13103105.0508 26.05.2008 8:53 Uhr Seite 1

570/13103105/0508

Directions for Use

B. Braun Melsungen AG · 34209 Melsungen, Germany

10% w/v Calcium Gluconate Inj.

Solution for Injection

Composition

Active substances:
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.

Excipients:
Calcium saccharate, water for injections

Pharmaceutical form
Solution for injection

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

Indications
Treatment of acute symptomatic hypocalcaemia

Contraindications
10% w/v Calcium Gluconate Inj. must not be administered in the following conditions:
- Hypersensitivity to calcium gluconate and to the excipient,
- elevated calcium level in blood (hypercalcaemia), e.g. in patients with hyperparathyroidism, hypervitaminosis D, decalcifying malignancies, renal insufficiency, immobilisation osteoporosis, sarcoidiosis, milk-alkali syndrome,
- increased calcium excretion in urine (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 "**Special Warnings ...**" and "**Interactions**").

Special warnings and precautions for use
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 "**Interactions**"), 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.
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, 10% w/v Calcium Gluconate Inj. 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 "**Undesirable effects**". Extravasation must be avoided; the injection site should be monitored carefully.
High Vitamin D intake should be avoided.

Pregnancy and Lactation

Pregnancy:
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.

Lactation:
Calcium is excreted in breast milk This should be borne in mind when administering calcium to women who are breast-feeding their infants.

Interactions
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 "**Contraindications**" and "**Special Warnings ...**").
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.
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, cephazolin sodium, cephamandole nafate, novobiocin sodium, dobutamine hydrochloride, prochlorperazine and tetracyclines.

Dosage
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 10% w/v Calcium Gluconate Inj., 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.

B BRAUN

Schwarz
210x297 mm
570/13103105/0508
Lätus: 702

13103105.0508 26.05.2008 8:53 Uhr Seite 2

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
(≙ 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
(≙ 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, ≙ 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, 10% w/v Calcium Gluconate Inj. 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 "**Special Warnings ...**" and "**Undesirable effects**". 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.

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.

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 made at adequate depth, 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.

Note:
Patients should inform their doctor or pharmacist if they notice any side effect not mentioned in this leaflet.

Expiry date
The product must not be used beyond the expiry date stated on the labelling.

Instructions for storage / use / handling
Do not store above 25 °C
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. 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.

Date of last revision: 06.2005

B. BRAUN

B. Braun Melsungen AG
34209 Melsungen
Germany

Schwarz
210x297 mm
570/13103105/0508
Lätus: 702