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DATA SHEET

Amargine

L-Arginine 100 mg in 1 mL Oral Solution

Product Code
A09, A09-ROW, A09a and A09a-ROW

Active Ingredient
L-Arginine Ph Eur.

Description of Product
Amargine is a clear, sugar-free strawberry flavoured oral solution containing 100 mg L-Arginine in 1 mL.

Presentation
The product is supplied as 200 mL oral solution in an amber PET bottle with a tamper-evident child-resistant closure.

Storage
Store upright in a dry place below 25°C. Keep out of direct sunlight. Do not refrigerate.

Shelf Life
Two years.

Excipients of Known Effect
This product contains:

- **Sodium methyl parahydroxybenzoate** (E219) and **sodium propyl parahydroxybenzoate** (E217): may cause allergic reactions (possibly delayed).
- Approximately 0.29 mg **Propylene glycol** (E1520) per ml, which is equivalent to 0.029% w/v.

Free-From Information
This product does not contain lactose, sugar, aspartame and ethanol.

Therapeutic Indications
L-Arginine is used in the maintenance treatment of hyperammonaemia in:

- Carbamylphosphate Synthetase (CPS)[1], Ornithine Transcarbamylase (OTC)[1] Argininosuccinate lyase (ASL)[2] and Argininosuccinate Synthetase (ASS)[2] deficiencies
- Citrullinaemia and arginosuccinic aciduria.[1]

L-Arginine can also be used with sodium 4-phenylbutyrate and sodium benzoate in the long-term management of urea cycle disorders.[2]

Dosage
<u>For maintenance treatment of hyperammonaemia in CPS and OTC deficiencies</u>
(specialist use only):[1]
Neonate: 100-200 mg/kg/day in 3-4 divided doses with feeds.
Child (body-weight up to 20 kg): 100-200 mg/kg/day in 3-4 divided doses with feeds or meals.

daily).

For maintenance treatment of hyperammonaemia in citrullinaemia, arginosuccinic aciduria (specialist use only):[1]
Neonate: 100-300 mg/kg/day in 3-4 divided doses with feeds.
Child (body-weight up to 20 kg): 100-300 mg/kg/day in 3-4 divided doses with feeds or meals.
Child (body-weight 20 kg and above): 2.5-6 g /m^2/day in 3-4 divided doses with meals (max. 6 g daily).

Administration
The product is designed to be taken orally. It can also be administered via a PEG tube.

Contraindications and Precautions
This product is not to be used in:

- Patients with hypersensitivity to L-Arginine or any of the product excipients.
- The treatment of arginase deficiency[1] or hyperargininaemia.[2]

Use with caution in patients with renal disease or anuria. Elevated plasma-potassium concentrations have been reported when L-Arginine is used in uraemic patients.[2]

Monitoring Requirements:
Regular checks of the plasma pH and chloride levels are recommended.[1]

Side-effects and Adverse Reactions
Following the use of L-Arginine the following has been reported:
Hypersensitivity reactions including rash and anaphylaxis have occurred, and treatment should be stopped if these are serious.[2] L- Arginine therapy has been associated with haematuria that sometimes occurred 1 or 2 days after dosing.[2] There have also been isolated reports of a decrease in platelet count.[2]

Mode of Action
Patients with OTC, CPS, ASS and ASL deficiencies cannot produce arginine. By supplementing arginine, the urea cycle continues to remove nitrogen and produce urea .[2] For every molecule of arginine administered two nitrogen atoms are removed from the urea cycle.[4]

Pharmacokinetics
Baseline plasma concentration of L-Arginine is 15.1 ± 2.6 micrograms mL^{-1}. The peak plasma concentration after oral administration (10 g) was 50 ± 13.4 micrograms mL^{-1} occurring 1 h after administration. The absolute bioavailability of a single oral 10 g dose of L-arginine is approximately 20%.[3]

Interactions with other Medications
Potentially fatal hyperkalemia reported in patients with hepatic disease taking concomitant spironolactone with L-Arginine.[2]

Pregnancy and Breastfeeding
No information available.

Legal Category
L-Arginine (Amargine) 100 mg in 1 mL Oral Solution is an 'Unlicensed Medicine' within the meaning of the current legislation, governed by the Human Medicines Regulations 2012.

This publication is solely for the technical guidance of prescribers and dispensers of L-Arginine (Amargine) 100 mg in 1 mL 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 exhaustive or reflective of all the information in the public domain.

Transmissible Spongiform Encephalopathies
All starting materials are certified as compliant with EMEA/410/01 (S.I. 2003/1680) for minimising the risk of BSE/TSE contamination.

References:

1) Paediatric Formulary Committee (2018). *BNF for Children 2018-2019*. London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. p. 613.
2) Brayfield A (ed), *Martindale: The Complete Drug Reference*. Arginine [online] London: Pharmaceutical Press. Available from http://www.medicinescomplete.com (accessed on 11-Sep-2018)
3) Tangphao, O., et al. (1999). Pharmacokinetics of intravenous and oral L-arginine in normal volunteers. *British Journal of Clinical Pharmacology*, 47(3), pp.261-266.
4) Berg JM, Tymoczko JL, Stryer L. *Biochemistry*. 5th edition. New York: W H Freeman; 2002. Section 23.4 ammonium ion is converted into urea in most terrestrial vertebrates. Available from: https://www.ncbi.nlm.nih.gov/books/NBK22450/.