

PRESCRIBING INFORMATION

2% Calcium Gluconate in Sodium Chloride Injection

Calcium Gluconate in Sodium Chloride Injection

Solution, 20 mg / mL (0.093 mEq / mL)

For Intravenous Use

Freeflex[®] bag: 1000 mg per 50 mL

Freeflex[®] bag: 2000 mg per 100 mL

ATC Code: B05BB01

Electrolyte Replenisher

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Date of Initial Authorization:

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RECENT MAJOR LABEL CHANGES

N/A

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Sections or subsections that are not applicable at the time of authorization are not listed.

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PART I: HEALTH PROFESSIONAL INFORMATION

1. INDICATIONS

2% Calcium Gluconate in Sodium Chloride Injection is used:

- for acute treatment of conditions arising from calcium deficiencies such as hypocalcemic tetany, hypocalcemia related to hypoparathyroidism and hypocalcemia due to rapid growth or pregnancy.
- In hyperkalemia, 2% Calcium Gluconate in Sodium Chloride Injection may aid in antagonizing the cardiac toxicity, provided the patient is not receiving digitalis therapy.

2. CONTRAINDICATIONS

2% Calcium Gluconate in Sodium Chloride Injection is contraindicated in patients with:

- hypersensitivity to the active substance or to any of the excipients
- ventricular fibrillation
- hypercalcemia
- severe renal failure
- hypercalciuria
- galactosaemia
- Patients taking cardiac glycosides (see WARNINGS AND PRECAUTIONS and DRUG INTERACTIONS)
- Neonates (28 days of age or younger) receiving ceftriaxone (see WARNINGS AND PRECAUTIONS)

2% Calcium Gluconate in Sodium Chloride Injection should not be given via the intramuscular or subcutaneous routes, as necrosis or sloughing may occur.

This product contains aluminum that may reach toxic levels (see WARNINGS AND PRECAUTIONS).

4. DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

2% Calcium Gluconate in Sodium Chloride Injection contains 20 mg of calcium gluconate per mL which contains 1.86 mg (i.e. 0.093 mEq) of elemental calcium. See Table 1 for amounts of elemental calcium in 2% Calcium Gluconate in Sodium Chloride Injection.

Table 1. Amount of Calcium Gluconate and Elemental Calcium

Total Strength per Total Volume	Strength per mL	Total Amount of Elemental Calcium (mg) per Total Volume	Total Amount of Elemental Calcium (mEq) per Total Volume
1000 mg per 50 mL	20 mg/mL	93 mg per 50mL	4.65 mEq per 50 mL
2000 mg per 100 mL	20 mg/mL	186 mg per 100 mL	9.3 mEq per 100 mL

The dose is dependent on the requirements of the individual patient. However, recommended doses are indicated in Table 2.

Table 2 – Dosing Recommendations in mg of calcium ion for Neonate, Pediatric, and Adult Patients

Patient Population	Initial Dose	Subsequent Doses (if needed)	
		Bolus	Continuous Infusion
Neonate (\leq 1 month)	100 – 200 mg/kg	100 – 200 mg/kg every 6 hours	Initiate at 17 – 33 mg/kg/hour
Pediatric (> 1 month to < 17 years)	29 – 60 mg/kg	29 – 60 mg/kg every 6 hours	Initiate at 8 – 13 mg/kg/hour
Adult	1000 – 2000 mg	1000 – 2000 mg every 6 hours	Initiate at 5.4 – 21.5 mg/kg/hour

4.4 Administration

- Do not dilute 2% Calcium Gluconate in Sodium Chloride Injection prior to use. Any unused portion should be discarded.

- Inspect 2% Calcium Gluconate in Sodium Chloride Injection visually prior to administration. The solution should appear clear and colorless. Do not administer if there is particulate matter or discoloration.
- Administer 2% Calcium Gluconate in Sodium Chloride Injection intravenously via a secure intravenous line to avoid calcinosis cutis and tissue necrosis (see WARNINGS AND PRECAUTIONS).
- Administer 2% Calcium Gluconate in Sodium Chloride Injection by continuous infusion at the rate recommended in Table 3 and monitor patients, vitals, calcium and ECG during the infusion (see WARNINGS AND PRECAUTIONS).
- Check solution container composition, lot number, and expiry date.
- Do not admix with other drugs.
- Do not use solution containers in series connections.
- Do not remove solution container from its overwrap until immediately before use.
- The intact port cap provides visual tamper evidence. Do not use if port cap is prematurely removed. Maintain strict aseptic technique during handling.

4.7 Instructions for Preparation and Use

INSTRUCTIONS FOR USE:

1. Always inspect the solution container before and after removal from the overwrap.
2. Place the solution container on a clean, flat surface. Remove the solution container from the overwrap.
3. Check the solution container for leaks by squeezing firmly. If leaks are found, discard.
4. Do not use if the solution is cloudy or a precipitate is present.

To Prepare for Administration:

1. Immediately before inserting the infusion set, break off BLUE Infusion Port Cap with the arrow pointing away from the solution container.
2. Use a non-vented infusion set or dose close the air-inlet on a vented set.
3. Close the roller clamp of the infusion set
4. Hold the base of the BLUE infusion port, twist and push spike until fully inserted.
5. The BLUE infusion port contains a self-sealing septum that helps prevent leakage after removing the spike. The infusion port is not intended to be spiked more than once.
6. Suspend solution container from hanger hole.
7. No preservative added. For Single Use Only. Discard unused portion.

Table 3 – Administration notes for bolus or continuous infusion

	Administration and Monitoring notes
Bolus Intravenous	DO NOT exceed an infusion rate of: <ul style="list-style-type: none">• 100 mg/minute in pediatric patients• 200 mg/minute in adult patients Measure serum calcium every 4 to 6 hours. Monitor patients, vitals, and electrocardiograph (ECG) during administration.
Continuous Infusion	Adjust rate as needed based on serum calcium levels. Measure serum calcium every 1 to 4 hours. Monitor patients, vitals, and electrocardiograph (ECG) during administration.

To avoid undesirable reactions that may follow rapid intravenous administration of calcium gluconate, the 2% Calcium Gluconate in Sodium Chloride Injection should be given slowly, e.g., approximately 1.5 mL over a period of one minute.

5. OVERDOSAGE

Overdosage of 2% Calcium Gluconate in Sodium Chloride Injection may result in hypercalcemia. Symptoms of hypercalcemia typically develop when the total serum calcium concentration is ≥ 12 mg/dL. Symptoms include anorexia, nausea, vomiting, abdominal pain, constipation, depression, mental disturbances, polydipsia, weakness, bone pain, fatigue, and confusion at lower levels, with patients experiencing hallucinations, disorientation, hypotonicity, seizures, and coma. Effects on the kidney include diminished ability to concentrate urine and diuresis, nephrocalcinosis, renal calculi. In severe cases, symptoms include cardiac arrhythmias and cardiac arrest.

If overdose of 2% Calcium Gluconate in Sodium Chloride Injection occurs, immediately discontinue administration and provide supportive treatments to restore intravascular volume as well as promote calcium excretion in the urine if necessary.

For management of a suspected drug overdose, contact your regional poison control centre.

6. DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 4 – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	2 % Solution Ca ⁺⁺ 0.093 mEq / mL	6.75 mg Sodium Chloride Sodium hydroxide and/or hydrochloric acid for adjustment to a final value of pH 6 to 8.2, water for injection. Aluminum not more than 100 mcg / L.

2% Calcium Gluconate in Sodium Chloride Injection is a sterile, preservative free, nonpyrogenic supersaturated solution of calcium gluconate that is stabilized with calcium saccharate, which provides 6% of the total calcium.

Each mL contains:

Calcium Gluconate (monohydrate), USP19.6 mg
 Calcium Saccharate (tetrahydrate), USP0.9 mg
 Total elemental Calcium.....1.86 mg (0.093 mEq)

2% Calcium Gluconate in Sodium Chloride Injection is supplied in freeflex® premixed bag..

Freeflex® premixed bag: Packaged in 24 bags per shipper carton.		
Fill Volume	Bag Size	Calcium Gluconate
50 mL	100 mL	1000 mg
100 mL	100 mL	2000 mg

7. WARNINGS AND PRECAUTIONS

For intravenous use only. Subcutaneous or intramuscular injection may cause severe necrosis and sloughing.

General: 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.

Aluminum Toxicity: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large

amounts of calcium and phosphate solutions which contain aluminum. Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg per kg per day accumulate aluminum at levels associated with central nervous system and bone toxicity.

Concomitant Cardiac Glycoside Use: Because of the danger involved in simultaneous use of calcium salts and drugs of the digitalis group, a digitalized patient should not receive an intravenous injection of a calcium compound unless indications are clearly defined (See CONTRAINDICATIONS and DRUG INTERACTIONS; Drug-Drug Interactions).

Concomitant Ceftriaxone Use: Concurrent use of intravenous ceftriaxone and 2% Calcium Gluconate in Sodium Chloride Injection can lead to formation of ceftriaxone-calcium precipitates.

Concomitant use of ceftriaxone and intravenous calcium-containing products is contraindicated in neonates (28 days of age or younger) (See CONTRAINDICATIONS).

In patients older than 28 days of age, ceftriaxone and calcium-containing products may be administered sequentially, provided the infusion lines are thoroughly flushed between infusions with a compatible fluid. Ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions via a Y-site in any age group.

7.1 Special Populations

7.1.1 Pregnant Women

It is not known whether calcium gluconate can cause fetal harm when administered to a pregnant woman or whether it can affect reproduction capacity. Animal reproduction studies have not been conducted with calcium gluconate. Calcium gluconate should be given to a pregnant woman only if clearly needed.

Infants born to mothers with hypocalcemia can have associated fetal and neonatal hyperparathyroidism, which in turn can cause fetal and neonatal skeletal demineralization, subperiosteal bone resorption, osteitis fibrosa cystica and neonatal seizures. Infants born to mothers with hypocalcemia should be carefully monitored for signs of hypocalcemia or hypercalcemia, including neuromuscular irritability, apnea, cyanosis and cardiac rhythm disorders.

7.1.2 Breast-feeding

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when 2% Calcium Gluconate in Sodium Chloride Injection is administered to a nursing woman.

8. ADVERSE REACTIONS

Administration site reactions: Local soft tissue inflammation, local necrosis, calcinosis cutis and calcification due to extravasation. Local necrosis and abscess formation may occur with intramuscular injection.

Cardiovascular: Vasodilation, decreased blood pressure, bradycardia, cardiac arrhythmias, syncope and cardiac arrest. Use in digitalized patients may precipitate arrhythmias.

Neurologic: Tingling sensations, a sense of oppression or heat wave, calcium or chalky taste.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

9. DRUG INTERACTIONS

9.3 Drug-Drug Interactions

2% Calcium Gluconate in Sodium Chloride Injection has been reported to be physically incompatible with intravenous solutions containing various drugs, including ceftriaxone,

amphotericin, cephalothin sodium, cephazolin sodium, cephamandole nafate, novobiocin, dobutamine, prochlorperazine, and fluids containing oxidising agents, citrates, soluble carbonates, bicarbonate, phosphates, tartrates and sulfates. Calcium salts can form complexes with many drugs, and this may result in a precipitate. Published data are too varied and/or limited to permit generalization, and specialized reference should be consulted for specific information.

Table 5 – Established or Potential Drug-Drug Interactions

Proper/Common name	Clinical Comment
Cardiac glycosides	The inotropic and toxic effects of cardiac glycosides and calcium are synergistic and arrhythmias may occur if these drugs are given together (particularly when calcium is given intravenously). Intravenous administration of calcium is contraindicated in patients receiving cardiac glycosides; if considered necessary, administer 2% Calcium Gluconate in Sodium Chloride Injection slowly in small amounts and monitor ECG closely.
Tetracycline antibiotics	Calcium complexes tetracycline antibiotics rendering them inactive. The two drugs should not be given at the same time orally, nor should they be mixed for parenteral administration.
Calcium Channel Blockers	Administration of calcium may reduce the response to calcium channel blockers.
Drugs that may cause Hypercalcemia	Vitamin D, vitamin A, thiazide diuretics, estrogen, calcipotriene and teriparatide administration may cause hypercalcemia. Monitor plasma calcium concentrations in patients taking these drugs concurrently.
Epinephrine	Co-administration of calcium and epinephrine attenuate epinephrine's β -adrenergic effects in postoperative heart surgery patients.
Magnesium	Calcium and magnesium mutually antagonise their effects.

9.7 Drug-Laboratory Test Interactions

Transient elevations of plasma 11-hydroxycorticosteroid levels (Glenn-Nelson technique) may occur when intravenous calcium is administered, but levels return to control values after one hour.

Intravenous 2% Calcium Gluconate in Sodium Chloride Injection can produce false-negative for serum and urinary magnesium.

10. CLINICAL PHARMACOLOGY

Calcium is the fifth most abundant element in the body and is essential for maintenance of the functional integrity of nervous, muscular and skeletal systems, and cell membrane and capillary permeability. It is also an important activator in many enzymatic reactions and is essential to a number of physiologic processes including transmission of nerve impulses; contraction of cardiac, smooth and skeletal muscles; renal function; respiration and blood coagulation. Calcium also plays regulatory roles in the release and storage of neurotransmitters and hormones, in the uptake and binding of amino acids, and in cyanocobalamin (vitamin B₁₂) absorption and gastrin secretion.

11. STORAGE, STABILITY AND DISPOSAL

The container closure is not made with natural rubber latex. Non-PVC, Non-DEHP, Sterile.

Store at 15 °C to 30 °C.

Preservative Free. Discard any unused portion in the single-dose container immediately.

12. SPECIAL HANDLING INSTRUCTION

This information is not available for this drug product.

PART II: SCIENTIFIC INFORMATION

13. PHARMACEUTICAL INFORMATION

This information is not available for this drug product.

14. CLINICAL TRIAL

This information is not available for this drug product.

15. MICROBIOLOGY

This information is not available for this drug product.

16. NON-CLINICAL TOXICOLOGY

This information is not available for this drug product.

17. SUPPORTING PRODUCT MONOGRAPHS

1. Calcium Gluconate Injection, USP 10%, Solution, 100 mg / mL (0.465 mEq / mL), submission control 229403, Prescribing Information, Fresenius Kabi Canada Ltd. February 24, 2020.

PAITIENT MEDICATION INFORMATION

This information is not available for this drug product.

MORE INFORMATION

If you want more information about 2% Calcium Gluconate in Sodium Chloride Injection:

- Talk to your healthcare professional.
- Find the full prescribing information that is prepared for healthcare professionals by visiting the Health Canada website (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>); the manufacturer's website (<https://www.fresenius-kabi.com/en-ca>), or by calling 1-877-821-7724.

This Prescribing Information is prepared by:

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