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This information is intended for use by health professionals

1. Name of the medicinal product

Calcium Gluconate Injection BP.

2. Qualitative and quantitative composition

10% of Calcium Gluconate in 10ml Each 1 ml of solution contains 100mg calcium gluconate,

For the full list of excipients, see section 6.1.

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 4.5-5.5 mEq 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.

Paediatric population:

Calcium Gluconate Injection is indicated for the treatment of neonatal tetany – it should not be routinely used in children less than 18 years of age.

Elderly:

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.

Method of administration

The intravenous administration rate should not exceed 2 ml (0.45 mmol of calcium) per minute.

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

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

4.3 Contraindications

• Hypersensitivity to the active substance or to any of the excipients listed in section 6.1;

• Patients with severe renal failure;

• Patients with hypercalcaemia (e.g. in hyperparathyroidism, hypervitaminosis D, neoplastic disease with decalcification of bone, renal insufficiency, immobilisation osteoporosis, sarcoidosis, milk-alkali syndrome);

• Patients with hypercalciuria;

• Patients receiving cardiac glycosides.

• Co-administration with ceftriaxone in:

o premature newborns up to a corrected age of 41 weeks (weeks of gestation + weeks of life) and

o 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)

• 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.

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).

4.4 Special warnings and precautions for use

Special warnings

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 only be used with caution and after careful establishment of the indication in patients with nephrocalcinosis, heart diseases, sarcoidosis (Boeck's disease), in patients receiving epinephrine (see section 4.5), or in the elderly.

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.

Renal impairment

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.

Patients receiving ceftriaxone

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). Sequential infusions of ceftriaxone and calcium-containing products must be avoided in case of hypovolaemia.

Precautions for use

Solutions containing calcium should be administered slowly to minimise peripheral vasodilation and cardiac depression.

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.

Plasma levels and urinary excretion of calcium should be monitored when high-dose parenteral calcium is administered.

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

Patients receiving calcium salts should be monitored carefully to ensure maintenance of correct calcium balance without tissue deposition.

High Vitamin D intake should be avoided.

4.5 Interaction with other medicinal products and other forms of interaction

Cardiac glycosides

The effects of digoxin and other cardiac glycosides may be potentiated by calcium, which may result in serious toxicity. Therefore, intravenous administration of calcium preparations to patients under therapy with cardiac glycosides is contraindicated.

Epinephrine

Co-administration of calcium and epinephrine attenuate epinephrine's β-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).

Thiazide diuretics

Combination with thiazide diuretics may induce hypercalcaemia as these medicinal products reduce renal calcium excretion.

Physical incompatibilities including interaction with ceftriaxone

See section 4.4 and section 6.2.

4.6 Pregnancy and lactation

Pregnancy

Calcium passes across the placental barrier and its concentration in foetal blood is higher than in maternal blood.

Calcium Gluconate Injection BP should not be used during pregnancy unless the clinical condition of the woman requires treatment with Calcium Gluconate Injection BP. The administered dose should be carefully calculated, and the serum calcium level regularly evaluated in order to avoid hypercalcaemia, which may be deleterious for the foetus.

Breast-feeding

Calcium is excreted in breast milk. 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/abstain from Calcium Gluconate Injection BP therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

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 ≥1/10

Common ≥1/100 to <1/10

Uncommon ≥1/1,000 to <1/100

Rare ≥1/10,000 to <1/1,000

Very rare < 1/10,000

Not known Frequency cannot be estimated from the available data

Cardiovascular 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.

Cardiac disorders

Not known: Bradycardia, cardiac arrhythmia.

Vascular disorders

Not known: Hypotension, vasodilatation, 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: Calcinosis cutis, possibly followed by skin ablation and necrosis, due to extravasation, has been reported.

Reddening of skin, burning sensation or pain during intravenous injection may indicate accidental perivascular injection, which may lead to tissue 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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms

Symptoms of hypercalcaemia may include: anorexia, nausea, vomiting, constipation, abdominal pain, polyuria, polydipsia, dehydration, muscle weakness, bone pain, renal calcification, drowsiness, confusion, hypertension and, in severe cases, cardiac arrhythmia up to cardiac arrest, and coma.

If intravenous injection is too rapid, symptoms of hypercalcaemia may occur as well as a chalky taste, hot flushes and hypotension.

Emergency treatment, antidotes

Treatment should be aimed at lowering the elevated plasma calcium concentration.

Initial management should include rehydration and, in severe hypercalcaemia, it may be necessary to administer sodium chloride by intravenous infusion to expand the extracellular fluid. Calcitonin may be given to lower the elevated serum calcium concentration. Furosemide may be administered to increase calcium excretion but thiazide diuretics should be avoided as they may increase renal absorption of calcium.

Haemodialysis or peritoneal dialysis may be considered where other measures have failed and where the patient remains acutely symptomatic. Serum electrolytes should be carefully monitored throughout treatment of overdose.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions affecting the electrolyte balance, electrolytes. ATC code: B05BB01.

Calcium is the most abundant mineral in the human organism (approx. 1.5 % of the entire body weight). More than 99% of the body's total calcium is located in bones and teeth, approx. 1% is dissolved in intra- and extracellular fluid.

Calcium is necessary for the functional integrity of nerves and muscles. It is essential for muscle contraction, cardiac function and blood coagulation.

The physiological level of the plasma calcium concentration is maintained at 2.25 – 2.75 mmol/l. As about 40-50% of the plasma calcium is bound to albumin, total plasma calcium is coupled to the plasma protein concentration. The concentration of ionised calcium lies between 1.23 and 1.43 mmol/l, regulated by calcitonin and parathormone.

Hypocalcaemia (total calcium below 2.25 mmol/l or ionised calcium below 1.23 mmol/l, respectively) may be caused by renal failure, vitamin D deficiency, magnesium deficiency, massive blood transfusion, osteoblastic malignant tumours, hypoparathyroidism, or intoxication with phosphates, oxalates, fluorides, strontium or radium.

Hypocalcaemia may be accompanied by the following symptoms: increased neuromuscular excitability up to tetany, paraesthesia, carpopedal spasms, spasms of smooth muscles e.g. in the form of intestinal colic, muscle weakness, confusion, cerebral convulsive seizures and cardiac symptoms like prolonged QT interval, arrhythmia and even acute myocardial failure.

The therapeutic effect of parenteral calcium substitution is normalisation of pathologically low serum calcium levels and thus relief of the symptoms of hypocalcaemia.

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

Excretion of calcium occurs in the urine although a large proportion undergoes renal tubular reabsorption.

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 sulfates. Physical incompatibility has also been reported with amphotericin, cephalothin sodium, cephazolin sodium, cephamandole 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, 50Ampoules.

6.6 Special precautions for disposal and other handling

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

7. Marketing authorisation holder

Ningbo Voice Biochemic Co., Ltd.

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