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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ardeaelytosol H 2/3 infusion solution

Ardeaelytosol H 1/2 infusion solution

Ardeaelytosol H 1/3 infusion solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ardeaelytosol	**H 2/3**	**H 1/2**	**H 1/3**
1000 ml o infusion solution contains:			
Natrii chloridum	4.00 g	3.00 g	2.00 g
Kalii chloridum	0.27 g	0.20 g	0.13 g
Calcii chloridum hexahydricum	0.13 g (or 0.09 g calcii chloridum dihydricum)	0.10 g (or 0.07 g calcii chloridum dihydricum)	0.07 g (or 0.05 g calcii chloridum dihydricum)
Magnesiii chloridum hexahydricum	0.13 g	0.10 g	0.07 g
Natrii lactas	2.02 g	1.51 g	1.01 g
Glucosum (as either glucosum or glucosum monohydricum)	16.67 g	25.00 g	33.33 g
Electrolyte content:			
Na^+ [mmol/l]	86.4	64.8	43.2
K^+ [mmol/l]	3.6	2.7	1.8
Ca^{2+} [mmol/l]	0.6	0.5	0.3
Mg^{2+} [mmol/l]	0.6	0.5	0.3
Cl^- [mmol/l]	74.5	55.9	37.2
Lactate ($C_3H_5O_3^-$) [mmol/l]	18.0	13.5	9.0
Osmotic pressure [kPa]	625	636	645
Energy value [kJ/l]	286	429	572
pH	3.5-6.0	3.5-6.0	3.5-6.0

Excipients with a known effect:

The medicinal product contains sodium bisulphite.

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

3. PHARMACEUTICAL FORM

Infusion solution

Description of the preparation: clear, colourless or no more than slightly yellowish solution

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Water and ion losses by sweating, breathing, in fever

Initial rehydration after operations

Rehydration in small children, new-borns and infants

4.2. Posology and method of administration

The posology is individual according to the losses, guided by the patient's condition.

Dosage rate is about 4-8 ml/kg/hour. Infants about 140 ml/kg/24 hours.

Method of administration:
Intravenous drop infusion in the closed system

4.3. Contraindications

Hypotonic dehydration

Hypotonic overhydration

4.4. Special warnings and precautions for use

Fluid balance, serum glucose, serum sodium and other serum electrolytes are necessary to be monitored before and during administration, 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.

Intravenous glucose infusion solutions are usually isotonic solutions. Nevertheless, solutions containing glucose become extremely hypotonic in the body due to rapid glucose metabolization (see sections 4.2, 4.5 and 4.8).

In physiologically hypotonic solutions, serum sodium monitoring is especially important.

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 and cerebral contusion) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatremia.

The product contains sodium bisulphite that can cause severe allergic reactions and bronchospasm.

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 such as:
  chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3,4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics.
- Drugs potentiating vasopressin action such as:
  chlorpropamide, NSAIDs, cyclophosphamide.
- Vasopressin analogues such as:
  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 2/3 (H 1/2, H 1/3) should be administrated with special caution in pregnant women during labour, particularly if administered in combination with oxytocin, because of the risk of hyponatremia (see sections 4.4, 4.5 and 4.8).

4.7. Effects on ability to drive and use machines

With regard to the character of the product and its indication is not relevant.

4.8. Undesirable effects

No direct undesirable effects are given with the product of Ardeaelytosol H 2/3 (H 1/2, H 1/3); 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
Cardiac disorders	Oedemas	Not known
	Cardiac failure	Not known
Renal and urinary disorders	Overhydration	Not known
Metabolism and nutrition disorders	Hyponatremia*	Not known
Nervous system disorders	Hyponatremic encephalopathy*	Not known

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

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

The overdose is manifested mainly as congested heart failure. The infusion should be necessarily stopped, or else diuretics be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

- Pharmacotherapeutic group: infundabilium, ATC code: B05BB02 (Intravenous solutions – solutions affecting the electrolyte balance – electrolytes with carbohydrates).
- Basic isosmotic hypoionic solution. It has a slight acidification effect after administration.
- The solution is intended for replacing water and electrolyte losses. It acts as a hypotonic solution after glucose utilization.

5.2. Pharmacokinetic properties

Electrolytes are distributed in the body according to concentration gradients in extracellular fluid. Free water is distributed in all body compartments according to concentration gradient.

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 metabolized into bicarbonate in the liver. Glucose is a basic substrate of cellular energy metabolism. Glucose is evenly distributed in the body and glucose enter into cells is dependent on insulin action. In kidneys, glucose goes through freely via glomerular filtration and is completely reabsorbed in tubules. If renal threshold is exceeded (approximately in glycaemia higher than 10 mmol/l), glycosuria occurs. In such case, glucose acts as an osmotic diuretic.

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 substance.

6. PHARMACEUTIAL PARTICULARS

6.1. List of excipients

Citric acid monohydrate

Sodium bisulphite

Aqua pro iniectione

6.2. Incompatibilities

If the product of Ardeaelytosol H 2/3 (H 1/2, H 1/3) is combined with other medicinal products, the difference in pH should be watched.

When mixed with the products containing oxalates, phosphates or bicarbonates, a precipitate can develop.

6.3. Shelf life

2 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.

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)

Ardeaelytosol H 2/3: 76/762/95-A/C

Ardeaelytosol H 1/2: 76/762/95-B/C

Ardeaelytosol H 1/3: 76/762/95-C/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: 19th October 2016

10. DATE OF REVISION OF THE TEXT

13th April 2018