Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

0.18 % w/v Sodium Chloride and 4 % w/v Glucose Intravenous Infusion BP, Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of the solution for infusion contain:
Sodium chloride 1.8 g
Glucose monohydrate 44.00 g
equivalent to glucose 40.00 g

Electrolyte concentrations:
Sodium 31 mmol/l
Chloride 31 mmol/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
Clear, colourless, upto faintly straw-coloured aqueous solution.

Energy 668kJ/l 160kcal/l
Theoretical osmolarity: 282mOsm/l
Acidity (titration to pH7.4): <0.5mmol/l pH: 3.5–5.5

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

§ Hypertonic dehydration
§ Partial coverage of energy requirements
§ Vehicle solution for compatible electrolyte concentrates and medicinal products

Paediatric Population
This product should only be used in paediatric specialist settings (such as renal, hepatic and cardiac units, high dependency units and intensive care units) for intravenous fluid therapy requiring the use of 0.18% sodium chloride and 4% glucose to maintain fluid and electrolyte balance.

4.2 Posology and method of administration

Posology

Adults
The dose is adjusted according to the individual requirements of fluid, electrolyte and energy. Thus the patient's age, weight, clinical and biological (acid-base balance) conditions and concomitant therapy should be taken into account. 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. 0.18 % w/v Sodium Chloride and 4 % w/v Glucose Intravenous Infusion BP may become extremely hypotonic after administration due to glucose metabolisation in the body (see sections 4.4, 4.5 and 4.8).

General guidelines

Maximum daily dose:
Up to 40 ml/kg body weight per day, corresponding to approx. 1.7 g glucose per kg body weight per day.

Maximum infusion rate:
Up to 5 ml per kg body weight per hour, corresponding to approx. 0.2 g glucose/kg body weight per hour.

Paediatric population

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 specialist. When administering this solution the total daily fluid and glucose requirements should be taken into account.

Elderly patients
Basically the same dosage as for adults applies, but caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that may frequently be associated with advanced age.

Other special patient groups
If the oxidative metabolism of glucose is impaired (e.g. in the early post-operative or posttraumatic period or in the presence of hypoxia or organ failure), the dosage should be adjusted to keep the blood glucose level close to normal values. See also section 4.4.

Method of administration

Intravenous use.
For instructions on dilution of the medicinal product before administration, see section 6.3.

4.3 Contraindications

- Hyperhydration states.
- Dehydration with hyponatraemia
- Head trauma (first 24 hours)
- Renal failure (oliguria or anuria) in the absence of renal replacement therapy
- Persistent hyperglycaemia not responding to insulin doses of up to 6 units/hour.

Paediatric population
This product should not be used in children except in paediatric specialist settings (such as renal, hepatic and cardiac units, high dependency units and intensive care units) under expert medical supervision. See also section 4.1.

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

4.4 Special warnings and precautions for use

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, burns, 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.

0.18 % w/v Sodium Chloride and 4 % w/v Glucose Intravenous Infusion BP, Solution for Infusion should not be used for fluid substitution, especially rehydration therapy, without adequate electrolyte administration, because this could lead to markedly decreased serum electrolyte values, notably severe hyponatraemia, with potentially detrimental effects on the patient, e.g. brain damage or heart affections. Especially children, elderly patients and patients in poor general condition are at risk.

0.18 % w/v Sodium Chloride and 4 % w/v Glucose Intravenous Infusion BP, Solution for Infusion shouldn't be used for routine rehydration or fluid maintenance therapy.

In patients with hyponatreaemia or hypokalaemia administration of this solution must be accompanied by additional substitution of sodium or potassium as necessary to normalise the serum levels of these electrolytes.

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

In patients with chronic hypernatraemia, the serum sodium concentration should not be lowered faster than at a rate of 0.5 $mmol \times l^{-1} \times h^{-1}$.

Administration of glucose solutions is not recommended after acute ischaemic strokes as hyperglycaemia was reported to worsen ischaemic brain damage and impair recovery.

Clinical monitoring should include checks of the serum electrolytes (especially potassium), glucose level, the acid-base and water balance.
If the oxidative metabolism of glucose is impaired close monitoring of blood glucose levels is recommended in order to prevent hyperglycaemia. See also section 4.2.

Please note: If this solution is used as vehicle solution the safety information of the additive provided by the respective manufacturer have to be taken into account.

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.

Paediatric population
Intravenous fluid therapy should be closely monitored in the paediatric population as they may have impaired ability to regulate fluids and electrolytes. Adequate urine flow must be ensured and careful monitoring of fluid balance, plasma and urinary electrolyte concentrations are essential.

The infusion of hypotonic fluids together with the non-osmotic secretion of ADH (in pain, anxiety, the post-operative state, nausea, vomiting, pyrexia, sepsis, reduced circulating volume, respiratory disorders, CNS infections, and metabolic and endocrine disorders) may result in hyponatraemia. Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death, therefore acute symptomatic hyponatraemia (e.g. hyponatraemic encephalopathy) is considered a medical emergency.

4.5 Interaction with other medicinal products and other forms of interactions

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

Pregnancy
There is a limited amount of data from the use of sodium chloride and glucose in pregnant women. Animal studies relating to physiological amounts of glucose and sodium chloride do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3).
Caution should be exercised when prescribing to pregnant women especially in the presence of (pre-) eclampsia.
Careful monitoring of blood glucose is necessary.

0.18% w/v Sodium Chloride and 4% w/v Glucose 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).

Breast-feeding
It is known that glucose/metabolites are excreted in human milk, but at therapeutic doses of Sodium Chloride 1.8 mg/ml (0.18%) and Glucose 40 mg/ml (4.0 %) solution for infusion no effects on the breastfed newborns/infants are anticipated.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Not relevant.

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)

Nervous system disorders:
Not known: Hyponatraemic encephalopathy

Metabolism and nutritiondisorders:
Not known:Hospital acquired hyponatraemia

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

General disorders and administration site conditions:
Not known: Local reactions at the site of administration, including local pain, vein irritation and thrombophlebitis

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

Symptoms
Overdose may result in hyperhydration, electrolyte imbalances (especially hypokalaemia and hyponatraemia) acid-base imbalances, and hyperglycaemia. Severe hyponatraemia could lead to death. Clinical symptoms of water intoxication may also occur, such as nausea, vomiting, spasms.

Treatment
Depending on the severity of the disorders 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.

In severe cases of overdose dialysis may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions affecting the electrolyte balance

ATC code: B05B B02 (Electrolytes with carbohydrates)

Mechanism of action
The solution contains equimolar proportions of sodium and chloride corresponding to one fifth of the physiological concentration in the plasma.

In addition the solution also contains 4 % (w/v) of carbohydrate in the form of glucose.

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 solution is mainly intended to supply free water in cases of hypertonic dehydration.

Pharmacodynamic effect
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.

Glucose is metabolized 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 ca. 17 kJ or 4 kcal/g. Nervous tissue, erythrocytes and medulla of the kidneys are amongst the tissues with an obligate requirement for glucose.

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 glucose 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 glucose concentration.

A normal electrolyte and acid-base status is a prerequisite for the optimal utilization 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 utilization 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.

5.2 Pharmacokinetic properties

Absorption
As the solution is administered by intravenous infusion the bioavailability of the solution is 100%.

Distribution
The total sodium content of the body is approx. 80 mmol per kg body weight, of which approx. 95 % is extracellular.
In adults, the concentration of glucose in the blood is 70 – 100 mg/100 ml, or 3.9 – 5.6 mmol/l (fasting).
On infusion glucose is first distributed in the intravascular space and then is taken up into the intracellular space.

Biotransformation
In glycolysis, glucose is metabolized to pyruvate. Under aerobic conditions pyruvate is completely oxidized to carbon dioxide and water. In case of hypoxia pyruvate is converted to lactate. Lactate can be partially re-introduced into the glucose metabolism (Cori cycle).

Elimination
The kidneys are the major regulator 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 keeping the volume of the extracellular space constant and regulating its fluid composition.
Chloride is exchanged for hydrogen carbonate in the tubule system and is, thus, involved in the regulation of the acid base balance.
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 associated with hyperglycaemia (e.g. diabetes mellitus, postaggression metabolism), glucose is also excreted via the kidneys (glucosuria) when (at blood glucose levels higher than 160-180 mg/100 ml or 8.8-9.9 mmol/l) the maximum tubular resorption capacity is exceeded.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, and toxicity to reproduction.

Since the components of Sodium Chloride 1.8 mg/ml (0.18%) and Glucose 40 mg/ml (4.0%). Solution for Infusion are physiologically present in human body, no harmful effects are to be expected with respect to genotoxicity and carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

When mixing with other medicinal products possible incompatibilities should be considered. It should be remembered that the solution has an acid pH, which can cause precipitation in the mixture.

6.3 Shelf life

Unopened
Polyethylene bottle: 3 years

After first opening the container
Containers once opened must be used immediately and must not be stored for later use. See also section 6.6.

After dilution
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 to 8 ° C, unless dilution has 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

0.18 % w/v Sodium Chloride and 4 % w/v Glucose Intravenous Infusion BP, Solution for Infusion is supplied in:

- 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 and other handling

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.

Only to be used if solution is clear, colourless up to faintly straw-coloured and the container and its closure are undamaged.

7 MARKETING AUTHORISATION HOLDER

B. Braun Medical Limited
3 Naas Road Industrial Park
Dublin 12
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0179/003/006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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