Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Glucose 50% w/v sterile concentrate, concentrate solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

50 ml of solution contains anhydrous glucose 25g (as glucose monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear, colourless or slightly yellowish aqueous solution.

Energy 420kJ/50ml = 100 kcal/50 ml
Theoretical osmolarity 2775 mOsm/l
Acidity (titration to pH 7.4) <1.5 mmol/l
pH 3.5 - 5.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Therapy of hypoglycaemia.

4.2 Posology and method of administration

Posology
Adults
For the treatment of hypoglycaemia the dose and the administration rate have to be adjusted according to the actual blood glucose concentration and the general condition of the patient.

Fluid balance, serum glucose, 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. Glucose 50% w/v sterile concentrate may become extremely hypotonic after administration due to glucose metabolisation in the body (see sections 4.4, 4.5 and 4.8).
Paediatric population
For the treatment of hypoglycaemia the dose and the administration rate have to be adjusted according to the actual blood glucose concentration and the general condition of the patient.

For correction of hypoglycaemia in children, it is recommended to dilute the glucose concentrate to a strength not higher than 100 mg/ml.

Method of administration

Intravenous infusion or slow intravenous injection after dilution.

Glucose concentrates must be administered diluted as an additive to infusion solutions.
Hypertonic glucose solutions should be preferably administered via a central venous catheter.

4.3 Contraindications

- Hyperglycaemia;
- Lactic acidosis.

4.4 Special warnings and precautions for use

Special warnings

Glucose 50% w/v sterile concentrate is a hypertonic solution. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization (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 metabolize glucose, intravenous administration of glucose can cause electrolyte disturbances most importantly hypo- or hyperosmotic hyponatraemia.

Consideration should be given to the correction of pre-existing thiamine (Vitamin B1) deficiency in at risk patients to prevent the development of Wernicke encephalopathy and/or lactic acidosis. If there is a thiamine deficiency (vitamin B1 deficiency), an appropriate dose of thiamine should be given as soon as possible.

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.

As hypertonic glucose solutions can cause skin necrosis and serious tissue damage a strict i.v. application has to be ensured.

Blood glucose concentrations should be monitored.

Close monitoring of blood glucose level is mandatory if the oxidative metabolism of glucose is impaired (e.g. in the early post-operative or post-traumatic period or in the presence of hypoxia or organ failure).

States of hyperglycaemia should be treated with insulin. The application of insulin causes additional shifts of potassium into the cells and may therefore cause or increase hypokalaemia.

Monitoring of serum electrolytes and acid-base balance is recommended.

Correction of fluid and electrolyte deficiencies should be ensured. This is especially important for potassium, because the administration of hypertonic glucose solutions may aggravate hypokalaemia.

Caution should be exercised in patients with increased serum osmolarity. In case of intracranial or intraspinal haemorhage solutions containing 10% or more w/v glucose should be avoided in the first 24 to 48 hours, unless the patient develops hypoglycaemia in the absence of nutritional support.

Hypertonic glucose solutions must be used with caution in patients with acute stroke as hyperglycaemia is associated with poor functional outcome in these patients.

Hypertonic glucose solutions should only be administered with caution in patients with renal failure.

Dehydration can be worsened by injection of hypertonic glucose solutions.

Glucose solutions should not be administered through the same infusion equipment, simultaneously with, before, or after administration of blood, because of the possibility of pseudo-agglutination.

Paediatric population

Newborns, especially preterm neonates with low birth weight, are especially at risk of hyperglycaemia. Close monitoring of the blood glucose level is mandatory to avoid long-term adverse events or fatal overdosage.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with medicinal products with an influence on glucose metabolism should be considered.

Drugs 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.

Prescribers should refer to the information provided with the product concerned.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited data (less than 300 pregnancy outcomes) from the use of glucose monohydrate in pregnant women.
Animal studies do not indicate direct or indirect harmful effects at the therapeutic dose with respect to reproductive toxicity (see section 5.3).
The medicinal product can be administered in pregnancy if indicated.
Nevertheless, an intrapartum infusion of glucose solution may predispose the infant to an increased risk of hypoglycaemia at 2 h of age. Therefore, it is recommended that during intrapartum glucose administration the blood glucose levels of the mothers should be monitored closely and kept in physiological limits to prevent maternal and foetal hyperglycaemia and subsequent risk of neonatal hypoglycaemia.
Glucose 50% w/v sterile concentrate 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
Glucose/metabolites are excreted in human milk, but at therapeutic doses of Glucose 50% w/v sterile concentrate no effects on breastfed infants are anticipated. Glucose 50% w/v sterile concentrate can be used during breastfeeding as indicated.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Glucose 50% w/v sterile concentrate has no influence on the ability to drive and use machines.

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 (frequency cannot be estimated from the available data)

General disorders and administration site conditions:
Not known: Local reactions at the site of administration, including local pain, vein irritation, thrombophlebitis or tissue necrosis in case of extravasation.

Metabolism and nutrition disorders:
Not known: Hospital Acquired Hyponatraemia
Nervous system 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).

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, Website: www.hpra.ie

4.9 Overdose

Symptoms
Overdose may cause hyperglycaemia, glucosuria, dehydration, hyperosmolarity, hyperglycaemic- hyperosmolar coma and electrolyte disorders.

Emergency treatment, antidotes

The primary therapy is dose reduction. Manifestations of overdose can additionally be treated by insulin administration. If necessary, disorders in fluid and electrolyte balance can be corrected by appropriate fluid and electrolyte administration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions for parentral nutrition, carbohydrates
ATC code: B05BA03

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. 17 kJ or 4 kcal/g. The obligate glucose consumption of an adult is about 200 g/d. Nervous tissue, erythrocytes and medulla of the kidneys are amongst the tissues with an obligate requirement for glucose. In adults the concentration of glucose in the blood is 60 – 100 mg/100 ml, or 3.3 – 5.6 mmol/l (fasting).
On 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 utilization of administered glucose. So an acidosis, in particular, can indicate impairment of the oxidative glucose metabolism.

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. Depending on its severity, hyperglycaemia can lead to osmotically induced renal fluid losses with consecutive hypertonic dehydration and to hyperosmotic disorders up to hyperosmotic coma.

Excessive glucose administration, particularly in conditions of post-operative or post-traumatic metabolic disorders, 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.

5.2 Pharmacokinetic properties

Absorption
As the solution is administered intravenously its bioavailability is 100 %.

Distribution
Parenterally administered glucose primarily adds to the blood glucose content and is then incorporated in the endogenous glucose pool.
In adults, the normal concentration of glucose in plasma is 70 – 100 mg/100 ml, or 3.9 – 5.6 mmol/l (fasting).

Biotransformation
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.
There are close metabolic relationships between the electrolytes and carbohydrate metabolism. The utilisation of glucose is associated with increased potassium, magnesium and phosphate requirements.
Uncorrected hypokalaemia may lead to massive cardiac arrhythmia.

Elimination
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 or in case of overdose, glucose is also excreted via the kidneys (glucosuria) when the maximum tubular resorption capacity is exceeded (at blood glucose levels of 180 mg/100 ml or 10 mmol/l or more).

5.3 Preclinical safety data

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

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. Glucose 50% w/v sterile concentrate has an acidic pH, incompatibilities can occur on mixing with other medicinal products.

6.3 Shelf life

- unopened
3 years
- after first opening the container
Once containers are opened contents must be used immediately. See section 6.6.
- after dilution according to directions
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

Vials of colourless glass of type II (Ph. Eur.), sealed with rubber stoppers.
contents: 50ml
available in packs of 20 x 50 ml.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Containers are for single use only. Discard container and any unused content after use.
Only to be used if the solution is clear, colourless or slightly yellowish 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

PA0179/001/039

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17 August 1992

Date of last renewal: 17 August 2007

10 DATE OF REVISION OF THE TEXT

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