Approved Professional Information for DEXTROSE FRESENIUS 10 %

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE

DEXTROSE FRESENIUS 10 % solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DEXTROSE FRESENIUS 10 % contains 100 g dextrose (anhydrous) per 1 000 ml.

Contains sugar (dextrose).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DEXTROSE FRESENIUS 10 % is indicated for use in adults and paediatric patients as a source of calories (energy) and water for hydration.

4.2 Posology and method of administration

Posology

The dosage is to be directed by a medical doctor and is dependent upon age, weight, clinical condition of the patient and laboratory determinations. Frequent laboratory determinations and clinical evaluations are essential to monitor changes in blood glucose and electrolyte concentrations, and fluid and electrolyte balance during prolonged parenteral therapy.

Fluid balance, serum glucose, serum sodium 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 medicines due to the risk of hyponatraemia.

Monitoring of serum sodium is particularly important for physiologically hypotonic fluids. DEXTROSE FRESENIUS 10 % may become extremely hypotonic after administration due to glucose metabolisation in the body (see sections 4.4, 4.5 and 4.8).

Special populations

Elderly patients

Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other medicine therapy.

Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see section 4.4).

Paediatric population

There is no specific paediatric dose. The dose is dependent on weight, clinical condition and laboratory results (see section 4.4).

Method of administration

For intravenous use only.

Use only if the solution is clear and container seals are intact.

When DEXTROSE FRESENIUS 10 % is to be administered peripherally, it should be slowly infused through a small bore needle, placed well within the lumen of a large vein to minimise venous irritation. Carefully avoid infiltration.

Fluid administration should be based on calculated maintenance or replacement fluid requirements for each patient.

4.3 Contraindications

The use of DEXTROSE FRESENIUS 10 % is contraindicated in patients with:

- hypersensitivity to dextrose (see sections 4.4 and 4.8 for maize allergies)
- uncompensated diabetes and diabetes insipidus
- hyperosmolar coma
- haemodilution and extracellular hyperhydration or hypervolaemia
- hyperglycaemia and hyperlactataemia
- severe renal insufficiency (with oliguria/anuria)
- uncompensated cardiac failure
- general oedema (including pulmonary and brain oedema) and ascitic cirrhosis

- other known glucose intolerances (such as metabolic stress situations)
- intracranial or intraspinal haemorrhage
- delirium tremens and where there is dehydration
- glucose-galactose malabsorption syndrome.

The contraindications related to any medicine that is added to DEXTROSE FRESENIUS 10 % should be considered.

4.4 Special warnings and precautions for use

DEXTROSE FRESENIUS 10 % should be used with care in patients with renal insufficiency, urinary tract obstruction, or impending or frank cardiac decompensation.

Hyperglycaemia

DEXTROSE FRESENIUS 10 % should be used with caution in patients with diabetes mellitus, as rapid infusion can lead to hyperglycaemia and a hyperosmolar syndrome.

To reduce the risk of hyperglycaemia-associated complications, the infusion rate must be adjusted and/or insulin administered.

DEXTROSE FRESENIUS 10 % should be administered with caution in patients with, for example:

- Impaired glucose tolerance (such as in patients with renal failure or diabetes mellitus or in the presence of sepsis, trauma or shock).
- Severe malnutrition (risk of precipitating a refeeding syndrome).
- Thiamine deficiency, e.g. in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolisation of pyruvate).
- Patients with ischaemic stroke or severe traumatic brain injury.

Avoid infusion within the first 24 hours following head trauma. Monitor blood glucose closely as early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury.

- Newborns.

Effects on insulin secretion

Prolonged intravenous administration of DEXTROSE FRESENIUS 10 % and associated hyperglycaemia may result in decreased rates of glucose-stimulated insulin secretion.

Hypersensitivity reactions

- Hypersensitivity/infusion reactions, including anaphylactic/ anaphylactoid reactions, have been reported with DEXTROSE FRESENIUS 10 % solution (see section 4.8). DEXTROSE FRESENIUS 10 % solution should therefore be used with caution, if at all, in patients with known allergy to maize or maize products (see section 4.3).
- DEXTROSE FRESENIUS 10 % solution must be stopped immediately, if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Refeeding syndrome

Refeeding severely undernourished patients may result in the refeeding syndrome that is characterised by the shift of potassium, phosphorus and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications.

Paediatric glycaemia-related issues

Newborns (especially those born premature and with low birth mass) are at increased risk of developing hypo- or hyperglycaemia and therefore, need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycaemic control in order to avoid potential long-term adverse effects. Hypoglycaemia in the newborn can cause prolonged seizures, coma and cerebral injury. Hyperglycaemia has been associated with intraventricular haemorrhage, late-onset bacterial and fungal infection, retinopathy of prematurity, necrotising enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stays and death.

Paediatric hyponatraemia-related issues

- In very low birth mass infants, excessive or rapid administration of DEXTROSE FRESENIUS 10 % may result in increased serum osmolality and possible intracerebral haemorrhage.
- In neonates and very small infants, even small volumes of fluid may affect fluid and electrolyte balance.
- Care must be exercised in treatment of neonates, especially pre-term neonates, whose renal function may be immature and whose ability to excrete fluid and solute loads may be limited.
- Fluid intake, urine output, and serum electrolytes should be monitored closely.
- Serum glucose concentrations should be monitored frequently when DEXTROSE FRESENIUS 10 % is prescribed to paediatric patients, particularly infants, neonates and low birth mass infants.
- Children (including neonates and older children) are at increased risk of developing hypoosmotic hyponatraemia as well as for developing hyponatraemic encephalopathy.

- Plasma electrolyte concentrations should be monitored closely in the paediatric population.
- Rapid correction of hypoosmotic hyponatraemia is potentially dangerous (risk of serious neurological complications). Dosage, rate, and duration of administration should be determined by a medical practitioner experienced in paediatric intravenous fluid therapy.

Blood

DEXTROSE FRESENIUS 10 % should not be administered simultaneously with blood through the same infusion set, as haemolysis and pseudoagglutination can occur.

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolisation (see section 4.2).

Dilution and other effects on serum electrolytes

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 DEXTROSE FRESENIUS 10 % can cause:

- hyperosmolality, osmotic diuresis and dehydration
- hypo-osmolality
- electrolyte disturbances such as:
  - hypo- or hyperosmotic hyponatraemia (see below)
  - hypokalaemia

- hypophosphataemia
- hypomagnesaemia
- overhydration/hypervolaemia and, for example,

congested states, including pulmonary congestion and oedema.

The above effects do not only result from the administration of electrolyte-free fluid but also from glucose administration.

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) characterised 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 of childbearing potential, 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.

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in the fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation.

Caution is advised in patients at increased risk of water and electrolyte disturbances that could be aggravated by increased free water load, hyperglycaemia or possibly required insulin administration (see below).

In case of prolonged administration or high dose of DEXTROSE FRESENIUS 10 %, care should be taken to avoid hypokalaemia by monitoring plasma potassium levels and administering a potassium supplement as required.

Special clinical monitoring is required at the beginning of any intravenous infusion.

4.5 Interaction with other medicines and other forms of interaction

Hypokalaemia and hyponatraemia may develop during parenteral administration of hypertonic dextrose solutions, such as DEXTROSE FRESENIUS 10 %. Sufficient amounts of potassium should be added to DEXTROSE FRESENIUS 10 % solutions administered to fasting patients with good renal function, especially those on digoxin therapy.

To minimise the risk of possible incompatibilities arising from mixing DEXTROSE FRESENIUS 10 % with other additives that may be prescribed, the final infusate should be inspected for cloudiness or precipitation immediately after mixing, prior to administration, and periodically during administration.

Both the glycaemic effects of DEXTROSE FRESENIUS 10 % and its effects on water and electrolyte balance should be considered when using DEXTROSE FRESENIUS 10 % in patients treated with other medicines that affect glycaemic control, or fluid and/or electrolyte balance.

Concomitant administration of catecholamines and steroids decreases the glucose uptake.

Medicines leading to an increased vasopressin effect

The below listed medicines 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 IV fluids (see sections 4.2, 4.4 and 4.8).

- Medicines stimulating vasopressin release, e.g. chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3,4-methylenedioxy-*N*-methamphetamine, ifosfamide, antipsychotics, narcotics.
- Medicines potentiating vasopressin action, e.g. chlorpropamide, NSAIDs, cyclophosphamide.
- Vasopressin analogues, e.g. desmopressin, oxytocin, terlipressin.

Other medicines increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Safety during pregnancy and lactation has not been established.

DEXTROSE FRESENIUS 10 % solutions are commonly used as hydrating fluids and as vehicles for other medicines. If given during labour, it has been suggested that the dextrose load on the mother may lead to fetal hyperglycaemia, hyperinsulinaemia, and acidosis, with subsequent neonatal hypoglycaemia and jaundice.

When a medicine is added, the nature of the medicine and its use during pregnancy and lactation have to be considered separately.

Pregnancy

DEXTROSE FRESENIUS 10 % solution can be used during pregnancy. However, caution should be exercised when DEXTROSE FRESENIUS 10 % solution is used intrapartum.

DEXTROSE FRESENIUS 10 % should be administrated with special 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).

Breastfeeding

There are no adequate data of using DEXTROSE FRESENIUS 10 % solution during breastfeeding.

However, no effect on breastfeeding is expected.

DEXTROSE FRESENIUS 10 % can be used during lactation.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Immune system disorders

Frequency not known:* anaphylactic reaction**, hypersensitivity reaction**

Metabolism and nutrition disorders

Frequency not known:* fluid and electrolyte disturbances (including hypokalaemia, hyponatraemia, hypomagnesaemia, hypophosphataemia), oedema, water intoxication and hyperglycaemia (due to prolonged or rapid infusion of large volumes of DEXTROSE

FRESENIUS 10 %), hyperglycaemia (may cause an osmotic diuresis, which may result in fluid and electrolyte losses), haemodilution, hypervolaemia, hospital-acquired hyponatraemia***

Nervous system disorders

Frequency not known: hyponatraemic encephalopathy***

Skin and subcutaneous tissue disorders

Frequency not known:* sweating, rash

Vascular disorders

Frequency not known:* vein irritation, thrombophlebitis, tissue necrosis (if extravasation occurs)

General disorders and administration site conditions

Frequency not known:* local pain, chills, shivering, pyrexia, febrile reaction, fever, infusion site infection, infusion site reactions (including infusion site phlebitis and infusion site erythema)

Investigations

Frequency not known:* glycosuria.

* Cannot be estimated from the available data.

** Potential manifestation in patients with allergy to maize, see section 4.4.

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

Reporting of suspected adverse reactions

Health care providers are asked to report any suspected adverse drug reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

Reporting suspected adverse reactions after authorisation of DEXTROSE FRESENIUS 10 % is important. It allows continued monitoring of the benefit/risk balance of DEXTROSE FRESENIUS 10 %. Health care providers are asked to report any suspected adverse reactions via the **Adverse Drug Reaction Reporting Form**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

See under section 4.8. In these cases, DEXTROSE FRESENIUS 10 % must be withdrawn.

Prolonged administration or rapid infusion of large volumes of DEXTROSE FRESENIUS 10 % may cause hyperosmolarity, hyponatraemia, dehydration, hyperglycaemia, hyperglycosuria, osmotic diuresis (due to hyperglycaemia), water intoxication and oedema. Severe hyperglycaemia and hyponatraemia may be fatal (see sections 4.4 and 4.8).

In case of suspected overdose, treatment with DEXTROSE FRESENIUS 10 % must be stopped immediately. Management of overdose is symptomatic and supportive, with appropriate monitoring.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 24 Mineral substitutes, electrolytes and trace elements.

Pharmacotherapeutic group “Carbohydrates”, ATC code: B05BA03

5.1 Pharmacodynamic properties

Dextrose is a hypertonic solution that provides calories and is a source of water.

5.2 Pharmacokinetic properties

Two different pathways are involved in the metabolism of glucose: one anaerobic and one aerobic.

Glucose is metabolised via pyruvic or lactic acid to carbon dioxide and water with the release of energy.

When medicine is added to DEXTROSE FRESENIUS 10 %, the pharmacokinetics of the additive will depend on the nature of the medicine used.

5.3 Preclinical safety data

No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (for pH-adjustment)

Sodium hydroxide (for pH-adjustment)

Water for injection

Osmolarity: 555 mOsm/l

pH: 4,5.

6.2 Incompatibilities

DEXTROSE FRESENIUS 10 % solution should not be given through the same infusion equipment as whole blood, as haemolysis and clumping can occur.

Incompatibility of the medicinal product to be added to DEXTROSE FRESENIUS 10 % must be assessed before its addition.

In the absence of compatibility studies, DEXTROSE FRESENIUS 10 % must not be mixed with other medicinal products.

The instructions for use of the medicine to be added must be consulted.

When a compatible medicine is added to DEXTROSE FRESENIUS 10 %, the solution must be administered immediately.

Those additives known to be incompatible should not be used.

6.3 Shelf life

24 months in PVC bags.

36 months in **free***flex*® bags.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

1 000 ml PVC or **free***flex*® bag.

Pack sizes: 12.

Not all container closure systems may be marketed.

6.6 Special precautions for disposal and other handling

DEXTROSE FRESENIUS 10 % should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. Use only if the solution is clear, without visible particles and if the container is undamaged. Administer immediately following the insertion of infusion set.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

Discard after single use.

Discard any unused portion.

Do not reconnect partially used bags.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten

Port Elizabeth 6020

South Africa

8. REGISTRATION NUMBER

C/24/226

9. DATE OF FIRST AUTHORISATION

09 July 1971

10. DATE OF REVISION OF THE TEXT

08 March 2022