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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ardeaelytosol H 1/1 infusion solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of infusion solution contains:

Natrii chloridum	6.00 g
Kalii chloridum	0.40 g
Calcii chloridum hexahydricum (or 0.13 g calcii chloridum dihydricum)	0.20 g
Magnesii chloridum hexahydricum	0.20 g
Natrii lactas	3.03 g

Electrolyte content:

Na^+	129.7 mmol/l
K^+	5.4 mmol/l
Ca^{2+}	0.9 mmol/l
Mg^{2+}	1.0 mmol/l
Cl^-	111.8 mmol/l
Lactate ($C_3H_5O_3^-$)	27.0 mmol/l
Osmotic pressure	276 mosm/l
pH:	4.8 – 7.0

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 water and electrolytes if acid base balance is in equilibrium or in case of a moderate tendency to acidosis without hypoxia. In case of isotonic or hypotonic dehydration of various origin, in losses of extracellular fluid as a short-term replacement of intravascular volume.

For rehydration after compensation with colloid plasma-expanders.

Vehiculum for other medicaments.

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

4.2. Posology and method of administration

Intravenous drop infusion in the closed system. It is usually administered by the infusion set into peripheral vein. It can be administered also in central vein.

The posology is strictly individual. The dosage must be adjusted to the age, body weight and clinical condition of each individual patient and running losses of fluids and electrolytes should be continuously monitored.

Maximum daily dose 30-45 ml/kg, administration rate usually 5-10 ml/kg/hour.

Average daily dose is 500 – 1,500 ml, in case of large electrolyte losses even a few litres daily, usually, however, in combination with other infusion solutions.

4.3. Contraindications

Hypertonic dehydration, hyperkalemia, hypernatremia, hyperchloremia, hypoxemia, hyperlactatemia, severe metabolic alkalosis.

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

4.4. Special warnings and precautions for use

The administration of the product should be considered very carefully in cases of renal insufficiency, cardiac insufficiency, circulatory failure and hypervolemia, hypoproteinaemia, urinary tract obstruction, in patients taking medicaments that cause sodium retention (e.g. corticosteroids).

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

In case of application of major amount of the product, central venous pressure and diuresis should be monitored and search for symptoms of cardiac failure, especially in elderly and critically ill patients.

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

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

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 H 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

With regard to the character and indication of the product, Ardeaelytosol H 1/1 has no influence on ability to drive and use machines.

4.8. Undesirable effects

There is a possibility of general undesirable effects connected with administration of Ardeaelytosol H 1/1 caused by an unsuitable management of the infusion therapy (the dose, administration rate).

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
Metabolism and nutrition disorders	Ion balance breakdown Hyperlactatemia Overhydration Hyponatremia*	Not known
Cardiac disorders	Oedemas Cardiac failure	Not known
Nervous system disorders	Acute hyponatremic encephalopathy *	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

If well-balanced water and ion balance is respected, then no overdose is to be taken into account. In case of accidental overdose, overhydration with subsequent overload of the circulation, hyperlactatemia, hyponatremia, oedema formation can occur. Primary therapy consists in immediate stop of infusion. If necessary, the therapy with diuretics can be started. Electrolytes levels should be monitored and adjusted in case of their imbalance.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

- Pharmacotherapeutic group: infundabilium, ATC code: B05BB01 (Intravenous solutions – solutions affecting the electrolyte balance - electrolytes).
- Basic, almost iso-osmotic infusion solution containing ions and lactate.
- Electrolyte composition of the product of Ardeaelytosol H 1/1 is similar to electrolyte composition of extracellular fluid. That is why it is used for achievement and maintaining of common osmotic conditions in extracellular and intracellular space.
- With regard to balanced chloride/lactate anions ratio, the administration of the solution has no significant influence on acid base balance; it has only a very slight alkalization effect.

5.2. Pharmacokinetic properties

a) General information – active metabolites are not generated with inorganic salts. These salts are water-soluble, fat-insoluble.

b) Characterization of the active substances – it contains mainly simple inorganic salts – body natural ions.

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 very easily.

d) Electrolytes are distributed in the body according to concentration gradients in extracellular fluid, free water is distributed according to the concentration gradient in all compartments. Ionic balance is dependent on excretion of individual ions by kidneys and is subordinated especially to mineralocorticoids regulation.

   Water homeostasis is controlled 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

The issue of safety of the preparation for the body is not relevant with regard to the composition and usage of the product as well as to the properties of the active substances. 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.

6. PHARMACEUTIAL PARTICULARS

6.1. List of excipients

Aqua pro iniectione

6.2. Incompatibilities

The solution contains Ca^{2+} and Mg^{2+} ions; after adding phosphates, carbonates, hydrogen carbonates or oxalates, a precipitate can be formed, especially in case of a prolonged standing.

When Ardeaelytosol H 1/1 is combined with other products, a difference in pH is necessary to be monitored.

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: 1 x 80 ml, 1 x 100 ml, 1 x 250 ml, 1 x 500 ml
20 x 80 ml, 20 x 100 ml, 10 x 250 ml, 10 x 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.

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 medicinal 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)

76/225/95-C

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of the first authorization: 19th April 1995

Date of the last renewal of the authorization: 1st July 2015

10. DATE OF REVISION OF THE TEXT

13th April 2018