Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paedisol Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of Paedisol solution for infusion contains:

Sodium chloride	6.429 mg
Potassium chloride	0.298 mg
Calcium chloride dihydrate	0.147 mg
Magnesium chloride hexahydrate	0.203 mg
Sodium acetate trihydrate	4.082 mg
Glucose monohydrate (equivalent to Glucose 10.0 mg)	11.0 mg

equivalent to:

Na^+	140 mmol/l;
K^+	4 mmol/l;
Ca^{2+}	1 mmol/l;
Mg^{2+}	1 mmol/l;
Cl^-	118 mmol/l;
Acetate ions	30 mmol/l;
Glucose	55.5 mmol/l

Total cation/anion content 148 mval/l each, glucose 10 mg/ml.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.
A clear, colourless to slightly yellow aqueous solution.

pH: 5.3–5.7
Theoretical osmolarity: 351 mOsmol/l
Titration acidity: to pH 7.4 £ 5 mmol/l
Energy content:168 kJ/l (40 kcal/l)
Carbohydrate content: 10 g/l

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Paedisol is indicated for paediatric patients such as neonates (0 to ≤28 days), infants (28 days to ≤2 years), children (2 to ≤12 years), and adolescents (12 to ≤14 years) as follows:

- Perioperative plasma-isotonic fluid and electrolyte replacement with partial coverage of carbohydrate requirements,
- Short-term intravasal volume replacement,
- Treatment of isotonic dehydration,
- Use as carrier solution for compatible electrolyte concentrates and medicinal products.

4.2 Posology and method of administration

Posology

Paediatric population

The dosage in perioperative intravenous infusion therapy depends on the fluid, electrolyte, and glucose requirements: During the first hour e.g. 10 – 20 ml/kg/hr, and thereafter for regulation of the infusion rate according to basic and correction requirements with monitoring of relevant cardiovascular and laboratory parameters.

For fluid requirements the following reference values apply:

Neonates (0 to ≤28 days), infants (28 days to ≤1 year):
100 – 140 ml/kg body mass and day

Infants aged 1 to ≤2 years:
80 – 120 ml/kg body mass and day

Children aged 2 to ≤5 years:
80 – 100 ml/kg body mass and day

Children aged 5 to ≤10 years:
60 – 80 ml/kg body mass and day

Children aged 10 to ≤12 years and adolescents aged 12 to ≤14 years:
50 – 70 ml/kg body mass and day

For the treatment of isotonic dehydration in the paediatric population the rate of infusion and the daily dose should be determined individually according to the nature and severity of the electrolyte and water imbalance by monitoring the relevant cardiovascular and laboratory parameters.

For short-term intravasalvolume replacement the dosage should be determined individually according to the fluid needs.

If Paedisol is used in combination with other solutions for infusion the current guidelines on the total fluid supply for the relevant age group should be considered upon dosage calculation.

The individual water, electrolyte, and carbohydrate requirements should be calculated and replaced accordingly; in particular, pre-term and underweight neonates, but also in all other exceptional therapeutic situations. Balancing needs to be more exact the pre-term, younger, and underweight the patient is.

Method of administration
For intravenous use.

Duration of administration
The duration of administration depends on the patient's fluid and electrolyte requirements.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1,
- Status of hyperhydration.

4.4 Special warnings and precautions for use

Monitoring of electrolyte and fluid status as well as the acid-base balance is necessary.

Particularly careful risk-benefit assessment is required when this medicinal product is used in patients with pre-existing hyperglycaemia and metabolic alkalosis because the use of this medicinal product can deteriorate such conditions. In this case, it is preferable to use similar electrolyte-containing solutions for infusion without glucose and/or acetate, if possible. In addition, in this patient group closer monitoring, particularly, blood glucose level and acid-base balance as well as electrolyte balance is required in order to detect resulting risks at an early stage.

Caution is required specifically in neonates and infants because the risk of developing lactic acidosis cannot be ruled out when using acetate as contained in this medicinal product in very rare disorders of acetate metabolism. These very rare disorders of acetate metabolism may appear for the first time when administering this medicinal product.

Paedisol should be used in paediatric patients with congenital disturbance of lactate utilisation after a careful risk-benefit-balance only.

Controls of blood glucose levels are required postoperatively, post-traumatically and in other disorders of glucose tolerance (hyperglycaemia).

Caution is required in case of hypernatraemia, hyperkalaemia, and hyperchloraemia.

4.5 Interaction with other medicinal products and other forms of interactions

There are no known interactions with other medicinal products.

4.6 Fertility, pregnancy and lactation

Paedisol is intended for use in the paediatric population (0 day to ≤14 years) only.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

As with all medicinal products for intravenous use, local site reactions associated with the method of administration cannot be excluded. The frequency of such reactions is not known (cannot be estimated from the available data). Local site reactions include febrile response, infections at the site of injection, venous thrombosis, phlebitis and extravasation extending from the site of injection.

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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose may lead to hyperhydration and hyperglycaemia.

Treatment:
Interruption of the infusion, renal elimination should beaccelerated, and administration of insulin, where appropriate.

For the intended use, no disturbances of electrolyte balance, osmolarity or acid-base balance are expected based on the composition of this medicinal product.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions affecting the electrolyte balance, electrolytes and carbohydrates, ATC code: B05BB02

Pharmacodynamic effects
Paedisol is an electrolyte solution for paediatric patients that has been adjusted in its most important cation composition to the respective plasma concentration and is used for the correction of fluid and electrolyte disturbances. The solution has been adapted in its composition to the typcial metabolic changes occurring in children during surgery and anaesthesia. The supply

of electrolytes restores or maintains normal osmotic conditions in the extra- and intracellular compartments. In addition, the solution also contains10 mg/ml carbohydrates as glucose.
Acetate is oxidised and has an alkalescent effect. Administration of Paedisol initially leads to replenishment of the interstitial space that accounts for approximately two-thirds of the extracellular compartment. Approximately one-third of the supplied volume remains in the intravascular space only. Therefore, the solution only has a short-term haemodynamic effect.

5.2 Pharmacokinetic properties

Distribution and Biotransformation
Upon infusion, glucose is first distributed intravascularly and then is taken up into the intracellular compartment.

Metabolism
Glucose, as a natural substrate of the cells in the organism, is ubiquitously metabolised. Under physiological conditions it is the most important energy-supplying carbohydrate with a caloric value of approximately 17 kJ/g or 4 kcal/g. Central nervous system tissues, erythrocytes and renal medulla are among others the obligatory glucose users. The normal fasting concentration of blood glucose range is 50 – 95 mg/100 ml or 2.8 – 5.3 mmol/l.

Glucose serves the formation of glycogen as the body's carbohydrate reserve and undergoes glycolysis to pyruvate or lactate for energy production in the cells. Glucose also enables the maintenance of the blood glucose level and the biosynthesis of important components of the organism. Insulin, glucocorticoids, and catecholamines are mainly involved in hormonal regulation of the blood glucose level.

By glycolysis, glucose is metabolised to pyruvate or lactate. Lactate can be partially re-introduced into the glucose metabolism (CORI cycle). Under aerobic conditions pyruvate is completely oxidised to carbon dioxide and water. The final products of this complete oxidation of glucose are eliminated via the lungs (carbon dioxide) and the kidneys (water).
A precondition for optimal utilisation of supplied glucose is a normal electrolyte and acid-base status. Particularly, acidosis can be a sign of impaired oxidative metabolism.

There is a strong correlation between electrolyte and carbohydrate metabolism which particularly affects potassium. Utilisation of glucose is associated with increased potassium requirements. If this relationship is not taken into account considerable disturbances of potassium metabolism may occur which can lead to massive cardiac arrhythmias amongst other conditions.

Under pathological metabolic conditions impairment of glucose utilisation (glucose intolerances) may occur. These include primarily diabetes mellitus as well as the hormonally-induced decrease of glucose tolerance resulting from metabolic stress (e.g. intra and post-surgery, serious illnesses, injuries) that may cause hyperglycaemia even without exogenous substrate supply. Hyperglycaemia – depending on the severity – may lead to osmotically based loss of fluid via the kidneys resulting in hypertonic dehydration, hyperosmolar disturbances and even hyperosmolar coma.

Excessive supply of glucose, in particular, in the course of a post-aggression syndrome, can considerably increase the disturbance of glucose utilisation and contribute to enhanced conversion of glucose to fat resulting from impaired oxidative glucose utilisation. This in turn may be associated with an increased carbon dioxide burden of the organism (problems with weaning from respirator) and additional fat infiltration in the tissues, specifically in the liver. Patients with intracranial injury and brain oedema possess a particular risk to disturbances of glucose homeostasis. In these patients, even slight disturbances of the glucose concentration and the associated increase in plasma (serum) osmolality can contribute to a significant increase of cerebral injury.

Upon infusion acetate is first distributed intravascularly and then is taken up into the interstitial compartment. Under physiological conditions acetate is converted to bicarbonate and carbon dioxide. The plasma bicarbonate and acetate concentrations are regulated by the kidneys; the carbon dioxide plasma concentration by the lungs.

Elimination
In healthy subjects, there is practically no renal elimination of glucose. In pathological metabolic situations (e.g. diabetes mellitus, post-aggression symptom) that are accompanied by hyperglycaemia (blood glucose concentrations above 120 mg/100 ml or 6.7 mmol/l) glucose is also eliminated via the kidneys (glucosuria) when the maximum tubular transport capacity (180 mg/100 ml or 10 mmol/l) is exceeded.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans others than those included in other sections of this text. Electrolytes and glucose contained in Paedisol are physiological components of animal and human plasma. Toxic effects are unlikely to occur at therapeutic doses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid 37 % (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

Incompatibility of the medicinal product to be added to Paedisol must be assessed before addition. In general, it can be stated that the following medicinal products (groups) must not be mixed with Paedisol:

- Medicinal products that might form hardly soluble precipitations with the constituents of the solution. (The preparation contains Ca^{2+} ions. Precipitation may occur with the addition of inorganic phosphate, hydrogen carbonate/ carbonate or oxalate.),
- Medicinal products that are not stable in an acid pH-range or do not exhibit optimum efficacy or decompose,
- Paedisol must not be mixed with other medicinal products or solutions for parenteral nutrition for which compatibility has not been tested.
- Solutions for infusion that contain glucose must not be administered simultaneously through the same infusion equipment with blood because of the possibility of pseudo-agglutination.

6.3 Shelf life

3 years

Use immediately after first opening.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C - 8°C, unless opening and storage have taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Paedisol is available in 100 ml, 250 ml, and 500 ml low-density polyethylene bottles (KabiPac) as primary packaging closed with a polyethylene or polyethylene/polypropylene cap containing a polyisoprene stopper.

Pack sizes:
40 x 100 ml bottles
20 x 250 ml bottles
10 x 500 ml bottles

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Use only if the solution is clear, without visible particles and if the container is undamaged.

For single use only.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/029/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16th September 2016

9 DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

15/09/2021

10 DATE OF REVISION OF THE TEXT

June 2019