Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Calcigluc 10% solution for injection

2. Qualitative and quantitative composition

Each 1 ml of solution contains 95 mg of calcium gluconate, equivalent to 0.21 mmol calcium
Each 10 ml of solution contains 950 mg of calcium gluconate, equivalent to 2.12 mmol calcium.

Excipients with known effect:
This medicinal product contains calcium saccharate equivalent to 0.01 mmol calcium/ml (0.11 mmol calcium/10 ml).

Total calcium content 0.22 mmol/ml (2.23 mmol/10 ml).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Clear, colourless to light brown solution for injection.

4. Clinical particulars

4.1 Therapeutic indications

Calcium Gluconate 10% solution for injection/infusion is indicated in **adults and children** aged **0**years **to < 18 years** for:

- Treatment of acute symptomatic hypocalcaemia.

- Fluoride or lead poisoning induced hypocalcaemia.

- Treatment of acute severe hyperkalaemia with or without ECG changes, as an emergency treatment aiming to reduce cardiac cell excitability (cardioprotective effect) while other measures to lower potassium levels are instituted.

- Cardiac arrest only due to severe hyperkalaemia.

4.2 Posology and method of administration

Posology

Treatment of acute symptomatic hypocalcaemia

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 in adults. Treatment should be aimed at restoring or maintaining this level.

During therapy, serum calcium levels should be monitored closely.

Adults

Slow intravenous injection or infusion in patients with normal renal function:

10 – 20 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 2.23 - 4.46 mmol calcium), can be administered **undiluted** as a *slow intravenous injection* over 10 minutes with plasma-calcium and ECG monitoring.

Or

10 – 20 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 2.23 - 4.46 mmol calcium), can be **diluted** in 50-100 ml of glucose 5% or sodium chloride 0.9% and administered as a *slow intravenous infusion* over 10 minutes with plasma-calcium and ECG monitoring.

If necessary, the dose can be repeated depending on the clinical condition of the patient. Subsequent doses should be adjusted according to the actual serum calcium level.

Paediatric population

Close plasma-calcium and ECG monitoring are necessary during administration until normal calcium values are achieved.

The dose should be individualised within the recommended range depending on the serum calcium levels, the severity of hypocalcaemic symptoms and the recommended limits for aluminium exposure (see section 4.4). The product can be administered either as a slow intravenous injection, or as a slow continuous infusion.

Urgent correction of acute, symptomatic hypocalcaemia administered as a ***slow intravenous injection***

Neonates (0 to 27 days)

A single dose of 1 ml/kg body weight of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.22 mmol calcium/kg body weight) can be administered undiluted as a *slow intravenous injection* over 5-10 minutes.

Lower doses of 0.5 ml/kg body weight of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.11 mmol calcium/kg body weight) have also been shown to be effective in alleviating hypocalcaemic symptoms.

The dose can be diluted 1:1 or 1:5 in glucose 5% and the rate of administration should not exceed 0.22 mmol calcium/min.

Children (28 days to < 18 years)

A single dose of 0.3 - 0.6 ml/kg body weight (corresponding to 0.07 - 0.13 mmol calcium/kg body weight) administered undiluted as *a slow intravenous injection* over 5-10 minutes.

The dose can be diluted 1:5 in glucose 5% or sodium chloride 0.9% and the rate of administration should not exceed 0.22 mmol calcium/min.

A maximum dose of 1ml/kg body weight of Calcium gluconate 10% solution for injection/infusion (corresponding to 0.22 mmol calcium/kg body weight) is recommended for administration in children from 0 to < 18 years due to the risk of exposure to aluminium (see section 4.4).

Urgent correction of acute, symptomatic hypocalcaemia administered as a ***slow continuous infusion*** *(rate of infusion adjusted according to serum calcium levels and severity of hypocalcaemic symptoms)*

Neonates (0 to 27 days)

Initially 0.2 - 0.3 ml/kg body weight/hour of Calcium Gluconate 10% solution for injection/infusion **(**corresponding to 0.04 - 0.07 mmol calcium/kg body weight) diluted 1:10 in sodium chloride 0.9% or glucose 5%.

An initial infusion rate of 0.1 ml/kg body weight/hour of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.02 mmol calcium/kg body weight/ hour) has also been shown to be effective for a correction of serum calcium levels.

The rate should then be adjusted according to the serum calcium levels and the severity of hypocalcaemic symptoms, however the maximum administration rate recommended in neonates (0 to 27 days) is 0.1 ml/kg body weight/hour (corresponding to 0.022 mmol/kg body weight/hour).

Children (28 days < 18 years)

Initially 0.08 ml/kg body weight/hour of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.02 mmol calcium/kg body weight/hour) diluted 1:10 in sodium chloride 0.9% or glucose 5%.

The rate should then be adjusted according to serum calcium levels and the severity of hypocalcaemic symptoms, however the maximum administration rate recommended in children (28 days <18 years) is 0.2 ml/kg body weight/hour (corresponding to 0.045 mmol/kg/hour).

A maximum dose of 1ml/kg body weight of Calcium gluconate 10% solution for injection/infusion (corresponding to 0.22 mmol calcium/kg body weight) is recommended for administration in children from 0 to < 18 years due to the risk of exposure to aluminium (see section 4.4).

Treatment of acute severe hyperkalaemia with or without ECG changes

Adults

Acute severe hyperkalaemia with or without ECG changes (serum potassium concentration above 6.5 mmol/L).

30 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 6.69 mmol calcium) administered undiluted as a *slow intravenous injection* over 10 minutes.

Further doses can be considered after 5 minutes, if needed, until ECG improvement is achieved.

Paediatric population

The dose regimen for cardiac arrest should be followed.

Treatment of cardiac arrest due to hyperkalaemia

Treatment should be tailored to the individual patient. The onset of action of intravenous calcium gluconate is within three minutes. With a relatively short duration of action (30 – 60 minutes) further doses may be necessary if hyperkalaemia remains uncontrolled.

Adults

30 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 6.69 mmol calcium) administered undiluted as *a rapid intravenous injection.*

Further doses can be repeated if return of spontaneous circulation is not achieved within 5-10 minutes, or if the resuscitation attempt is prolonged.

Paediatric population

Neonates (0 to 27 days)

0.5 ml/kg body weight of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.11 mmol calcium/kg body weight) administered undiluted (in the case of emergency) as a *slow intravenous injection* over 5-10 minutes.

The dose should be given centrally whenever possible. If no central access is available, the dose should be diluted with sodium chloride 0.9% to five times the volume.

The dose can be repeated if ECG changes persist after 5-10 minutes following administration of the first dose.

Children (28 days to < 18 years)

0.5 ml/kg of body weight of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.11 mmol calcium/kg body weight) by *slow intravenous injection* over 5-10 minutes.

In the case of emergency, Calcium gluconate 10% solution for injection/infusion can be administered undiluted via central IV access.

The dose can be diluted to 50 ml with sodium chloride 0.9% over 10 minutes.

The dose can be repeated if ECG changes persist after 5-10 minutes following administration of the first dose.

In children with a body weight ≥ 20 kg a maximum recommended dose of 20 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 4.46 mmol calcium) can be given.

A maximum dose of 1ml/kg body weight of Calcium gluconate 10% solution for injection/infusion (corresponding to 0.22 mmol calcium/kg body weight) is recommended for administration in children from 0 to < 18 years due to the risk of exposure to aluminium (see section 4.4).

Fluoride (e.g. hydrofluoric acid) or lead poisoning-induced hypocalcaemia:

The UK National Poisons Information Service (NPIS) should be consulted for further specific advice.

Adults

10-30 ml of Calcium Gluconate 10% solution for injection/infusion intravenously (corresponding to 2.23-6.69 mmol calcium).

In severe hypocalcaemia, an infusion may be required e.g. 40 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 8.92 mmol calcium) administered intravenously over 1 hour.

The serum calcium should be monitored if repeated doses are administered or if calcium is given as an infusion.

Paediatric population (children aged 0 years to < 18 years)

0.5 ml/kg of Calcium Gluconate 10% solution for injection/infusion (corresponding to 0.11 mmol calcium/kg body weight) over 5 minutes.

In children with a body weight ≥ 20 kg a maximum recommended dose of 20 ml of Calcium Gluconate 10% solution for injection/infusion (corresponding to 4.46 mmol calcium) can be given.

A maximum dose of 1ml/kg body weight of Calcium gluconate 10% solution for injection/infusion (corresponding to 0.22 mmol calcium/kg body weight) is recommended for administration in children from 0 to < 18 years due to the risk of exposure to aluminium (see section 4.4).

Special populations

Elderly

Although there is no evidence that tolerance of Calcium Gluconate 10% solution for injection/infusion 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% solution for injection/infusion is contraindicated (See section 4.3) for repeated or prolonged

administration in patients with impaired renal function (see section 4.4).

Renal insufficiency

Patients with renal dysfunction have an increased risk of hypercalcaemia. For urgent correction of hypocalcaemia (short term use) Calcium Gluconate 10% solution for injection/infusion should be titrated to response as the desired effect may be achieved with less calcium in patients with renal impairment and serum calcium levels should be monitored closely (see section 4.4). In patients with severe renal insufficiency and renal failure, appropriate blood purification methods (i.e. haemodialysis or peritoneal dialysis) should be available.

Calcium Gluconate 10% solution for injection/infusion is contraindicated for repeated or prolonged treatment in patients with impaired renal function due to risk of aluminium accumulation and toxicity (see sections 4.3 and 4.4).

Hepatic insufficiency

Hepatic function does not impact the availability of ionized calcium after intravenous administration of calcium gluconate. Dose adjustments in hepatically impaired patients may not be necessary.

Method of administration

Slow intravenous injection and/or infusion.

The intravenous administration rate should not exceed 0.45 mmol of calcium per minute in adults and 0.22 mmol of calcium per minute as a bolus in children.

For continuous infusions, the rate should be adjusted based on the serum calcium levels and the severity of the hypocalcaemic symptoms with a maximum administration rate of 0.022 mmol/kg body weight /hour in neonates (0 to 27 days) and 0.045 mmol/kg body weight /hour in children (28 days to < 18 years).

For the management of acute severe hyperkalaemia further doses can be considered and adjusted according to ECG resolution of arrythmias.

For instruction on dilution of the medicinal product before administration, see section 6.6.

Calcium Gluconate 10% solution for injection/infusion can be diluted with glucose 5% or sodium chloride 0.9%.

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

Appropriate venous access should be ensured as extravascular administration can result in severe skin injuries including tissue necrosis.

4.3 Contraindications

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

• 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;

• Poisoning with cardiac glycosides;

• Patients receiving cardiac glycosides. The only exception may be that intravenous calcium administration is imperative for treatment of severe hypocalcaemia symptoms or acute severe hyperkalaemia putting the patient at immediate vital risk, if safer therapeutic alternatives are not available and calcium administration via the oral route is not possible (see also sections 4.4 and 4.5).

• 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, in children (less than 18 years of age) and those with impaired renal function, due to the risk of exposure to aluminium (see section 4.2, 4.4 and 5.1).

Calcium Gluconate 10% solution for injection/infusion is indicated for acute, symptomatic treatment **only**. 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 pharma ltd Calcium Gluconate 10% solution for injection/infusion BP should not be used in the preparation of Total Parenteral Nutrition (TPN), due to the risk of exposure to aluminium (see section 4.4).

4.4 Special warnings and precautions for use

Special warnings

Calcium gluconate and calcium chloride are presented in 10 ml ampoules 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 2.23 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.

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.

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 (see also sections 4.2, 4.3 and 4.5). Calcium Gluconate 10% solution for injection/infusion should be administered slowly (in 100 ml glucose 5% over 20 minutes). Rapid calcium administration may precipitate myocardial digoxin toxicity therefore other methods e.g. haemodialysis should also be considered after consultation with specialists.

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.

Calcium Gluconate 10% solution for injection/infusion must not be mixed with or administered through the same intravenous line as sodium bicarbonate (sometimes used for treatment of severe hyperkalaemia) due to the risk of precipitation.

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. In patients with severe renal insufficiency and renal failure, appropriate blood purification methods (i.e. haemodialysis or peritoneal dialysis) should be available due to higher risk of hypercalcemia.

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.

Aluminium oxide

Aluminium oxide can be leached from ampoule glass by calcium gluconate. Increased aluminium levels can lead to risks associated with aluminium toxicity, such as adverse effects on bone mineralisation and neurological (brain and nervous system) development, particularly in vulnerable patients such as those with renal impairment and children (less than 18 years of age). Also see section 4.8.

Precautions for use

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 are directly related to the administration rate and the administered dose.

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. **Reddening of skin, burning sensation or pain during intravenous injection may indicate accidental perivascular injection, which may lead to tissue necrosis.**

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.

Paediatric population

Due to the risk of aluminium exposure and accumulation, a maximum dose of 1 ml/kg body weight/day of Calcium Gluconate 10% solution for injection/infusion is recommended for administration in children 0 to < 18 years and those with impaired renal function.

Taking into account the content of aluminium in one ampoule (when measured at the end of shelf life) and considering current scientific knowledge, it cannot be excluded that exposure to aluminium (from administering more than the recommended number of ampoules) could contribute to future total aluminium exposure (from the environment, drinking water and food) and potential toxicity in patients (See section 4.2 and 5.1).

A study by Bishop et al. (1997) assessed aluminium neurotoxicity in preterm infants receiving intravenous feeding solutions. Either standard parenteral feeding solutions containing aluminium at a dose of 45 µ g/kg/day or solutions with depleted aluminium content at a dose of 4.0 – 5.0 µ g/kg/day were administered to the infants.

Bayley Mental Development Index (MDI) was used to compare neurologic development between the studied groups. The MDI scores in all groups of infants receiving the intravenous feeding solutions for 10 days or less were similar. However, in infants receiving the standard solutions for more than 10 days a statistically significant 10-point deficit in MDI scores (P = 0.02) was observed when compared with those receiving the aluminium-depleted solutions.

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.

The only exception may be that intravenous calcium administration is imperative for treatment of severe hypocalcaemia symptoms or acute severe hyperkalaemia putting the patient at vital risk, if safer therapeutic alternatives are not available and calcium administration via the oral route is not possible (see also sections 4.3 and 4.4).

Adrenaline / Epinephrine

Co-administration of calcium and adrenaline/epinephrine attenuates 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 and sodium bicarbonate

See section 4.4 and section 6.2.

4.6 Fertility, pregnancy, and lactation

Pregnancy

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

Calcium Gluconate 10% solution for injection/infusion BP should not be used during pregnancy unless the clinical condition of the woman requires treatment with Calcium Gluconate 10% solution for injection/infusion 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 10% solution for injection/infusion 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.

Not applicable

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); Not known (cannot be estimated from the available data)		
System Organ Class (SOC)	Frequency	Adverse Reactions
Cardiac disorders	Not known	Bradycardia, cardiac arrhythmia, cardiac arrest, syncope.
Vascular disorders	Not known	Hypotension, vasodilatation, circulatory collapse (possibly fatal), flushing.
Gastrointestinal disorders	Not known	Nausea, vomiting.
General disorders and administration site conditions	Rare Not known Not known	Severe, and in some cases fatal, adverse reactions following intravenous administration of ceftriaxone and calcium salt in preterm and full-term newborns (aged <28 days)*. Calcinosis cutis, possibly followed by skin ablation and necrosis, due to extravasation, cardiovascular and other systemic undesirable effects**. Heat sensations, sweating.

Description of selected adverse reactions

*** Precipitation of ceftriaxone-calcium salts**

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, 4.4 and 4.5).

**** Adverse reactions only occurring with improper administration technique**

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 (see section 4.4).

Aluminium accumulation and toxicity

In the paediatric population, aluminium toxicity is often manifested in the form of osteopenia, fractures and rickets and usually occurs after months to years of therapy but may appear after shorter periods of time in infants. Neonates are at an increased risk of aluminium toxicity because of anatomic, physiologic and nutrition-related factors not present in other populations. Aluminium has a potential to accumulate in presence of advanced renal dysfunction (see section 4.4).

Potential adverse reactions from aluminium toxicity, occurring as a result of aluminium exposure in cases of repeated or prolonged treatment in the paediatric population, in the elderly and in patients with renal impairment: microcytic anaemia, osteopenia, fractures,

rickets, impaired bone mineralisation (reduced bone mass and mineral content), neurotoxicity (affecting brain and nervous system development) and hepatotoxicity.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

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

Further administration of calcium should be discontinued.

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.

Mechanism of action

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

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.

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.

Pharmacodynamic effects

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

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.

Hyperkalaemia

In acute severe hyperkalaemia (with or without ECG changes), which is defined as a serum potassium concentration above 6.5 mmol/L in adults, calcium is given to reduce the threshold potential of cardiac cells by restoring the normal gradient with the resting potential that has been increased with the elevated potassium levels. Calcium does not affect potassium levels.

5.2 Pharmacokinetic properties

Absorption

After intravenous administration, the bioavailability of calcium gluconate is 100%.

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. Calcium is excreted also in the faeces.

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
Water for Injection

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

24 months

6.4 Special precautions for storage:

Do not store above 30°C

6.5 Nature and contents of container

10 grams cream packed in collapsible Aluminium tubes embossed with batch number, manufacturing date and expiry dates packed in unit box with an insert

6.6 Special precautions for disposal and other handling:

Use as directed by the physician. If only part used, discard the remaining solution. Keep out of reach of children.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Tasa Pharma Limited Unit C1-C3 Kay complex Nairobi Kenya

Manufacturing site address:

Tasa Pharma Ltd Unit C1-C3, Kay Complex, Mombasa Road, Nairobi, P.O. Box 3959-00506 Kenya

8. Marketing authorization number

H2024/CTD10958/24317

9. Date of first registration

28/02/2024

10. Date of revision of the text:

November 2024