

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Calcium Gluconate 10 % w/v Injection BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml ampoule contains
940 mg Calcium Gluconate for Injection,
equivalent to 2.26 mmol calcium in 10 ml.

Each 1 ml contains
94 mg Calcium Gluconate for Injection,
equivalent to 0.23 mmol calcium in 1 ml.

For excipients see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection
Clear, colourless to light brown aqueous solution, practically free from particles

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of acute symptomatic hypocalcaemia

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 this level. During therapy, serum calcium levels should be monitored closely.

Recommended dosage schedule

Adults:

The usual initial dose in adults is 10 ml of Calcium Gluconate 10 % w/v Injection BP, corresponding to 2.26 mmol or 4.52 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.

Children and adolescents (< 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.

The following table gives usual **initial** dosage values for guidance:

Age	Body wt. (kg)	ml	Equiv. to mmol (mEq) calcium
3 mo.	5.5	2 – 5	0.45 – 1.13 (0.9 – 2.26)
6 mo.	7.5	2 – 5	0.45 – 1.13 (0.9 – 2.26)
1 yr.	10	2 – 5	0.45 – 1.13 (0.9 – 2.26)
3 yr.	14	5 – 10	1.13 – 2.26 (2.26 – 4.52)
7.5 yr.	24	5 – 10	1.13 – 2.26 (2.26 – 4.52)
12 yr.	38	5 – 10	1.13 – 2.26 (2.26 – 4.52)
> 12 yr.	> 38		as for adults

This corresponds approximately to:

- 0.4 – 1 ml/kg body weight
(\triangleq 0.09 – 0.23 mmol [0.18 – 0.45 mEq] of calcium per kg body weight)
for children up to 3 years,
- 0.2 – 0.5 ml/kg body weight
(\triangleq 0.05 – 0.1 mmol [0.1 – 0.2 mEq] of calcium per kg body weight)
for children from 4 to 12 years.

For patients above 12 years of age the adult dosages should be applied.

In cases of severe symptoms of hypocalcaemia, e.g. cardiac symptoms, higher initial doses (up to 2 ml per kg body weight, \triangleq 0.45 mmol [0.9 mEq] 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.

IV 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 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.

Method of administration

Adults:

Slow intravenous or deep intramuscular injection

Children and adolescents:

Only slow intravenous injection or intravenous infusion after dilution, in order to achieve sufficiently low administration rates and to avoid irritation/necrosis in case of accidental extravasation. For intravenous infusion, Calcium Gluconate 10 % w/v Injection BP may be diluted 1:10 to a concentration of 10 mg/ml with the following two infusion fluids: 0.9% w/v Sodium Chloride Intravenous Infusion or 5% w/v Glucose Intravenous Infusion. Intramuscular injections should not be performed in children.

The intravenous administration rate should not exceed 50 mg of calcium gluconate per min. The patient should be in the lying position and should be closely observed during injection. Monitoring should include heart rate or ECG.

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 position-

ing of the injection into the muscle and not into adipose tissues. If repeated injections are necessary, the injection site should be changed every time.

4.3 Contraindications

Calcium Gluconate 10 % w/v Injection BP must not be administered in the following conditions:

- Hypersensitivity to calcium gluconate and to the excipient (see section 6.1),
- Hypercalcaemia (e.g. in patients with hyperparathyroidism, hypervitaminosis D, decalcifying malignancies, renal insufficiency, immobilisation osteoporosis, sarcoidosis, milk-alkali syndrome),
- Hypercalciuria,
- Intoxication with cardiac glycosides,
- Therapy with cardiac glycosides

The only exception may be that IV calcium administration is imperative for treatment of severe hypocalcaemia symptoms 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).

4.4 Special Warnings and Precautions for Use

Special warnings

In the exceptional case of IV 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.

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.

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

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.

In children, Calcium Gluconate 10 % w/v Injection BP should not be injected IM but only slowly IV.

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

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

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 also section 4.8. Extravasation must be avoided; the injection site should be monitored carefully.

High Vitamin D intake should be avoided.

4.5 Interactions with Other Medicinal Products and Other Forms of Interaction

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 IV calcium administration is imperative for treatment of severe hypocalcaemia symptoms 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 4.3 and 4.4).

Co-administration of calcium and *epinephrine* may lead to cardiac arrhythmia.

Calcium and *magnesium* mutually antagonise their effects.

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

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

4.6 Pregnancy and Lactation

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

Calcium gluconate injections should be used during pregnancy only if considered to be essential by the physician. 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.

Calcium is excreted in breast milk. 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

Cardiovascular and other systemic undesirable effects are likely to occur as symptoms of acute hypercalcaemia resulting from IV overdose or too rapid IV injection. Their occurrence and frequency is directly related to the administration rate and the administered dose. Under the conditions of proper administration, they are rare (< 1:1000).

Cardiac and vascular disorders

Hypotension, bradycardia, cardiac arrhythmia, vasodilatation, vasomotor collapse (possibly fatal), flushing, mainly after too rapid injection.

Gastro-intestinal disorders

Nausea, vomiting

General disorders

Heat sensations, sweating

Administration site conditions

Common (< 1:10, ≥ 1:100):

Intramuscular injection may be accompanied by pain sensations or erythema.

Adverse reactions only occurring with improper administration technique:

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

Soft tissue calcification, 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.

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, somnolence, 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 i.v. 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 overdosage.

5 PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic Properties**

Pharmaco-therapeutic group: Solutions affecting the electrolyte balance, electrolytes.

ATC-code: B05B B01.

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

The physiological level of the plasma calcium concentration is maintained at 2.25-2.75 mmol/l. As about 50 per cent of the plasma calcium is bound to albumin, total plasma cal-

cium is coupled to the plasma protein concentration. The concentration of ionised calcium is between 1.23 and 1.43 mmol/l, regulated by calcitonin and parathormone.

Hypocalcaemia (total calcium below 2.25 mmol/l or ionized 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, dysarthria, confusion, and cerebral convulsive seizures.

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 50% of the total plasma calcium is in the physiologically active ionised form, about 45% is bound to proteins, mainly albumin, and 5% is complexed with anions.

Metabolism

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.

Excretion

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

5.3 Preclinical Safety Data

Preclinical data from studies of safety pharmacology, chronic and reproduction toxicity did not reveal any particular risk for the use of the product in humans.

There are no preclinical data relating to genotoxicity or oncogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Calcium saccharate,
Water for injections

6.2 Incompatibilities

The medicinal product should not be mixed with any other drug, unless compatibility has been satisfactorily demonstrated.

Calcium salts can form complexes with many drugs and this may result in a precipitate.

Calcium salts are incompatible with oxidising agents, citrates, soluble carbonates, bicarbonates, oxalates, phosphates, tartrates and sulphates.

Physical incompatibility has also been reported with amphotericin, cephalothin sodium, cephalozin sodium, cephmandole nafate, novobiocin sodium, dobutamine hydrochloride, prochlorperazine and tetracyclines.

6.3 Shelf Life

Shelf life of the medicinal product as packaged for sale

3 years

Shelf life after first opening the container

For single dose use only. Any unused solution should be discarded immediately after initial use.

Shelf life after dilution according to directions

When diluted to 10 mg per ml, according to directions, with the recommended infusion fluids, 0.9% w/v Sodium Chloride Intravenous Infusion or 5% w/v Glucose Intravenous Infusion, physical in-use stability has been demonstrated for 48 hours, when stored at room temperature. 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 exceed than 24 hours at 2 to 8° C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special Precautions for Storage

Do not store above 25 °C

When diluted according to directions with the recommended infusion fluids, 0.9% w/v Sodium Chloride Intravenous Infusion or 5% w/v Glucose Intravenous Infusion, physical in-use stability has been demonstrated for 48 hours, when stored at room temperature. 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 exceed than 24 hours at 2 to 8° C, unless dilution has taken place in controlled and validated aseptic conditions.

6.5 Nature and Contents of Container

10 ml LDPE (low density polyethylene) ampoule.
Pack size: Cardboard box containing 20 ampoules.

6.6 Instructions for Use and Handling

The product is intended for single dose use only. Any unused solution should be discarded immediately after initial use.

Visually inspect the sterile solution for injection for particulate matter, discoloration and the integrity of the container prior to use.

The solution should only be used if it is clear and the container is undamaged.

For intravenous infusion, Calcium Gluconate 10% B. Braun may be diluted 1:10 to a concentration of 10 mg/ml with the following two infusion fluids: 0.9% w/v Sodium Chloride Intravenous Infusion or 5% w/v Glucose Intravenous Infusion. When diluted with these recommended infusion fluids, the resulting solutions are intended for immediate single use. The

rate of intravenous infusion should not exceed 50 mg of calcium gluconate per minute (see Posology 4.2). Dilution should be performed under controlled and validated aseptic conditions. After mixing, the container should be gently agitated to ensure homogeneity.

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen AG
Carl-Braun-Str. 1,
D-34212 Melsungen, Germany

8 MARKETING AUTHORISATION NUMBER(S)

PL 03551/0098-0001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

18.05.2006

10 DATE OF (PARTIAL) REVISION OF THE TEXT

June 2005