Approved Professional Information for DEXTROSE 5 % FRESENIUS

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE

DEXTROSE 5 % FRESENIUS solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DEXTROSE 5 % FRESENIUS contains 50 g dextrose (as dextrose monohydrate) per 1 000 ml.

Excipient with known effect:

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 5 % FRESENIUS is indicated for use in adults and paediatric patients as a source of calories (energy) and water for hydration.

DEXTROSE 5 % FRESENIUS is also used as a vehicle and diluent for compatible medicinal products for parenteral administration.

4.2 Posology and method of administration

Posology

The dosage is to be determined by a medical doctor and is dependent upon age, body mass, clinical condition of the patient and laboratory test results. 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 should 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 5 % FRESENIUS may become extremely hypotonic after administration due to glucose metabolisation in the body (see sections 4.4, 4.5 and 4.8).

The recommended dosage for treatment of carbohydrate and fluid depletion is:

- for adults: 500 ml to 3 litres in 24 hours
- for babies and children:

0 – 10 kg body mass	100 ml/kg per 24 hours
10 – 20 kg body mass	1 000 ml + 50 ml/kg over 10 kg per 24 hours
> 20 kg body mass	1 500 ml + 20 ml/kg over 20 kg per 24 hours

The infusion rate depends on the patient's clinical condition.

Infusion rate should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycaemia. Therefore, the maximum dose ranges from 5 mg/kg/min for adults to 10 – 18 mg/kg/min for babies and children depending on the age and the total body mass.

The recommended dosage when used as a vehicle or diluent ranges from 50 to 250 ml per dose of DEXTROSE 5 % FRESENIUS to be administered.
When DEXTROSE 5 % FRESENIUS is used as a diluent for injectable preparations of other medicines, the dosage and the infusion rate will be principally dictated by the nature and the dose regimen of the prescribed medicine.

Special populations

Paediatric population

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

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).

Method of administration

For intravenous use only.

For single use only. Discard unused portion.
Use only if the solution is clear and container seals are intact.

When DEXTROSE 5 % FRESENIUS 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 5 % FRESENIUS is contraindicated in patients with:

- hypersensitivity to dextrose (see section 4.4 for maize allergies)
- uncompensated diabetes or other known glucose intolerances such as metabolic stress situations and glucose-galactose malabsorption syndrome
- hyperglycaemia
- hyperlactataemia.

4.4 Special warnings and precautions for use

Blood

DEXTROSE 5 % FRESENIUS must not be administered with blood through the same infusion set, as there is a risk of haemolysis and pseudo-agglutination.

Adding other medicine or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In case of an adverse reaction, the infusion must be stopped immediately.

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylactic/ anaphylactoid reactions, have been reported with glucose solutions such as DEXTROSE 5 % FRESENIUS (see section 4.8).

Solutions containing glucose, including DEXTROSE 5 % FRESENIUS, should be used with caution, if at all, in patients with a known allergy to maize or maize products (see sections 4.3 and 4.8).

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.

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 5 % FRESENIUS 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.

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 develop into acute hyponatraemic encephalopathy (brain oedema) characterised by headache, nausea, seizures, lethargy, coma, vomiting, cerebral oedema and death.

Patients with brain oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, the elderly, women of childbearing potential, post-operative patients, patients with hypoxia and patients with central nervous system disease (e.g. meningitis, intracranial bleeding, and cerebral contusion) or psychogenic polydipsia are at particular risk for this complication caused by acute hyponatraemia.

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

Particular 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).

Hyperglycaemia

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.

Rapid administration of glucose solutions may produce substantial hyperglycaemia and a hyperosmolar syndrome.

If hyperglycaemia occurs, the rate of infusion should be adjusted and/or insulin administered. If necessary, provide parenterally supplement in potassium levels.

DEXTROSE 5 % FRESENIUS should be administered with caution in patients with, for example:

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

Effects on insulin secretion

Prolonged intravenous administration of DEXTROSE 5 % FRESENIUS and associated hyperglycaemia may result in decreased rates of glucose-stimulated insulin secretion.

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 intake while avoiding overfeeding can prevent these complications.

Paediatric population

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

In order to avoid potentially fatal over-infusion of intravenous fluids to the neonate, special attention needs to be paid to the method of administration. When using a syringe pump to administer intravenous fluids or medicines to neonates, a bag of fluid should not be left connected to the syringe.

When using an infusion pump all clamps on the intravenous administration set must be closed before removing the administration set from the pump or switching the pump off. This is required regardless of whether the administration set has an anti-free-flow device.

The intravenous infusion device and administration equipment must be frequently monitored.

Paediatric glycaemia-related issues

Newborns – especially those born prematurely and with low birth body mass – are at increased risk of developing hypo- or hyperglycaemia and therefore need close monitoring during treatment with intravenous glucose solutions, such as DEXTROSE 5 % FRESENIUS, to ensure adequate glycaemic control in order to avoid potential long-term side 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 stay and death.

Paediatric hyponatraemia-related issues

Children (including neonates and older children) are at increased risk of developing hypo-osmotic hyponatraemia as well as for developing hyponatraemic encephalopathy.

Plasma electrolyte concentrations should be closely monitored in the paediatric population.

Rapid correction of hypo-osmotic hyponatraemia is potentially dangerous (risk of serious neurologic complications).

Dosage, rate, and duration of administration should be determined by a medical practitioner experienced in paediatric intravenous fluid therapy.

Elderly patients (> 65 years)

When selecting the type of infusion solution and the volume/rate of infusion for an elderly patient, consider that older patients are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant medicine therapy.

Risk of air embolism

Do not use plastic containers in series connections.

Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

Pressurising intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

Both the glycaemic effects of DEXTROSE 5 % FRESENIUS and its effects on water and electrolyte balance should be taken into account when it is administered to patients that are also treated with other substances that affect glycaemic control, 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.

4.6 Fertility, pregnancy and lactation

Safety during pregnancy and lactation has not been established.

DEXTROSE 5 % FRESENIUS 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 metabolic acidosis, with subsequent neonatal hypoglycaemia and jaundice.

Pregnancy

DEXTROSE 5 % FRESENIUS solution can be used during pregnancy. However, caution should be exercised when DEXTROSE 5 % FRESENIUS solution is used intrapartum.

DEXTROSE 5 % FRESENIUS 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 5 % FRESENIUS solution during breastfeeding.

However, no effect on breastfeeding is expected.

DEXTROSE 5 % FRESENIUS 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 (maize allergy)

Metabolism and nutrition disorders

Frequency not known: Electrolyte imbalance, hypokalaemia, hypomagnesaemia, hypophosphataemia, hyperglycaemia, dehydration, hypervolaemia, hospital-acquired hyponatraemia**

Nervous system disorders

Frequency not known: Hyponatraemic encephalopathy**

Skin and subcutaneous tissue disorders

Frequency not known: Rash

Vascular disorders

Frequency not known: Venous thrombosis, phlebitis

Renal and urinary disorders

Frequency not known: Polyuria

General disorders and administration site conditions

Frequency not known: Chills*, pyrexia*, infusion site infection, infusion site irritation (such as erythema, extravasation, local reaction, localised pain).

*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

Reporting suspected adverse reactions after authorisation of DEXTROSE 5 % FRESENIUS is important. It allows continued monitoring of the benefit/risk balance of DEXTROSE 5 % FRESENIUS. 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.

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.

4.9 Overdose

Prolonged administration or rapid infusion of large volumes of DEXTROSE 5 % FRESENIUS may cause hyperosmolarity and hyponatraemia, dehydration, hyperglycaemia, hyperglycosuria, osmotic diuresis (due to the hyperglycaemia) and 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 5 % FRESENIUS 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.

ATC code: B05BA03

5.1 Pharmacodynamic properties

DEXTROSE 5 % FRESENIUS is an isosmotic solution that is a principal source of energy in cellular metabolism and provides water supplementation. Each 1 000 ml of DEXTROSE 5 % FRESENIUS provides 840 kilojoules of energy.

5.2 Pharmacokinetic properties

Glucose is metabolised via pyruvic or lactic acid to carbon dioxide and water with the release of energy. The pharmacokinetics of the additive will depend on the nature of the medicine used.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (for pH-adjustment)

Sodium hydroxide (for pH-adjustment)

Water for injection

Osmolarity: 278 mOsml/l

pH approximately 4,5.

6.2 Incompatibilities

DEXTROSE 5 % FRESENIUS solution should not be given through the same infusion equipment as whole blood as haemolysis and clumping can occur.

To minimise the risk of possible incompatibilities arising from mixing DEXTROSE 5 % FRESENIUS 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.

6.3 Shelf life

24 months in **free***flex*® bags and PVC bags.

36 months in KabiPac (PE) bottles.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

50 ml PVC/**free***flex*® bag

100 ml PVC/**free***flex*® bag or KabiPac (PE) bottle

200 ml PVC bag

250 ml **free***flex*® bag or KabiPac (PE) bottle

500 ml PVC/**free***flex*® bag or KabiPac (PE) bottle

1 000 ml PVC/**free***flex*® bag or KabiPac (PE) bottle.

Not all container closure systems and pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicine should be disposed of in accordance with local requirements.

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

Electrolyte supplementation may be indicated according to the clinical needs of the patient.

Additives may be introduced before or during infusion through the injection site.

When introducing additives, the final osmolarity of solutions need to be checked.

Administration of hyperosmolar solutions may cause venous irritation and phlebitis.

Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored.

Please see section 4.4 for the risk of air embolism.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten 6020

Gqeberha

South Africa

8. REGISTRATION NUMBER

C/25.2/228

9. DATE OF FIRST AUTHORISATION

Date of registration: 29 May 1972

10. DATE OF REVISION OF THE TEXT

17 May 2022