

## **SUMMARY OF PRODUCT CHARACTERISTICS**

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

Calcium gluconate 10% w/v Solution for injection

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

Each mL contains 0.095 g calcium gluconate as monohydrate, equivalent to 0.212 mmol of calcium.

Each 10 mL ampoule contains 0.95 g calcium gluconate as monohydrate equivalent to 2.12 mmol of calcium.

Excipient with known effect: The product also contains an amount of the excipient calcium saccharate equivalent to 0.0112 mmol calcium per mL (or 0.112 mmol calcium per 10 mL).

Total calcium content: 0.223 mmol per mL (2.23 mmol per 10 mL).

For the full list of excipients, see section 6.1.

### **3 PHARMACEUTICAL FORM**

Solution for Injection.

Clear, colourless to pale yellow aqueous sterile solution, with a pH between 6 and 8.2, practically free from particles.

### **4 CLINICAL PARTICULARS**

#### **4.1 Therapeutic 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, and some cases of neonatal tetany.

Intravenous injections of calcium have been used in the treatment of the acute colic of lead poisoning. Advice should be sought from specialist centres (National Poisons

Information Service, tel: 111) regarding the treatment of symptoms of acute lead poisoning.

Calcium gluconate 10% w/v Solution for injection is used in the treatment of acute fluoride poisoning. Advice should be sought from specialist centres (National Poisons Information Service, tel: 111) regarding treating patients with this condition.

## 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 4.5-5.5 mEq per litre. Treatment should be aimed at restoring or maintaining this level.

During therapy, serum calcium levels should be monitored closely.

### *Posology*

#### Acute hypocalcaemia

##### Adults

The usual initial dose in adults is 10 mL of Calcium gluconate 10% w/v Solution for injection, corresponding to 2.23 mmol or 4.46 mEq of calcium. If necessary, the dose may be repeated, depending on the patient's clinical condition. Subsequent doses should be adjusted according to the actual serum calcium level.

##### Paediatric patients (< 18 years)

The dose and the route of administration depend on the degree of hypocalcaemia and the nature and severity of the symptoms. In the case of mild neuromuscular symptoms oral calcium administration should be preferred.

<b>Age</b>	<b>mL / kg</b>
3 months	0.4-0.9
6 months	0.3-0.7
1 year	0.2-0.5
3 years	0.4-0.7
7.5 years	0.2-0.4
12 years	0.1-0.3
> 12 years	As for adults

In cases of severe symptoms of hypocalcaemia in neonates or infants, e.g. cardiac symptoms, higher initial doses (up to 2 mL per kg body weight, □ 0.45 mmol calcium per kg body weight) may be necessary for a quick restoration of a normal serum calcium level.

Also, if necessary, the dose may be repeated, depending on the patient's clinical condition. Subsequent doses should be adjusted according to the actual serum calcium level.

Intravenous therapy should be followed by oral administration if indicated, e.g. in cases of calciferol deficiency.

### Elderly patients:

Although there is no evidence that tolerance of Calcium gluconate 10% w/v Solution for 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 10% w/v Solution for injection is contraindicated (See section 4.3) for repeated or prolonged administration in patients with impaired renal function.

### Neonatal tetany

Intravenous administration of 10% calcium gluconate as a bolus of 100-200 mg/kg (1-2 mL/kg) over approximately 10-20 minutes, followed by a continuous infusion (0.5-1 g/kg/d) over 1-2 days.

Heart rate should be monitored during the infusion.

The IV site should also be watched closely because tissue infiltration by a calcium solution is irritating and may cause local tissue damage or necrosis.

### Fluoride poisoning

Calcium gluconate regime for hypocalcaemia in fluoride poisoning:

#### Immediate:

- give 10 mL of 10% calcium gluconate intravenously on presentation, repeat at 1 hour, or
- give 30 mL of 10% calcium gluconate intravenously if tetany present.

#### Maintenance:

- Maintain serum calcium with intravenous 10% calcium gluconate 10 mL every 4 hours, adjusting according to frequent serum calcium concentrations.

Mild to moderate dermal toxicity due to hydrofluoric acid/fluoride exposure:

Subcutaneous calcium gluconate (10%) for dermal exposure of hydrofluoric acid > 20%.

- Infiltrate each square centimeter of the exposed area with 0.5 mL of 10% calcium gluconate.

In the case of significant burn due to hydrofluoric acid /fluoride exposure, calcium salts may be administered intravenously (for systemic toxicity) or intra-arterially (for hand burns predominantly).

- 10 mL of 10% calcium gluconate plus heparin 5000 units in a total volume of 40 mL is administered intravenously.
- 10 mL of 10% calcium gluconate in 50 mL of 0.9% sodium chloride solution is intra-arterially infused over 4 h.

### Hypocalcaemia during transfusion

#### Adults

Calcium should be administered during massive transfusion if  $\text{Ca}^{2+}$  concentration is low, in order to preserve normocalcaemia.

10 mL of a 10% solution of Calcium gluconate 10% w/v Solution for injection IV diluted in 100 mL D5W (5% Glucose in water), given over 10 min or 10-20 mL Calcium gluconate for each 500 mL of blood infused.

#### Pediatric patients (< 18 years)

During transfusion / exchange transfusion the patient's clinical condition and the calcium serum concentration have to be monitored, and a clinically significant hypocalcaemia should be treated according to dosing recommendations for acute hypocalcaemia.

#### Method of administration

The patient should be in the lying position and should be closely observed during injection. Monitoring should include heart rate or ECG.

#### *Adults*

Slow intravenous or deep intramuscular injection.

**For the intramuscular route, if intravenous injection is not possible, only the 10% w/v solution should be used. Because of the risk of local irritation, intramuscular injections should only be performed if intravenous injection is not possible.** Care should be taken to administer the intramuscular injections sufficiently deep IM, preferably into the gluteal region. See also sections 4.4 and 4.8. In the case of adipose patients a longer needle will have to be chosen for safe positioning of the injection into the muscle and not into adipose tissues. If repeated injections are necessary, the injection site should be changed every time.

The intravenous administration rate should not exceed 2 mL (0,45 mmol of calcium) per minute.

#### Paediatric patients (<18 years)

Only slow intravenous injection or intravenous infusion (both after dilution), in order to achieve sufficiently low administration rates and to avoid irritation/necrosis in case of accidental extravasation. The intravenous administration rate should not exceed 5 mL of a 1:10 dilution per minute (see section 6.6) of Calcium gluconate 10% w/v Solution for injection in children and adolescents.

Intramuscular injections should not be performed in paediatric patients.

### **4.3 Contraindications**

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1

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

Calcium gluconate 10% w/v Solution for 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.

In the exceptional case of intravenous administration of calcium gluconate to patients receiving cardiac glycosides, adequate cardiac monitoring is mandatory and emergency treatment of cardiac complications such as serious arrhythmias must be available.

Intravenous injections should be accompanied by heart rate or ECG control because bradycardia with vasodilatation or arrhythmia can occur when calcium is administered too quickly.

Renal impairment may be associated with hypercalcaemia and secondary hyperparathyroidism. Therefore, in patients with renal impairment, parenteral calcium should be administered only after careful assessment of the indication and the calcium-phosphate balance should be monitored.

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

Calcium salts should only be used with caution and after careful establishment of the indication in patients with sarcoidosis (Boeck's disease), in patients receiving epinephrine (see section 4.5).

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 medicinal products 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).

In children, Calcium gluconate 10% w/v Solution for injection should not be injected intramuscularly but only slowly intravenously.

Calcium is insoluble in adipose tissue and may therefore cause infiltration and subsequent abscess formation, tissue induration and necrosis.

After perivascular or superficial IM injection local irritation, possibly followed by skin ablation or tissue necrosis, may occur (see section 4.8). Extravasation must be avoided; the injection site should be monitored carefully.

## **4.5 Interaction with other medicinal products and other forms of interaction**

### *Cardiac glycosides*

The effects of digoxin and other cardiac glycosides may be accentuated by calcium and digitalis intoxication may be precipitated.

### *Thiazide diuretics*

There is increased risk of hypercalcaemia with thiazides.

### *Epinephrine*

Co-administration of calcium and epinephrine attenuate epinephrine's  $\beta$ -adrenergic effects in postoperative heart surgery patients (see section 4.4).

#### *Magnesium*

Calcium and magnesium mutually antagonise their effects.

#### *Calcium antagonists*

Calcium may antagonise the effect of calcium antagonists (calcium channel blockers).

#### *Interaction with ceftriaxone*

See sections 4.4 and 6.2.

#### *Physical incompatibilities*

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

## **4.6 Fertility, pregnancy and lactation**

### **Pregnancy**

Calcium passes the placental barrier and its concentration in fetal blood is higher than in maternal blood. Calcium gluconate should be used during pregnancy only if considered to be essential by the physician. The administered dose should be carefully calculated, and serum calcium levels regularly evaluated in order to avoid hypercalcaemia, which may be deleterious to the fetus.

### **Lactation**

Calcium is excreted in breast milk and this should be borne in mind when administering calcium to women who are breast-feeding their infants. A decision must be made whether to discontinue breast-feeding or to discontinue Calcium gluconate therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the mother.

### **Fertility**

No data available.

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

None

#### 4.8 Undesirable effects

The frequency of undesirable effects listed below is defined using the following convention:

Very common  $\geq 1/10$

Common  $\geq 1/100$  to  $< 1/10$

Uncommon  $\geq 1/1,000$  to  $< 1/100$

Rare  $\geq 1/10,000$  to  $< 1/1,000$

Very rare  $< 1/10,000$

Not known: Frequency cannot be estimated from the available data

Vascular and other systemic undesirable effects are likely to occur as symptoms of acute hypercalcaemia resulting from intravenous overdose or too rapid intravenous injection. Their occurrence and frequency is directly related to the administration rate and the administered dose.

##### *Vascular disorders*

Not known: Hypotension, circulatory collapse (possibly fatal), flushing, mainly after too rapid injection.

##### *Gastrointestinal disorders*

Not known: Nausea, vomiting.

##### *General disorders and administration site conditions*

Not known: Heat sensations, sweating

##### *Ceftriaxone-calcium salt precipitation*

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).

*Adverse reactions only occurring with improper administration technique:*

Not known: Soft tissue calcification due to extravasation of calcium solutions has been reported.

Intramuscular injection may be accompanied by pain sensations or erythema.

If intramuscular injection is not performed sufficiently deep intramuscularly, infiltration into the adipose tissue may occur with subsequent abscess formation, tissue induration, and necrosis.

#### 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 Yellow Card Scheme, Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

## **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 medicinal products which may be used include calcitonin, bisphosphonates, disodium edetate and phosphates. Haemodialysis may be considered as a last resort. During treatment of overdose, serum electrolytes should be monitored carefully.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: mineral supplements, calcium gluconate.

ATC code: A12AA03

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.

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.

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**

### Distribution

After injection the administered calcium shows the same distribution behaviour as the endogenous calcium. About 45-50% of the total plasma calcium is in the physiologically active ionised form, about 40-50% is bound to proteins, mainly albumin, and 8-10% is complexed with anions.

### Biotransformation

After injection the administered calcium adds to the intravascular calcium pool and is handled by the organism in the same manner as the endogenous calcium.

#### Elimination

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 saccharate

Water for Injections

### **6.2 Incompatibilities**

Calcium salts can form complexes with many ingredients of medicinal products, 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, cephazolin sodium, cephamandole nafate, ceftriaxone, novobiocin sodium, dobutamine hydrochloride, prochlorperazine, and tetracyclines.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

### **6.3 Shelf life**

3 years

*After dilution*

When diluted to 10 mg per mL, according to directions, with the recommended infusion fluids, sodium chloride 9 mg/mL (0.9%) solution for injection or 50 mg/mL (5%) glucose solution for injection, physical in-use stability has been demonstrated for 48 hours at 23°C - 27°C and 2°C - 8°C.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 48 hours at 23°C - 27°C or 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

#### **6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

#### **6.5 Nature and contents of container**

Polypropylene ampoules of 10 mL. Packed in cartons to contain 10, 20 or 50 ampoules x 10 mL.

Not all pack sizes may be marketed.

#### **6.6 Special precautions for disposal**

##### Handling

The product is intended for single use only. Discard any unused solution.

**NOTE:** The specific product is a supersaturated solution of calcium gluconate. Supersaturated solutions are prone to precipitation.

The medicinal product should be visually inspected for particulate matter or discoloration. The solution should only be used if it is clear, colourless to pale yellow aqueous solution, practically free from particles.

##### Dilution

For intravenous infusion, Calcium gluconate 10% w/v Solution for injection may be diluted 1:10 to a concentration of 10 mg/ mL with the following two infusion fluids: sodium chloride 9 mg/ mL (0.9%) solution for injection or 50 mg/ mL (5%) glucose solution for injection. When diluted with these recommended infusion fluids, the resulting solutions are intended for immediate single use. Dilution should be performed under controlled and validated aseptic conditions. After mixing, the container should be gently agitated to ensure homogeneity.

Use as directed by a physician.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

**7      MARKETING AUTHORISATION HOLDER**

DEMO SA Pharmaceutical Industry

21<sup>st</sup> km National Road Athens - Lamia

14568 Krioneri, Attiki, Greece

**8      MARKETING AUTHORISATION NUMBER(S)**

PL 17589/0012

**9      DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
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14/07/2025

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