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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ardeaelytosol conc. natriumhydrogenkarbonát 4,2% concentrate for solution for infusion
Ardeaelytosol conc. natriumhydrogenkarbonát 8,4% concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ardeaelytosol conc. natriumhydrogenkarbonát	**4,2%**	**8,4%**
1000 ml of the concentrate for infusion solution contains:		
Natrii hydrogenocarbonas	42.0 g	84.0 g
Electrolyte content:		
Na^+	500 mmol/l	1000 mmol/l
HCO_3^-	500 mmol/l	1000 mmol/l
pH	7.0-8.5	7.0-8.5
Osmotic pressure	2 418 kPa	4 835 kPa

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

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion
Description of the product: clear, colorless solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Metabolic acidosis (in urgent conditions). Therapy of acute hyperkalemia.

4.2 Posology and method of administration

Dosage is individual. Dilution 1:3 - 1:6 by adding into a carrying solution. The calculation of the dose according to the base deficit: $NaHCO_3$ (mmol/l) = body weight (kg) x 0.3 x negative BE (mmol/l). Base deficit should be corrected gradually; no more than 50 % of the calculated amount is administered in practice. Also the values of pH and pCO_2 should be considered as well as the patient's general clinical condition. In urgent conditions, the solution can be used undiluted. One half of the calculated amount is administered within about 2 hours, further then as a slow infusion according to the total amount of fluids and electrolytes applied within 24 hours, under repeated laboratory check-ups.

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

4.3 Contraindications

Metabolic alkalosis, respiratory acidosis, hypokalemia, hypernatremia (higher than 150 mmol/l).

4.4 Special warnings and precautions for use

With regard to sodium content, the product should be applied very cautiously in patients with congestive heart failure, impaired renal functioning, hepatic cirrhosis, hypertension and in patients treated with corticoids.

The concentrate administered undiluted (e.g. in urgent resuscitation) irritates endothelium of peripheral veins due to the high osmolality

Paravenous administration can result in tissue necrosis.

4.5 Interaction with other medicinal products and other forms of interaction

In common short-term usage for adjustment of internal environment, no major interactions occur. However, the long-term administration of major doses can lead to urine alkalization, then the elimination may be changed and efficacy of some drugs may thus be influenced. In case of urine alkalization (above pH 7.5), the efficacy and toxicity of ephedrine, pseudoephedrine and quinidine are increased (due to lowering of renal excretion). The efficacy and toxicity of chlorpropamide, lithium, salicylates and barbiturates are lowered (an increase in renal excretion). An increase in blood pH results in a decrease in kalemia, and that is why the efficacy and toxicity of cardiac glycosides are increased.

4.6 Fertility, pregnancy and lactation

If the administration of the medicinal product is required by the patient's condition, then such use during pregnancy and lactation is not contraindicated.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

No undesirable effects are given with the products of Ardeaelytosol conc. natriumhyrogenkarbonát 4,2 % (8,4%). However, there is a possibility of general undesirable effects connected with an unsuitable management of the infusion therapy such as metabolic alkalosis, hypernatremia, cardiac failure, oedemas, ion balance breakdown.

Organ system class according to MedDRA database	**Character of undesirable effect**	**Frequency of occurrence**
Blood and lymphatic system disorders	Ion balance breakdown	Accurate data are not available; it can be expected that they occur rarely with the frequency of occurrence >1/10,000 and < 1/1,000.
Metabolism and nutrition disorders	Metabolic alkalosis	Accurate data are not available; it can be expected that they occur rarely with the frequency of occurrence >1/10,000 and < 1/1,000.
Cardiac disorders	Oedemas	Accurate data are not available; it can be expected that they occur rarely with the frequency of occurrence >1/10,000 and < 1/1,000.
	Cardiac failure	Accurate data are not available; it can be expected that they occur rarely with the frequency of occurrence >1/10,000 and < 1/1,000.
Renal and urinary disorders	Hyperhydration	Accurate data are not available; it can be expected that they occur rarely with the frequency of occurrence >1/10,000 and < 1/1,000.

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 with the product can result in metabolic alkalosis (especially in patients with impairment of renal functioning). The most frequent symptoms include shortness of breath, muscle weakness (especially with concurrent hypokalemia), muscle hypertonicity, twitching and cramps, disorders of central nervous system (restlessness, convulsions, coma). The therapy is based on the adjustment of electrolyte balance, especially correction of potential calcium, potassium and chloride deficits, under parallel monitoring of acid base balance, ionogram and osmolality.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: infundabilium, ATC code: B05XA02 (Intravenous solution additives – electrolyte solutions – sodium bicarbonate).

Concentrated infusion solution is used for the adjustment of metabolic acidosis.

Basic infusion solution for the adjustment of acid base balance. After administration, it has an alkalisation effect.

5.2 Pharmacokinetic properties

$NaHCO_3$ is dissociated in aqueous solution into sodium cation (Na^+) and bicarbonate anion (HCO_3^-). The product administration increases bicarbonate blood levels directly. It crosses hemato-encephalic barrier having a delay. It goes through placental barrier easily. After intravenous application, bicarbonate anion reacts with hydrogen cation developing carbonic acid which is dissociated into carbon dioxide and water. A decrease in concentration of hydrogen cations leads to an increase in blood pH. Excessive bicarbonate together with Na^+ is eliminated by kidneys and the urine is alkalized.

5.3 Preclinical safety data

The product is not toxic. The active substance is contained in blood as a dissociated form.

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

Glacial acetic acid

Disodium edetate dihydrate

Aqua pro iniectione

6.2. Incompatibilities

Hydrocortisone and theophylline medicinal products must not be added into hydrogen carbonate infusion. With regard to alkali reaction, it should not be mixed with products containing Ca^{2+}, Mg^{2+} or phosphates.

6.3. Shelf life

2 years provided that the package is intact.

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 provided that the opening/dilution 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 200 ml
20x 80 ml, 10x 200 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.

The product must not be used undiluted! The preparation is not intended for direct infusion. It is administered intravenously diluted with a larger amount of carrying infusion solution.

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 infusion solution is a concentrated solution, and therefore it should not be stored at the temperature lower than common room temperature. Crystals that may be developed during the storage can be dissolved by warming of the bottle. As a preventive precaution against unwantedly infused crystals with the solution, an infusion set provided with a filter is necessarily to be used.

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 conc. natriumhydrogenkarbonát 4,2%: 76/758/95-A/C

Ardeaelytosol conc. natriumhydrogenkarbonát 8,4%: 76/758/95-B/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: 15th February 2017

10. DATE OF REVISION OF THE TEXT

4th September 2018