Arginine HCl

Brand names	R-Gene 10
Medication error potential	Overdose in children has resulted in hyperchloremic metabolic acidosis, cerebral edema, and death; hence, dosing calculations should be carefully checked prior to administration.[1] (See Overdose in the Comments section.)
Contraindications and warnings	Known hypersensitivity to arginine or any ingredient contained in the formulation.[1] Anaphylactic reactions have been reported in two children.[2,3] The manufacturer notes that confluent macular rash with reddening and swelling of the hands and face resolved quickly after termination of the infusion and administration of diphenhydramine.[1] One group recommends administration of a 1:1000 arginine intradermal skin test.[3]
Infusion-related cautions	Flushing, nausea, vomiting, numbness, headache, and local venous irritation are associated with rapid infusion.[1] Diphenhydramine should be available in the event of an allergic reaction.[1] The product is hypertonic (i.e., 950 mOsmol/L)[1]; hence extravasation, causing full thickness tissue necrosis, has been reported in three children (ages 3.5–7 years) who received a 10% solution.[4,5] Infuse via antecubital or other suitable vein that is patent. Some had advocated diluting the dose so that the formulation is isotonic before administration.[4]
Dosage	**Pituitary function test/growth hormone reserve test:** 500 mg/kg not to exceed a total dose of 30 g (*adult* dose = 300 mL or 30 g) over 30 minutes. (See the Preparation and Delivery section.)[6-8] Inadequate dosing or prolonged infusion period may diminish the stimulus to the pituitary and nullify the test.[1] **Inborn errors of urea synthesis (pending diagnosis):** Arginine is given with sodium benzoate and sodium phenylacetate to treat hyperammonemia.[9-11] Continue treatment until serum ammonia concentrations are within the normal range. Monitor acid–base balance closely. **Argininosuccinic acid lyase or argininosuccinic acid synthetase deficiency:** Loading dose of 600 mg/kg (12 g/m^2) infused over 90 minutes followed by 600 mg/kg/day (12 g/m^2/day) as a continuous infusion via central venous line.[9,11] **Carbamyl phosphate synthetase or ornithine transcarbamylase deficiency:** Loading dose of 200 mg/kg (4 g/m^2) followed by 200 mg/kg/day (4 g/m^2/day) as a continuous infusion via central venous line.[9] The loading dose should only be repeated in neonates with severe disorders or in those receiving dialysis. If an additional dose is given, the two doses should be given at least 6 hours apart.[9] (See the Maximum Dosage section.) **Other uses** **Necrotizing enterocolitis (NEC) (prevention):** 261 mg/kg/day administered on days 2–5 of life and continued for 28 consecutive days.[12] This recommendation is based on one, randomized controlled study in 152 preterm infants neonates (75 received arginine), which showed that arginine supplementation significantly reduced the incidence of all cases of NEC. It is not known whether the hydrochloride salt was used in this study. There continues to be insufficient evidence to recommend arginine supplementation for infants at risk for NEC.[13,24] **Severe hypochloremia:** Chloride deficit dose (mEq) = 0.2 × weight (kg) × [103 – patient's serum chloride (mEq/L)].[14] Give 50% to 75% of estimated dose over 12 hours and reassess serum chloride. R-Gene 10 contains 0.475 mEq/mL of chloride ions. **Severe metabolic alkalosis:** Arginine should be used only after sodium and potassium chloride supplementation has failed (serum pH >7.55). or Base excess (mEq) = 0.5 × weight (kg) × [patient's plasma bicarbonate (mEq/L) – 24].[14] Give 50% to 75% of estimated dose over 12 hours and reassess plasma bicarbonate. R-Gene 10 contains 0.475 mEq/mL of hydrogen ions. **Pulmonary hypertension:** 500 mg/kg over 30 minutes[16-18]

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Dosage adjustment in organ dysfunction	Patients with renal and hepatic insufficiency may accumulate arginine.[1] Arginine is metabolized to nitrogen-containing products that are renally eliminated; hence, accumulation of arginine may result in an overproduction of nitric oxide, leading to vasodilation and hypotension.[1]
Maximum dosage	The manufacturer recommends a maximum total dose of 30 g.[1]
Additives	Contains 0.475 mEq/mL of chloride. Each 1 mEq chloride delivers 1 mEq hydrogen.[1] (See the Comments section.) R-Gene 10 is a preservative-free product.
Suitable diluents	D10W[1]
Maximum concentration	100 mg/mL (commercially available).[1] Because the solution is hypertonic (950 mOsm/L) it should only be given via a secure IV line.[1]
Preparation and delivery	*Parenteral products should be visually inspected for particulate matter and discoloration before use. Refer to appropriate references for more information on compatibility with other drugs and solutions; compatibility following Y-site delivery, and suggested storage and extended stability.*[15] **Preparation:** For pediatric patients weighing <60 kg, withdraw a weight-based dose from a sealed R-Gene 10 bottle and place in a separate container for IV infusion. This should avoid the inadvertent delivery and administration of the total volume from the commercially available container.[1] The dose (600 mg/kg) can be diluted in 25–35 mL D10W.[20] **Delivery system issues:** Stable in polypropylene syringes and plastic containers made of either polyvinyl chloride or ethylene vinyl acetate.[1] **Compatibility:** Compatible with sodium phenylacetate and sodium benzoate.[1] **Stability:** Store at room temperature (25°C).[1] Postpenetration storage (including infusion time) should not exceed 4 or 24 hours at room (25°C) or refrigerated (2°C to 8°C) temperatures, respectively.[1] Inspect solution prior to administration and discard if it is not clear.
IV push	Not recommended
Intermittent infusion	Over 30 minutes for growth hormone reserve test[1] and over 90–120 minutes for inborn errors of metabolism[9,18]
Continuous infusion	Used for treatment of inborn errors of urea synthesis and hyperammonemia[9-11]
Other routes of administration	None[1]
Comments	**Hyperkalemia:** Because of the high chloride content, those with electrolyte abnormalities may experience hyperkalemia as arginine induces a shift of intracellular potassium extracellularly. Two patients with severe hepatic disease and moderate renal insufficiency developed hyperkalemia following treatment for metabolic alkalosis with L-arginine.[21] Despite aggressive treatment, one of these died.[21] Four *adults* with chronic renal failure on hemodialysis underwent an evaluation of growth hormone metabolism and developed significant hyperkalemia.[22] Those being treated for hyperammonemia may experience hyperchloremic metabolic acidosis. Serum concentrations of chloride and bicarbonate should be monitored to determine the need for bicarbonate therapy. **Hypotension:** Decrease in blood pressure was noted within 10 minutes of drug administration in 11 children (9.4 ± 4.1 years) receiving 500 mg/kg of arginine for pituitary function testing. Blood pressure returned to normal within 30 minutes.[8]