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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ardeanutrisol G 5% infusion solution

Ardeanutrisol G 10% infusion solution

Ardeanutrisol G 20% infusion solution

Ardeanutrisol G 40% infusion solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of infusion solution contains:

Ardeanutrisol	**G 5%**	**G 10%**	**G 20%**	**G 40%**
Glucosum:	50.0 g	100.0 g	200.0 g	400.0 g
Osmotic pressure:	670 kPa	1342 kPa	2684 kPa	5369 kPa
Energy value	858 kJ/l	1716 kJ/l	3432 kJ/l	6864 kJ/l
pH	3.0 – 6.5	3.0 – 6.5	3.0 – 6.5	3.0 – 6.5

Excipients with a known effect: sodium bisulphite E 222 (G 20%, G 40%)

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

Covering the need of energy and fluids within parenteral infusion therapy in post-operative conditions, shock, intoxications, liver diseases, in protracted vomiting and diarrhoea, in intoxications as a part of forced diuresis.

Prophylaxis of hypoglycaemia in overdose by peroral antidiabetics or insulin.

The solution of 50 g/l glucose is iso-osmotic with blood plasma; it is used for the supplementation of body fluids volume, especially in case of "pure water" loss, in combination with electrolytes to supplement fluids in isotonic dehydration, as a carrying solution for other drugs.

The solution of 100 g/l glucose is used as a carrying solution for other drugs, as a source of energy and water in parenteral nutrition.

The solutions of 200 g/l and 400 g/l glucose are used as a source of energy in parenteral nutrition, as a part of all-in-one mixtures, in the therapy of hypoglycaemic conditions, in osmo-therapy of pulmonary oedema, in intracranial hypertension and eclampsia.

4.2. Posology and method of administration

Intravenous drop infusion in the closed system.

The dosage is individual and should be necessarily adjusted to the age, body weight and patient's clinical condition.

Total dose and administration rate is guided by the indication and patient's clinical condition. In the therapy of hypoglycaemic conditions, the administered dose should necessarily be managed by current values of glycaemia and patient's clinical condition.

Recommended posology:

50 g/l solution: max. 40 ml/kg of BW/day, usually 2 - 4 ml/kg/hour, totally 500 - 2000 ml per day

100 g/l solution: max. 30 ml/kg of BW/day, usually 2 ml/kg/hour, totally 500 - 1000 ml per day

200 g/l solution: max. 30 ml/kg of BW/day, usually 1 – 1.5 ml/kg/hour, totally 500 - 1000 ml per day

400 g/l solution: max. 20 ml/kg of BW/day, usually 0.5 ml/kg/hour, totally 500 ml per day

50 g/l and 100 g/l solutions are administered usually into peripheral vein, the solutions with higher concentrations via central venous catheter.

In case of danger of hypoglycaemia, also the 400 g/l solution can be administered slowly into peripheral vein, the maximum administration rate is 3 ml/min.

4.3. Contraindications

Hyperglycaemia, diabetes mellitus not compensated properly, acute phase in cerebral ischaemia, hypoxaemia, hypotonic dehydration, hyperhydration conditions, major disorders of renal functioning, hypokalaemia

50 g/l solution: hyperhydration, hypo-osmolality, oedemas

Hypertonic solutions: hyper-osmolality, intracranial and intraspinal bleeding, dehydration.

4.4. Special warnings and precautions for use

- There is need to observe adequate infusion flow rate, to monitor the patients' clinical condition continuously, and, especially in diabetics also glycaemia levels.
- 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.
- Special caution should be exercised in the administration of concentrated glucose solutions in patients with advanced cerebral atherosclerosis.
- Application of glucose solutions with the concentration higher than 10 % in the therapy of hypoglycaemic conditions in infants and children under 3 years of age is not recommended due to not negligible osmotic effect and due to danger of induction of significant hyperglycaemia and insulin secretion stimulation.
- The solution must not be applied concurrently before or after the blood transfusion via the same infusion set with regard to the risk of pseudo-agglutination.
- The products of Ardeanutrisol G 20% and Ardeanutrisol G 40% contain sodium bisulphite as an antioxidative excipient, which can rarely cause severe allergic reactions and bronchospasm. Total prevalence of hypersensitivity to bisulphites in common population is low and is not known (it is

estimated up to 0.5 % according to some sources). The incidence of hypersensitivity to bisulphites is more common in asthmatics (especially in corticoid dependent asthma) and even more common in children's asthmatics. Precise medical history is necessary to be taken before the application of glucose infusion, and then, in case of asthmatic patient or patients suffering from known bisulphite food intolerance, any different glucose infusion without bisulphites is more suitable.

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

High doses of catecholamines and steroids can have an influence on insulin resistance condition.

The use of peroral antidiabetics or insulin leads to a decrease in blood glucose.

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 Ardeanutrisol G 5% (G 10%, G 20%, G 40%) 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, method of administration and indications of the product, it has no influence on ability to drive and use machines.

4.8. Undesirable effects

General characteristics – hyperglycaemia or else local irritation of the vascular wall at the application site can be expected after the application of high concentrations (G 20%, G 40%).

Long-term administration or rapid infusion of large volumes of iso-osmotic solutions (G 5%) can result in oedemas and water intoxication. It can be avoided by a decrease in infusion rate.

Long-term or rapid administration of hypertonic solutions can result in hyperglycaemia, glycosuria and dehydration. Concurrent insulin administration in case of the administration of high concentrations can prevent glycosuria and hyperglycaemia.

In hypoxemia, there is a danger of conversion of administered glucose into lactate with risk of hyperlactatemia.

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	Hyperglycaemia Hyperlactataemia Hyponatremia*	Not known
Cardiac disorders	Oedemas	Not known
Vascular disorders	Local irritation of the vascular wall	Not known
Renal and urinary disorders	Dehydration Glycosuria Water intoxication	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

If contraindications and correct dosage are respected, then no overdose is to be taken into account.

In case of accidental overdose, hyperglycaemia, glycosuria, hyperosmolality, hyponatraemia, hyperglycaemic and hyperosmolar coma may occur. Primary therapy consists in immediate stop of infusion. In case of overhydration, the therapy with diuretics can be started.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

- Pharmacotherapeutic group: infundabilium, ATC code: B05BA03 (Intravenous solutions – solutions for parenteral nutrition - carbohydrates).
- Mechanism of action: Glucose is an important source of energy almost for all cells of the body. Depending on insulin action, glucose enters into cells where is metabolized into pyruvate and under anaerobic conditions into lactate. Both of these substances are oxidised into carbon dioxide and water within Krebs cycle. Glucose goes through freely via glomerular filtration and is completely reabsorbed in tubules if renal threshold in glycaemia higher than 10 mmol/l is not exceeded.
- Pharmacodynamic properties: Glucose infusion solutions are intended for covering the need of energy and water supplementation in the body. 1 g of glucose corresponds to energy of 17.16 kJ (4 kcal).

5.2. Pharmacokinetic properties

a) General information: Glucose is monosaccharide which is a basic source of energy of intracellular metabolism. Glucose is evenly distributed in the body and glucose enter into most cells is dependent on insulin action. Active metabolites are not generated. Glucose is water-soluble, fat-insoluble.

b) Characterization of the active substances:

- Glucose is evenly distributed in the body after intravenous administration; first glucose enters intravascular and later intracellular space. Glucose enter into most cells is dependent on insulin action – glucose enter into brain and some other organs is non-insulin dependent.
- Biotransformation: all cells have the ability to oxidise glucose either aerobically into pyruvate or anaerobically into lactate. Pyruvate and lactate can further be oxidised in Krebs cycle into carbon dioxide and water under energy release. Final products from glucose metabolization are then eliminated by lungs and kidneys.
- Elimination: glucose goes through freely via glomerular filtration and is completely reabsorbed in tubules. In healthy people, practically no glucose is eliminated by kidneys. Maximum glucose utilization rate is from 500 to 750 mg/kg of body weight/hour. If renal threshold is exceeded (approximately in glycaemia higher than 10 mmol/l), glycosuria occurs. In such case, glucose acts as an osmotic diuretic.

c) Characterization after the administration in patients:

- Relations between active substance concentration and potential undesirable effects: high concentrations (G 20%, G 40%) may cause hyperglycaemia, glycosuria and dehydration.
- Other factors (age, sex, smoking) have not an influence on the effectiveness of glucose infusion solutions.

5.3. Preclinical safety data

With regard to the composition, method of the use of the product and glucose properties as a body natural active substance, the issue of the safety for the body is not relevant. The solution has been used for many years without problems.

6. PHARMACEUTIAL PARTICULARS

6.1. List of excipients

Aqua pro iniectione

Citric acid monohydrate (G 20%, G 40%)

Sodium bisulphite (G 20%, G 40%)

6.2. Incompatibilities

The product is not administered by infusion set concurrently with plasma and blood derivates.

When the glucose infusion solutions are used as vehiculum, pH of glucose solution is necessarily to be taken into account. Compatibilities with various active substances are necessarily to be considered with regard to the acid reaction.

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

For intravenous use.

Instructions for use – if the products (G 5% or G 10%) are used as carrying solutions for other drugs, then it is necessary to check whether no clot or opacity is developing after the mixing and **before** the use of the mixture. Such medicine **must not be administered in glucose solution!**

Use the solution only when it is clear, no visible solid particles are present and the package is intact.

The preparation is intended only for a single use.

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

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)

Ardeanutrisol G 5%: 76/232/95-A/C

Ardeanutrisol G 10%: 76/232/95-B/C

Ardeanutrisol G 20%: 76/232/95-C/C

Ardeanutrisol G 40%: 76/232/95-D/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: 29th July 2015

10. DATE OF REVISION OF THE TEXT

13th April 2018