

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **PRODUCT SUMMARY**

#### **1. NAME OF THE MEDICINAL PRODUCT**

Calcium Gluconate Injection BP.

#### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

9.5% of Calcium Gluconate in 10ml

#### **3. PHARMACEUTICAL FORM**

Sterile Injection.

#### **4. CLINICAL PARTICULARS**

##### **4.1 Therapeutic indications**

Properties: Calcium is an essential body electrolyte. It is necessary for the functional integrity of nerve and muscle and is essential for the muscle contraction, cardiac function and coagulation of the blood.

Calcium homeostasis is mainly regulated by three endocrine factors: parathyroid hormone is secreted in response to a fall in plasma calcium concentration and acts by accelerating calcium transfer from bone and by increasing its intestinal absorption and its renal reabsorption; calcitonin lowers plasma calcium by decreasing bone resorption and by increasing renal excretion of the ion; vitamin D stimulates intestinal absorption of calcium and decreases its renal excretion.

Indications: Parenteral administration of calcium is indicated where the pharmacological action of a high calcium ion concentration is required, as for example, in acute hypocalcaemia, cardiac resuscitation and some cases of neonatal tetany.

Intravenous injections of calcium have been used in the treatment of the acute colic of lead poisoning, and as an adjunct in the treatment of acute fluoride poisoning. Also, for the prevention of hypocalcaemia in exchange transfusions.

## 4.2 Posology and method of administration

The normal concentration of calcium in plasma is within the range of 2.25 -2.75 mmol or 4.5-5.5mEq per litre. Treatment should be aimed at restoring or maintaining this level.

During therapy, serum calcium levels should be monitored closely.

Acute hypocalcaemia: 10-20ml (2.2-4.4mmol)

Fluoride or lead poisoning: 0.3ml/kg (0.07mmol/kg)

Neonatal tetany: 0.3ml/kg (0.07mmol/kg)

Cardiac resuscitation: 7-15ml (1.54-3.3mmol). It should be noted that the absolute amount of calcium required for this indication is difficult to determine and may vary widely.

In hypocalcaemic tetany, an initial intravenous injection of 10ml of the 10% solution (2.25mmol) should be followed by a continuous infusion of about 40ml (9mmol) daily. Plasma calcium should be monitored.

Intravenous injections should be given very slowly (3 minutes for 10ml).

Calcium Gluconate Injection can be diluted with glucose 5% or sodium chloride 0.9%. Dilution into a solution containing bicarbonate, phosphate or sulphate should be avoided.

Elderly patients: Although there is no evidence that tolerance of Calcium Gluconate Injection is directly affected by advanced age, factors that may sometimes be associated with ageing, such as impaired renal function and poor diet, may indirectly affect tolerance and may require a reduction in dosage. Renal function declines with age and prior to prescribing this product to elderly patients it should be considered that Calcium Gluconate injection is contraindicated (See section 4.3) for repeated or prolonged administration in patients with impaired renal function.

### 4.3 Contraindications

Aluminium oxide can be leached from ampoule glass by Calcium Gluconate. In order to limit the exposure of patients to aluminium, especially those with impaired renal function and children (less than 18 years of age), Hameln Pharmaceuticals Ltd Calcium Gluconate Injection BP is not intended for use in the preparation of Total Parenteral Nutrition (TPN).

This product should not be used for repeated or prolonged treatment, including as an intravenous infusion, in children (less than 18 years of age) and those with impaired renal function, due to the risk of exposure to aluminium.

This product is contraindicated in severe renal failure, hypercalcaemia (e.g. in hyperparathyroidism, hypervitaminosis D, neoplastic disease with decalcification of bone), severe hypercalciuria, severe renal failure and in patients receiving cardiac glycosides.

Calcium Gluconate Injection must not be co-administered with ceftriaxone in:

- premature newborns up to a corrected age of 41 weeks (weeks of gestation + weeks of life),
- full-term newborns (up to 28 days of age)

because of the risk of precipitation of ceftriaxone-calcium (see section 4.4, 4.8 and 6.2)

#### **4.4 Special warnings and precautions for use**

Plasma calcium levels and calcium excretion should be monitored when calcium is administered parenterally, especially in children, in chronic renal failure or where there is evidence of calculi formation within the urinary tract. If plasma calcium exceeds 2.75mmol per litre or if 24 hour urinary calcium excretion exceeds 5mg/kg, treatment should be discontinued immediately as cardiac arrhythmias may occur at these levels. Also see section 4.3.

Calcium salts should be used with caution in patients with impaired renal function or with nephrocalcinosis. Care is also required in patients with cardiac disease.

Calcium salts are irritant. The infusion site must be monitored regularly to ensure extravasation injury has not occurred.

Calcium gluconate is physically incompatible with many other compounds (see section 6.2). Care should be taken to avoid admixture of calcium gluconate and incompatible drugs in giving sets, or in the circulation after separate administration. Serious complications, including fatalities, have occurred following microcrystallisation of insoluble calcium salts in the body following separate administration of physically incompatible solutions or total parenteral nutrition solutions containing calcium and phosphate.

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 vitro studies demonstrated that newborns have an increased risk of precipitation of ceftriaxone-calcium compared to other age groups.

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 another if 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. (see sections 4.3, 4.8, and 6.2).

#### **4.4 Special warnings and precautions for use (*Continued*)**

The label shall state the following:

WARNING: Check each ampoule for clarity of solution. Use only if clear

#### **4.5 Interactions with other medicinal products and other forms of interactions**

The effects of digoxin and other cardiac glycosides may be accentuated by calcium and digitalis intoxication may be precipitated. There is increased risk of Hypercalcaemia with thiazides.

##### *Physical incompatibilities*

See section 4.4 (Special warnings and precautions for use) and section 6.2 (Incompatibilities).

#### **4.6 Pregnancy and lactation**

Calcium Gluconate Injection should be used during pregnancy only if considered to be essential by the physician. Calcium is excreted in breast milk and this should be borne in mind when administering calcium to women who are breast-feeding their infants.

#### **4.7 Effects on ability to drive and use machines**

None

#### **4.8 Undesirable effects**

If Calcium Gluconate Injections is administered too rapidly, nausea, vomiting, hot flushes, sweating, hypotension and vasomotor collapse, possibly fatal, may occur. Soft tissue calcification due to extravasation of calcium solutions has been reported.

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).

## **4.9 Overdose**

Excessive administration of calcium salts leads to hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, polydipsia, polyuria, mental disturbances, bone pain, nephrocalcinosis, renal calculi and if severe, cardiac arrhythmias and coma.

Severe hypercalcaemia should be treated with infusion of sodium chloride, intravenously, to expand the extracellular fluid volume. This may be given with or followed by furosemide to increase calcium excretion. If this treatment is unsuccessful, other drugs which may be used include calcitonin, the bisphosphonates, disodium edetate, phosphates. Haemodialysis may be considered as a last resort. During treatment of overdosage, serum electrolytes should be monitored carefully.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Calcium is an essential body electrolyte. It is necessary for the functional integrity of nerve and muscle and is essential for muscle contraction, cardiac function and coagulation of the blood.

The cytoplasmic concentration of calcium is normally maintained at very low levels of about 0.1-1.0  $\mu\text{mol}$  per litre by the extrusion of calcium from the cell and by its sequestration within cellular organelles, particularly the endoplasmic reticulum (called the sarcoplasmic reticulum, in muscle fibres). Various electrical or chemical stimuli trigger the influx of calcium ions across the plasma membrane or release of the ion from cellular stores. These calcium ions interact with high-affinity binding sites on specific intracellular proteins, such as troponin, and thus regulate a number of functional and metabolic processes.

Calcium ions are essential for normal function of the neuromuscular apparatus. Hypocalcaemia causes a decrease in the threshold for excitation, resulting in tetany. Hypercalcaemia increases the threshold for excitation of nerve and muscle, leading to muscle weakness and lethargy. Calcium ions are necessary for muscle contraction. By binding to troponin, calcium removes the inhibitory effect of troponin on the interaction of actin and myosin.

Calcium ions also play an important role in stimulus-secretion coupling in most exocrine and endocrine glands.

Calcium ions are essential for normal excitation-contraction coupling in cardiac muscle, and for the conduction of electrical impulses in certain regions of the heart, especially through the AV node. The initiation of contraction in vascular and other smooth muscle is also dependent on calcium ions.

These cardiac and vascular smooth muscle effects can be opposed by various calcium-channel blocking drugs in the treatment of angina, hypertension and cardiac arrhythmias.

Calcium ions are also involved in both the intrinsic and extrinsic pathways of blood coagulation.

## **5.2 Pharmacokinetic properties**

Calcium is absorbed from the small intestine and, generally, about one third of ingested calcium is absorbed. Absorption is facilitated by Vitamin D and by parathyroid hormone. Calcium is excreted mainly in the urine with some faecal loss. Urinary excretion is the net result of the quantity filtered and the amount reabsorbed. The tubular reabsorption of calcium is enhanced by Vitamin D and by parathyroid hormone, whereas calcitonin increases the urinary excretion of calcium ions. Calcium is also excreted in saliva, bile, pancreatic juice, sweat and breast milk.

## **5.3 Preclinical safety data**

No further information other than that which is included in the Summary of Product Characteristics.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Calcium D Saccharate USP  
Water for Injections Ph. Eur.

### **6.2 Incompatibilities**

Calcium salts can form complexes with many drugs, and this may result in a precipitate (See section 4.4). Calcium salts are incompatible with oxidising agents, citrates, soluble carbonates, bicarbonates, phosphates, tartrates and sulphates. Physical incompatibility has also been reported with amphotericin, cephalothin sodium, cephalozin sodium, cephmandole nafate, ceftriaxone, novobiocin sodium, dobutamine hydrochloride, prochlorperazine, and tetracyclines.

**6.3 Shelf life**

36 months.

**6.4 Special precautions for storage**

Store at less than 25 C.

**6.5 Nature and contents of container**

Type I clear glass ampoule, 10ml. Packed in cardboard cartons to contain 10 ampoules x 10ml.

**6.6 Instructions for use, handling and disposal**

Use as directed by a physician.

**ADMINISTRATIVE DATA**

**7. MARKETING AUTHORISATION HOLDER**

hameln pharmaceuticals ltd  
Gloucester  
UK

**8. MARKETING AUTHORISATION NUMBER**

PL 1502/0038

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION**

12/08/83 –28/11/2000

**10. DATE OF (PARTIAL) REVISION OF TEXT**

23/07/2010