DIRECTIONS FOR USE

1 NAME OF THE MEDICINAL PRODUCT

GLUCOSE INJECTION BP 50%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml of solution contains

Glucose (monohydrate)	55.0 g
(equivalent to anhydrous glucose)	(50.0 g)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion
Clear and colourless or faintly yellow solution, free from particles

Energy:	8375 KJ/l ≙ 2000 kcal/l
Theoretical osmolarity:	2775 mOsm/l

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 Injection BP 50%* may become hypotonic after administration due to glucose metabolization 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 concentrates to a strength not higher than 100 mg/ml.

Method of administration
Intravenous infusion or slow intravenous injection.

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

4.3 Contraindications

- Hypersensitivity to the active substance. See section 4.4 for corn allergies
- Lactic acidosis

4.4 Special warnings and precautions for use

Special warnings

Glucose Injection BP 50% 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.

Due to the risk of developing a severe lactic acidosis and/or a Wernicke encephalopathy a pre-existing thiamine (Vitamin B1) deficiency must be corrected before infusion of glucose containing solutions.

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.

Effective

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 *Glucose Injection BP 50%* 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.

Glucose Injection BP 50% must be used with caution in patients with acute stroke as hyperglycaemia is associated with poor functional outcome in these patients.

Glucose Injection BP 50% should only be administered with caution in patients with renal failure.

Dehydration can be worsened by injection of *Glucose Injection BP 50%*.

Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, have been reported with Glucose solutions. Solutions containing glucose should therefore be used with caution, if at all, in patients with known allergy to corn or corn products (see section 4.3).

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

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.

Effective

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 from the use of glucose solutions in pregnant women.

Animal studies do not indicate direct or indirect harmful effects at the therapeutic does 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 Injection BP 50% 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 Injection BP 50%* no effects on breastfed infants are anticipated.

Glucose Injection BP 50% can be used during breastfeeding as indicated.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Glucose Injection BP 50% 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

Neurological disorders:
Not known: Hyponatraemic encephalopathy

Effective

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

Note

Patients should inform their doctor or nurse if they notice any of these reactions or other adverse reactions.

4.9 Overdose

Symptoms

Excessive glucose infusions can cause hyperglycaemia, glucosuria, hypertonic dehydration, hyperglycaemic- hyperosmolar coma and electrolyte disorders.

Treatment

The primary treatment is discontinuation of the therapy. 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 parenteral nutrition, carbohydrates
ATC code: B05B A03

Pharmacodynamic effects

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/g or 4 kcal/g. In adults the concentration of glucose in the blood is 70 – 100 mg/dl, or 3.9 – 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
Since the solution is administered intravenously, its bioavailability is 100 %.

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

Biotransformation
In glycolysis glucose is metabolised 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.

Effective

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, post-aggression metabolism) associated with hyperglycaemia or in case of overdose, 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

No non-clinical studies have been carried out with *Glucose Injection BP 50%*. Glucose is a physiological component of animal and human plasma. Limited toxicological data with different glucose solutions for injection reveal at therapeutic doses no special hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Because *Glucose Injection BP 50%* has an acidic pH, incompatibilities can occur on mixing with other medicinal products.

Erythrocyte concentrates must not be suspended in *Glucose Injection BP 50%* because of the risk of pseudo-agglutination. See also section 4.4.

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

Do not store above 25 °C.

For storage conditions of the diluted medicinal product, see section 6.3.

6.5 Nature and contents of the container

• ampoules of low-density polyethylene (Mini-Plasco or Mini-Plasco connect), contents 20 ml, available in packs of 20 x 20 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.

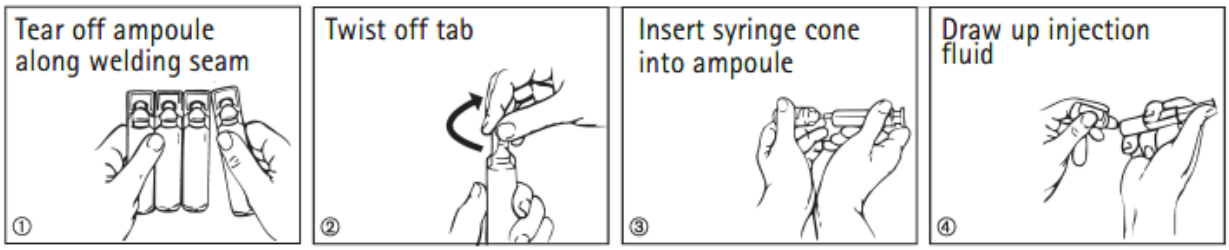
Only to be used if the solution is clear and colourless or faintly yellow solution, free from particles and the container and its closure are undamaged.

7. DATE OF REVISION OF THE TEXT

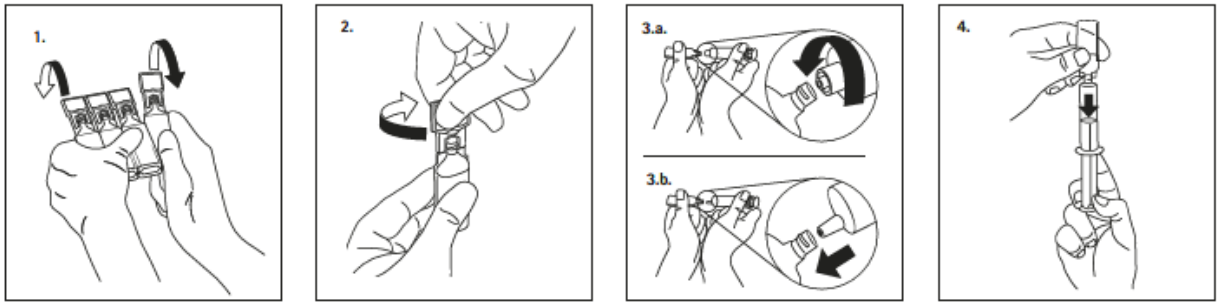
Last internal revision: 10.2024

Effective

Mini-Plasco® Handling



Mini-Plasco® Connect Handling



8. Manufactured by:
B. Braun Medical Industries Sdn. Bhd.
11900 Bayan Lepas, Penang, Malaysia

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