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INSTRUCTION
for medical use

ARSTIFEN®

Composition:
active substance: citric acid anhydrous, trisodium citrate anhydrous, potassium hydrocarbonate;
1 tablet contains citric acid anhydrous 1197 mg; trisodium citrate anhydrous 835.5 mg; potassium hydrocarbonate 967.5 mg;
excipients: lactose monohydrate, mannitol (E 421), sodium saccharin, Powdarome Lemon Premium flavour, adipic acid, polyethylene glycol.

Pharmaceutical form. Effervescent tablets.
Basic physical and chemical properties: round, flat, bevelled edged tablets, white to off white, plain on both sides.

Pharmacotherapeutic group. Urinary concrement solvents. ATC code G04B C.

Pharmacological properties.
Pharmacodynamics.
While dissolving the effervescent tablets Arstifen® in water, potassium-sodium hydrocitrate is formed and carbon dioxide is released.
In this case, residual alkaline ions are formed, which are extracted by the kidneys. Thus, there is an increase in the level of urine pH (depending on the dosage, it is neutralized or alkalized).
This increases the degree of dissociation and at the same time – the degree of dissolution of uric acid/cysteine. Confirmation of the litholysis of uric acid concretions is performed by X-ray.
When taking the drug the allocation of citrates increases and the allocation of calcium in the urine decreases. Alkalization of urine, increased secretion of citrates, and decreased calcium excretion lead to a decrease in the amount of calcium oxalate in urine, since citrate forms stable, complex compounds with calcium in a weak alkaline environment. In addition, citrate ion should be considered as the most effective physiological inhibitor of crystal formation and accumulation of oxalate and calcium phosphate.
Pharmacokinetic.
After a one-day administration of Arstifen® effervescent tablets, the amount of sodium and potassium introduced is excreted from the body by the kidneys within 24–48 hours. With prolonged use of the drug daily intake of potassium and sodium corresponds to daily intake. There are no significant changes in blood gases or electrolytes in blood or blood serum. This means that due to the renal regulation, the acid-base balance in the body is stored, and the accumulation of sodium and potassium with normal kidney function does not occur.

Clinical characteristics.

Indications.

Arstifen® is used for the treatment of urinary stone disease with the purpose of:

- alkalization of urine in patients with urate stones, in the presence of concomitant calcium stones or without them;
- metaphysics of calcium-oxalate concretions (prevention of re-formation of new stones and/or growth of residual fragments).

Contraindications.

- Hypersensitivity to the components drug.
- Renal insufficiency.
- Urinary tract infections caused by bacteria that dilute urea (risk of the formation of struvite stones).
- Metabolic alkalosis.
- Episodic hereditary adynamia.

Interaction with other medicinal products and other forms of interactions.

Interaction studies were performed in adults only. Simultaneous ingestion of substances containing citrate and aluminium can cause increasing the resorption of aluminium, therefore, it is recommended to observe a two-hour pause between the doses of these drugs and Arstifen®.

The drug enhances the therapeutic effect of allopurinol.

Some antihypertensives (aldosterone antagonists and other low potassium diuretics such as triamterenes, spironolactones and amyloidids), ACF inhibitors, sartans, as well as analgesic and anti-inflammatory drugs (non-steroidal anti-inflammatory drugs and peripheral analgesics) can reduce the excretion of potassium, which should be taken into account when concurrently prescribed with Arstifen® (increased risk of hyperkalaemia). The growth of extracellular potassium concentrations reduces the efficacy of cardiac glycosides, while decreasing it increases the effect of arrhythmogenic cardiac glycosides.

In the long-term use of Arstifen®, the accumulation of quinidine in the body in case of its simultaneous administration, as well as the reduction of the effectiveness of nitrofurantoin (alkaline reaction of the medium), salicylates and lithium preparations (accelerated withdrawal) is possible.

Special warnings and precautions for use.

In relation to conditions that promote the formation of urinary concretions (for example, adenoma of the parathyroid gland, uric acid concretions associated with malignomy), it is necessary to take measures of etiotropic therapy.

When uric acid stones are dissolved, it should not be allowed to multi-day excessive urine excretion (pH above 7.8) in view of the possible appearance of a phosphate salt precipitate on the surface of uric acid, which may hinder its further dissolution. In addition, the long-term and pronounced alkaline state of metabolism is undesirable.

Before use it is necessary to determine the level of electrolytes in serum and to check the function of the kidneys. In case of suspicion of renal tubule acidosis, it is necessary to further control the acid-base balance.

During treatment it is necessary to check the parameters of urine and blood tests regularly.

Special attention should be paid to the acid-base balance.

Patients with heart failure should take into account the effect of potassium on myocardial infarction: 1 tablet of Arstifen® contains 380 mg of potassium ions or 9.7 mmoles of potassium, which may affect the effect of cardiac glycosides (increased extracellular potassium concentration reduces the effectiveness of glycosides, and increases its decrease arrhythmogenic effect).

Patients with a disorder of uric acid metabolism should combine the drug administration with allopurinol.
Individuals who adhere to a diet restricting sodium intake should take into account the increased sodium content in this drug (1 tablet contains 220 mg of sodium ions or 9.7 mmol sodium equivalent to 0.57 g of salt).
1 effervescent tablet contains 9.7 mmol (380 mg) of potassium. This should be considered when treating patients with renal impairment or those on a potassium-restricted diet.
During therapy, it is recommended to follow a low-protein diet, i.e. to restrict the use of foods rich in purine content (e.g. meat, sausage products, animal offal, sardines), as well as to reduce the consumption of salt.
Every day it is necessary to drink 2–3 litres of liquid in the form of tea, fruit juice or alkaline mineral water.
The drug does not contain carbohydrates and can be used to treat patients with diabetes mellitus.
Patients with severe hepatic insufficiency should only take Arstifen® under careful monitoring.
The drug contains lactose monohydrate. In this regard, when establishing an intolerance to some sugars, it is necessary to consult a doctor before taking this drug.

Use during pregnancy and lactation.
When using the drug in accordance with the instructions, no adverse effects in the period of pregnancy or breastfeeding have been observed.

Effects on ability to drive and use machines.
Does not affect.

Posology and method of administration.
The optimal daily dose of Arstifen® is determined individually by determining the pH of urine.
For alkalizing urine in patients with uric acid (urate) stones.
To prevent recurrence, the pH of fresh urine should be within 6.2–6.8. The required daily dose of Arstifen® is individual for different patients. Usually the daily dose is 3 effervescent tablets. The daily dose is divided into three equal single doses, which are taken during the day. If the pH of the urine is below 6.2, the dose should be increased. This adjustment should be made by increasing the evening dose to 2, and in exceptional cases – to 3 effervescent tablets. If the pH value exceeds 6.8, the dose should be reduced. It is desirable to adjust the dosage for the account of the evening dose.
For dissolution (hemolitolysis) of uric acid (urate) stones, the pH of urine should be within 7.0 and 7.2.
For the metaphylaxis of calcium stones and alkalization of urine in patients with uric acid stones, in the presence of concomitant calcium stones.
The pH of fresh urine should be adjusted to 6.8–7.4. The dose should be determined on a case-by-case basis to achieve this pH range. Usually it is 3 effervescent tablets. If necessary, the dose can be increased, but in most cases, 5 effervescent tablets are sufficient to achieve results in the specified range of pH values.
The daily dose of 3 effervescent tablets can be taken as a single evening dose or divided into three equal individual doses taken during the day. At higher doses, it is advisable to take 1 effervescent tablet in the morning, 1 – in the afternoon and 2–3 tablets in the evening.
Arstifen® is contraindicated in children under 18 years of age (see section “Children”).
Method of administration
Effervescent tablets of Arstifen® should be dissolved in a glass of water, stirred and drunk immediately.
The liquid may be slightly turbid and have some undissolved particles on the surface.
Usually the control of efficacy is carried out 3 times a day by determining the pH of urine. To do this, use the standard indicator strips included in each package. The indicator area of the test

strip should be briefly immersed in urine. The color of the test strip is then compared with the color scale for 2 minutes, the pH value is read and entered into the control calendar.
Children.
The effectiveness and safety of the use of the drug for children is not sufficiently studied, therefore it is not recommended to prescribe Arstifen® to this age group (under the age of 18).

Overdose.
With normal renal function, the undesirable effect of the drug on the change in physiological parameters of the metabolism is not observed either at the usual recommended dose or in higher, since the removal of excess alkali by the kidneys is a natural mechanism of regulation of acid-base balance in the body.
The upper limit of the pH range of the urine, as indicated above, should not be exceeded over several days, because as a result of an increase in the pH (pH > 7.8), there is an increased risk of crystallization of phosphates; in addition, explicit alkaline metabolic status is not a long-term problem.
Possible overdose can be corrected by reducing the dose of the drug. If necessary, measures should be taken to treat metabolic alkalosis.

Undesirable reactions.
In the case of individual intolerance of any components of the drug possible reactions of hypersensitivity. In some cases, taking pills may cause gastrointestinal infections disorders in patients prone to these. There was reported the appearance of wheezing, heartburn, pain in stomach, flatulence, diarrhea, nausea, vomiting.
Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after drug registration is an important procedure. This allows you to continue to monitor the benefit/risk ratio for this medicine. Medical staff are asked to report all suspected adverse reactions to the State Expert Centre of the Ministry of Health of Ukraine and the applicant via the feedback form website: https://kusum.ua/pharmacovigilance/.

Shelf life.
2 years.

Storage conditions.
Store in the original package at the temperature not more than 25°C.
Keep out of reach of children.

Package.
20 effervescent tablets in a tube, 4 tubes in a carton package with indicator paper and a control calendar.

Condition of supply.
Without prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Manufacturer's location and address of the place of business.
Plot No. M-3, Indore Special Economic Zone, Phase-II, Pithampur, Distt. Dhar, Madhya Pradesh, Pin 454774, India.

Date of last revision