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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ardeaelytosol D 1/1 infusion solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of infusion solution contains:

Natrii chloridum	4.00 g
Kalii chloridum	2.67 g
Natrii lactas	5.94 g

Electrolyte content:

Na^+ [mmol/l]	121.3
K^+ [mmol/l]	35.8
Cl^- [mmol/l]	104.2
Lactate ($C_3H_5O_3^-$) [mmol/l]	52.9
Osmotic pressure [kPa]	695
pH	4.8-6.5

For the full list of excipients, see the section 6.1.

3. PHARMACEUTICAL FORM

Infusion solution

Description of the product: clear, colorless solution

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

It is used for replacing body fluids losses, especially in conditions associated with hypokalemia and acidosis or with a tendency to acidosis.

In cases of potassium losses mainly caused by losses of gastric or intestinal digestive juices including bile and pancreatic juices (by drainage, probe, diarrhoea etc.)

In potassium losses caused by a long-term administration of peroral non-potassium sparing diuretics without potassium supplementation.

4.2. Posology and method of administration

The posology is strictly individual and is guided by the patient's condition. The administration rate is usually about 4 ml/kg/hour; maximum potassium administration rate should not exceed 20 mmol/hour (40 mmol/hour according to some recent sources); it is usually recommended not to exceed the total daily dose of 150 – 200 mmol K^+ /24 hours.

The average daily dose of Ardeaelytosol D 1/1 solution is usually given as 500 – 1,000 ml.

The product is suitable for adults or children without any age restriction.

Method of administration:
Intravenous drop infusion in the closed system.

4.3. Contraindications

Hyperkalaemia, severe alkalosis, hypoxemia, general or local lactatemia.

Overhydration, renal failure (oliguria, anuria), decompensated cardiac failure, pulmonary or cerebral oedema, a major stage of hypertension.

4.4. Special warnings and precautions for use

With regard to the presence of lactate, the product is suitable only in patients with normoxemia, unimpaired liver functioning and sufficient liver perfusion.

Fluid balance, serum electrolytes and acid base balance may need to be monitored before and during administration.

It is necessary to monitor potassium serum levels during the therapy.

Sodium serum levels should be monitored very carefully, especially in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist drugs due to the risk of hyponatraemia (see sections 4.4, 4.5 and 4.8).

High volume infusions must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hyponatraemia (see below).

Hyponatremia

Acute hyponatremia can lead to acute hyponatremic encephalopathy (cerebral oedema).

Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and cerebral oedema) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.

It is necessary to maintain an adequate infusion flow rate. Special precaution is needed with co-therapy by cardiac glycosides.

4.5. Interaction with other medicinal products and other forms of interaction

The product should be administered very carefully in case of concomitant therapy with medicaments that lead to an increase in potassium level such as nonsteroidal anti-rheumatics, beta-blockers, heparin, ACE inhibitors, aldosterone effect blockers.

Special precaution is also needed in case of simultaneous therapy with cardiac glycosides (e.g. digoxin) because they also lead to a potassium blood level increase as the medicaments mentioned above. A parallel increased calcium supply has an influence on the balance between calcium and potassium ions which can result in cardiac arrhythmia.

Drugs leading to an increased vasopressin effect

The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and an increased risk of hyponatremia following inappropriately balanced treatment with i.v. solutions (see sections 4.2, 4.4 and 4.8).

- Drugs stimulating vasopressin release include:
  chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3,4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics.
- Drugs potentiating vasopressin action include:
  chlorpropamide, NSAIDs, cyclophosphamide.
- Vasopressin analogues include:
  desmopressin, oxytocin, vasopressin, terlipressin.

Other medicinal products increasing the risk of hyponatremia also include diuretics in general and antiepileptics such as oxcarbazepine.

4.6. Fertility, pregnancy and lactation

The medicinal product of Ardeaelytosol D 1/1 should be administrated with special caution in pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see sections 4.4, 4.5 and 4.8).

4.7. Effects on ability to drive and use machines

The medicinal product of Ardeaelytosol D 1/1 is administered only in medical facilities and that is why the assessment of its impact on ability to drive or use machines is not relevant.

4.8. Undesirable effects

No direct undesirable effects are given with the product of Ardeaelytosol D 1/1; there is a possibility of general undesirable effects connected with an unsuitable management of the infusion therapy.

Frequency of undesirable effects, as given below, is defined according to the following convention:

Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000); not known (cannot be established from the available data).

Organ system class according to MedDRA database	**Character of undesirable effect**	**Frequency of occurrence**
Blood and lymphatic system disorders	Ion balance breakdown	Not known
Metabolism and nutrition disorders	Hyperkalemia	Not known
	Hyponatremia*	Not known
Nervous system disorders	Acute hyponatremic encephalopathy *	Not known
Cardiac disorders	Oedemas	Not known
	Cardiac failure	Not known
Renal and urinary disorders	Overhydration	Not known

* Hyponatremia may cause irreversible brain injury and death due to development of acute hyponatremic encephalopathy (see sections 4.2, 4.4 and 4.5).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the address:

Státní ústav pro kontrolu léčiv (State Institute for Drug Control)
Šrobárova 48
100 41 Praha 10

Website: www.sukl.cz/nahlasit-nezadouci-ucinek

4.9. Overdose

In case of overdose, hyperkalemia associated with cardiac arrhythmia, hyperlactatemia can occur.

Inadequately managed infusion therapy can also result in disorders of ionic balance, overhydration, hyponatremia, oedemas, cardiovascular decompensation. In such case the infusion should be interrupted, or else diuretics to be administered.

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: infundabilium, ATC code: B05BB01 (Intravenous solutions – solutions affecting the electrolyte balance - electrolytes).

Basic iso-osmotic electrolyte solution with an increased content of potassium and lactate.

With regard to an increased content of lactate, it has a slight alkalization effect after administration.

5.2. Pharmacokinetic properties

a) General information – no active metabolites are generated

b) Characterization of the active substances – it contains simple inorganic salts – body natural ions. They are water-soluble, fat-insoluble.

c) Characterization after the administration in patients – it is a product intended for intravenous use. It persists in the blood circulation only for a few tens of minutes after i.v. administration; it leaks into extravascular compartment easily.

Fully dissociated ions are distributed in the body according to concentration gradients in extracellular fluid; free water is distributed according to concentration gradient in all compartments.

Ionic balance is dependent on the excretion of individual ions by kidneys and is particularly subordinated to mineralocorticoids regulation. Water homeostasis is regulated by antidiuretic hormone.

Lactate is changed into pyruvate and then into bicarbonate provided that the liver cells are undamaged having a sufficient oxygen supply.

5.3. Preclinical safety data

It is a product with a long-term usage ("well implemented therapeutic use") in which no preclinical studies had been performed with its introduction into the therapy.

There have been no undesirable effects known from the literature. The product used according to the recommended method is entirely safe.

6. PHARMACEUTIAL PARTICULARS

6.1. List of excipients

Aqua pro iniectione

6.2. Incompatibilities

The product is compatible with the most of commonly used medicaments. No physical or chemical incompatibilities are known except of those with solutions with oxidants content or solutions showing a different pH value.

6.3. Shelf life

3 years provided that the package is intact.

The shelf life after the first opening:

Chemical and physical stability before the use after the opening was confirmed for 48 hours at 25°C.

From microbiological point of view, the product should be used immediately. If it is not used immediately, then the period and storage conditions of the product after the opening before the use are within the reliability of the user and in common case it should not be longer than 24 hours
at 2-8 °C as far as the opening was not performed under the controlled and validated aseptic conditions.

6.4. Special precautions for storage

Protect from frost.

6.5. Nature and contents of container

Infusion glass bottle with a rubber stopper and a metallic closure, carton box.

Package size: 1x 80 ml, 1x 100 ml, 1x 250 ml, 1x 500 ml
20x 80 ml, 20x 100 ml, 10x 250 ml, 10x 500 ml

Not all package sizes may be marketed.

6.6. Special precautions for use, disposal and other handling

This medicinal product is dispensed entirely on the base of medical prescription.

It is usually administered by an infusion set into peripheral vein.

Parenteral products should be checked up visually before the use. The product must not be administered if visible solid particles are present or the package is not intact.

The preparation is intended only for a single use.

Any unused product or waste should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

ARDEAPHARMA, a.s., Třeboňská 229, 373 63 Ševětín, Česká republika (Czech Republic)

8. MARKETING AUTHORISATION NUMBER(S)

76/785/95-C

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of the first authorization: 11th October 1995

Date of the last renewal of the authorization: 8th February 2017

10. DATE OF REVISION OF THE TEXT

13th April 2018