Approved Professional Information for SUSTENANCE FRESENIUS

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

SUSTENANCE FRESENIUS solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 000 ml contains:

Potassium chloride	1,86 g
Sodium chloride	2,05 g
Magnesium chloride	0,51 g
Dextrose anhydrous	50,00 g

Ionic concentration:

Sodium ion:	35 mmol/l
Chloride ion:	65 mmol/l
Potassium ion:	25 mmol/l
Magnesium ion:	2,5 mmol/l

Excipient with known effect:

Contains sugar (dextrose): Each 1 000 ml solution contains 50 g dextrose anhydrous.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

Clear, colourless to light straw-coloured solution.

Osmolarity: 404,5 mOsml/l (approximately).

pH: 3,5 – 4,5 (approximately).

Energy: 836 kilojoules/l.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SUSTENANCE FRESENIUS is indicated as a source of water (fluid), electrolytes, and calories, or as an alkalinising agent.

4.2 Posology and method of administration

Posology:

The dosage, rate and duration of administration are to be individualised and depend upon the indication for use, the patient's age, weight, clinical condition and concomitant treatment and on the patient's clinical and laboratory response to treatment.

If patients need IV fluids for routine maintenance alone, restrict the initial prescription* to:

- 25 – 30 ml/kg/day of water **and**
- approximately 1 mmol/kg/day of potassium, sodium and chloride, **and**
- approximately 50 – 100 g/day of dextrose to limit starvation ketosis.

For patients who are obese, adjust the IV fluid prescription to their ideal body weight. Use lower range volumes per kg (patients rarely need more than a total of 3 litres of fluid per day) and seek expert help if their BMI is more than 40 kg/m^2.

Consider prescribing less fluid (for example, 20–25 ml/kg/day fluid) for patients who:

- Are older or frail.
- Have renal impairment or cardiac failure.
- Are malnourished and at risk of refeeding syndrome.

* These are initial prescriptions and further prescriptions should be guided by monitoring (see *General considerations* below).

General considerations:

Prescribing more than 2,5 litres IV fluid per day increases the risk of hyponatraemia (also see section 4.4).

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 agonists due to the risk of hyponatraemia.

Monitoring of serum sodium is particularly important for physiologically hypotonic fluids.
SUSTENANCE FRESENIUS may become extremely hypotonic after administration due to glucose metabolisation in the body (see section 4.4).

Special populations:

Paediatrics: Currently, there are no dosing recommendations for use in children (please see section 4.4: Paediatric use).

Method of administration:

For intravenous administration only.

SUSTENANCE FRESENIUS should be inspected visually for particulate matter and discolouration prior to administration. This solution should not be administered unless it is clear and the seal is intact (see section 6.6).

Additives may be incompatible. Those additives known to be incompatible should not be used. The pharmacist should be consulted if available. If, in the informed judgement of the medical doctor, it is deemed advisable to introduce additives, aseptic technique should be used. Mix thoroughly when additives have been introduced. Solutions containing additives should not be stored (see section 6.2).

4.3 Contraindications

- Hypersensitivity to the active ingredients (see section 2) or to any of the excipients of SUSTENANCE FRESENIUS listed in section 6.1.
- Solutions containing dextrose may be contraindicated in patients with known allergy to maize or maize products
- SUSTENANCE FRESENIUS must not be used in patients with clinically significant hyperglycaemia.

4.4 Special warnings and precautions for use

SUSTENANCE FRESENIUS should not be administered simultaneously with blood through the same administration set because of the possibility of pseudo-agglutination or haemolysis (see section 4.5).

SUSTENANCE FRESENIUS should be used with caution. Excess administration may result in metabolic alkalosis.

SUSTENANCE FRESENIUS should be used with great care in patients with:

- congestive heart failure
- severe renal insufficiency (see “Use in patients with severe renal impairment” below)
- in clinical states in which there exists oedema with sodium retention (see “Use in patients with hypervolaemia or overhydration, or conditions that cause sodium retention and oedema” below)
- hyperkalaemia (see “Use in patients with or at risk of hyperkalaemia”)
- severe renal failure
- conditions in which potassium retention is present
- metabolic or respiratory alkalosis
- severe hepatic insufficiency.

Hypersensitivity reactions:

Hypersensitivity/infusion reactions, including anaphylactoid reactions, have been reported with SUSTENANCE FRESENIUS. 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.

Hypertonic solution:

SUSTENANCE FRESENIUS is a hypertonic solution. Administration of hypertonic solutions may cause venous irritation including phlebitis. Hypertonic solutions should be administered with caution to patients with hyperosmolar states, e.g. hypochloraemic hypokalaemic alkalosis due to prolonged vomiting, pyloric stenosis, or prolonged nasogastric suctioning.

Fluid and/or solute overload and electrolyte disturbances:

Depending on the volume and rate of infusion, SUSTENANCE FRESENIUS can cause:

- fluid and/or solute overload resulting in overhydration/hypervolaemia and, for example, congested states including pulmonary congestion and oedema
- clinically relevant electrolyte disturbances and acid-base imbalance. See “Paediatric use” below.

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

Hyponatraemia:

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose-containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolisation. Monitoring of serum sodium is particularly important for hypotonic fluids.

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.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired 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 (cerebral oedema)

characterised by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening cerebral injury.
Children, women of childbearing 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.

Use in patients with or at risk of hypermagnesaemia:

Solutions containing magnesium should be used with caution in patients with:

- hypermagnesaemia or conditions predisposing to hypermagnesaemia including, but not limited to, severe renal impairment or magnesium therapy, such as eclampsia
- myasthenia gravis.

Use in patients with hypervolaemia or overhydration, or conditions that cause sodium retention and oedema:

The risk of dilutional states is inversely proportional to the electrolyte concentrations of SUSTENANCE FRESENIUS. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of SUSTENANCE FRESENIUS.

SUSTENANCE FRESENIUS should be administered with particular caution to hypervolaemic or overhydrated patients.
SUSTENANCE FRESENIUS should be used with great care in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists oedema with sodium retention, fluid overload and oedema, such as patients with primary hyperaldosteronism, secondary hyperaldosteronism (associated with, for example, hypertension, congestive heart failure, renal artery stenosis or nephrosclerosis) or pre-eclampsia.

Use in patients with hypocalcaemia:

SUSTENANCE FRESENIUS contains no calcium and an increase in plasma pH due to its alkalinising effect may lower the concentration of ionised (not protein-bound) calcium. SUSTENANCE FRESENIUS should be administered with particular caution to patients with hypocalcaemia.

Use in patients with or at risk of hyperkalaemia:

SUSTENANCE FRESENIUS is not for use in patients with hyperkalaemia. It should be used with caution in patients with conditions predisposing to hyperkalaemia (such as severe renal impairment or adrenocortical insufficiency, acute dehydration or
extensive tissue injury or burns) and in patients with cardiac disease, and in conditions where potassium retention is present.

Use in patients with severe renal impairment:

In patients with diminished renal function, administration of SUSTENANCE FRESENIUS may result in sodium or potassium retention.

Use in patients with or at risk of hyperglycaemia:

SUSTENANCE FRESENIUS contains 50 g dextrose (anhydrous) per infusion bag. This should be taken into account in patients with diabetes mellitus.
SUSTENANCE FRESENIUS should be used with caution in patients with impaired glucose tolerance or diabetes mellitus.
In order to avoid hyperglycaemia, the infusion rate should not exceed the patient's ability to utilise glucose. Hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery after acute ischaemic strokes. Caution is recommended in using glucose-containing solutions in such patients.

Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury. Glucose-containing solutions should, therefore, be used with caution in patients with head injury, in particular during the first 24 hours following the trauma.

Newborns, especially those born prematurely and with low birth weight, 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 (see “Paediatric use” below).

If hyperglycaemia occurs, the rate of glucose administration should be reduced and/or insulin administered, or the insulin dose adjusted.

Use in the elderly:

Reported clinical experience with SUSTENANCE FRESENIUS has not identified differences in responses between the elderly and younger patients. In general, 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 medicine therapy.

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

Paediatric use:

Safety and effectiveness of SUSTENANCE FRESENIUS in paediatric patients have not been established.

The infusion rate and volume depend on the age, weight, clinical and metabolic conditions of the patient, and concomitant therapy, and should be determined by the medical practitioner experienced in paediatric intravenous fluid therapy.

In very low birth weight infants, excessive or rapid administration of SUSTENANCE FRESENIUS may result in increased serum osmolality or possible haemorrhage.

Newborns, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia and therefore need close monitoring during treatment with SUSTENANCE FRESENIUS to ensure adequate glycaemic control in order to avoid potential long-term adverse effects. Hypoglycaemia in the newborn can cause prolonged seizures, coma and brain damage. 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.

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes.

The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death. Therefore, acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

4.5 Interaction with other medicines and other forms of interaction

SUSTENANCE FRESENIUS should not be administered simultaneously with blood through the same administration set because of the possibility of pseudo-agglutination or haemolysis (see sections 4.4 and 6.2).

Caution should be exercised in the administration of SUSTENANCE FRESENIUS to patients receiving corticosteroids or corticotrophin.

Caution is advised when administering SUSTENANCE FRESENIUS to patients treated with medicines for which renal elimination is pH dependent. Due to its alkalinising effect (formation of bicarbonate), SUSTENANCE FRESENIUS may interfere with the elimination of such medicines:

- renal clearance of acidic medicines such as salicylates, barbiturates and lithium may be increased
- renal clearance of alkaline medicines such as sympathomimetics (e.g. ephedrine, pseudoephedrine, quinidine or dextroamphetamine (dexamphetamine) sulphate) may be decreased.

Because of its potassium content, SUSTENANCE FRESENIUS should be administered with caution in patients treated with medicines that can cause hyperkalaemia or increase the risk of hyperkalaemia, such as:

- potassium-sparing diuretics (amiloride, spironolactone)
- angiotensin converting enzyme inhibitors (ACEIs)
- Angiotensin II receptor antagonists
- immunosuppressants such as tacrolimus and ciclosporin.

Administration of potassium in patients treated with such medicines can produce severe and potentially fatal hyperkalaemia, particularly in patients with severe renal insufficiency.

Caution is advised when administering SUSTENANCE FRESENIUS to patients treated with medicines leading to an increased vasopressin effect. The below listed medicines increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatraemia following treatment with IV fluids (see sections 4.4 and 4.8):

- medicines stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3,4-methylenedioxy-*N*-methamphetamine, ifosfamide, antipsychotics, opioids

- medicines potentiating vasopressin action such as chlorpropamide, nonsteroidal anti-inflammatories (NSAIDS), cyclophosphamide
- vasopressin analogues such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering SUSTENANCE FRESENIUS to patients treated with medicines that may increase the risk of hyponatraemia, such as diuretics and antiepileptics (e.g. oxcarbazepine).

Also see section 6.2 (Incompatibilities).

4.6 Fertility, pregnancy and lactation

The safety of POST SUSTENANCE FRESENIUS during pregnancy and lactation has not been established.

Studies with POST SURGISOL SOLUTION FRESENIUS have not been performed to evaluate effect on fertility.

4.7 Effects on ability to drive and use machines

There is no information of the effects of SUSTENANCE FRESENIUS on the ability to drive and use machines. Patients should be advised to take special care before performing tasks requiring their attention, until they know how SUSTENANCE FRESENIUS will affect them.

4.8 Undesirable effects

The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA system organ class (SOC), then in order of severity, where feasible. The frequency of the adverse reactions listed in this section is not known (cannot be estimated from the available data).

System organ class (SOC)	**Not known (cannot be estimated from the available data)**
Immune system disorders	*Hypersensitivity/infusion reactions, including anaphylactoid reaction
Metabolism and nutrition disorders	Hyperkalaemia Hyperglycaemia Hypervolaemia Hyponatraemia
Nervous system disorders	Seizures Hyponatraemic encephalopathy
Vascular disorders	Thrombophlebitis Venous thrombosis
General disorders and administration site conditions	Infusion site reactions (e.g. burning sensation pyrexia injection site pain injection site reaction injection site phlebitis injection site irritation injection site infection extravasation)
Metabolism and nutrition disorders	Electrolyte disturbance

*Include the following manifestations: hypotension, chest discomfort, dyspnoea, wheezing, flushing, hyperaemia, asthenia, urticaria, cold sweat, pyrexia and chills.

If an adverse reaction does occur, discontinue the infusion with SUSTENANCE FRESENIUS, evaluate the patient, institute appropriate therapeutic countermeasures, and save the remainder of the fluid for examination if deemed necessary.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of SUSTENANCE FRESENIUS is important. It allows continued monitoring of the benefit/risk balance of SUSTENANCE FRESENIUS. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions 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

In overdose, side effects will be exaggerated and exacerbated.

Excessive administration of SUSTENANCE FRESENIUS may lead to metabolic alkalosis. Metabolic alkalosis may be accompanied by hypokalaemia as well as a decrease in ionised serum calcium and magnesium (see section 4.4).

An excessive volume of SUSTENANCE FRESENIUS may lead to fluid and sodium overload with a risk of oedema (peripheral and/or pulmonary) particularly when renal sodium excretion is impaired (see section 4.4).

Excessive administration of potassium may lead to the development of hyperkalaemia, especially in patients with severe renal impairment (see section 4.4).

Excessive administration of magnesium may lead to hypermagnesaemia (see section 4.4).

Excessive administration of glucose-containing solution may lead to hyperglycaemia, hyperosmolarity, osmotic diuresis and dehydration.

When assessing an overdose, any additives in the solution must be considered.

Acute treatment:

The infusion should be interrupted immediately. Administration of diuretics and continuous monitoring of serum electrolytes, correction of electrolyte balance and acid-base balance may be required. Treatment is supportive and symptomatic.

Patients with hypermagnesaemia can be treated using assisted ventilation, calcium chloride administered intravenously, and forced diuresis with mannitol infusions.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 24 Mineral substitutes, electrolytes

Pharmacotherapeutic group: Electrolytes with carbohydrates.

ATC code: B05BB02.

SUSTENANCE FRESENIUS has value as a source of water, electrolytes, and calories. It is capable of inducing diuresis depending on the clinical condition of the patient.

SUSTENANCE FRESENIUS produces a metabolic alkalinising effect.

5.2 Pharmacokinetic properties

Potassium: Factors influencing potassium transfer between intracellular and extracellular fluid such as acid base disturbances can distort the relationship between plasma concentrations and total body stores. Potassium is excreted mainly by the kidneys; it is secreted in the distal tubules in exchange of sodium or hydrogen ions. The capacity of the kidneys to conserve potassium is poor and some urinary excretion of potassium continues even when there is severe depletion. Some potassium is excreted in the faeces and small amounts may also be excreted in sweat.

Sodium: Sodium is predominantly excreted by the kidney, but there is extensive renal reabsorption. Small amounts of sodium are lost in the faeces and sweat.

Dextrose: After intravenous administration glucose exhibits fast (approximately 20 minutes) and slow phases of equilibrium. Distribution is largely through extracellular water, and intracellular water of the liver.

Magnesium: Parenterally administered magnesium is excreted mainly in the urine. Small amounts of magnesium are distributed into breast milk and it crosses into the placenta.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection.

6.2 Incompatibilities

Additives may be incompatible. Those additives known to be incompatible should not be used (see

section 4.2).

Dextrose anhydrous as contained in SUSTENANCE FRESENIUS should not be administered concomitantly with blood in the same infusion set, due to the risk of clotting of red blood cells (see sections 4.4 and 4.5).

6.3 Shelf life

Unopened:

24 months.

In use:

After opening the container, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used containers.

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*® (non-PVC/polyolefine) bags.

6.6 Special precautions for disposal and other handling

SUSTENANCE FRESENIUS should be inspected visually for particulate matter and discolouration prior to administration. This solution should not be administered unless it is clear and the seal is intact.

Check for minute leaks by squeezing bag.

For single use only.

Discard any unused solution.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd.

6 Gibaud Road

Korsten

Port Elizabeth 6020

South Africa

8. REGISTRATION NUMBER

V/24/142

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13 January 1989

10. DATE OF REVISION OF THE TEXT

07 October 2021