SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sodium Chloride 0.45% w/v and Glucose 2.5% w/v Intravenous Infusion BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000ml of the solution for infusion contains:

Sodium chloride	4.5g
Glucose monohydrate	27.50g
equivalent to s glucose	25.00g

Electrolyte concentrations:

Sodium	77mmol/l
Chloride	77mmol/l

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for infusion.

A clear, colourless up to faintly straw-coloured aqueous solution.

Energy	418 kJ/l 100 kcal/l
Theoretical osmolarity:	293mOsm/l
Acidity (titration to pH 7.4):	< 0.5mmol/l
pH:	3.5 – 5.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Hypertonic dehydration
- Vehicle solution for compatible electrolyte concentrates and medicinal products

4.2 Posology and method of administration

Adults, the Elderly and Children

The dosage depends on the age, weight, clinical and biological (acid-base balance) conditions of the patient, concomitant therapy and should be determined by the consulting physician.

Fluid balance, serum glucose, serum sodium and other electrolytes may need 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.
Monitoring of serum sodium is particularly important for physiologically hypotonic fluids. Sodium Chloride 0.45% w/v and Glucose 2.5% w/v Intravenous Infusion BP Solution for Infusion may become hypotonic after administration due to glucose metabolisation in the body (see sections 4.4. 4.5 and 4.8).

General guidelines

Daily dose:
Up to 40 ml/kg body weight per day, corresponding to 2 g glucose/kg body weight per day.

Infusion and drop rate*:*
Up to 5 ml/kg body weight per hour, corresponding to 0.25 g glucose/kg body weight per hour.
The prescribing doctor may determine individual adaptation of the dose and infusion rate, especially for children.

Monitoring
Adequate urine flow must be ensured and careful monitoring of serum electrolytes and glucose is essential.

Method of administration

Intravenous infusion

This container contains a significant volume of air. To avoid risk of air embolism, this product must not be administered by pressure infusion.

4.3 Contraindications

Sodium Chloride 0.45 % w/v and Glucose 2.5 % w/v Intravenous Infusion must not be used in cases of
- hyperhydration
- hypotonic dehydration
- acute ischaemic stroke
- head trauma (first 24 hours)

4.4 Special warnings and precautions for use

Special warnings

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolisation (see section 4.2)

Depending on the tonicity of the solution, the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolise glucose, intravenous administration of glucose can cause electrolyte disturbances most importantly hypo- or hyperosmotic hyponatraemia.

Hyponatraemia:

Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, bums, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (brain oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain oedema are at particular risk of severe, irreversible and life-threatening brain injury.

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 hyponatraemia.

In diabetic patients, the amount of infused glucose has to be taken into account and insulin requirements may be modified.

Sodium Chloride 0.45 % w/v and Glucose 2.5 % w/v Intravenous Infusion should only be administered with caution in cases of:
– hyponatraemia,
– hyperglycaemia,
– renal insufficiency.

Precautions for use

The solution should be administered with caution to patients with conditions associated with sodium retention (e.g. hypertension, heart failure).

Clinical supervision should include checks of the serum electrolytes and the water balance. Special attention should be paid to regular monitoring of the serum potassium concentration.

In post-operative and post-traumatic conditions and in conditions of impaired glucose tolerance: only administer with monitoring of blood glucose level.

For correction of hypertonic dehydration, solutions containing not less than 70 mmol/l of sodium should be used. The time for correction should not be shorter than 48 hours.

4.5 Interaction with other medicinal products and other forms of interaction

The solution should not be administered through the same infusion equipment simultaneously, before or after an administration of blood because of the possibility of pseudo-agglutination.

Corticosteroids are associated with the retention of sodium and water.

Medicinal products leading to an increased vasopressin effect
The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i. v. fluids (see sections 4.2, 4.4 and 4.8)

Drugs stimulating vasopressin release, e.g.:
Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine , ifosfamide, antipsychotics, narcotics

Drugs potentiating vasopressin action, e.g.:
Chlorpropamide, NSAIDs, cyclophosphamide

Vasopressin analogues, e.g.:
Desmopressin, oxytocin, vasopressin, terlipressin
Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

4.6 Fertility, pregnancy and lactation

Data from preclinical and clinical studies of the use of this product in these conditions are not available. Therefore Sodium Chloride 0.45 % w/v and Glucose 2.5 % w/v Intravenous Infusion should be administered with caution during pregnancy and lactation.

It has been suggested that if used during labour, the glucose load on the mother may lead to foetal hyperglycaemia, hyperinsulinaemia, and acidosis, with subsequent neonatal hypoglycaemia and jaundice. Others have found no evidence of such an effect.

Sodium Chloride 0.45% w/v and Glucose 2.5% w/v Intravenous Infusion BP should be administrated with special caution for pregnant women during labour particularly if administered in combination with oxytocin due to the risk of hyponatraemia (see section 4.4, 4.5 and 4.8).

4.7 Effects on Ability to Drive and Use Machines

Not applicable

4.8 Undesirable effects

Undesirable effects are listed according to their frequencies as follows:

Very common	(≥ 1/10)
Common	(≥ 1/100 to < 1/10)
Uncommon	(≥ 1/1,000 to < 1/100)
Rare	(≥ 1/10,000 to < 1/1,000)
Very rare	(< 1/10,000)
Not known	(cannot be estimated from the available data)

Metabolism and nutrition disorders:
Not known: Hospital Acquired Hyponatraemia

Neurological disorders:
Not known: Hyponatraemic encephalopathy

Hospital acquired hyponatraemia may cause irreversible brain injury and death due to development of acute hyponatraemic encephalopathy (see sections 4.2 and 4.4).

Adverse reactions may be associated with the technique of administration including febrile response, infection at the site of injection, local pain or reaction, vein irritation, venous thrombosis or phlebitis.

Adverse reactions may be associated with the medications added to the solution; the nature of the additive will determine the likelihood of any other undesirable effects.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

Overdose may result in hyperhydration with increased skin tension, venous congestion, oedema - possibly also lung or brain oedema -, hypokalaemia and acid-base imbalances, and hyperglycaemia.

Retention of excess sodium when there is defective renal sodium excretion may result in pulmonary and peripheral oedema.

Hypernatraemia rarely occurs after therapeutic doses of sodium chloride. The most serious effect of hypernatraemia is dehydration of the brain which causes somnolence and confusion progressing to convulsions, coma, respiratory failure and death. Other symptoms include thirst, reduced salivation and lacrimation, fever, tachycardia, hypertension, headache, dizziness, restlessness, irritability and weakness.

Excessive administration of chloride salts may cause a loss of bicarbonate with an acidifying effect.

Prolonged or rapid administration of hypertonic solutions containing glucose may result in dehydration as a consequence of the induced hyperglycaemia.

Emergency treatment, antidotes

Immediate stop of infusion, administration of diuretics with continuous monitoring of serum electrolytes, correction of electrolyte and acid-base imbalances, administration of insulin if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmaco-therapeutic group: B05 BB02: Electrolytes with carbohydrates

The solution contains equimolar proportions of sodium and chloride corresponding to half the physiological concentration in the plasma. In addition this solution also contains 2.5 % (w/v) of carbohydrate in the form of glucose. The solution is practically isotonic.

Sodium is the primary cation of the extracellular space and together with various anions, regulates the size of this. Sodium and potassium are the major mediators of bioelectric processes within the body.

The sodium content and the liquid metabolism of the body are closely coupled to each other. Each deviation of the plasma sodium concentration from the physiological one simultaneously affects the fluid status of the body.

An increase in the sodium content of the body results also means reduction of the body's free water content independent of the serum osmolality.

Glucose is metabolised ubiquitously as the natural substrate of the cells of the body. Under physiological conditions glucose is the most important energy-supplying carbohydrate with a caloric value of approx. 16 kJ or 3.75 kcal/g. Nervous tissue, erythrocytes and medulla of the kidneys are amongst the tissues with an obligate requirement for glucose. The concentration of glucose in the blood is reported as 50-95 mg/100 ml, or 2.8-5.3 mmol/l (fasting).

One the one hand, glucose serves for the synthesis of glycogen as the storage form of carbohydrates and, on the other hand, it is subject to glycolysis to pyruvate and lactate for energy production in the cells. Glucose also serves to maintain the blood sugar level and for the synthesis of important body components. It is primarily insulin, glucagon, glucocorticoids and catecholamines that are involved in the regulation of the blood sugar concentration.

A normal electrolyte and acid-base status is a prerequisite for the optimal utilisation of administered glucose. So an acidosis, in particular, can indicate impairment of the oxidative glucose metabolism.

There are close metabolic relationships between the electrolytes and carbohydrate metabolism; potassium, in particular, is affected. The utilisation of glucose is associated with an increased potassium requirement. Not taking this relationship into account can lead to considerable disturbances of potassium metabolism, which can, amongst other things, lead to massive cardiac arrhythmia.

Glucose utilisation disturbances (glucose intolerance) can occur under conditions of pathological metabolism. These mainly include diabetes mellitus and states of metabolic stress (e.g. intra-, and postoperatively, severe disease, injury), hormonally mediated depression of glucose tolerance, which can even lead to hyperglycaemia without exogenous supply of the substrate. Hyperglycaemia can - depending on its severity - lead to osmotically mediated renal fluid losses with consecutive hypertonic dehydration, to hyperosmotic disorders up to and including hyperosmotic coma.

Excessive glucose administration, particularly in the condition of a postaggression syndrome, can lead to an appreciable aggravation of the impairment of glucose utilisation and, as a result of the limitation of oxidative glucose utilisation, to an increased conversion of glucose into lipids. This in

turn can be associated, amongst other things, with an increased carbon dioxide load of the body (problems with weaning from the respirator) and increased fatty infiltration of the tissues, particularly the liver. Patients with skull and brain injury and cerebral oedema are particularly at risk from disturbances of the glucose homeostasis. Here even slight disturbances of the blood glucose concentration and the associated increase in plasma (serum) osmolality can lead to a considerable increase in the degree of cerebral damage.

At the maximum dose level, (40 ml/kg body weight per day, corresponding to 1 g of glucose/ kg BW/day) this solution can partially cover minimum obligatory carbohydrate requirements.

5.2 Pharmacokinetic Properties

The total sodium content of the body is approx. 80 mmol/kg of which approx. 97 % is extracellular and approx. 3 % intracellular. The daily turnover is approx. 100 - 180 mmol (corresponding to 1.5 - 2.5 mmol/kg body weight).

The kidneys are the major regulators of the sodium and water balances. In co-operation with the hormonal control mechanisms (renin-angiotensin-aldosterone system, antidiuretic hormone) and the hypothetical natriuretic hormone they are primarily responsible for the volume.

Chloride is exchanged for hydrogen carbonate in the tubule system and is, thus, involved in the regulation of the acid base balance.

On infusion glucose is first distributed in the intravascular space and then is taken up into the intracellular space.

In glycolysis glucose is metabolised to pyruvate or to 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 the complete oxidation of glucose are eliminated via the lungs (carbon dioxide) and the kidneys (water).

Practically no glucose is excreted renally by healthy persons. In pathological metabolic conditions (e.g. diabetes mellitus, postaggression metabolism) associated with hyperglycaemia (blood glucose concentrations of more than 120 mg/100 ml or 6.7 mmol/l), glucose is also excreted via the kidneys (glucosuria) when the maximum tubular resorption capacity (180 mg/100 ml or 10 mmol/l) is exceeded.

5.3 Preclinical Safety Data

There are no pre-clinical data of relevance to the prescriber which are additional to those already stated in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened
Polyethylene bottle: 3 years

After first opening the container
From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately.

6.4 Special Precautions for Storage

The product does not need any special storage conditions within Europe. (Climatic zone 2).

6.5 Nature and contents of container

Polyethylene (LDPE) bottles, contents: 500 ml, 1000 ml

available in packs of 10 x 500 ml, 10 x 1000 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.
Containers are for single use only. Discard container and any unused content after use.
Do not re-connect partially used containers.
Administer immediately following the insertion of infusion set.
Only to be used if solution is clear without visible particles, colourless up to faintly straw-colored and the container and its closure are undamaged.

7 MARKETING AUTHORISATION HOLDER

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