medicaments

Sodium valproate	Increases hyperammonaemia by inhibiting any residual action of the affected urea cycle enzyme
Haloperidol	
Corticosteroids	
Probenecid	May decrease urinary excretion of hippurate

Interactions in Pregnancy/Breast-Feeding
No information available

Cautions/Special Warnings
500mg of Sodium Benzoate contains 3.5mmol (81mg) of sodium ions and caution should be exercised when treating patients with:

i) Severe hypertension
ii) Renal insufficiency
iii) Congestive heart failure
iv) Sodium retention with oedema

Use with caution in neonates with hyperbilirubinaemia (benzoate competes with bilirubin binding sites on albumin).

Additional Information
Sodium Benzoate conjugates with the amino acid glycine to form hippurate, which is excreted in the urine. The administration of one molecule of Sodium Benzoate results in the excretion of one atom of waste nitrogen.

Specifications

Description	Clear, colourless and odourless liquid
Identity: Sodium Benzoate	Sodium Benzoate present
Flame test	Positive
Ferric Chloride test	Positive
Hydrochloric Acid test	Positive
Magnesium Sulphate test	Positive
pH	7.0-9.0
Extractable volume	Not less than 10ml
Sterility	Conforms to BP
Assay: Sodium Benzoate	18.0-20.0% (w/v)

Legal Category
Sodium Benzoate 2g in 10ml Injection is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.

References
Medicines for Children. Great Britain: RCPCH Publications Ltd; 2003, 566-567

Dr. G. A. March PhD, MRPharmS
Managing Director
August 2007

THE PRODUCTS

Strong in the area of inborn errors of metabolism (IEM), Special Products has a particular interest in meeting the formulation needs of children; indeed, many of our medicines were originally targeted specifically at children and later extended for adult use.

Benefits

- All have active ingredients which have been used in hospitals for many years.
- All have stability data and a long shelf-life.
- All are palatable to children.
- All are free from lactose, sucrose, colourants and transmissible spongiform encephalopathy.
- All are manufactured by contractors with a manufacturing licence to manufacture 'specials'.
- All have a Certificate of Analysis signed by a Qualified Person.
- All have an excellent reputation and safety & efficacy track record.
- The recommended dose described in each data sheet is evidence-based.

Existing IEM Medicines

Products for Urea Cycle Disorders (see also overleaf):

Active Ingredient	Strength/Presentation/Pack Size
L-Arginine	500mg/Tablet/100 Tablets
	100mg in 1ml/Powder for Oral Solution/200ml
	5g in 10ml/Injection/10 Ampoules
Sodium 4-Phenylbutyrate	500mg/Film-Coated Tablet/100 Tablets
	250mg in 1ml/Powder for Oral Solution/100ml
	/Powder/100g
	2g in 10ml/Injection/10 Ampoules
Sodium Benzoate	500mg/Tablet/100 Tablets
	500mg in 5ml/Oral Liquid/100ml
	/Powder/250g
	2g in 10ml/Injection/10 Ampoules

Other Products:

Active Ingredient	Strength/Presentation/Pack Size
Betaine	250mg/Tablet/200 Tablets
	500mg in 1ml/Powder for Oral Liquid/100ml
L-5-Hydroxytryptophan	20mg/Capsule/250 Capsules
	50mg/Capsule/50 Capsules
L-Isoleucine	10mg in 1ml/Powder for Oral Solution/200ml
L-Phenylalanine	10mg in 1ml/Powder for Oral Solution/200ml
L-Valine	10mg in 1ml/Powder for Oral Solution/200ml
Sodium Dichloroacetate	50mg in 1ml/Powder for Oral Liquid/200ml

Suggestions for New IEM Medicines

We always welcome suggestions from healthcare professionals on medicines which would address an existing unmet medical need in addition to hard-to-find medicines, ie medicines that have been or are in the process of being discontinued by major pharmaceutical manufacturers and suppliers.

For further information please contact:
Dr Graham March PhD, MRPharmS, QP
Managing Director
Special Products Limited
Unit 25 Boundary Business Centre, Boundary Way, Woking, Surrey GU21 5DH United Kingdom
T: +44 (0)1483 736950
F: +44 (0)1483 721926
E: Graham.March@specialproducts.biz

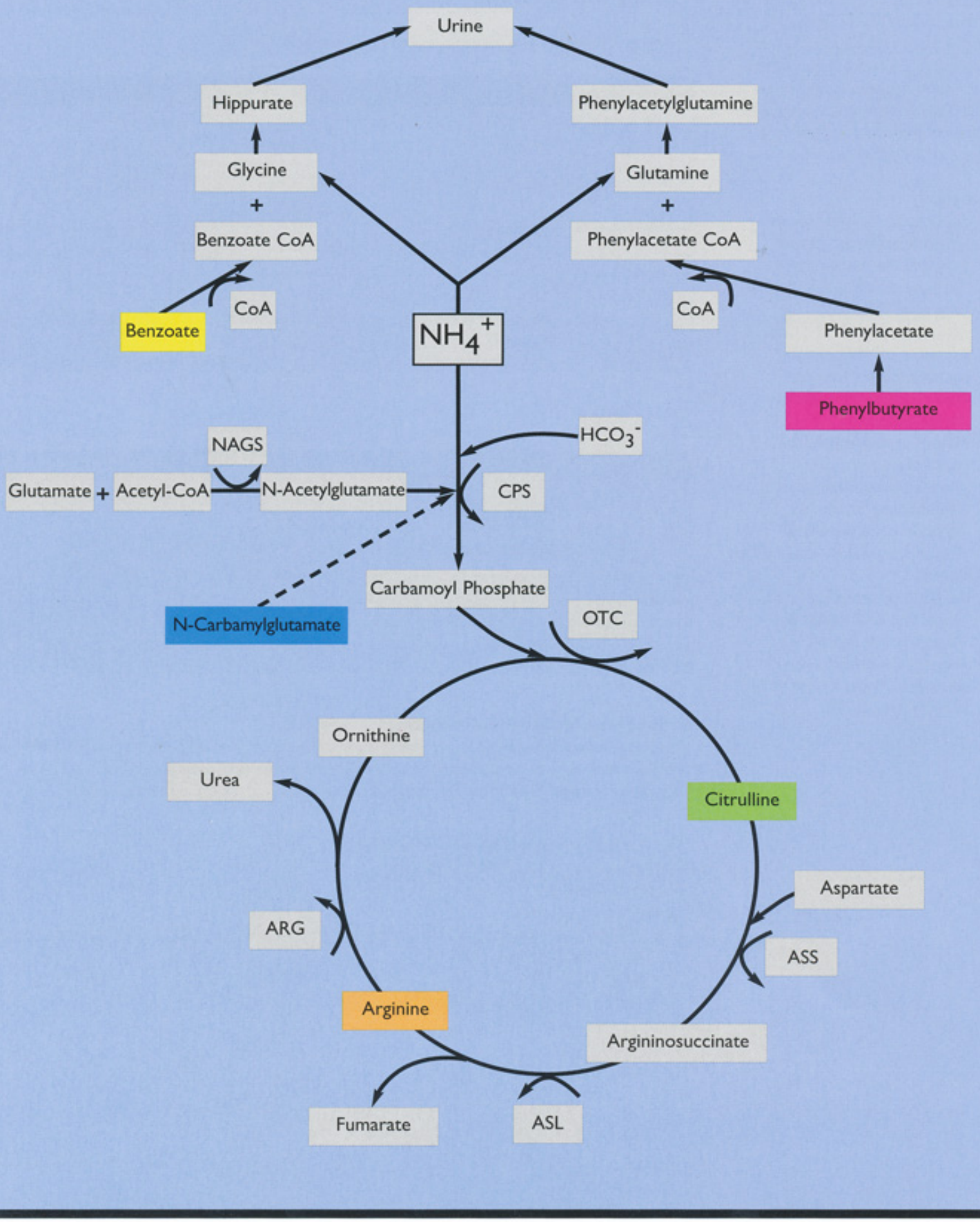
Our Products for Urea Cycle Disorders:

- **L-Arginine**
- **L-Citrulline***
- **N-Carbamy-L-Glutamic Acid***
- **Sodium 4-Phenylbutrate**
- **Sodium Benzoate**

Enzymes:

ARG	Arginase
ASS	Argininosuccinate Synthetase
ASL	Argininosuccinate Lyase
CPS	Carbamoyl Phosphate Synthetase
NAGS	N-Acetylglutamate Synthetase

* Denotes the products of Chemical Developments Limited (www.chemicaldevelopments.com) and are available directly from the company or through its affiliated company Special Products Limited.



Special Products Ltd ● Unit 16 Trade City ● Avro Way ● Brooklands Business Park ● Weybridge ● Surrey ● KT13 0YF ● UK

Telephone : +44 (0)1932 690325
Fax : +44 (0)1932 341091
Web : www.specialproducts.biz
Email : info@specialproducts.biz

DATA SHEET

SODIUM-D, L-3-HYDROXYBUTYRATE
50g

Product Code
H03

Active Ingredient
Sodium-D,L-3-hydroxybutyrate

Description of Product
A hygroscopic white crystalline powder.

Presentation
50g of a loose white powder supplied in a white tamper-evident plastic container

Storage
Store below 25C in a dry place.

Shelf Life
2 years.

Active Excipients
None.

Allergenic Information
Supplied as a pure powder so it is lactose-free, colour-free, aspartame-free etc.

Therapeutic Indication[1]
Multiple acyl-CoA dehydrogenase deficiency (MADD).

Sodium D,L 3-hydroxybutyrate is a naturally occurring ketone in the body. It is used as an an energy source for the brain and muscles. Patients that have multiple acyl-CoA dehydrogenase deficiency (MADD) cannot produce D,L3-hydroxybutyrate.

MADD is a genetic defect of the electron transfer flaviprotein (ETF) chain causing dysfunction of dehydrogenases linked to flavin adenine dinucleotide (FAD), including those of fatty acid β oxidation.

The clinical presentation varies widely. Neonates with a severe deficiency sometimes die in infancy with malformations and severe metabolic decompensations. Patients who first present as infants and children have a less severe enzyme deficiency. They present with a milder metabolic decompensation and exhibit hepatic dysfunction, myopathy, and cardiomyopathy.

Since fats cannot provide a source of energy, due to the enzyme deficiency, patients lack energy and can suffer spastic quadriplegia and cardiomyopathy.

Dosage[1]
80-900mg/kg/day in three divided doses (4 hourly). Start at the lower dose and increase to obtain measurable concentrations of physiological ketone bodies (sum of D-3-hydroxybutyrate and acetoacetate) at all times.

Administration
This is a pure powder intended to be used as an ingredient for extemporaneoud preparations. The product may be divided into individual powders . The powder can be weighed into individual tablet bottles and

dispensed to the patient. The individual powders can be mixed with water and taken orally or via a gastrostomy tube. Alternatively, the powder could be sprinkled onto cold food and consumed immediately.

Contraindications and Precautions
The high sodium intake limits the maximum dose.

Side-effects and Adverse Reactions
No side-effects were reported[1].

Mode of Action
D,L-3-hydroxybutyrate is a ketone body that can cross the blood/brain barrier and provide an alternative energy source for the brain. It also provides an energy source for the heart, kidney and muscle. This results in the return of mobility.

Pharmacokinetics[1]
C_{max}: 30-60 minutes after administration via a gastrostomy tube.
Free fatty acids decreased by up to 75% 1 hour after administration, returning to pretreatment concentrations after 3 hours. This suggests that the product should be administered every 3-4 hours.

Interactions with Other Medications
No information available.

Pregnancy and Breastfeeding
No information available.

Legal Category
Sodium-D,L 3-hydroxybutyrate is an 'Unlicensed Medicine' within the meaning of the current legislation, governed by the UK Medicines Act 1968.

This publication is solely for the technical guidance of prescribers and dispensers of Sodium-D,L 3-hydroxybutyrate and must not be considered as a recommendation or endorsement for the clinical use of the product. The information provided in this publication may not be comprehensive.

Transmissible Spongiform Encephalopathies
Sodium-D,L 3-hydroxybutyrate complies with the Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003 [S.I. No.1608].

Sodium D,L 3-hydroxybutyrate Powder 99% w/w
Version: 4 14 May 2009
Produced by: G. March PhD, MRPharmS
Approved by: S. Sidhu MPharm, MRPharmS

Reference:
1 Van Hove J:K et al; D,L-3-hydroxybutyrate treatment of multiple acyl-CoA dehydrogenase deficiency (MADD); The Lancet; 2003; 361; 1433-1435

Special Products Limited

Orion House, 49 High Street, Addlestone, Surrey KT15 1TU

Telephone: 01932 820666 Fax: 01932 850444

DATA SHEET

L-Citrulline Powder

Active Ingredient
L-Citrulline (base)

Pack size
100 g of powder

Therapeutic Indications
Used in lysinuric protein intolerance (LPI) and as an alternative to L-Arginine in severe carbamylphosphate synthase (CPS) and ornithine camyltrnsferase (OTC) deficiencies.

Dosage (birth–adult)

Route	Age (birth-adult)	Frequency (times daily)
Oral	42.5 mg/kg	4

Side-Effects and Adverse Reactions
Oral: None reported

Contraindications
Do not use in arginase deficiency

Interactions, Pregnancy, Breast-Feeding
No information available

Pharmacodynamic Properties
L- Citrulline is converted to L-Arginine, thus preventing Arginine deficiency. However, Citrulline contributes one less nitrogen atom to the free amino acid pool than does Arginine.

Legal Category
L-Citrulline powder is an 'Unlicensed Medicine' within the meaning of current legislation governed by the UK Medicines Acts and EU Pharmaceutical Directives.