YURIA·PHARM

ARGININE HYDROCHLORIDE

TIVORTIN
42 mg/mL (4.2% w/v) Solution for Infusion (I.V.)
Amino Acid

Rx

Formulation:
Active component: Arginine hydrochloride
1 mL contains 42 mg of arginine hydrochloride (100 mL contains 20 mmol of arginine and 20 mmol of chlorides);
Auxiliary component: Water for injections.

Pharmaceutical form: Solution for Infusion

Pharmacotherapeutic group: Blood transfusion and perfusion solutions. Electrolytes combined with other drugs.
Amino acids. ATC code B05X B01.

Clinical characteristics:
Indications for use:
Arteriosclerotic heart disease and cerebral atherosclerosis, peripheral vessels disease, including the manifestations of angiosclerotic myasthenia, diabetic angiopathy, coronary heart disease, arterial hypertension, states after acute myocardial infarction and acute cerebrovascular accident, myocardiopathy, chronic heart failure, hypercholesterinemia, stenocardia, chronic obstructive pulmonary disease, interstitial pneumonia, idiopathic pulmonary hypertension, chronic postembolic pulmonary hypertension, acute and chronic hepatitis with different etiology, hyperammoniemia, hypoxic states, asthenic states in recovery, including those after inflectional diseases and operative treatment, metabolic alkalosis, depression of thymus function, fetal growth retardation and preeclampsia.

Contraindications:
Increased sensitivity to the drug. Severe renal function impairment, hyperchloremic acidosis; history of allergic reactions; administration of potassium-sparing diuretics or spironolactone.

Dosage and Administration:
The drug is administered intravenously by drops with rate of 10 dpm during the first 10-15 min, then the rate can be increased up to 30 dpm.
The daily dose of the drug is 100 mL of solution.
In patients with severe circulation failure in central and peripheral vessels, in case of pronounced intoxication, hypoxia, asthenic states the dose can be increased up to 200 mL per day.
The maximal infusion rate should not exceed 20 mmol/hour. The dose for children under 12 is 5-10 mL per 1 kg of body mass per day.
The dose for treatment of metabolic alkalosis is calculated as follows:

$$\frac{\text{arginine hydrochloride (mmol)}}{\text{bases excess (Be) (mmol/L)}} \times 0.3 \text{ kg of body mass}$$

The administration is started with a half of the calculated dose. The additional correction can be made after the results of renewed acid-base balance have been obtained.

Adverse reactions:
General disorders: hyperthermia, fever sensation, body pain.
Musculoskeletal system: joint pain.
Alimentary tract: dry mouth, nausea, vomiting.
Skin and skin structure: changes in administration site, including hyperemia, itchiness sensation, skin pallor down to acrocyanosis.
Immune system: hypersensitivity reactions, including rash, urticarial fever, angioedema.
Cardiovascular system: heterotonia, heart rhythm changes, pain in the region of heart.
Nervous system: headache, dizziness, apprehension, asthenia, convulsions, tremor, more often in case of infusion rate exceedance.
Laboratory indicators: hyperkalemia.

Overdosing:
Symptoms: renal failure, hypoglycemia, metabolic acidosis.
Treatment: In case of overdosing, drug infusion must be discontinued. Physiologic reactions monitoring and basic life support should be made. The alkalizing agents and the saluretics, electrolyte solutions (0.9% sodium chloride solution, 5% glucose solution) are administered as appropriate. The therapy is symptomatic.

Administration during pregnancy or lactation:
The drug penetrates the placenta, so it can only be administered during pregnancy when the expected benefit for the mother exceeds the potential risk for the fetus.
No data exist for administration of the drug during lactation.

Administration in children:
The drug is administered to children above 3 years old.

Administration details:
In patients with renal failure the diuresis and the potassium blood level should be verified as the drug may cause the development of hyperkalemia.
The drug should be administered with caution to patients with endocrine dysfunction. The drug can stimulate the insulin and growth hormone release.

In case of dry mouth the blood sugar level should be verified. Caution must be exercised in patients with electrolyte exchange disruptions and kidney diseases. If asthenic symptoms increase concurrently with the drug therapy, therapy must be discontinued.

Effect on ability to drive and operate machines:
Caution must be exercised when driving or operating machinery as the drug can cause dizziness.

Drug interaction and other forms of interaction:
During the use of ARGININE HYDROCHLORIDE (TIVORTIN), it should be taken into consideration that the drug can cause a pronounced and refractory hyperkalemia and a concurrent renal failure in patients who are taking or were taking spironolactone. The prior administration of potassium-sparing diuretics may stimulate increase in the blood potassium level. The concurrent use of aminophylline may increase the blood insulin level.

Pharmacologic properties:
Pharmacodynamics. Arginine (α-amino-δ-guanidinovaleric acid) is an amino acid belonging to the class of conditionally essential amino acids and it is an active and many-sided cellular regulator of many vital functions of the body, and has the protector effects that are important in the critical state of body.
ARGININE HYDROCHLORIDE (TIVORTIN) has antihypoxic, membrane-stabilizing, cytoprotective, anti- oxidative, antiradical, disintoxicating action and acts as an active regulator of intermediary metabolism and power supply processes, takes part in maintaining hormonal balance. It is known that arginine increases the blood level of insulin, glucagon, somatotrophic hormone and prolactin, participates in the synthesis of proline, polyamine, agmatine, is included into the processes of fibrinogenolysis, spermatogenesis, and has membrane depolarizing action. Arginine is one of the main substrates in the cycle of ureapoiesis in liver. Hyperammonemia effect of the drug is realized due to the activation of transformation of ammonia into urea. It has a hepatoprotective action due to its antioxidant, antihypoxic and membrane stabilizing potency, and has a positive influence on the power supply processes in hepatocytes.
ARGININE HYDROCHLORIDE (TIVORTIN) is a substrate for NO-synthase; an enzyme that catalyzes the synthesis of nitric oxide in endotheliocytes. The drug activates guanylate cyclase and increases the level of cyclic guanidine monophosphate in the vessel's endothelium, inhibits the synthesis of protein of VCAM-1 and MCP-1 adhesion and in such a way prevent the formation and development of atherosclerotic plaques, inhibits the synthesis of endothelin-1 which is a powerful vasoconstrictor and stimulator of proliferation and migration of vascular smooth muscle cells. ARGININE HYDROCHLORIDE (TIVORTIN) inhibits the synthesis of asymmetric dimethyl-arginine, which is a powerful endogenous stimulator of oxidative stress. The drug stimulates the function of the thymus gland which produces the T-cells, regulates the blood level of glucose during physical exercise. ARGININE HYDROCHLORIDE (TIVORTIN) has an acid-forming action and helps to correct the acid-base balance.
Pharmacokinetics. At continuous intravenous infusion the maximal concentration of arginine hydrochloride in the blood plasma is reached 20-30 min after the beginning of infusion. ARGININE HYDROCHLORIDE (TIVORTIN) penetrates the placenta, is filtered in malpighian tubes but is almost completely reabsorbed in renal tubules.

Pharmaceutical characteristics:
Main physical and chemical properties: Transparent, colorless or slightly yellowish-brownish liquid; pH 5.0-6.5.
Theoretical osmolarity: 398 mOsm/L.

Incompatibility:
The drug is incompatible with thiopental.

Shelf life:
24 months.

Storage condition:
Store at temperatures not exceeding 30°C. Protect from light. Keep out of reach of children.

Packaging:
100 mL USP Type II glass bottle (Box of 1's)

Caution:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

Manufacturer:
Yuria-Pharm Ltd.
108, Verbovetskogo Str., Cherkassy,
Cherkassy Region, Ukraine 18030
Tel.:+38(044)2810101
www.uf.ua

Importer and Distributor:
despina
Despina Pharma Inc.
3/F #12 A Moonbeam Corner Armstrong Avenue, Moonwalk Subdivision Phase 1, Moonwalk, Parañaque City, Philippines

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