

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Glucose Intravenous Infusion BP 5% w/v, Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 50 mg glucose as glucose monohydrate
1000 ml contain 50.0 g glucose (as glucose monohydrate, 55.0 g)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Infusion.
Clear, colourless or almost colourless, aqueous solution.

Energy: 837kJ/l \triangleq 200kcal/l

Theoretical osmolarity: 278 mOsm/l

Acidity titre (titration to pH 7.4): < 0.5 mmol/l

pH: 3.5 – 5.5

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Vehicle solution for compatible electrolyte concentrates and medicinal products.

For use in prophylactic and replacement therapy requiring the use of glucose.

4.2 Posology and method of administration

Posology

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 Intravenous Infusion BP 5% w/v may become extremely hypotonic after administration due to glucose metabolism in the body (see sections 4.4, 4.5 and 4.8).

Prophylactic and replacement therapy requiring the use of glucose

The quantity and rate of administration is dependent on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician.

Vehicle solution for compatible medicinal products

The volume to be chosen depends on the desired concentration of the medicinal product for which the solution is to be used as vehicle, having regard to the maximum dose stated below. Of note, provision of the entire daily fluid supply with this solution alone is contraindicated. See sections 4.3 and 4.4.

*Adults*Maximum daily intake

Up to 40 ml per kg body weight per day, corresponding to 2 g of glucose per kg body weight per day.

Maximum infusion rate

Up to 5 ml per kg body weight per hour, corresponding to 0.25 g of glucose per kg body weight per hour.

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

Paediatric population

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician experienced in paediatric intravenous fluid therapy.

Generally, dosing of this solution should be as restrictive as possible and must be accompanied by adequate electrolyte substitution. See sections 4.3 and 4.4. When administering this solution the total daily fluid and glucose requirements should be taken into account.

Method of Administration

Intravenous use.

The possibility of peripheral venous infusion depends on the osmolarity of the prepared mixture.

4.3 Contraindications

- Hyperglycaemia, not responding to insulin doses of up to 6 units insulin/hour;
- Lactic Acidosis.

If it is necessary to administer large volumes, further contraindications can arise on account of the fluid load:

- Hypotonic hyperhydration
- Isotonic hyperhydration
- Acute congestive heart failurePulmonary oedema

This solution must not be used alone for fluid supply/rehydration because it does not contain electrolytes. See section 4.4.

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

4.4 Special warnings and precautions for useSpecial warnings

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

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.

In patients with disturbed glucose metabolism, as present e.g. in postoperative or posttraumatic conditions or in patients with diabetes mellitus, Glucose Intravenous Infusion BP 5% w/v must be administered with caution, i.e. with frequent monitoring (see below), and dosage must be adapted as required.

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

Patient monitoring should include regular checks of the blood glucose level, serum electrolytes (especially potassium and sodium) and the acid-base and water balance.

This fluid should also be administered with great caution to patients with renal insufficiency.

Administration of glucose solutions is not recommended after acute ischaemic strokes as hyperglycaemia has been reported to worsen ischaemic brain damage and impair recovery. In prehospital management of acute ischemic stroke, glucose-containing solutions should be avoided unless hypoglycaemia is present or strongly suspected.

Glucose solutions should not be administered through the same infusion equipment, simultaneously, before, or after 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 hydration and urine flow must be ensured and careful monitoring of fluid balance, plasma and urinary electrolyte concentrations are mandatory.

The infusion of hypotonic fluids such as Glucose Intravenous Infusion BP 5% w/v 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 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 doses with respect to reproductive toxicity (see section 5.3).

Glucose Intravenous Infusion BP 5% w/v can be used during pregnancy, if indicated as vehicle solution.

Glucose Intravenous Infusion BP 5% w/v should be administered 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 Intravenous Infusion BP 5% w/v no effects on the breast-fed newborns/infants are anticipated.

Glucose Intravenous Infusion BP 5% w/v can be used during breast-feeding as indicated.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Glucose Intravenous Infusion BP 5% w/v 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 ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very rare ($< 1/10,000$)

Not known (frequency cannot be estimated from the available data)

Metabolism and nutrition disorders:

Not known: Electrolyte imbalance, e.g. hyponatraemia and hypokalaemia.

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, 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 of glucose overdose

Excessive glucose infusions can cause hyperglycaemia, glucosuria, hyperosmolar dehydration and in extreme cases overdose can lead to hyperglycaemic-hyperosmolar coma.

Symptoms of fluid overdose

Fluid overdose may result in hyperhydration with increased skin tension, venous congestion, oedema – possibly also lung or brain oedema -, dilution of serum electrolytes, electrolyte imbalances, notably hyponatraemia and hypokalaemia (see section 4.4), and acid-base imbalances.

Clinical symptoms of water intoxication may occur like nausea, vomiting, spasms.

Further symptoms of overdose may arise depending on the nature of the additive.

Emergency treatment, antidotes

The disturbances can – depending on the type and the degree of severity – be treated by stopping the infusion, by administration of electrolytes, diuretics, or insulin.

For correction of hyponatraemia the following formula⁽¹⁾ can be used:

$$\text{mmol of Na}^+ \text{ required} = (\text{target Na}^+ \text{ level}^{(2)} - \text{actual Na}^+ \text{ level}) \times \text{TBW}^{(3)}$$

(1) modified from [2])

(2) should not be lower than 130 mmol/l

(3) TBW: Total body water, calculated as a fraction of body weight: 0.6 in children, 0.6 and 0.5 in nonelderly men and women, respectively, and 0.5 and 0.45 in elderly men and women, respectively

During treatment, serum electrolytes should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Solvents and diluting agents incl. irrigating solutions

ATC code: V07AB

Pharmacodynamic effects

Low concentration glucose solutions are suitable diluents for drugs because glucose, as a natural substrate of the cells in the organism, is ubiquitously metabolised. Under physiological conditions glucose is the most important energy supplying carbohydrate with a calorific value of approximately 17kJ or 4 kcal/g. In adults, the normal concentration of glucose in blood is reported to be 70 – 100 mg/100 ml, or 3.9 – 5.6 mmol/l (fasting).

5.2 Pharmacokinetic properties

Absorption

Since the solution is administered intravenously, its bioavailability is 100 %.

Distribution

On infusion glucose initially distributes in the intravascular space and is then taken up in the intracellular space.

Biotransformation

In glycolysis, glucose is metabolized to pyruvate. Under aerobic conditions pyruvate is completely oxidised to carbon dioxide and water. In case of hypoxia, pyruvate is converted to lactate. Lactate can be partially reintroduced into the glucose metabolism (CORI cycle).

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.

Metabolism of glucose and electrolytes are closely related to each other. Insulin facilitates potassium influx into cells. Phosphate and magnesium are involved in the enzymatic reactions associated with glucose utilization. Potassium, phosphate and magnesium requirements may therefore increase following glucose administration and may therefore have to be monitored and supplemented according to individual needs. Especially cardiac and neurological functions may be impaired without supplementation.

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 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/dl 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, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections.

6.2 Incompatibilities

Because Glucose Intravenous Infusion BP 5% w/v has an acid pH incompatibilities can occur on mixing with other medicinal products.

Erythrocyte concentrates must not be suspended in Glucose Intravenous Infusion BP 5% w/v because of the risk of pseudoagglutination. See also section 4.4.

6.3 Shelf life

- Unopened

Container: 3 years.

- After first opening the container:

Containers once opened must be used immediately. See section 6.6.

- after admixture of additives

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.

6.4 Special precautions for storage

Do not store above 25°C.

Store in original container.

For storage conditions after admixture of additives see section 6.3.

6.5 Nature and contents of container

Bottles of low-density polyethylene with integral on-welded closure of the same material.

Contents 50ml, 100ml:

Available in packs of:

20 x 50 ml, 20 x 100 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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

The medicinal product is supplied in containers for single use only. After first use discard container and remaining contents.

Do not re-connect partially used containers.

Only to be used if solution is clear and colourless or almost colourless and if the container or its closure are undamaged.

Administration should commence immediately after connecting the container to the giving set or infusion equipment.

When admixing additives observe usual precautions of asepsis strictly.

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen A.G.
P.O. Box 1110 + 1120
D-34209 Melsungen
Germany

8 MARKETING AUTHORISATION NUMBER

PA0736/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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