Approved Professional Information for Half Strength Darrows Solution with 5 % Dextrose Fresenius

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 000 ml contains:

Dextrose monohydrate	55 g
equivalent to dextrose anhydrous	50 g
Potassium chloride	1,3 g
Sodium chloride	2 g
Sodium lactate	2,95 g

Contains:

Chloride ions	51,5 mmol/l
Lactate	26,5 mmol/l
Potassium ions	17,5 mmol/l
Sodium ions	60,5 mmol/l

Contains sugar (55 g dextrose monohydrate equivalent to 50 g dextrose anhydrous per 1 000 ml).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

A clear colourless to light straw-coloured solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fluid and/or electrolyte deficiency states where dextrose supplementation is required.

4.2 Posology and method of administration

Posology

Adults

In adults somewhat less than the average daily maintenance dose of potassium is supplied in one litre.

In potassium deficiency 70 – 80 mmol of potassium (or more) should be given daily.

Intravenously the maximum rate is 3 ml per minute for adults. It is desirable not to give more than 10 mmol of potassium per hour to adults if large amounts are indicated and correspondingly less to infants and children.

Special populations

Paediatric population

After adequate hydration and renal function are assumed by means of the initial hydrating solution, the dose is usually 80 ml per kilogram of body weight for the first 24 hours. After the first day, 22 – 53 ml per kilogram of body weight per day may be given as long as the stools remain watery. Additional fluid required daily may be provided by carbohydrate in water in amounts calculated so that the total fluid (with and without potassium) will be 150 – 200 ml per kilogram of body weight.

Method of administration

For IV use.

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.
HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may become extremely hypotonic after administration due to glucose metabolisation in the body (see sections 4.4, 4.5 and 4.8).

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may cause venous irritation and phlebitis. Therefore, it is recommended that HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS be administered through a large central vein, for thorough and rapid dilution of the hyperosmolar solution.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be inspected visually for particulate matter and discolouration prior to administration, whenever the solution and container permit (see section 4.4). Do not administer unless the solution is clear, and seal is intact. Only sterile and nonpyrogenic equipment must be used for intravenous administration.

The equipment should be primed with the solution to prevent air embolism due to residual air in the system. Additives may be introduced before infusion or during infusion through the injection site. Additives may be incompatible. Check additive compatibility with both the solution and container prior to use. Complete information is not available. Those additives known to be incompatible should not be used.

A gradual increase of flow rate should be considered when starting administration of glucose-containing products, as in HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS.

If in the informed judgment of the medical practitioner, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly and carefully when additives have been introduced. Do not store the solution containing additives.

4.3 Contraindications

- Hypersensitivity to any active ingredient, maize (maize is the raw material used in the production of dextrose), or to any ingredient of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS (see section 6.1).
- Renal insufficiency.
- Crush syndrome.
- Severe haemolytic reactions.
- Adrenocortical insufficiency.
- Hyperkalaemia.
- Early postoperative oliguria, except when gastrointestinal drainage is being done.
- Hypernatraemia.
- Hyperchloraemia.
- Uncompensated cardiac failure.
- Uncompensated diabetes, other known glucose intolerances (such as metabolic stress situations), hyperosmolar coma, hyperglycaemia and hyperlactataemia.

4.4 Special warnings and precautions for use

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).

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.

Hypersensitivity reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported (see section 4.8). Stop the infusion immediately if signs or symptoms of hypersensitivity/infusion reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Risk of hyperkalaemia

Hyperkalaemia is the most frequently occurring and serious hazard of potassium treatments. Since an exact measurement of potassium deficiency is not usually possible, potassium supplement should be administered slowly and with caution.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administered with caution to patients with conditions predisposing to hyperkalaemia and/or associated with increased sensitivity to potassium, such as patients with potassium-aggravated skeletal muscle channelopathies (e.g. hyperkalaemic periodical paralysis, congenital paramyotonia, and potassium-aggravated myotonia/patamyotonia).

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be used with great care, if at all, in patients with cardiac disease including congestive heart failure or AV block (especially if they receive digitalis), conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration or extensive tissue destruction as occurs with severe burns.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administered with considerable care to patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia or clinical states in which there exist oedema with sodium retention.

The administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS can cause fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations, overhydration, congested states, or pulmonary oedema. The risk of dilution states is inversely proportional to the electrolyte concentrations of the infusions. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of the infusions.

Use in patients with or at risk of alkalosis

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administered with particular caution, if at all, to patients with alkalosis or at risk of alkalosis, because lactate is metabolised to bicarbonate and administration may result in, or worsen, metabolic alkalosis. The effect of the sodium lactate component in HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS on patients with metabolic or respiratory alkalosis should be monitored closely.

Use in patients with or at risk for increased lactate levels or with impaired lactate utilisation

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administered with extreme caution, if at all, to patients with conditions associated with increased lactate levels, impaired lactate utilisation such as cardiac disease, shock and severe hepatic insufficiency or otherwise at risk of alkalosis. Hyperlactataemia (i.e. high lactate levels) can develop in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. In addition, HALF STRENGTH DARROWS SOLUTION WITH

5 % DEXTROSE FRESENIUS may not produce its alkalinising action in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. Less frequently seizures may be precipitated by the alkalosis induced by lactate.
Lactate-containing solutions should be administered with particular caution to neonates and infants less than 6 months of age (see also "**Paediatric patients**").

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be used with care in patients with subclinical diabetes mellitus (see section 4.5), hyperkalaemia, severe renal failure, and in conditions in which potassium retention is present. Careful monitoring of plasma levels is recommended in these clinical situations.

Administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may lead to hyperglycaemia, therefore it is not recommended to use this solution after acute ischaemic strokes, as hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery. If hyperglycaemia occurs, rate of infusion should be adjusted, or insulin administered (see section 4.5).

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administered with caution to patients who are at risk of experiencing hyperosmolarity, acidosis or undergoing correction of alkalosis (conditions associated with a shift of potassium from intracellular to extracellular space) and patients treated concurrently or recently with medicine that can cause hyperkalaemia.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be used with caution in patients with cardiac dysrhythmia. Dysrhythmias can develop at any time during hyperkalaemia. Frequently, mild or moderate hyperkalaemia is asymptomatic and may be manifested only by increased serum potassium concentrations, and possibly characteristic electrocardiogram (ECG) changes.

Hyponatraemia

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be used with particular caution in patients with or at risk of hyponatraemia.
Glucose intravenous infusions, such as HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS, 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.

Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, postoperative stress, infections, burns and central nervous system (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. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

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.

Risk of hypo- and hyperosmolality, serum electrolytes and water imbalance

Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolise glucose, intravenous administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS can cause:

- hypoosmolality
- hyperosmolality, osmotic diuresis and dehydration
- electrolyte disturbances such as
    - hyponatraemia
    - hypophosphataemia
    - hypomagnesaemia.
- overhydration/hypervolaemia and, for example, congested states, including central (e.g. pulmonary congestion) and peripheral oedema.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS can also cause:

- acid-base imbalance
- an increase in serum glucose concentration is associated with an increase in serum osmolality. Osmotic diuresis associated with hyperglycaemia can result in or contribute to the development of dehydration and electrolyte losses.

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.

Risk of hyperglycaemia

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

Lactate is a substrate for gluconeogenesis and since HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS contains glucose and lactate (which is metabolised to glucose), administration that exceeds the metabolic capacity for glucose may lead to hyperglycaemia.

In order to avoid hyperglycaemia, the infusion rate should not exceed the patient's ability to utilise glucose. To reduce the risk of hyperglycaemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

Intravenous glucose should be administered with caution in patients with, for example:

- impaired glucose tolerance (such as in diabetes mellitus, renal impairment, 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 metabolism of pyruvate)
- water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be used with caution in:

- Patients with ischaemic stroke. Hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery after acute ischaemic strokes.
- Patients with severe traumatic brain injury. Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury.
- Newborns.

Prolonged intravenous administration of glucose 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.

Patients with severe renal impairment

Administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be discontinued if signs of renal insufficiency develop. Close medical supervision with frequent electrocardiograms and serum potassium determinations should guide parenteral potassium therapy.

Assurance of normal kidney function is the key to safe potassium therapy. Such assurance may be provided by the use of the initial hydrating solution 5 % dextrose in 0,2 % saline solution.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administered with particular caution to patients at risk of severe renal impairment.

In such patients, administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may result in sodium retention, fluid overload, and/or may predispose to hyperkalaemia.

Risk of air embolism

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container. Pressurising intravenous solutions

contained in flexible 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.

Elderly patients

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

Paediatric patients

Neonates, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia. Therefore, close monitoring during treatment with HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS is required to ensure adequate glycaemic control to avoid potential long-term adverse effects.
Hypoglycaemia in the neonate can cause prolonged seizures, coma and brain damage.
Hyperglycaemia has been associated with cerebral injury, including intraventricular haemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotising enterocolitis, bronchopulmonary dysplasia, increased oxygen requirements, prolonged length of hospital stay, and in some cases, death.
Infants and children may have an impaired ability to regulate fluid and electrolytes.
Plasma electrolyte concentrations should be closely monitored in the paediatric population.
Rapid correction of 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.

Lactate-containing solutions should be administered with particular caution to neonates and infants less than 6 months of age (see also "**Use in patients with or at risk for increased lactate levels or with impaired lactate utilisation**" above).

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS contains sugar (50 g dextrose per 1 000 ml). Patients with rare glucose-galactose malabsorption should not receive this medicine.

4.5 Interaction with other medicines and other forms of interaction

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, nonsteroidal anti-inflammatory drugs (NSAIDs), cyclophosphamide.
- Vasopressin analogues, e.g. desmopressin, oxytocin, vasopressin, terlipressin.

Medicine increasing the risk of hyponatraemia

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

Blood

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should not be administered simultaneously with blood through the same administration set because of the possibility of haemolysis and pseudo-agglutination.

Medicines or products causing hyperkalaemia or increasing the risk of hyperkalaemia

Use with caution in patients treated with medicines or products that can cause hyperkalaemia or increase the risk of hyperkalaemia, e.g. potassium-sparing diuretics (such as amiloride, spironolactone, triamterene), angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists. The simultaneous administration of these medicines can result in increased risk of severe and potentially fatal hyperkalaemia, in particular in the presence of other risk factors for hyperkalaemia.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should also be used with caution concomitantly with ciclosporin, tacrolimus and medicines that contain potassium.

Medicine affecting glycaemic control

Concurrent use of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS with insulin will decrease serum potassium. Use of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may necessitate review of a patient's oral hypoglycaemic or insulin requirements, so close monitoring of serum glucose levels is also required. Both the glycaemic effects of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS and its effects on water and electrolyte balance should be taken into account when using these products in patients treated with other medicines that affect glycaemic control, or fluid and/or electrolyte balance.

Lithium

Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be increased during administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS and can result in decreased lithium levels.

Medicines for which renal elimination is pH dependent

Due to the alkalinising action of lactate (formation of bicarbonate), HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may interfere with the elimination of such medicines:

- renal clearance of acidic medicines such as salicylates, barbiturates and lithium (see also "**Lithium**" above) may be increased
- renal clearance of alkaline medicines such as sympathomimetics (e.g. pseudoephedrine), dexamphetamine sulphate and fenfluramine hydrochloride may be decreased.

Beta adrenergic agonist

Beta adrenoceptor blockade increases both peak serum potassium concentration and the time required for serum potassium to return to basal levels in subjects receiving an acute intravenous potassium load.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

These may cause hyperkalaemia by inducing secondary hypoaldosteronism following inhibition of renal prostaglandin synthesis.

Heparin

Reduces the synthesis of aldosterone, which may result in hyperkalaemia, especially in patients with underlying renal insufficiency or other problems that impair potassium excretion.

Digoxin

Potassium supplementation is not recommended with concurrent digoxin in those patients with severe or complete heart block. Careful monitoring is necessary if potassium chloride is used to correct hypokalaemia in such patients.

Sodium bicarbonate

Concurrent use will decrease serum potassium.

Corticosteroids or corticotropin

Caution must be exercised in the administration of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS to patients receiving corticosteroids or corticotropin, as it may lead to sodium and water retention, oedema and hypertension.

4.6 Fertility, pregnancy and lactation

The safety of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS in pregnancy and lactation has not been established.

HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be administrated with special caution to pregnant woman during labour, particularly if administered in combination with oxytocin, due to the risk of hyponatraemia (see sections 4.4, 4.5 and 4.8).

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Immune system disorders

Frequency not known: anaphylactic reactions, hypersensitivity, pyrexia and chills

Metabolism and nutrition disorders

Frequency not known: hospital-acquired hyponatraemia**, hyperkalaemia, hyperchloraemic acidosis

Nervous system disorders

Frequency not known: hyponatraemic encephalopathy**

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

Cardiac disorders

Frequency not known: cardiac arrest

General disorders and administrative site conditions

Frequency not known: fluid and electrolyte disturbances.

Reporting of suspected adverse reactions

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

Symptoms

There is no overdose experience with HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS IV infusion preparations.

However, an excessive volume or too high a rate of administration may lead to fluid and sodium overload with a risk of oedema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired.

Excessive administration of lactate may lead to metabolic alkalosis, which may be accompanied by hypokalaemia.

Excessive administration or impaired excretion of potassium may lead to:

- hyperglycaemia, adverse effects on water and electrolyte balance, and corresponding complications (e.g. severe hyperglycaemia and severe dilutional hyponatraemia and their complications, can be fatal)
- hyponatraemia (which can lead to CNS manifestations including seizures, coma, cerebral oedema and death)
- hypernatraemia, especially in patients with severe renal impairment
- fluid overload (which can lead to central and/or peripheral oedema)
- development of potentially fatal hyperkalaemia (see section 4.8). If hyperkalaemia is present or suspected, discontinue the infusion immediately and institute close ECG, laboratory and other monitoring and, as necessary, corrective therapy to reduce serum potassium levels. Manifestations of hyperkalaemia may include:

- disturbances in cardiac conduction and dysrhythmias, including bradycardia, heart block, asystole, ventricular tachycardia, ventricular fibrillation
- hypotension
- muscle weakness up to and including muscular and respiratory paralysis, paresthesia of extremities
- gastrointestinal symptoms (ileus, nausea, vomiting, abdominal pain).

- dysrhythmias and conduction disorders, in addition to dysrhythmias and conduction disorders, the ECG shows progressive changes that occur with increasing potassium levels. Possible changes include:
  - peaking of T waves
  - loss of P waves
  - QRS widening.

However, the correlation between potassium levels and ECG changes is not precise, and whether or at which potassium level certain ECG signs develop depends on factors such as patient sensitivity, the presence of other electrolytes disorders, and the rapidity of the development of hyperkalaemia. The presence of any ECG findings that are suspected to be caused by hyperkalaemia should be considered a medical emergency.

When assessing an overdose, any additives in the solution must also be considered. Clinically significant overdose of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS may, therefore, constitute a medical emergency.

Overdose is usually asymptomatic and may only be manifested by increased serum potassium levels and characteristic ECG features (see sections 4.4 and 4.8).

Treatment

No specific antidotes to this preparation are known, interventions include discontinuation of HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

Should overdose occur, treatment should be discontinued and the patient should be observed for symptoms of the infusion, including any additives, with appropriate supportive measures instituted as required. The use of potassium-containing foods or medicine causing potassium retention must also be discontinued.

Treatment of hyperkalaemia depends on its severity. If hyperkalaemia is present or suspected, discontinue the infusion immediately and institute close ECG, laboratory and other monitoring and, as necessary, corrective therapy to reduce serum potassium levels. It must be kept in mind that rapid lowering of serum potassium concentrations in digitalised patients can cause cardiac toxicity.

Clinically, only the intravascular potassium concentration causes cardiac disorders. Therefore, infusion of the potassium chloride solution and other exogenous sources of potassium, such as potassium-rich containing foods or medicine causing potassium retention (potassium-sparing diuretic) must be discontinued immediately. In patients with severe hyperkalaemia, measures, which facilitate the shift of potassium ions from the vascular to the intracellular space, should be initiated. It can be achieved by administration of sodium bicarbonate, glucose/insulin, or calcium gluconate infusions.

In patients with serum potassium concentrations greater than 6,5 mmol/l, intravenous infusion of 40 – 160 mmolar of sodium bicarbonate over a 5-minute period has been recommended. This dose may be repeated every 15 minutes if ECG abnormalities persist. This treatment results in a temporary alkalosis and lowers serum potassium levels by 0,6 mmol/l for every 0,1 increase of the pH.

Glucose/insulin infusion is another treatment for an overdose episode with potassium chloride medicine. It consists of 300 – 500 ml of 10 – 25 % glucose intravenous infusion containing 5 – 10 IU insulin per 20 g of glucose infused over a 1-hour period.
Patients whose ECGs show the absence of P waves or a broad QRS complex and who are not receiving cardiac glucosides should immediately be given intravenously 0,5 – 1,0 g (5 – 10 ml of a 10 % solution) of calcium gluconate or another calcium salt over a 2- minute period (with continuous ECG monitoring) to antagonise the cardiac toxic effects of potassium. If ECG abnormalities persist, repeated doses of calcium salt may be given, allowing 1 – 2 minutes between doses.

When the ECG approaches normal, efforts should be directed toward removal of excess potassium from the body. This is a choice of treatment, when the removal of the potassium should be initiated as soon as possible. This is accomplished by administration of sodium polystyrene sulphonate resin orally or rectally, where sodium is exchanged with potassium in the gastrointestinal tract. One gram of resin will remove 1 mmol of potassium, but at the same time it will add 2 – 3 mmol of sodium, which may lead to a sodium overload. To overcome the constipating effect of the resin, it is formulated in sorbitol solution (20 %).

The initial dose of 30 – 60 g of resin in 120 – 240 ml of 20 % sorbitol has been recommended. It can be repeated every 1 – 2 hours.

As a last resort, haemodialysis or peritoneal dialysis can be used to remove potassium from the body, in particular, in patients with renal impairment. The infusion of furosemide (high dose diuretics) with a substantial amount of sodium chloride and bland solution will excrete potassium at the distal tubules of the renal system by sodium exchange mechanism into the urine.

5. PHARMACOLOGICAL PROPERTIES

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

Pharmacotherapeutic group: Electrolytes with carbohydrates

ATC code: B05BB02

5.1 Pharmacodynamic properties

It is a dextrose-containing electrolyte solution for intravenous infusion.

Glucose is readily metabolised into carbon dioxide and water with a release of energy. Thus, administration of a glucose solution either by oral or parenteral route will provide water for body hydration as well as energy. In addition, it may reduce catabolic loss of nitrogen from the body and aid in prevention of depletion of liver glycogen. That is, in the absence of glucose, amino acids undergo deamination followed by oxidation in order to release energy.

Potassium is the major cation of intracellular fluid (160 mEq/litre of intracellular water) and functions principally in the control of body fluid composition and electrolyte balance. Potassium participates in carbohydrate utilisation and protein synthesis and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart.

In contrast, sodium is a major cation of extracellular fluid and functions principally in the control of water distribution, fluid and electrolyte balance, and osmotic pressure of the body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of acid-base balance. A membrane bound enzyme, sodium-potassium activated ATP-ase (Na/K-ATPase), actively pumps sodium ions out of the cells into extracellular compartments, whilst the potassium ions are pumped into the cells against concentration gradients in order to maintain homeostasis of cell electrolytes.

Chloride, the major extracellular anion, closely follows the physiological disposition of sodium cation in maintenance of acid-base balance, isotonicity and electrodynamic

characteristic of the cells. An increase of chloride concentration may result in a decrease of bicarbonate level, which leads to plasma acidosis.

Sodium lactate is an alkalising medicine. Lactate is slowly metabolised to bicarbonate and water. This reaction depends on the cellular oxidative activity. Under normal physiological condition conversion of sodium lactate to bicarbonate requires about 1 - 2 hours. The bicarbonate metabolite then has similar actions to those of sodium bicarbonate preparations. That is, bicarbonate metabolites react with acid to produce carbon dioxide and water.

5.2 Pharmacokinetic properties

Absorption

As the HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS is directly administered to the systemic circulation by infusion, the bioavailability (absorption) of the active ingredients is complete (100 %).

Distribution

After its distribution into extracellular compartments, these ions follow the physiological pathways of the individual ion. That is, potassium ions and sodium ions are pumped into and out of the cells, respectively, by the action of Na/K-ATPase.

Elimination

Sodium and potassium ions are principally excreted by the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection.

37 % hydrochloric acid (for pH-adjustment)

Theoretical osmolarity: 434 mOsmol/l

pH (approximately): 5

Kilojoules (approximately): 840

Sterile, pyrogen free.

6.2 Incompatibilities

Additives may be incompatible. The compatibility with both the solution and container should be reviewed prior to use. Additives known to be incompatible should not be used.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Any unused portion should be discarded.

6.5 Nature and contents of container

200 ml, 500 ml and 1 000 ml in PVC bags or **free***flex*® (non-PVC) bags. Not all pack sizes and container systems may be marketed.

6.6 Special precautions for disposal and other handling

Do not use if solution is cloudy or if there is a deposit or visible particles in it. Check for minute leaks by squeezing the bag. HALF STRENGTH DARROWS SOLUTION WITH 5 % DEXTROSE FRESENIUS should be used once only. Any unused portion should be discarded. Do not reconnect partially used bags.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten 6020

Gqeberha

South Africa

8. REGISTRATION NUMBER

H/24/276

9. DATE OF FIRST AUTHORISATION

Date of registration: 21 April 1976

10. DATE OF REVISION OF THE TEXT

25 May 2022