AUSTRALIAN PRODUCT INFORMATION

CALCIUM CHLORIDE 10%

(calcium chloride dihydrate) 1 g in 10 mL Injection

1 NAME OF THE MEDICINE

Calcium chloride dihydrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Calcium Chloride 10% Injection contains 1 g of calcium chloride dihydrate. Each 10 mL contains 6.8 mmol (13.6 mEq) calcium ions and 13.6 mmol (13.6 mEq) chloride ions.

For the full list of excipients, see Section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

Calcium Chloride 10% Injection is a clear, colourless sterile solution of calcium chloride dihydrate in Water for Injections BP with a pH of between 5 and 8.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Parenteral administration of calcium is indicated in the treatment of hypocalcaemia where a rapid increase in plasma calcium is required, such as in hypocalcaemic tetany and tetany due to parathyroid deficiency.

Intravenous calcium is also indicated to antagonise the cardiotoxicity of hyperkalaemia.

4.2 DOSE AND METHOD OF ADMINISTRATION

Calcium Chloride 10% Injection should not be administered if the solution is cloudy or contains particles. After use, the unused portion of each vial must be discarded. The injection should not be given via the subcutaneous or intramuscular route. Use in one patient on one occasion only and discard.

Each mL of Calcium Chloride 10% Injection contains approximately 0.68 mmol of calcium ions and 1.36 mmol of chloride ions.

To aid in converting: 1 g elemental calcium = 25 mmol elemental calcium = 50 mEq elemental calcium = 3.7 g calcium chloride.

Calcium Chloride 10% Injection must be administered slowly via a small needle into a large vein at a rate not exceeding 0.35 - 0.7 mmol (0.7 to 1.4 mEq) per minute to avoid venous damage and to prevent a high concentration of calcium reaching the heart and causing syncope. The injection should be stopped if the patient experiences pain or redness at the injection site as this may indicate extravasation of the drug.

It is recommended that the patient remain recumbent for a short time after the intravenous injection of calcium. The dose, and dose rate, should be individualised according to the patient's condition using frequent determinations of plasma calcium concentrations.

Acute hypocalcaemia

Adults. An initial dose of 3.5 - 7 mmol (7 to 14 mEq) calcium is recommended repeated every 1 - 3 days as necessary.

Children. An initial dose of 0.5 - 3.5 mmol (1 to 7 mEq) calcium/kg is recommended. The dose may be repeated every 1 - 3 days as necessary.

Hypocalcaemic tetany

Adults. An initial dose of 2.25 - 8 mmol (4.5 to 16 mEq) calcium is recommended, repeated until a response is achieved.

Children. An initial dose of 0.25 - 0.35 mmol calcium/kg is recommended, repeated every 6 - 8 hours until a response is achieved.

Hyperkalaemia with secondary cardiac toxicity

Adults. An initial dose of 1.12 - 7 mmol (2.25 to 14 mEq) calcium is recommended. The dose may be repeated after 1 - 2 minutes if necessary. ECG should be monitored during administration.

Compatibilities

Calcium Chloride10% Injection is reported to be compatible with glucose 5% and sodium chloride 0.9%.

4.3 CONTRAINDICATIONS

The administration of calcium salts is contraindicated where hypercalcaemia, hypercalciuria or severe renal disease are present.

Due to the increased risk of arrhythmias, intravenous calcium administration is contraindicated in patients with ventricular fibrillation.

Administration of calcium salts is also contraindicated in patients with renal calculi, since it may exacerbate the condition, and in patients with sarcoidosis, since it may potentiate the hypercalcaemia, which may occur in this condition.

The administration of calcium preparations is also contraindicated in digitalised patients (see Section 4.5 Interactions with Other Medicines and Other Forms of Interactions).

Calcium Chloride 10% Injection should never be administered orally to infants since it may result in severe irritation to the gastrointestinal tract.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Calcium gluconate and calcium chloride are presented in 10 mL vials at 10% (w/v) for injection but are **not equivalent** in calcium content:

- 10 mL of Calcium Gluconate 10 % solution for injection/infusion BP contains 2.2 mmol calcium
- 10 mL of calcium chloride 10% solution contains 6.8 mmol of calcium

The difference in calcium content should be accounted for to achieve the correct calcium dose when using either salt to avoid medication errors.

Solutions of calcium salts, particularly calcium chloride, are irritant and should not be administered intramuscularly or subcutaneously or into perivascular tissue, since severe necrosis or sloughing may occur. The injection should be stopped if the patient complains of discomfort. Direct injection into heart tissues should be avoided.

Intravenous calcium chloride must be administered slowly via a small needle into a large vein, at a rate not exceeding 0.35 - 0.7 mmol per minute, to avoid venous damage and to prevent a high concentration of calcium reaching the heart and causing syncope. Continuous ECG monitoring should be performed when using calcium salts to antagonise cardiac toxicity associated with hyperkalaemia.

Intravenous administration of calcium chloride may cause vasodilatation, which may result in a moderate fall in blood pressure.

Since calcium chloride is acidifying, caution should be extended in administering intravenous calcium chloride in conditions where acidification may cause problems, such as renal disease, cor pulmonale, respiratory acidosis, or respiratory failure.

Caution should be extended in administering intravenous calcium solutions in conditions where there may be an increased risk of hypercalcaemia, such as chronic renal function impairment, dehydration, or electrolyte imbalance.

Since calcium salts may increase the risk of cardiac arrhythmia, caution should be extended in administering intravenous calcium preparations in patients with cardiac disease.

Use in the elderly

No data available.

Paediatric use

See Section 4.2 Dose and Method of Administration.

Effects on laboratory tests

Careful monitoring of serum calcium levels is advised at frequent intervals during therapy to ensure that normal serum calcium levels are not exceeded. Urinary calcium concentrations may also need to be monitored to avoid hypercalciuria since hypercalciuria can occur in the presence of hypocalcaemia.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Cardiac glycosides/digitalis. Since the inotropic and toxic effects of intravenous calcium chloride and cardiac glycosides are synergistic, concurrent use may increase the risk of arrhythmia.

Calcium channel blockers. Concurrent use of calcium salts in quantities sufficient to raise the serum calcium concentrations above normal with calcium channel blocking agents may reduce the response to verapamil and probably other calcium channel blockers.

Calcium containing or magnesium containing medications. Concurrent use with other calcium-containing or magnesium containing medications may increase the risk of hypercalcaemia or hypermagnesaemia, especially in patients with renal disease.

Neuromuscular blocking agents. Concurrent use with parenteral calcium salts usually reverses the effects of nondepolarising neuromuscular blocking agents; also concurrent use with calcium salts has been reported to enhance or prolong the neuromuscular blocking action of tubocurarine.

Tetracyclines. Calcium salts may complex with tetracyclines, and therefore tetracyclines and calcium salts should not be mixed for parenteral administration.
Magnesium sulfate. Mixing calcium salts with magnesium sulfate may cause precipitation of calcium sulfate and therefore magnesium sulfate and calcium salts should not be mixed for parenteral administration.

Phosphate-containing medications. Mixing calcium salts with phosphates may cause precipitation of calcium phosphate and therefore phosphate-containing medications and calcium salts should not be mixed for parenteral administration.

Carbonate-containing medications. Mixing calcium salts with carbonates may cause precipitation of calcium carbonate and therefore carbonate-containing medications and calcium salts should not be mixed for parenteral administration.

Tartrate-containing medications. Mixing calcium salts with tartrates may cause precipitation of calcium tartrate and therefore tartrate-containing medications and calcium salts should not be mixed for parenteral administration.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Animal reproduction studies have not been conducted with this product. It is not known whether this product can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Therefore, Calcium Chloride 10% Injection is not recommended during pregnancy.

Use in lactation

Calcium is a normal constituent of breast milk, but it is not known whether calcium chloride is distributed into breast milk. Therefore, Calcium Chloride 10% Injection is not recommended during lactation.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Solutions of calcium salts, particularly calcium chloride, may cause venous irritation when injected intravenously. Local reactions such as skin redness or rash and pain may indicate extravasation, which can lead to severe necrosis. Tissue calcification has also been reported.

Excessive intravenous administration of calcium chloride may cause hypercalcaemia, but this is rare except in cases of chronic renal failure. Adverse reactions associated with hypercalcaemia include: thirst, nausea, vomiting, constipation, polyuria, abdominal pain, muscle weakness, mental disturbances and, in severe cases, cardiac arrhythmia and coma.

Too rapid injection of calcium chloride may cause the patient to experience hot flushes, chalky taste, peripheral vasodilation, a decrease in blood pressure and abnormal heart activity (bradycardia, arrhythmia, syncope) (see Section 4.2 Dose and Method of Administration).

If calcium chloride is injected into the myocardium, cardiac tamponade or pneumothorax, leading to ventricular fibrillation, may result.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Clinical features

Hypercalcaemia may occur when large doses of calcium salts are given, especially in patients with renal failure. Symptoms associated with hypercalcaemia include thirst, nausea, vomiting, constipation, polyuria, abdominal pain, muscle weakness, mental disturbances and, in severe cases, cardiac arrhythmia and coma.

Treatment

Plasma concentrations exceeding 2.6 mmol/L are considered hypercalcaemia. Plasma calcium concentrations should be monitored at frequent intervals to guide therapy.

For mild cases of overdose, treatment involves immediately discontinuing administration of calcium chloride, other calcium containing medications.

For more serious cases (plasma concentration > 2.9 mmol/L), the following measures may be required.

- rehydration with 0.9% sodium chloride infusion
- use of non-thiazide diuretics to increase calcium excretion
- monitoring of serum potassium and magnesium levels; early use of replacement therapy
- monitoring of cardiac function; use of beta-blockers to protect the heart against arrhythmia
- haemodialysis may need to be considered.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Calcium is essential for the maintenance of the functional integrity of the nervous, muscular and skeletal systems and cell membrane and capillary permeability. This cation is an important activator in many enzymatic reactions and is essential to a number of physiological processes including the transmission of nerve impulses; contraction of cardiac, smooth and skeletal muscles; renal function; respiration and blood coagulation. Calcium also plays a regulatory role in the release and storage of neurotransmitters and hormones, in the uptake and binding of amino acids, in cyanocobalamin (vitamin B_{12}) absorption and in gastrin secretion.

The calcium of bone is in constant exchange with the calcium of plasma. Plasma calcium concentration is kept within narrow limits by an endocrine control mechanism involving parathyroid hormone, calcitonin and Vitamin D. Under the influence of this control mechanism, calcium may be released from bone if plasma calcium decreases, and may be sequestered into bone if plasma calcium rises. Thus, on a chronic basis, normal mineralisation of bone requires adequate amounts of total body calcium.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

No data available.

Distribution

The normal concentration range of total calcium in plasma is 2.15 - 2.60 mmol/L. Approximately 99% of total body calcium is contained in the bones and teeth, primarily as hydroxy apatite [$Ca_{10}(PO_4)_6(OH)_2$], with small amounts of calcium carbonate and amorphous calcium phosphates. The remaining 1% is contained in other body tissues and fluids.

Approximately 50% of calcium in plasma is in the physiologically active, ionised form, 45% is bound to protein (principally albumin) and 5% is complexed with phosphates, citrates and other anions. For a change in serum albumin of 1 g/dL, the calcium concentration may change about 0.02 mmol/dL. Hyperproteinaemia is associated with increased total serum concentration of calcium; in hypoproteinaemia, total serum calcium concentration decrease. Acidosis results in increased concentration of ionic calcium, while alkalosis promotes a decrease in the ionic serum calcium concentration.

Metabolism

No data available.

Excretion

Approximately 80% of calcium is excreted via faeces and consists of non-absorbed calcium and calcium secreted via bile and pancreatic juice into the lumen of the gastrointestinal tract. The remaining 20% of calcium is excreted renally. More than 95% of the calcium filtered by the renal glomeruli is reabsorbed in the ascending limb of the loop of Henle and the proximal and distal tubules. Urinary excretion of calcium is decreased by parathyroid hormone, thiazide diuretics and Vitamin D and increased by calcitonin, other diuretics and growth hormone.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Calcium Chloride 10% Injection contains calcium chloride dihydrate BP 1 g in Water for Injections BP to 10 mL. Sodium hydroxide and/or hydrochloric acid may be used for pH adjustment. The product contains no antimicrobial preservative.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG)[1]. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

It is presented in a 10 mL glass vial in a pack of 10 vials.
The vial stopper is not made with natural rubber latex.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Name: calcium chloride dihydrate Molecular formula: $CaCl_2.2H_20$ Molecular weight: 147.01

CAS number

10035-04-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled in Australia.

General Sales Classification in New Zealand.

8 SPONSOR

Phebra[2] Pty Ltd,
19 Orion Road, Lane Cove West, NSW 2066, Australia
Ph: 1800 720 020

Distributed in New Zealand by AFT Pharmaceuticals Ltd,
PO Box 33-203, Takapuna, Auckland.

9 DATE OF FIRST APPROVAL

19 June 2007

10 DATE OF REVISION

10 November 2023

SUMMARY TABLE OF CHANGES

[1] AUST R 137325
[2] Phebra and the Phi symbol are trademarks of Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia

Section Changed	Summary of new information
4.4	Safety added to warn of the potential for underdosing
All	Minor editorial changes throughout the PI