Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Calcium Chloride Injection Minijet 10% w/v, Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Calcium Chloride Dihydrate 100mg in 1 ml.
Contains 0.68mmol/ml calcium ions.

Available as 1000mg in 10 ml.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
The solution is contained in a type I glass vial with an elastomeric closure; it is specially designed for use with the IMS Minijet injector provided. The product is available as 10 ml.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Calcium Chloride Injection 10% w/v is indicated in the immediate treatment of hypocalcaemic tetany. Other therapy, such as parathyroid hormone and/or vitamin D, may be indicated according to the etiology of the tetany. It is also important to institute oral calcium therapy as soon as practicable.

In cardiac resuscitation, particularly after open heart surgery, calcium chloride has been used when adrenaline has failed to improve weak or ineffective myocardial contractions.

Calcium salts have been used as adjunctive therapy in a number of conditions, including the following:

1. In severe hyperkalaemia, calcium may be injected slowly while the ECG is monitoring the heart.
2. As an aid in the treatment of depression due to overdosage of magnesium sulfate (calcium is the antagonist of magnesium toxicity).

Routes of administration:
For intracardiac or slow intravenous use only.

4.2 Posology and method of administration

Intracardiac use:
In cardiac resuscitation, injection may be made into the ventricular cavity. Do not inject into the myocardium.

Adult dosage: 200-400mg (2-4ml).
Paediatric dosage: 0.2ml/kg of body weight.

Intravenous use:

Hypocalcaemic disorders
Adult dosage: 500mg to 1g (5-10ml) at intervals of 1 to 3 days, depending on response of the patient or serum calcium determinations. Repeated injection may be required.

Paediatric dosage: 0.2ml/kg of bodyweight. Maximum 1-10ml/day.

Magnesium Intoxication
Adult dosage: 500mg (5ml) administered promptly. Observe patient for signs of recovery before further doses are given.

Hyperkalaemic ECG disturbances of cardiac function
Adult dosage: Adjust dosage by constant monitoring of ECG changes during administration.

Geriatric patient dosage is the same as an adult.

4.3 Contraindications

In cardiac resuscitation, the use of calcium is contraindicated in the presence of ventricular fibrillation.

Calcium chloride is also contraindicated in those patients with conditions associated with hypercalcaemia and hypercalcuria (e.g. some forms of malignant disease) or in those with conditions associated with elevated vitamin D levels (e.g. sarcoidosis) or in those with renal calculi or a history of calcium renal calculi.

Ceftriaxone is contraindicated inpremature newborns up to a corrected age of 41 weeks (weeks of gestation + weeks of life) and full-term newborns (up to 28 days of age) if they require (or are expected to require) IV calcium treatment, or calcium-containing infusions because of the risk of precipitation of ceftriaxone-calcium (see sections 4.4 and 4.5).

The treatment of asystole and electromechanical dissociation.
Hypersensitivity to any component.

4.4 Special warnings and precautions for use

A moderate fall in blood pressure due to vasodilation may attend the injection. Since calcium chloride is an acidifying salt, it is usually undesirable in the treatment of hypocalcaemia of renal insufficiency.

Calcium chloride injection, 10% w/v is for intracardiac or slow intravenous injection only. Care should be taken not to infiltrate the perivascular tissue due to possible necrosis. Solutions should be warmed to body temperature. Injections should be made slowly through a small needle into a large vein to minimize venous irritation and avoid undesirable reactions.

It is particularly important to prevent a high concentration of calcium from reaching the heart because of danger of cardiac syncope. If injected into the ventricular cavity in cardiac resuscitation care must be taken to avoid injection into the myocardial tissue. Calcium chloride injection should never be given to infants orally because of severe irritation to the gastrointestinal tract. Infant injections should not be given through the scalp.

The use of calcium chloride is undesirable in patients with respiratory acidosis or respiratory failure due to the acidifying nature of the salt.

Cases of fatal reactions with calcium-ceftriaxone precipitates in lungs and kidneys in premature and full-term newborns aged less than 1 month have been described. At least one of them had received ceftriaxone and calcium at different times and through different intravenous lines. In the available scientific data, there are no reports of confirmed intravascular precipitations in patients, other than newborns, treated with ceftriaxone and calcium-containing solutions or any other calcium-containing products.

In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites. However, in patients older than 28 days of age ceftriaxone and calcium-containing solutions may be administered sequentially one after anotherif infusion lines at different sites are used, or if the infusion lines are replaced or thoroughly flushed between infusions with physiological salt-solution to avoid precipitation. In patients requiring continuous infusion with calcium-containing TPN solutions, healthcare professionals may wish to consider the use of alternative antibacterial treatments which do not carry a similar risk of precipitation**.** If use of ceftriaxone is considered necessary in patients requiringcontinuous nutrition,TPN solutions and ceftriaxone can be administered simultaneously, albeit via different infusion lines at different sites. Alternatively, infusion of TPN solution could be stopped for the period of ceftriaxone infusion, considering the advice to flush infusion lines between solutions.

Calcium chloride injection is irritating to veins and must not be injected into tissues, since severe necrosis and sloughing may occur. 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.

4.5 Interaction with other medicinal products and other forms of interactions

For interaction between calcium containing products and ceftriaxone, please see sections 4.3 and 4.4 above.

Calcium-containing products may decrease the effectiveness of calcium channel blockers.

Because of the danger involved in the simultaneous use of calcium salts and drugs of the digitalis group, a digitalized patient should not receive an intravenous injection of a calcium compound unless the indications are clearly defined. Calcium salts should not generally be mixed with carbonates, phosphates, sulfates or tartrate in parenteral mixtures.

Biphosphonates may interact with calcium chloride causing reduced absorption of biphosphates. Thiazide diuretics may increase the risk of hypercalcaemia.

4.6 Fertility, pregnancy and lactation

Studies on the effects of calcium chloride on pregnant women have not been carried out and problems have not been documented. Calcium crosses the placenta. The benefits of administration must outweigh any potential risk.

Calcium is excreted in breast milk but there are no data on the effects, if any, on the infant.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Rapid intravenous injections may cause the patient to complain of tingling sensations, a calcium taste, a sense of oppression 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. Soft tissue calcification, bradycardia or arrhythmias have also been reported.

Hypertension

Venous thrombosis

Hypercalcemia

Rarely, severe, and in some cases fatal, adverse reactions have been reported in preterm and full-term newborns (aged <28 days) who had been treated with intravenous ceftriaxone and calcium. Precipitations of ceftriaxone-calcium salt have been observed in lung and kidneys post-mortem. The high risk of precipitation in newborns is due to their low blood volume and the longer half life of ceftriaxone compared with adults (see sections 4.3 and 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms: anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi and, in severe cases, cardiac arrhythmias and coma.

Treatment: withholding calcium administration will usually resolve mild hypercalcaemia in asymptomatic patients, provided renal function is adequate.

When serum calcium concentrations are greater than 12mg per 100ml, immediate measures may be required such as hydration, loop diuretics, chelating agents, calcitonin and corticosteroids. Serum calcium concentration should be determined at frequent intervals to guide therapy adjustments.

Cardiac arrhythmia and cardiac arrest may occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Calcium is essential for the functional integrity of the nervous and muscular systems. It is necessary for normal cardiac function. It is also one of the factors involved in the mechanism of blood coagulation.

Calcium ions increase the force of myocardial contraction. In response to electrical stimulation of muscle, calcium ions enter the sarcoplasm from the extracellular space. Calcium ions contained in the sarcoplasmic reticulum are rapidly transferred to the sites of interaction between the actin and myosin filaments of the sarcomere to initiate myofibril shortening. Thus, calcium increases myocardial function. Calcium's positive inotropic effects are modulated by its action on systemic vascular resistance. Calcium may either increase or decrease systemic vascular resistance. In the normal heart, calcium's positive inotropic and vasoconstricting effect produces a predictable rise in systemic arterial pressure.

5.2 Pharmacokinetic properties

The precise mechanism of action of calcium is not known.

Excretion is renal and varies directly with serum calcium ion concentration.

5.3 Preclinical safety data

Not applicable since calcium chloride has been used in clinical practice for many years and its effects in man are well known.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydroxide
Hydrochloric acid
Water for injections

6.2 Incompatibilities

Calcium salts should not be mixed with carbonates, phosphates, sulfates, tartrates or tetracycline antibiotics in parenteral mixtures.

Calcium containing solutions should not be mixed with Ceftriaxone because a precipitate can form. Calcium containing solutions should not be administered simultaneously with Ceftriaxone (see section 4.2, 4.3, 4.4 and 4.8).

6.3 Shelf life

Unopened: 3 years.
The product should be used immediately after opening. Discard any unused portion.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The solution is contained in a type I glass vial with an elastomeric closure and is supplied with an IMS minijet injector which meets all the relevant specifications. The product is available as 10ml. Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The container is specially designed for use with the IMS Minijet injector.

7 MARKETING AUTHORISATION HOLDER

DLRC Pharma Services Limited
Chesterfield House
Clonmannon
Ashford
Wicklow
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22684/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 September 1977

Date of last renewal: 08 September 2007

10 DATE OF REVISION OF THE TEXT

May 2019