SESLHDMG/128

Medicine Guideline

Arginine IV for treatment of acute stroke-like episode in patients with confirmed or suspected MELAS

(Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes)

Synonym	L-arginine
Areas where Protocol/Guideline applicable	SESLHD Inpatients
Authorised Prescribers:	• Neurologists or their representatives (Advanced trainees, registrars, JMOs). • Medical teams, following discussion with the Neurology service.
Indication for use	Treatment of acute stroke-like episode in MELAS, to improve endothelial function and clinical symptoms. Aim to commence within 3 hours of onset of symptoms.
Clinical condition	Stroke-like episode Characterised by headache, nausea, vomiting, encephalomyopathy, focal onset-seizures (with or without associated focal neurological deficits). Neuro-imaging will show cortical and sub-cortical signal abnormalities that may not be confined to vascular territories.
Proposed Place in Therapy	At the discretion of treating or consulting neurologist.
Adjunctive Therapy	Arginine should be used in conjunction with best supportive care for stroke-like episodes as per published patient care standards.
Contra-indications	• Known hypersensitivity to arginine • Severe acidosis (pH <7.2) • pH <7.0 if concomitant lactataemia and patient otherwise clinically well • Hypotension • Disease related to nitric oxide production
Precautions	• Renal impairment - Use with caution in patients with moderate renal insufficiency. Elevated plasma potassium concentrations have been reported in uraemic patients. • Hepatic impairment - Use with caution in patients with severe hepatic impairment. • Allergic reaction • Electrolyte disturbance, particularly the risk of hyperchloraemic metabolic acidosis. • Arginine may enhance the hypotensive effect of Blood Pressure Lowering Agents.

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Important Drug Interactions	Arginine may enhance the hypotensive effect of **vasodilating** or **antihypertensive** agents and dose adjustment may be required. **Spironolactone** – may increase risk of hyperkalaemia.
Dosage	*Acute management* **Bolus:** arginine 0.5 g/kg IV (up to 30 g), in 250mL sodium chloride 0.9% given as intravenous infusion over 30 to 60 minutes *followed by* **Continuous Infusion:** Maximum daily dose 30 g. • 0.5 g/kg (per day) given as continuous IV infusion for 3-5 days. *OR as an alternative to the continuous IV infusion (eg. if patient doesn't tolerate due to agitation or otherwise)* • 0.25 g/kg (each dose up to 15g) twice daily IV infusion over 1-2 hours. Maximum daily dose 30 g. After 3 days of intravenous arginine therapy, patients can be transitioned to oral arginine at 0.5 g/kg daily in three divided doses (up to maximum 30 g daily), provided they are safe to swallow and under the direction of the treating or consulting neurologist. *Prophylaxis* After 5 days of arginine therapy (or as per treating Neurologist), the patient can be transitioned to 0.15 to 0.3 g/kg arginine PO in 3 divided doses, as secondary prevention of further stroke-like episode. Duration of treatment is at the discretion of treating or consulting neurologist.
Presentation	arginine 15g/ 25mL injection
Duration of therapy	See above.
Prescribing Instructions	Must be prescribed on the eMR or eRIC. In the absence of eMM systems, the appropriate paper medication chart may be used.
Administration Instructions	Administer via central line, or large peripheral vein (e.g., antecubital fossa). Dilute with sodium chloride 0.9% as outlined under dosage section above. Sodium chloride 0.9% is preferred over glucose as patients with MELAS may have issues with blood glucose control. Initial bolus given over 30 to 60 mins, followed by continuous infusion daily for 3 to 5 days (or alternative twice daily dosing).

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Monitoring requirements Safety Effectiveness	Monitor blood pressure every 15 minutes and finger-prick blood glucose every 30 minutes, during initial bolus infusion. Monitor blood pressure every 4 hours during 3 to 5 days of continuous infusions. If the alternative of twice daily infusions is implemented, then monitor blood pressure every 30 minutes during the infusions. Daily bloods • FBC – monitor Hb • EUC / LFT – monitor K, eGFR and liver function • VBG – monitor for metabolic acidosis. • Serum lactate Monitor BP for 24 hours after the infusion.
Adverse effects	**Uncommon adverse reactions** • Nausea, vomiting, GI upset, flushing, headache. • Local venous irritation may occur if arginine solutions are infused too rapidly. • Normal anion gap metabolic acidosis (often a hyperchloraemic metabolic acidosis). **Rare Adverse Reactions** • Hypotension • Anaphylactic reaction or severe allergic reaction • Severe hyperkalaemia

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Management of Complications	**Hypotension** • Stop or slow the infusion and treat accordingly • Urgent medical review if symptomatic or concerns otherwise • Consider IV sodium chloride 0.9% hydration **Metabolic acidosis** • Withhold L-arginine infusion and monitor with twice daily venous blood gas assessment **Allergic reaction** • Anaphylaxis – manage as per local protocol and cease L-arginine. • Mild allergic reaction. Stop or slow L-arginine infusion, consult treating team. Give oral antihistamine therapy for symptomatic relief. **Hyperkalaemia** • Withhold L-arginine infusion and manage hyperkalaemia as per established hospital guidelines.
Basis of Protocol/Guideline:	1. Sue, C. M., Balasubramaniam, S., Bratkovic, D., Bonifant, C., Christodoulou, J., Coman, D., Crawley, K., Edema-Hildebrand, F., Ellaway, C., Ghaoui, R., Kava, M., Kearns, L. S., Lee, J., Liang, C., Mackey, D. A., Murray, S., Needham, M., Rius, R., Russell, J., Smith, N. J. C., … Wools, C. (2022). Patient care standards for primary mitochondrial disease in Australia: an Australian adaptation of the Mitochondrial Medicine Society recommendations. Internal medicine journal, 52(1), 110–120. https://doi.org/10.1111/imj.15505 2. Australian Register of Therapeutic Goods – Arginine Product Information. Accessed: 24/04/2024 3. Koenig MK, Emrick L, Karaa A, Korson M, Scaglia F, Parikh S, Goldstein A (2016) Recommendations for the management of stroke-like episodes in patients with mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes. JAMA Neurol 73(5):591–594 4. In-use Stability Report for Arginine 60% injection. Medical Information- Phebra.Email correspondence 2/12/2024.
Groups consulted in development of this guideline	POWH Pharmacy POWH Neurology Clinic Nurse Specialist

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GOVERNANCE	
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