SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Glucose 50%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 mL concentrate for solution for infusion contain

Glucose monohydrate 55.0 g
(≙ 50.0 g anhydrous glucose)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion
Clear, colourless up to faintly, straw-colored solution, practically free from particles.

Energy:	835 kJ/100 mL ≙ 200 kcal/100 mL
Theoretical osmolarity:	2,770 mOsm/L
Titratable acidity (pH 7.4):	< 1.5 mmol/L
pH:	3.5-5.5

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

High caloric carbohydrate infusion, (in a minimal volume of water), Hypoglycemia.

4.2 Posology and method of administration

Dosage
Adults:
The dosage depends on age, weight and clinical condition of the patient.
Up to 14 ml/kg body weight/day.

Flow rate:
Up to 1.0 ml/kg bw/h or (for 70 kg patient) up to 23 drops/min = 70 ml/h.
For patients in a markedly depleted nutritional state, the above drop/flow rates have to be reduced accordingly.

Insulin induced hypoglycemia:
Determine blood glucose before injecting dextrose.

Children:
According to individual requirements.

Route of Administration
I.V. via a central venous catheter.

For total parenteral nutrition Glucose Injection is administered by slow intravenous infusion (a) after admixture with amino acid solutions via an indwelling catheter with the tip positioned in a large central vein, preferably the superior vena cava, or (b) after dilution with sterile water for injection. Dosage should be adjusted to meet individual patient requirements.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Hyperglycaemia
- Hypokalaemia
- Acidosis

4.4 Special warnings and precautions for use

Glucose 50% is a hypertonic solution. In the body, however, glucose-containing fluids can become extremely hypotonic due to rapid glucose metabolisation.

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

Hyponatraemia:
Patients with non-osmotic vasopressin release (e.g., in acute illness, pain, postoperative stress, infections, burns and CNS disorders), patients with cardiac, hepatic and renal disorders, and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia following infusion of hypotonic fluids.
Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema), characterised by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.
Children, women of childbearing potential and patients with reduced cerebral compliance (e.g., meningitis, intracranial bleeding and cerebral contusion) are at particular risk of severe, life-threatening brain swelling caused by acute hyponatraemia.

Care must be taken in case of increased serum osmolarity.

Blood glucose levels must be monitored according to metabolic condition and administered amount.

Monitoring of the electrolyte and acid-base balance and of potassium levels is necessary.

Solutions containing glucose must not be administered simultaneously with stored blood through the same infusion equipment, as pseudoagglutination may occur (see section 6.2).

Paediatric population

There is an increased risk of hyperglycaemia in neonates, particularly in premature infants with a low birth weight. To prevent possible long-term undesirable effects in such cases, adequate glycaemic control is necessary by means of close monitoring during treatment with a solution containing glucose.

The solution must be administered with particular caution to prevent a possible fatal overdose of intravenous fluid in neonates.

4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products leading to an increased vasopressin effect

The medicinal products listed below increase the vasopressin effect, leading to reduced renal electrolyte-free fluid excretion and increasing the risk of hospital-acquired hyponatraemia following insufficiently balanced treatment with IV fluids (see sections 4.4 and 4.8).

- Medicinal products that stimulate vasopressin release, e.g.: chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, amphetamines, ifosfamide, antipsychotics, narcotics
- Medicinal products that potentiate the vasopressin effect, e.g.: chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues, e.g.: desmopressin, oxytocin, vasopressin, terlipressin

Other medicinal products that increase the risk of hyponatraemia also include diuretics in general and antiepileptic drugs such as oxcarbazepine.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of glucose solutions in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity at therapeutic doses (see section 5.3).
The use of Glucose 50% may be considered during pregnancy, provided that blood glucose and electrolyte and fluid balance are carefully monitored and remain within the physiological range. Glucose 50% should be administered with particular caution to pregnant women during labour, particularly if administered in combination with oxytocin, due to the risk of hyponatraemia (see sections 4.4, 4.5 and 4.8).

If a medicinal product is added, the type of additive and its use during pregnancy and breastfeeding must be considered separately.

Breast-feeding
Glucose/metabolites are excreted in human milk, but at therapeutic doses of Glucose 50%, no effects on the breastfed newborns/infants are anticipated.
Glucose 50% can be used during breast-feeding.

Fertility
No data from humans are available. At therapeutic doses, no effects are anticipated.

4.7 Effects on ability to drive and use machines

Glucose 50% has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The undesirable effects listed in this section are categorised according to the recommended frequency convention: 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).

List of undesirable effects

System organ class	Undesirable effect	Frequency
Metabolism and nutrition disorders	Hypertonic dehydration (see section 4.9) Hospital-acquired hyponatraemia*	not known
Nervous system disorders	Hyponatraemic encephalopathy*	not known

General disorders and administration site conditions	Irritation at the administration site Irritation of veins Thrombophlebitis Extravasation Local pain	not known

*Hospital-acquired hyponatraemia may cause irreversible brain injury and death due to the development of acute hyponatraemic encephalopathy (see section 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il

4.9 Overdose

Overdose may result in hyperglycaemia and hypertonic dehydration. Hyperglycaemia may be treated by reducing glucose administration and giving insulin.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: solutions for parenteral nutrition, carbohydrates
ATC code: B05B A03

Mechanism of action

Glucose, as a natural substrate of the cells in the body, is ubiquitously metabolised. Under physiological conditions, glucose is the most important energy-supplying carbohydrate with a calorific value of approx. 17 kJ/g or 4 kcal/g. Nerve tissue, erythrocytes and renal medulla are among those dependent on glucose supply. The normal range for blood glucose concentration is reported to be 60-100 mg/100 mL or 3.3-5.6 mmol/L (fasting).

On the one hand, glucose is used to produce glycogen as the storage form of carbohydrates, while on the other hand it is broken down by glycolysis to pyruvate or lactate in order to generate energy in the cells. Furthermore, glucose serves to maintain blood glucose levels and the biosynthesis of important body constituents. Primarily insulin, glucagon, glucocorticoids and catecholamines are involved in the hormonal regulation of blood glucose levels.

Clinical efficacy and safety

A normal electrolyte and acid-base balance is the prerequisite for optimum utilisation of supplied glucose. In particular, acidosis may indicate impaired oxidative utilisation.

There are close interrelationships between electrolytes and carbohydrate metabolism which affect potassium in particular. Increased glucose utilisation is associated with increased potassium requirements. If this relationship is not taken into account, this may cause considerable potassium metabolism abnormalities, which may result in significant cardiac arrhythmias, among other conditions.

Abnormal glucose utilisation (glucose intolerance) can occur under conditions of pathological metabolism. These mainly include diabetes mellitus and the hormone-mediated reduction of glucose tolerance that occurs in so-called states of metabolic stress (e.g., intra- and postoperative, serious illness, injury), which can lead to hyperglycaemia even without exogenous supply of the substrate.

Hyperglycaemia can - depending on its severity - lead to osmotically mediated renal fluid losses with consequential hypertonic dehydration and hyperosmotic disorders culminating in hyperosmotic coma.

Excessive administration of glucose, particularly in the context of a post-traumatic metabolism, may result in a pronounced exacerbation of the glucose utilisation disorder and, due to impaired oxidative glucose utilisation, contribute to increased conversion of glucose to fat. This may in turn be accompanied by, for instance, increased carbon dioxide levels in the body (issues whilst weaning from the respirator), as well as increased fatty infiltration of tissues, in particular in the liver. Recent literature reports furthermore also suggest a negative impact of the administration of carbohydrates in high doses in an intensive-care setting on the peripheral nervous system (paralysis). Patients with traumatic brain injury and cerebral oedema are at a particular risk of glucose homoeostasis abnormalities. Even minor blood glucose level abnormalities and the associated increase in plasma (serum) osmolarity may result in a significant worsening of cerebral damage.

5.2 Pharmacokinetic properties

Distribution

On injection, 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 or lactate. Under aerobic conditions, pyruvate is completely oxidised to carbon dioxide and water. The end products of the complete oxidation of glucose are eliminated via the lungs (carbon dioxide) and the kidneys (water).

Elimination

Practically no glucose is eliminated renally by healthy persons. In pathological metabolic conditions (e.g., diabetes mellitus, post-traumatic metabolism) associated with hyperglycaemia (blood glucose concentration of more than 120 mg/100 mL or 6.7 mmol/L), glucose is also excreted via the kidneys (glycosuria) if the maximum tubular transport capacity (180 mg/100 mL or 10 mmol/L) is exceeded.

5.3 Preclinical safety data

No preclinical toxicity or safety pharmacology studies have been conducted with Glucose 50%. Glucose is a natural component of human and animal plasma. Limited toxicological data with various glucose solutions reveal no special hazard for humans at therapeutic doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Solutions containing glucose must not be administered simultaneously with stored blood through the same infusion equipment, because pseudo-agglutination can occur.

Packed red blood cells must not be suspended in Glucose 50%, as this can lead to pseudoagglutination.

Due to the acidic pH value of Glucose 50%, incompatibilities may occur when this product is mixed with other medicinal products.

6.3 Shelf life

- *unopened*

The expiry date of the product is indicated on the packaging materials

- *after first opening of the container*

Not applicable. See also section 6.6.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

- 50 ml glass vials (type II glass) with rubber stoppers
  Pack sizes: 20 × 50 mL
- 20 ml plastic ampoules (LDPE)
  Pack sizes: 20 × 20 mL

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Instructions for handling
Use only if the container is intact and the solution for injection is clear.
The vials are intended for single use only.

7. MANUFACTURER

B. Braun Melsungen AG
Carl-Braun Str. 1
D-34209 Melsungen, Germany

8. REGISTRATION HOLDER

Lapidot Medical Import and Marketing Ltd.
8 Hashita st., Industrial park, Caesarea 38900, Israel

9. LICENSE NUMBER

134-97-25555-00

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