Approved Professional Information for CALCIUM CHLORIDE 10 % FRESENIUS

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

CALCIUM CHLORIDE 10 % FRESENIUS solution for injection or infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml ampoule contains 1 g calcium chloride dihydrate.

Each 10 ml ampoule contains 6,803 millimoles or 13,605 milliequivalents of calcium.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection or infusion.

A clear, colourless solution in 10 ml clear glass ampoules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of calcium deficiency and hypocalcaemia. It is also used as an adjunct in the treatment of severe hyperkalaemia and hypermagnesaemia. It has an inotropic effect in cardiac resuscitation. Alleviation of pain in lead colic.

4.2 Posology and method of administration

Up to 10 ml CALCIUM CHLORIDE FRESENIUS injection is given according to the patient's need in an intravenous infusion or very slow intravenous injection (not more than 1 ml per minute) – too rapid administration will cause vasodilation or clotting. A maximum of 8 g in 24 hours must not be exceeded. There are about three times more calcium ions in calcium chloride than in an equivalent amount of calcium gluconate. The pulse rate should be monitored during administration and should bradycardia develop, the intravenous infusion should be stopped immediately.

Treatment should be stopped at once if blood calcium exceeds 2,625 mmol to 2,75 mmol per litre.

4.3 Contraindications

CALCIUM CHLORIDE FRESENIUS is contraindicated in:

- Patients that are hypersensitive to calcium chloride or any of the excipients in CALCIUM CHLORIDE FRESENIUS listed in section 6.1.
- Patients being treated with cardiac glycosides.
- Patients with ventricular fibrillation or hypercoagulability of blood.
- Hypercalcaemia and severe hypercalciuria (e.g. hyperparathyroidism, vitamin D overdosage, decalcifying tumours such as plasmacytoma and skeletal metastases).
- Renal failure.
- Osteoporosis due to immobilisation.
- Sarcoidosis and milk-alkali syndrome.

4.4 Special warnings and precautions for use

Do not inject intramuscularly or subcutaneously. It is irritant to tissues and causes necrosis. Intravenous infusions must be given very slowly. Injection given too quickly can cause hypotension and cardiovascular collapse (see section 4.8).

Hypercalcaemia can occur because of underlying hyperparathyroidism of neoplastic disease and excessive vitamin D intake, prolonged immobilisation, sarcoidosis, hyperthyroidism, milk-alkali syndrome and acidosis (see section 4.3).

Give cautiously to patients with impaired renal function or renal stone formation.

Serum calcium levels should be assessed regularly, particularly with renal insufficiency and if large doses of vitamin D are used concurrently.

CALCIUM CHLORIDE FRESENIUS, because of its acidifying nature, is unsuitable for the treatment of hypocalcaemia caused by renal insufficiency or in patients with respiratory acidosis or failure.

Ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites.

A moderate fall in blood pressure due to vasodilation may attend CALCIUM CHLORIDE FRESENIUS injection.

CALCIUM CHLORIDE FRESENIUS is irritating to veins and must not be injected into tissues, since severe necrosis and sloughing may occur (see section 5.8). Great care should be taken to avoid extravasation or accidental injection into perivascular tissues. Should perivascular infiltration occur, IV administration at that site should be discontinued at once. Local infiltration of the affected area with 1 % procaine hydrochloride, to which hyaluronidase may be added, will often reduce venospasm and dilute the calcium remaining in the tissues locally. Local application of heat may also be helpful.

Excessive amounts of calcium salts may cause hypercalcaemia (see section 4.8). Careful monitoring of serum electrolyte concentrations is essential throughout therapy.

It is particularly important to prevent a high concentration of calcium from reaching the heart because of the danger of cardiac syncope. If injected into the ventricular cavity in cardiac resuscitation, care must be taken to avoid injection into the myocardial tissue.

4.5 Interaction with other medicines and other forms of interaction

CALCIUM CHLORIDE FRESENIUS potentiates effects of digitalis glycosides and may cause intoxication. It could increase the gastric acid secretion enormously.

For interaction between calcium-containing products and ceftriaxone, please see section 4.4 above.

CALCIUM CHLORIDE FRESENIUS is not compatible for simultaneous administration with other intravenous solutions containing citrates, soluble carbonates, phosphates, sulphates, cefalotin sodium, clindamycin phosphate, magnesium sulphate, novobiocin sodium and prednisolone sodium phosphate.

In addition, incompatibilities have occurred with oxytetracycline hydrochloride, prochlorperazine, sodium bicarbonate, streptomycin sulphate and tetracycline hydrochloride.

Hypercalcaemia has occurred when CALCIUM CHLORIDE FRESENIUS was given with thiazide diuretics or vitamin D.

CALCIUM CHLORIDE FRESENIUS may decrease the effectiveness of calcium channel blockers.

CALCIUM CHLORIDE FRESENIUS may reduce the absorption of bisphosphonates (in the treatment of Paget's disease or hypercalcaemia of malignancy) and must be given at least 12 hours apart.

4.6 Fertility, pregnancy and lactation

The safety of CALCIUM CHLORIDE FRESENIUS in pregnancy and lactation has not been established.

4.7 Effects on ability to drive and use machines

No adverse effects have been reported.

4.8 Undesirable effects

Gastrointestinal disorders:

Frequency unknown: Nausea, vomiting.

Skin and subcutaneous tissue disorders:

Frequency unknown: Tingling of the skin, peripheral vasodilation, sweating and hot flushes.

General disorders and administration site conditions:

Frequency unknown: Chalk-like taste.

Description of selected adverse reactions:

Rapid intravenous injections may cause the patient to complain of tingling sensations, a calcium (chalk-like) taste, and a sense of distress or “heat wave”. Injections of calcium chloride are accompanied by peripheral vasodilation as well as a local burning sensation and there may be a

moderate fall in blood pressure.

Necrosis and sloughing with subcutaneous or intramuscular administration or if extravasation occurs have been reported (see section 4.4). Soft tissue calcification, bradycardia or dysrhythmias have also been reported.

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 CALCIUM CHLORIDE FRESENIUS is important. It allows continued monitoring of the benefit/risk balance of CALCIUM CHLORIDE 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.

4.9 Overdose

Symptoms:

An overdose of CALCIUM CHLORIDE FRESENIUS would lead to hypercalcaemia.

Symptoms of hypercalcaemia may include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, thirst, polyuria, drowsiness, confusion, nephrocalcinosis, and in severe cases – cardiac dysrhythmias, coma and cardiac arrest.

Treatment:

Initial management of hypercalcaemia should include withholding calcium administration. This will usually resolve mild hypercalcaemia in asymptomatic patients, provided renal function is adequate. When serum calcium concentrations are greater than 12 mg per 100 ml, immediate measures may be required such as rehydration by either the oral or intravenous route. In severe hypercalcaemia, administration of sodium chloride by intravenous infusion to expand the extracellular fluid may be necessary.

Intravenous rehydration may be given with, or followed by, furosemide or other loop diuretics to increase calcium excretion. Thiazide diuretics should be avoided as they may increase the renal absorption of calcium.

Other medicines which may be used if this treatment proves unsuccessful include calcitonins, the bisphosphonates, medicines with chelating properties, corticosteroids and plicamycin.

Phosphates may be useful, but should be given by mouth and only to patients with low serum phosphate concentrations and normal renal function.

Haemodialysis may be considered as a last resort.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 24 Mineral substitutes, electrolytes.

Pharmacotherapeutic group: Mineral supplements.

ATC code: A12AA07.

Calcium is an essential electrolyte of the tissues and the blood, in ionised and colloidal form. It is essential for normal muscle and nerve function, cardiac function and blood clotting.

5.2 Pharmacokinetic properties

The body contains about 1 200 g of calcium (or 300 to 500 mmol per kg body weight), approximately 99 % of which is found in the skeleton. The normal concentration of calcium in plasma is between 2,15 to 2,60 mmol per litre.

Calcium is absorbed from the small intestine. The amount of calcium absorbed varies depending on several factors including the requirements of the body, but is normally only about 30 % of the dietary intake.

The absorption of calcium is increased during periods of high physiological requirement such as during pregnancy and lactation.

The amount of dietary calcium required by an adult is about 700 to 800 mg (17,5 – 20 mmol) per day.

After absorption calcium is eventually incorporated into bones and teeth with 99 % of the body's calcium content being present in such skeletal tissue. The remaining calcium is present in both the intra- and extracellular fluids.

About 50 % of the total blood calcium content is in the physiologically active ionised form with 5 % being complexed to citrate, phosphate or other anions and 45 % being bound to proteins.

Excretion of calcium occurs in the urine although a large proportion is reabsorbed in the renal tubules. Excretion also occurs in the faeces, this consisting of unabsorbed calcium as well as that secreted in the bile and pancreatic juice. Minor amounts are lost in the sweat. Calcium crosses the placenta and is also excreted in breast milk.

5.3 Preclinical safety data

No information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection

Hydrochloric acid (for pH-adjustment).

6.2 Incompatibilities

See sections 4.4 and 4.5.

6.3 Shelf life

60 months.

Use immediately after first opening.

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

10 ml clear, Type 1 glass OPC ampoules, packed into a blister tray and outer carton.

Pack size: 10 ampoules per outer carton.

6.6 Special precautions for disposal and other handling

For single use only. Discard any unused contents after first use.

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/24/221

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12 August 1988

10. DATE OF REVISION OF THE TEXT

07 February 2022