12.2022

רופא/ה רוקח/ת נכבד/ה,

ברצוננו להודיעך על עדכון בעלון לרופא בעקבות "אימוץ עלון כלשונו" עבור התכשירים:

Glucose 20 %

חומר פעיל :

Glucose monohydrate 220.0g

התוויה מאושרת:

High caloric carbohydrate infusion
Hypoglycemia

להלן עלון לרופא כפי שאומץ מעלון אסמכתא כלשונו (טקסט מסומן ירוק משמעותו עדכון ,טקסט מסומן צהוב משמעותו החמרה):

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Glucose 20%

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution for infusion contains:
Glucose monohydrate 220.0g (equivalent to anhydrous glucose) (200.0g)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion

Clear, colourless or slightly yellowish aqueous solution.

Caloric value	3350 kJ/l ≅ 800 kcal/l
Theoretical osmolarity	1110 mOsm/l
Titration acidity (to pH 7.4)	< 1 mmol/l
pH	3.5 - 5.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- High caloric carbohydrate infusion
- Hypoglycemia

4.2 Posology and method of administration

Dosage

Adults:
The dosage depends on age, weight and clinical condition of the patient.
Glucose 20 %: Up to 35 ml/kg body weight/day
Glucose 50 %: Up to 14 ml/kg body weight/day

Flow rate:
Glucose 20 %: Up to 2.5 ml/kg bw/h or (for 70 kg patient) up to 58 drops/min = 175 ml/h
Glucose 50 %: 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, not responding to insulin doses of up to 6 units insulin/hour
- Delirium tremens if such patients are already dehydrated
- Acute states of shock or collapse
- Metabolic acidosis
- Since the administration of glucose solutions is accompanied by the administration of free water, further contraindications may arise e.g.:
- Hyperhydration
- Pulmonary oedema
- Acute congestive heart failure

4.4 Special warnings and precautions for use

General

20% w/v Glucose Intravenous Infusion BP is a hypertonic solution. In the body, however, glucose containing fluids can become 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.

Administration of glucose solutions is not recommended after acute ischaemic strokes as

hyperglycaemia has been reported to worsen ischaemic brain damage and impair recovery.

Application of hyperosmolar glucose solutions in patients with damaged haematoencephalic barrier may lead to increase of intracranial/intraspinal pressure.

Glucose infusions should not be started before existing fluid and electrolyte deficiencies like hypotonic dehydration, hyponatraemia and hypokalaemia have adequately been corrected.

This solution should be used with caution in patients with
- Hypervolaemia
- Renal insufficiency
- Cardiac insufficiency
- Increased serum osmolarity
- Known subclinical diabetes mellitus or carbohydrate intolerance for any reason.

Unstable metabolism (e.g. postoperatively or after injuries, hypoxia, organ insufficiencies) impairs oxidative metabolism of glucose and may lead to metabolic acidosis.

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.

Profound hypoglycemia may follow sudden discontinuation of high glucose infusion rates because of the accompanying high serum insulin concentrations. This applies especially to children less than 2 years of age, patients with diabetes mellitus and patients with other disease states associated with impaired glucose homeostasis. In obvious cases, the glucose infusion should be tapered off within the last 30 – 60 minutes of the infusion. As a precaution it is recommended that each individual patient be monitored for 30 minutes for hypoglycemia on the first day of abrupt discontinuation of parenteral nutrition.

Clinical monitoring should include blood glucose, serum electrolytes, fluid and acid- base balance in general. A focus should be put on the sodium level as glucose solutions provide free water to the body and may therefore cause or worsen hyponatraemia. Frequency and kind of laboratory testing depend on the overall condition of the patient, the prevailing metabolic situation, the administered dose and the duration of treatment. Also monitor total volume and amount of glucose administered.

Parenteral nutrition in malnourished or depleted patients with full doses and full infusion rates from the very beginning and without adequate supplementation of potassium, magnesium and phosphate may lead to the refeeding syndrome, characterised by hypokalaemia, hypophosphataemia and hypomagnesaemia. Clinical manifestations may develop within a few days of starting parenteral nutrition. In such patients, infusion regimens should be built up gradually. Adequate supplementation of electrolytes according to deviations from normal values is necessary.

Special attention should be paid to hypokalaemia. Then, supplementation of potassium is mandatory.

Electrolytes and vitamins must be supplied as necessary. Vitamin B, especially thiamine, is needed for glucose metabolism.

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

It should be noted that this solution constitutes only one component of parenteral nutrition. In total parenteral nutrition, glucose infusions should always be combined with an adequate supply of amino acids, lipids, electrolytes, vitamins and trace elements.

Paediatric population
For treatment of hypoglycaemia in children, use of 10% glucose solution is recommended. Children in the 1st and 2nd year of life are especially at risk for rebound hypoglycaemia after abrupt discontinuation of high infusion rates, see above.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or 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 with respect to reproductive toxicity (see section 5.3).

The use of 20% w/v Glucose Intravenous Infusion BP may be considered during pregnancy, if clinically needed.

20% 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).

Careful monitoring of blood glucose is necessary.

Breast-feeding
Glucose/metabolites are excreted in human milk, but at therapeutic doses of 20% w/v Glucose Intravenous Infusion BP no effects on the breast-fed newborns/infants are anticipated. 20% w/v Glucose Intravenous Infusion BP can be used during breast- feeding as indicated.

Fertility
No special precautions.

4.7 Effects on ability to drive and use machines

The solution has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

General

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)

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

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

Symptoms

Symptoms of glucose overdose
Excessive glucose infusions can cause hyperglycaemia, glucosuria, hyperosmolar dehydration and in extreme case overdose can lead up to hyperglycaemic- hyperosmotic coma. In cases of gross overdosing lipogenesis resulting in hepatic steatosis is possible.

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 and spasms.

Treatment
The primary therapeutic measure is dose reduction or cessation of infusion, depending on the severity of symptoms. Disorders of the carbohydrate and electrolyte metabolism are treated by insulin administration and appropriate electrolyte substitution, respectively.

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. 16.7 kJ/g or 4 kcal/g. In adults, the normal concentration of glucose in blood is reported to be 70 – 100 mg/dl or 3.9 to
5.6 mmol/l (fasting).

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 or to lactate. 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).
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 (e.g. diabetes mellitus, postaggression metabolism) associated with hyperglycaemia, glucose is also excreted via the kidneys (glucosuria) when the maximum tubular resorption capacity is exceeded (at blood glucose levels higher than 160-180 mg/dl or 8.8-9.9 mmol/l).

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
Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Erythrocyte concentrates must not be suspended in glucose solutions because of the risk of pseudo-agglutination. See also section 4.4.

6.3 Shelf life

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

After first opening the container
Not applicable, see section 6.6.

After reconstitution or 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.
Observe the directions given by the manufacturer of the respective additive or drug to be diluted.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Bottles of colourless low-density polyethylene, contents: 500, 1000 ml.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Single-dose container. Discard containers and any unused contents after use. Do not re-connect partially used containers.
Only to be used if the solution is clear and colourless or slightly yellowish and if the bottle and its closure are undamaged.

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

Before addition of an additive or preparing a nutrient mixture, physical and chemical

compatibility must be confirmed. Because glucose solutions have an acidic pH, incompatibilities can occur on mixing with other medicinal products. Information on compatibility can be requested from the manufacturer of the added drug.

When adding additives observe usual precautions of asepsis strictly.

7 MANUFACTURER

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8 REGISTRATION HOLDER

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9 MARKETING AUTHORISATION NUMBER

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העלון לרופא נשלח למאגר התרופות שבאתר משרד הבריאות www.health.gov.il לצורך העלאתו לאתר וניתן לקבלו מודפס על ידי פניה לבעל הרישום Lapidot Medical Import & Marketing Ltd, רח' השיטה 8, פארק התעשיה קיסריה 3088900 ישראל.

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