PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Calcium Chloride Injection USP

100 mg/mL
(27 mg [0.7 mmol or 1.4 mEq] Ca^{++}/mL)

10% Hypertonic solution for intravenous injection

Calcium Replenisher

Pfizer Canada ULC

17300 Trans-Canada Highway

Kirkland, Québec

H9J 2M5

Date of Initial Authorization:
December 31, 1981

Date of Revision:
August 25, 2022

Submission Control Number: 262054

RECENT MAJOR LABEL CHANGES

CONTRAINDICATIONS (2)	08/2022

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

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Calcium Chloride Injection USP is indicated:

- For the treatment of hypocalcemia in those conditions requiring a prompt increase in blood plasma calcium levels,
- In the treatment of magnesium intoxication due to overdosage of magnesium sulfate
- To combat the deleterious effects of hyperkalemia as measured by electrocardiography (ECG), pending correction of the increased potassium level in the extracellular fluid.
- In cardiac resuscitation when weak or inadequate contractions return following defibrillation or when epinephrine injection has failed to strengthen myocardial contractions.

2 CONTRAINDICATIONS

Calcium Chloride Injection USP is contraindicated:

- For cardiac resuscitation in the presence of ventricular fibrillation.
- In patients with the risk of existing digitalis toxicity.
- In the treatment of asystole and electromechanical dissociation.
- When mixed or administered simultaneously with ceftriaxone intravenous solutions, even via different infusion lines or at different infusion sites, as it can lead to precipitation of ceftriaxone-calcium (see **7 WARNINGS AND PRECAUTIONS**).
- For injection into tissues, since it is irritating to veins and severe necrosis and sloughing may occur.
- In patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING**.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- **Caution: This solution must not be injected intramuscularly or subcutaneously.**

4.2 Recommended Dose and Dosage Adjustment

- The usual adult dosage in hypocalcemic disorders ranges from 200 to 1000 mg at intervals of 1 to 3 days, depending on the response of the patient and/or results of serum calcium determinations. Repeated injections may be required because of rapid excretion of calcium.
- In magnesium intoxication, an initial adult dose of 500 mg (5 mL) should be administered promptly and the patient observed for signs of recovery before further doses are given.
- In hyperkalemic ECG disturbances of cardiac function, the dosage of calcium chloride injection should be titrated by constant monitoring of ECG changes during administration.
- In cardiac resuscitation, the usual adult dosage ranges from 500 mg to 1 g (5 to 10 mL) intravenously, or from 200 to 800 mg (2 to 8 mL) when injected into the ventricular cavity.

4.4 Administration

Calcium Chloride Injection USP is administered only by **slow** intravenous injection (not to exceed 1 mL/min) and/or in cardiac resuscitation, by injection into the ventricular cavity. It must not be injected into the myocardium.

The usual precautions for intravenous therapy should be observed. If time permits, the solution should be warmed to body temperature. The injection should be halted if the patient complains of any discomfort; it may be resumed when symptoms disappear. Following injection, the patient should remain recumbent for a short time.

To prevent needle-stick injuries, needles should not be recapped, purposely bent or broken by hand. Place all needles in a sharps disposal container immediately after they have been used.

4.5 Missed Dose

This information is not applicable for this drug product.

5 OVERDOSAGE

Too rapid injection may produce lowering of blood pressure and cardiac syncope. Persistent hypercalcemia from calcium overdosage is unlikely because of rapid excretion. In the event of untoward effects from excessive calcium administration, the drug should be discontinued promptly, the patient re-evaluated and appropriate countermeasures instituted, if necessary. Symptoms of overdosage include: anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi and, in severe cases, cardiac arrhythmias and coma (see **7 WARNING AND PRECAUTIONS** and **8 ADVERSE REACTIONS**).

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

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Intravenous or intraventricular cavity injection	10 mL Calcium Chloride solution in a pre-filled, single use syringe **(see Table 2 Dosage Forms)** / 100 mg/mL / Calcium Chloride Dihydrate	Hydrochloric Acid and/or Sodium Hydroxide for pH adjustment, Water for Injection USP

Calcium Chloride Injection USP is supplied in single-use containers as follows:

Table 2 – Dosage Forms & Packaging

Container	Volume	Needle
LifeShield® Abboject® Syringe[1]	10 mL	20-gauge
Pre-filled Abboject® Syringe[2]	10 mL	20-gauge
Pre-filled Ansyr® Syringe[3]	10 mL	Needle-free, with luer lock adapter

1: LifeShield® Abboject® Syringe: Flexible and reliable, the ready-to-use LifeShield® Abboject® syringe minimizes errors and protects caregivers and patients alike. It can be used for needle-free or shrouded needle access. The design features two pieces - a calibrated glass drug vial and a matching plastic syringe barrel with integral injector needle. Medication, fluid path, and needle are sterile and nonpyrogenic if caps and needle cover are undisturbed and package intact.

2. Abboject® Syringe: Flexible and reliable, the ready-to-use Abboject® syringe minimizes errors and protects caregivers and patients alike. It can be used for needle-free access. The design features two pieces - a calibrated glass drug vial and a matching plastic luer lock syringe barrel. Medication, fluid path, and needle are sterile and nonpyrogenic if caps and luer end cover are undisturbed and package intact.

3: Ansyr® Syringe: The Ansyr® syringe is a proprietary delivery option offering one-piece, polypropylene plastic construction with a needle-free male luer lock adapter. Ansyr® syringes are available prefilled with a wide range of emergency medications. Graduated markings on the syringe barrel conform to ISO standards and clearly show any drug remaining. Medication and fluid path are sterile and nonpyrogenic if protective cover is undisturbed and package intact.

7 WARNINGS AND PRECAUTIONS

General

Risk of Ceftriaxone-Calcium Precipitation

Ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites as it can lead to precipitation of ceftriaxone-calcium (see **2 CONTRAINDICATIONS**).

Calcium chloride and ceftriaxone intravenous 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.

Aluminum Toxicity

This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired.

Research indicates that patients with impaired kidney function, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicities. Tissue loading may occur at even lower rates of administration.

Risk of Cardiac Toxicity

Because of its additive effect, calcium should be administered very cautiously to a patient who is digitalized or who is taking effective doses of digitalis or digitalis-like preparations (see **9 DRUG INTERACTIONS)**.

It is particularly important to prevent a high concentration of calcium from reaching the heart because of the danger of cardiac syncope. Too rapid an injection exceeding 1 mL/min may lead to hypotension and cardiac syncope (see **4 DOSAGE AND ADMINISTRATION**). If injected into the ventricular cavity in cardiac resuscitation, it must not be injected into the myocardial tissue.

Injection Site Reactions

Calcium Chloride Injection USP is irritating to veins and must not be injected into tissues, since severe necrosis and sloughing may occur (see **2 CONTRAINDICATIONS**).

Injections should be made slowly through a small needle into a large vein to minimize venous irritation and avoid undesirable reactions. Great care should be taken to avoid extravasation or accidental injection into perivascular tissues. Should perivascular infiltration occur, intravenous administration at that site should be discontinued at once. Local infiltration of the affected area with 1% procaine hydrochloride, to which hyaluronidase may be added, will often reduce venospasm and dilute the calcium remaining in the tissues locally. Local application of heat may also be helpful.

7.1 Special Populations

7.1.1 Pregnant Women

Calcium crosses the placenta. There are no adequate and well-controlled studies in pregnant women. Therefore, it is not known whether developmental toxicity may occur with the use of calcium chloride. There are no available animal data that evaluate the drug-associated risk. Calcium chloride should be given to a pregnant woman only if clearly needed.

7.1.2 Breastfeeding

It is not known whether calcium chloride injection would have an impact on the calcium content of the human milk in lactating women. Calcium chloride should be administered to lactating women only if clearly indicated. Studies assessing the effects of calcium chloride in breastfed children have not been performed. Studies to assess the effect of calcium chloride on milk production or excretion have not been performed. The developmental and health benefits of breastfeeding should be considered along with

the mother's clinical need for calcium chloride, and any potential adverse effects on the breastfed child from calcium chloride or from the underlying maternal condition.

7.1.3 Pediatrics

Pediatrics (< 18 years of age**):** No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Patients over 65 years of age: An evaluation of current literature revealed no clinical experience identifying differences in response between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8 ADVERSE REACTIONS

8.2 Clinical Trial Adverse Reactions

This information is not available for this drug product.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

This information is not available for this drug product.

8.3 Less Common Clinical Trial Adverse Reactions

This information is not available for this drug product.

8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics

This information is not available for this drug product.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

This information is not available for this drug product.

8.5 Post-Market Adverse Reactions

Nervous system disorders: Paraesthesia (upon rapid injection), calcium taste

General disorders and administration site conditions: Sense of oppression, sense of "heat wave", local burning sensation, injection site extravasation, injection site reactions

Vascular disorders: Peripheral vasodilatation

Investigations: Blood pressure decreased

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 3 - Established or Potential Drug-Drug Interactions

Proper/Common name	Source of Evidence	Effect	Clinical comment
Calcium Channel Blockers	C	Administration of calcium may reduce the response to calcium channel blockers.	Calcium-containing products, like Calcium Chloride Injection, may decrease the effectiveness of calcium channel blocker.
Ceftriaxone	C	Ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites as it can lead to precipitation of ceftriaxone-calcium (see **2 CONTRAINDICATIONS**).	Calcium chloride and ceftriaxone intravenous 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.
Digitalis or digitalis-like preparations	C		Because of its additive effect, calcium should be administered very cautiously to a patient who is digitalized or who is taking effective doses of digitalis or digitalis-like preparations see **7 WARNINGS AND PRECAUTIONS**).

Legend: C = Case Study

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Calcium chloride in water dissociates to provide calcium (Ca^{++}) and chloride (Cl^{-}) ions. They are normal constituents of the body fluids and are dependent on various physiologic mechanisms for maintenance of balance between intake and output.

10.2 Pharmacodynamics

The normal serum calcium concentrations range from 8.8 to 10.4 mg/dL (2.2 to 2.6 mM).

10.3 Pharmacokinetics

Distribution

Body calcium exists in two major compartments in which the skeleton accounts for 99% of the total body calcium, and only 1% of the total body calcium is in the body fluids. The calcium in the body fluids can exist in three forms: ionized (~50%), protein-bound (~40%) and complexed with other anions (~10%). The main calcium-binding proteins include albumin and globulin in serum.

Metabolism

Calcium does not undergo any direct metabolism.

Elimination

Approximately 80% of body calcium is excreted in the feces as insoluble salts; urinary excretion accounts for the remaining 20%.

Specific Populations and Conditions

The effect of age, gender, race, renal or hepatic impairments on the pharmacokinetics of calcium have not been evaluated in clinical studies.

11 STORAGE, STABILITY AND DISPOSAL

Store between 20 and 25°C.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. Do not use unless the solution is clear and the container or seal is intact. Discard if the solution contains a precipitate.

Single-use; discard unused portion.

12 SPECIAL HANDLING INSTRUCTIONS

Liquid in glass vial. Handle with care. Inspect vial for damage prior to assembly.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

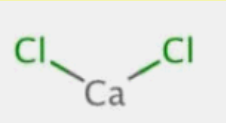
Drug Substance

Proper name: Calcium chloride

Chemical name: Calcium; dichloride; dihydrate

Molecular formula and molecular mass: $CaCl_2$ $2H_2O$ (dihydrate) 110.98 147.01 (dihydrate)

Structural formula:



Physicochemical properties:

Calcium Chloride Injection USP is a sterile, nonpyrogenic, hypertonic solution for containing 100 mg/mL (0.7 mmol/mL or 1.4 mEq/mL) of calcium chloride, dihydrate (0.7 mmol/mL or 1.4 mEq/mL of Ca^{++} and 1.4 mmol/mL or 1.4 mEq/mL of Cl^-) in Water for Injection USP. It is provided in a 10 mL single-use syringe to facilitate intravenous injection. The solution is administered only by intravenous or intraventricular cavity injection as a calcium replenisher.

The solution contains no bacteriostat, antimicrobial agent nor added buffer (except for pH adjustment) and is intended only for use as a single-use injection. When smaller doses are required, the unused portion should be discarded. As per USP testing, when diluted with water for injection to make a 5% solution, the pH of calcium chloride injection is 5.5 to 7.5. The solution may contain hydrochloric acid and/or sodium hydroxide for pH adjustment. The osmolar concentration is 2.04 mOsm/mL (calc.). Calcium Chloride Injection, USP is oxygen sensitive.

Calcium Chloride USP dihydrate is chemically designated $CaCl_2 \cdot 2H_2O$ (dihydrate) white, odourless fragments or granules freely soluble in water.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

This information is not available for this drug product.

14.2 Study Results

This information is not available for this drug product.

14.3 Comparative Bioavailability Studies

This information is not available for this drug product.

14.4 Immunogenicity

This information is not available for this drug product.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

This information is not available for this drug product.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

CALCIUM CHLORIDE INJECTION USP

Read this carefully before you start taking **Calcium Chloride Injection USP** and each time you get an injection. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Calcium Chloride Injection USP**.

What is Calcium Chloride Injection USP used for?

Calcium Chloride Injection USP is used in **adults**:

- to treat low calcium levels in the blood
- to treat magnesium intoxication due to overdosage of magnesium sulfate
- to treat high potassium levels in blood
- as part of the resuscitation procedure following a cardiac arrest (when defibrillation leaves the heart weak, or when epinephrine does not work)

How does Calcium Chloride Injection USP work?

Calcium Chloride Injection USP works by supplying more calcium and chloride minerals to your body when your body does not have the right balance.

What are the ingredients in Calcium Chloride Injection USP?

Medicinal ingredients: calcium chloride dihydrate

Non-medicinal ingredients: Hydrochloric Acid and/or Sodium Hydroxide for pH adjustment, Water for Injection USP

Calcium Chloride Injection USP comes in the following dosage forms:

Solution in a single-use pre-filled syringe: 100 mg/mL

Do not use Calcium Chloride Injection USP if:

- you are allergic to calcium chloride, or to any other ingredient in the formulation
- you have ventricular fibrillation (a dangerous irregular heartbeat)
- you are at risk of existing digitalis toxicity
- you are being treated for asystole and electromechanical dissociation
- administered for injection into tissues, since it is irritating to veins and severe death of body tissue and shedding may occur
- you are currently receiving ceftriaxone (an antibiotic) injections

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Calcium Chloride Injection USP. Talk about any health conditions or problems you may have, including if you:

- have any kidney problems
- are taking or have recently taken digitalis, or digitalis-like preparations for heart problems

- are taking any calcium channel blockers
- are pregnant, or think you are pregnant
- are breastfeeding

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Calcium Chloride Injection USP:

- ceftriaxone (an antibiotic)
- digitalis or digitalis-like preparations for heart problems
- medicines called “calcium channel blockers”

How to take Calcium Chloride Injection USP:

- Calcium Chloride Injection USP is given to you by a healthcare professional in a healthcare setting.
- Calcium Chloride Injection USP is given by slow injection into a vein.
- If you feel any discomfort during the injection, tell your healthcare professional.

Usual dose:

The dose of Calcium Chloride Injection USP is decided by a healthcare professional.

Overdose:

Since the injection is given to you by a healthcare professional, it is unlikely that you will be given too much. However, symptoms of an overdosage may include:

- anorexia
- nausea or vomiting
- constipation or stomach pain
- muscle weakness
- mental disturbances
- feeling thirsty
- frequent urination
- bone pain
- kidney stones
- irregular heartbeat
- coma

If you think you, or a person you are caring for, have taken too much Calcium Chloride Injection USP, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using Calcium Chloride Injection USP?

These are not all the possible side effects you may have when taking Calcium Chloride Injection USP. If you experience any side effects not listed here, tell your healthcare professional.

- calcium taste in the mouth
- hot flushes

- burning sensation at the site of injection
- temporary low blood pressure
- tingling or pricking ("pins and needles") sensation

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

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

Storage:

Calcium Chloride Injection USP is stored by a healthcare professional, between 20 and 25°C.

Keep out of reach and sight of children.

If you want more information about Calcium Chloride Injection USP:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website [www.pfizer.ca], or by calling 1-800-463-6001.

This leaflet was prepared by Pfizer Canada ULC

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