NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DBL™ Calcium Gluconate Injection BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DBL™ Calcium Gluconate Injection BP contains in each 10 mL, Calcium Gluconate BP 953 mg and Calcium Saccharate U.S.P. 30 mg. Each mL of the injection contains 0.22 mmol (0.45 mEq), equivalent to 8.9 mg of calcium ions.

DBL™ Calcium Gluconate Injection BP contains aluminium which is leached from the glass ampoules the product is packaged in. Aluminium levels of up to 6.1 ppm have been reported for similar products.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

DBL™ Calcium Gluconate Injection BP is a clear, colourless solution .

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Parenteral administration of calcium gluconate is required in acute hypocalcaemia and hypocalcaemic tetany.

It may be administered intravenously as an adjunct in the treatment of severe hyperkalaemia and as an aid in the treatment of depression due to overdosage of magnesium sulphate (calcium is the antagonist of magnesium toxicity).

Intravenous injections of calcium have been used in the treatment of acute renal, biliary and intestinal colic.

Calcium has been used as an inotrope in cardiac resuscitation.

Calcium salts may also be used for the prevention of hypocalcaemia in exchange transfusions and in long term electrolyte replacement therapy.

4.2 Dose and method of administration

Dose

Calcium gluconate is usually administered intravenously as a 10% solution, by slow direct

intravenous injection, or by continuous or intermittent intravenous infusion. Various maximum rates of administration have been recommended for direct intravenous injection, including 2 mL/min, 1.5 to 3 mL/min, and 5 mL/min. By intermittent infusion, a maximum rate of 2 mL/min (0.9 mEq of calcium ions/min) is suggested. During I.V. administration of calcium, close monitoring of serum calcium levels is essential.

Calcium gluconate has also been given by intramuscular or, rarely, subcutaneous injection to adults, but these routes are not recommended because of the possibility of tissue necrosis, sloughing, and abscess formation. Extravasation should also be avoided for this reason. Subcutaneous injection and intramuscular injection is contraindicated in children.

Table of Equivalence of Calcium ions in DBL™ Calcium Gluconate Injection BP

	mmol	**mEq**	**mg**
per mL	0.22	0.45	8.9
per 10 mL	2.2	4.5	89

The dose of calcium is dependent on the requirements of the individual patient. The usual initial dose for elevating serum calcium is 7 to 14 mEq for adults. Doses may be repeated every one to three days if necessary. In hypocalcaemic tetany, doses of 4.5 to 16 mEq may be administered until response occurs. The maximum daily dose should not exceed 15g of calcium gluconate (67.5 mEq of calcium ion).

For children and infants, initial doses of 1 to 7 mEq and less than 1 mEq respectively, are usually used to elevate serum calcium. If needed, doses may be repeated every one to three days. For children with hypocalcaemic tetany, dosages of 0.5 to 0.7 mEq/kg, repeated every six to eight hours until response is seen, are recommended. Neonatal tetany may be treated with divided doses totalling about 2.4 mEq/kg/day.

Calcium salts may be administered intravenously in a dose of 4.5 to 9.0 mEq of calcium as an adjunct in the treatment of severe hyperkalaemia, repeated as required under ECG control.

For the treatment of hypermagnesemia in adults, an initial dose of 7 mEq I.V. may be given with subsequent doses adjusted according to response.

In cardiac resuscitation, the recommended intravenous dose is 7-14 mEq for adults and 0.5 mEq for children.

Calcium salts may also be added to parenteral nutrition solutions for the prevention of hypocalcaemia.

Compatibilities

It is recommended that DBL™ Calcium Gluconate Injection BP be diluted with either 0.9% Sodium Chloride, 5% Glucose in Water, Lactated Ringers Injection, or 5% Glucose in 0.9% sodium Chloride when intended to be administered as an intravenous infusion. It has been reported that at a concentration of 1.0 - 2.0 g/L, Calcium Gluconate is compatible in all of the infusion fluids listed above for 24 hours.

To reduce microbiological contamination hazards, it is recommended that any further dilution

of the product should be effected immediately prior to use and infusion commenced as soon as practicable after preparation of the mixture. Infusion should be completed within 24 hours and any residue discarded. Any solutions which are discoloured, hazy or contain visible particulate matter should not be used.

Supersaturated solutions of calcium gluconate are prone to precipitation. Crystals may be redissolved by warming the ampoule to 80°C for 1 hour and shaking vigorously. Allow to cool to room temperature before dispensing. The solution should not be used if the precipitate remains after following the above procedures.

The phenomenon of compatibility/incompatibility of calcium salts with phosphates in solution is a very complex one and may be affected by solubility and concentration phenomena, pH, as well as temperature and time of storage of the admixture and the presence of other substances. Consequently, DBL™ Calcium Gluconate Injection BP should not be further diluted with phosphate-containing infusion fluids.

4.3 Contraindications

Aluminium 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), DBL™ Calcium Gluconate Injection BP is not intended for use in the preparation of Total Parenteral Nutrition (TPN).

This product should not be used for repeated or prolonged treatment, including as an intravenous infusion, in children (less than 18 years of age) and those with impaired renal function, due to the risk of exposure to aluminium (See section 4.4).

Calcium gluconate is contraindicated in patients with hypercalcaemia and hypercalciuria (eg hyperparathyroidism, vitamin D overdosage, decalcifying tumours such as plasmocytoma, bone metastases); severe renal disease; and calcium loss due to immobilisation.

The injection of calcium preparations is strictly contraindicated in the digitalised patients. Calcium enhances the effects of digitalis on the heart and may precipitate digitalis intoxication. Parenteral calcium therapy is therefore contraindicated in patients receiving cardiac glycosides.

Although no concrete evidence is available about the metabolic process leading from calcium glucono-galacto- gluconate to galactose, it is advisable not to administer calcium gluconate to galactosaemic patients.

Intravenous administration of calcium is contraindicated when serum calcium concentrations are above normal levels (ie 4.5 - 5.2 mEq/L).

Calcium gluconate should not be given by the intramuscular or subcutaneous route as necrosis or sloughing can occur.

4.4 Special warnings and precautions for use

Calcium Gluconate Injection contains aluminium (See section 2). This product should not be used for repeated or prolonged treatment in children younger than 18 years and in patients

with renal impairment due to potential increased risk of exposure to aluminium. Premature neonates requiring high doses of calcium gluconate are particularly at risk. Short term (acute) use of this product is not contraindicated in these patient populations.

Aluminium might reach toxic levels with prolonged or repeated administration if renal function is impaired. Premature neonates are particularly at risk because they require large amounts of calcium and their ability to eliminate aluminium from the body is reduced due to the immaturity of their kidneys. Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminium at greater than 4 to 5 mcg/kg/day accumulate aluminium at levels associated with central nervous system and bone toxicity.

Solutions of calcium salts, particularly calcium chloride, are irritant, and care should be taken to prevent extravasation during intravenous injection.

Calcium salts should be given cautiously to patients with impaired renal function, cardiac disease, or sarcoidosis. When used in large doses, serum calcium concentrations and kidney function should be determined weekly or at the first sign of hypercalcaemia, which is characterised by symptoms such as anorexia, lassitude, muscular and joint pains, nausea and vomiting, thirst and polyuria.

Frequent determinations of serum calcium concentrations should be performed. Hypercalcaemia is rarely produced by administrations of calcium alone, but may occur when large doses are given to patients with chronic renal failure. Since hypercalcaemia may be more dangerous than hypocalcaemia, overtreatment of hypocalcaemia should be avoided.

In mild hypercalciuria (exceeding 300 mg/ 24 hours) as well as in chronic renal failure, or when there is evidence of stone formation in the urinary tract, adequate checks must be kept on urinary calcium excretion. If necessary the dosage should be reduced or calcium therapy discontinued. In patients prone to formation of calculi in the urinary tract an increased fluid intake is recommended.

ECG monitoring is required when calcium is administered by intravenous injection for treatment severe hyperkalaemia.

Calcium gluconate is a supersaturated solution. Do not use if a precipitate is present.

4.5 Interaction with other medicines and other forms of interaction

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 should be avoided in patients receiving cardiac glycosides. If considered necessary, calcium should be given slowly in small amounts.

Tetracyclines: Calcium is known to complex with tetracycline antibiotics, thus rendering them inactive. The two drugs should therefore not be mixed prior to parenteral administration.

High vitamin D intake should be avoided during calcium therapy unless especially indicated.

Administration of calcium may reduce the response to verapamil and possibly other calcium channel blockers.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

There is no information available on the use of calcium gluconate during pregnancy. The decision to treat pregnant women with calcium gluconate should therefore consider the potential benefits to the mother against the potential harm to the foetus.

Lactation

Calcium crosses into the breast milk. Problems have not been documented with the administration of calcium to women who are breastfeeding. Nevertheless, the decision to treat breastfeeding mothers with calcium should weight the potential benefits to the mother against the potential harm to the infant.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

Calcium salts are irritating to tissue when administered by intramuscular or subcutaneous injection and cause mild to severe local reactions including burning, necrosis and sloughing of tissue, cellulitis, and soft tissue calcification; venous irritation may occur with intravenous administration. When injected intravenously, calcium salts should be administered slowly through a small needle into a large vein to avoid too rapid an increase in serum calcium and extravasation of calcium solution into the surrounding tissue with resultant necrosis. Patients may complain of tingling sensations, a sense of oppression or heat waves, and a calcium or chalky taste following intravenous administration of calcium salts.

Rapid intravenous injection of calcium salts may cause vasodilation, decreased blood pressure, bradycardia, cardiac arrhythmias, syncope, and cardiac arrest.

Hypercalcemia is rarely produced by administration of calcium alone, but may occur when large doses are given to patients with chronic renal failure. Since hypercalcemia may be more dangerous than hypocalcemia, overtreatment of hypocalcemia should be avoided.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Hypercalcaemia may occur when large doses of calcium gluconate are given, especially when such doses are given to patients with chronic renal failure. Symptoms of hypercalcaemia include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi, and in severe cases, cardiac arrhythmias, coma and cardiac arrest.

Treatment

A serum calcium concentration exceeding 10.5 mg per 100 mL (2.6 mmol/L) is considered a hypercalcaemic condition. Withholding additional administration of calcium and any other medications that may cause hypercalcaemia usually resolves mild hypercalcaemia in asymptomatic patients, when renal function is adequate.

When serum calcium concentrations are greater than 12 mg per 100 mL, immediate measures may be required with possible use of the following:

- Hydration with intravenous 0.9% Sodium Chloride Injection and forced diuresis with frusemide to rapidly increase calcium excretion.

- Monitoring of potassium and magnesium serum concentrations and early replacement to prevent complications of therapy.

- ECG monitoring and the possible use of beta-adrenergic blocking agents to protect the heart against serious arrhythmias.

- Possible treatment with calcitonin, diphosphonate dmp and other measures.

- Determining serum calcium concentrations at frequent intervals to guide therapy adjustments.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Calcium gluconate is a calcium salt used primarily for the prevention and treatment of calcium deficiency.

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

The calcium of bone is in a constant exchange with the calcium of plasma. Since the metabolic functions of calcium are essential for life, when there is a disturbance in the calcium balance because of dietary deficiency or other causes, the stores of calcium in bone may be depleted to fill the body's more acute needs. Therefore, on a chronic basis, normal mineralization of bone depends on adequate amounts of total body calcium.

5.2 Pharmacokinetic properties

Dietary calcium is absorbed from the small intestine. About one third of ingested calcium is absorbed although this can vary depending upon dietary factors and the state of the small intestine.

Following absorption, calcium first enters the extracellular fluid and is then rapidly incorporated into skeletal tissue. Bone formation, however is not stimulated by administration of calcium. Bone contains 99% of the body's calcium; the remaining 1% is distributed equally between the intracellular and extracellular fluids.

Normal total serum calcium concentration ranges from 9-10.4 mg/dL (4.5-5.2mEq/L), but only ionized calcium is physiologically active. Serum calcium concentrations are not necessarily accurate indications of total body calcium; total body calcium may be decreased in the presence of hypercalcemia, and hypocalcemia can occur even though total body calcium is increased. Of the total serum calcium concentration, 50% is in the ionic form and 5% is complexed by phosphates, citrates, and other anions. Approximately 45% of the serum calcium is bound to plasma proteins; for a change in serum albumin of 1 g/dL, the serum calcium concentration may change about 0.8 mg/dL (0.04 mEq/dL). Hyperproteinamia is associated with increased total serum calcium concentrations; in hypoproteinemia, total serum calcium concentrations decrease. Acidosis results in increased concentrations of ionic calcium, while alkalosis promotes a decrease in the ionic serum calcium concentration.

CSF concentrations of calcium are about 50% of serum calcium concentrations and tend to reflect ionized serum calcium concentrations. Calcium crosses the placenta and reaches higher concentrations in fetal blood than in maternal blood. Calcium is distributed into milk.

Calcium is excreted mainly in the faeces and consists of unabsorbed calcium and that secreted via bile and pancreatic juice into the lumen of the GI tract. Most of the calcium filtered by renal glomeruli is reabsorbed in the ascending limb of the loop of Henle and proximal and distal convoluted tubules. Only small amounts of the cation are excreted in urine. Parathyroid hormone, vitamin D, and thiazide diuretics decrease urinary excretion of calcium, whereas other diuretics, calcitonin, and growth hormone promote renal excretion of the cation. Urinary excretion of calcium decreases with reduction of ionic serum calcium concentrations but is proportionately increased as serum ionised calcium concentrations increase. In healthy adults on a regular diet, urinary excretion of calcium may be as high as 250-300 mg daily. With low calcium diets, urinary excretion usually does not exceed 150 mg daily. Urinary excretion of calcium decreases during pregnancy and in the early stages of renal failure. Calcium is also excreted by the sweat glands.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

Reproductive and developmental toxicity

No data available.

6. PHARMACEUTICAL PARTICUALRS

6.1 List of excipients

- Calcium Saccharate
- Water for Injections

6.2 Incompatibilities

No data available.

6.3 Shelf life

No data available.

6.4 Special precautions for storage

Store below 30°C. Do not refrigerate.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Strength	Pack
10%	10 x 10 mL Ampoules

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

General Sale Medicine.

8. SPONSOR

Pfizer New Zealand Limited

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Auckland, New Zealand

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

10 November 1983

10. DATE OF REVISION OF THE TEXT

15 January 2019

Summary table of changes

Section changed	Summary of new information
All	Reformatting according to Medsafe datasheet guidance