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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ardeaelytosol R 1/2 infusion solution
Ardeaelytosol R 1/3 infusion solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ardeaelytosol	**R 1/2**	**R 1/3**
1000 ml of infusion solution contains:		
Natrii chloridum	4.30 g	2.87 g
Kalii chloridum	0.15 g	0.10 g
Calcii chloridum hexahydricum	0.25 g (or 0.17 g calcii chloridum dihydricum)	0.17 g (or 0.11 g calcii chloridum dihydricum)
Glucosum (as either glucosum or glucosum monohydricum)	25.00 g	33.33 g
Electrolyte content:		
Na^+ [mmol/l]	73.6	49.0
K^+ [mmol/l]	2.0	1.3
Ca^{2+} [mmol/l]	1.1	0.8
Cl^- [mmol/l]	77.9	51.9
pH	3.5 – 6.0	3.5 – 6.0
Osmotic pressure [kPa]	675	676
Energy value [kJ/l]	429	572

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

3. PHARMACEUTICAL FORM

Infusion solution
Description of the product: clear, colorless or slightly yellowish solution

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Hypertonic dehydration (in cases when the patient's kidneys are able to compensate acidosis caused by Cl^- ions that are present in the solution in a higher amount in comparison with ECF).
A carrying solution for other drugs.

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.
Method of administration:

Intravenous drop infusion in the closed system

4.3. Contraindications

Hypotonic dehydration

Hypotonic overhydration

Acidosis

Decompensated heart functioning

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.

Additional medicinal or other substances must not be added if it is not clear that these substances are compatible.

The product contains Ca^{2+} ions – if any clot is visible after the addition of other preparation, for which Ardeaelytosol R1/2 (R1/3) is a carrying solution, then such solution must not be used – a different carrying infusion solution, which will be compatible, should be used for the added drug.

It is necessary to maintain an adequate infusion flow rate

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 R 1/2 (R 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 R 1/2 (R 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 encefalopathy*	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

If well-balanced water and ion balance is respected, then no overdose is to be taken into account.

In case of inadequately managed infusion therapy, disorders of ionic balance, overhydration, oedemas, cardiovascular decompensation can occur. If necessary, the therapy means immediate stop of infusion, it is possible to start the therapy with diuretics.

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: infundabilium, ATC code: B05BB02 (Intravenous solutions – solutions affecting the electrolyte balance – electrolytes with carbohydrates).

Basic infusion solution containing sodium, potassium, calcium, chloride ions and glucose.

It has a slight acidification effect after administration. It acts as a hypotonic solution after glucose utilization.

5.2. Pharmacokinetic properties

a) General information – no active metabolites are generated.

b) Characterization of the active substances –the solution contains simple inorganic salts and glucose - body natural substances, 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.

Sodium and chloride 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.

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

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 because all components of the solution are naturally contained in animal and human plasma.

There have been no undesirable effects known from the literature. The product used according to the recommended method is entirely safe. The safety of drugs potentially added should be assessed separately.

6. PHARMACEUTIAL PARTICULARS

6.1. List of excipients

Aqua pro iniectione

6.2. Incompatibilities

The product is compatible with most of medicines commonly used. Additives with known incompatibility should not be used

No physical or chemical incompatibilities are known except of those with solutions with oxidants content or solutions showing a different pH value.

It contains Ca^{2+} ions; after adding of phosphates, carbonates, hydrogen carbonates or oxalates, clots formation can occur, especially in case of a prolonged standing.

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.

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)

Ardeaelytosol R 1/2: 76/923/95-A/C
Ardeaelytosol R 1/3: 76/923/95-B/C

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of the first authorization: 22nd November 1995

Date of the last renewal of the authorization: 19th October 2016

10. DATE OF REVISION OF THE TEXT

13th April 2018