

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DBL™ Sodium Acetate Concentrated Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DBL™ Sodium Acetate Concentrated Injection contains 272.16 milligrams of sodium acetate (trihydrate) in each mL of water for injections. This is equivalent to 164 milligrams of sodium acetate (anhydrous) or 46 milligrams of sodium in each mL. DBL™ Sodium Acetate Concentrated Injection contains 2 mEq (2 mmol) of sodium ions, and 2 mEq (2 mmol) of acetate ions in each 1 mL.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

DBL™ Sodium Acetate Concentrated Injection is a clear, colourless solution.

Sodium acetate trihydrate is a white granular crystalline powder, or white flakes or colourless transparent crystals. It is odourless, or has a slight odour of acetic acid.

The pH of the solution ranges between 8.2 and 9.2.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DBL™ Sodium Acetate Concentrated Injection is indicated for inclusion in total parenteral nutrition (TPN) solutions as an electrolyte source. Sodium acetate may also be added to parenteral solutions to increase pH.

DBL™ Sodium Acetate Concentrated Injection may also be used for the treatment of hyponatraemia (sodium depletion) states, in cases where oral sodium therapy is contraindicated or not tolerated.

4.2 Dose and method of administration

Dose

DBL™ SODIUM ACETATE CONCENTRATED INJECTION MUST BE DILUTED WITH A SUITABLE INFUSION SOLUTION PRIOR TO ADMINISTRATION.

Each mL of DBL™ Sodium Acetate Concentrated Injection contains 2 mEq (2 mmol) of sodium ions and 2 mEq (2 mmol) of acetate ions.

1. Use in total parenteral nutrition (TPN) solutions or other parenteral solutions

The desired quantity of DBL™ Sodium Acetate Concentrated Injection should be added to the TPN or other solution. Serum sodium levels should be monitored as a guide to dosage.

2. Treatment of hyponatraemia (sodium depletion)

The concentration and dosage of sodium solutions for intravenous use is determined by several factors including the age, weight and clinical condition of the patient and in particular the patient's hydration state. Serum electrolyte concentrations and total body water should be carefully monitored throughout. Hypernatraemia should not be allowed to develop.

Therapy should be guided by the rate and degree of development of hyponatraemia. Volume depletion should also be corrected where necessary.

4.3 Contraindications

Sodium Acetate Concentrated Injection is contraindicated in patients who are hypersensitive to sodium or acetate. It should not be administered to patients with hypernatraemia, fluid retention or severe renal impairment.

Sodium Acetate Concentrated Injection should not be administered to patients suffering from conditions which are likely to lead to dehydration (e.g. severe burns, severe or prolonged diarrhoea or vomiting, or uncontrolled diabetes mellitus).

Sodium acetate forms the bicarbonate after metabolism; therefore, sodium acetate should not be administered to patients with metabolic or respiratory alkalosis, hypocalcaemia, chloride depletion or hypokalaemia.

4.4 Special warnings and precautions for use

SODIUM ACETATE CONCENTRATED INJECTION MUST BE DILUTED WITH A COMPATIBLE INFUSION FLUID PRIOR TO ADMINISTRATION.

Diluted solutions of sodium acetate must be administered slowly, as rapid intravenous injection of sodium may lead to hypernatraemia and fluid overload. Hypernatraemia is more likely to occur if sodium acetate is administered intravenously to patients with impaired mechanisms for excreting sodium (e.g. chronic renal disease). Potentially fatal hypernatraemia can develop rapidly and asymptotically. Therefore, careful monitoring of serum sodium concentration and appropriate dosage adjustment is recommended.

Elevated plasma sodium concentration may cause dehydration of the brain, which can result in somnolence and confusion, progressing to convulsions, coma, respiratory failure and death.

Sodium acetate should be used with extreme caution in patients with congestive heart failure, other oedematous states, renal function impairment, cirrhosis, eclampsia, hypertension or aldosteronism. It should also be used with caution in patients with oliguria or anuria.

Solutions containing sodium ions should be administered cautiously to patients receiving corticosteroids or corticotropin.

Acetate should be administered with caution in those conditions where there is an increased level or impaired utilisation of the acetate ion, such as severe hepatic impairment.

4.5 Interaction with other medicines and other forms of interaction

Alkalinisation of the urine by sodium acetate may increase the renal clearance of acidic drugs such as salicylates, barbiturates and tetracyclines, especially doxycycline.

Urinary alkalinisation may decrease the renal clearance of basic drugs, such as quinidine, amphetamines, ephedrine, pseudoephedrine and lithium, and may result in toxicity.

Hypochloreaemic alkalosis may occur if sodium acetate is used in conjunction with potassium depleting diuretics such as bumetanide, ethacrynic acid, frusemide and thiazides. Concurrent use in patients taking potassium supplements may reduce serum potassium levels by promoting an intracellular ion shift.

Solutions containing sodium ions should be administered with caution to patients receiving corticosteroids or corticotropin.

Effect on laboratory tests

Alkalinisation of the urine by sodium acetate may cause a false positive Labstix test for urinary protein.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

Sodium is a natural constituent of human tissues and fluids. Since high levels of sodium may lead to dehydration, serum levels should be closely monitored in pregnant women being treated with sodium salts. Serum potassium levels and pH should also be closely monitored, as the acetate ion may cause hypokalaemia or metabolic alkalosis.

Sodium Acetate Concentrated Injection should only be used in pregnant women if the expected benefits outweigh the possible risks to the mother or foetus.

Lactation

Sodium is likely to be excreted into breast milk. Sodium Acetate Concentrated Injection should only be used in women who are breast feeding if the expected benefits to the mother outweigh the possible risks to the infant.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

Excessive doses of sodium salts may lead to hypernatraemia. The most serious effect of hypernatraemia is dehydration of the brain, which causes somnolence and confusion, progressing to convulsions, coma, respiratory failure and death. Other symptoms include thirst, reduced salivation and lachrymation, fever, tachycardia, hypertension, headache, dizziness, restlessness, irritability and weakness.

Excessive administration of compounds which are metabolised to form the bicarbonate anion (such as acetate) may lead to hypokalaemia and metabolic alkalosis, especially in patients with impaired renal function. Symptoms may include mood changes, tiredness, shortness of breath, muscle weakness and irregular heartbeat. Hyperirritability, muscle hypertonicity, twitching and tetany may develop, especially in hypocalcaemic patients. These may occur as a result of rapid shifts of free ionised calcium, or serum protein alterations arising from the pH changes.

Extravasation of hypertonic solutions containing sodium acetate may result in chemical cellulitis and ulceration.

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

Symptoms

Excessive administration or impaired excretion of sodium leads to the development of potentially fatal hypernatraemia, while excessive administration of the acetate may lead to hypokalaemia and metabolic alkalosis (see section 4.8).

Treatment

Serum sodium concentrations should be measured, and if severe hypernatraemia is present, this should be treated. Treatment of hypernatraemia usually requires water replacement. In some cases, oral administration of water and restriction of sodium intake may be sufficient. In more severe cases, glucose 5% may be administered by slow intravenous infusion.

If the total body sodium content is too high, loop diuretics may be used to increase sodium excretion, with fluid losses being replaced by an infusion of glucose 5% and potassium chloride. Dialysis may be necessary if there is significant renal impairment, if the patient is moribund, or if the serum sodium concentration is greater than 200 mmol/L.

If alkalosis occurs, administration of the acetate should be stopped, and the patient managed according to the degree of alkalosis present. Rebreathing expired air may help control the symptoms of alkalosis. Sodium chloride 0.9% may be administered intravenously. Calcium gluconate may be necessary to control the hyperirritability and tetany which may occur with more severe alkalosis. Ammonium chloride could be administered intravenously in cases of severe alkalosis, except in patients with pre-existing hepatic disease. Potassium chloride should be administered if hypokalaemia is present.

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

Sodium is the principal cation in the extracellular fluid, comprising more than 90% of total cations at its normal plasma concentration (between 135 to 145 millimol/L). Potassium ions predominate in the intracellular fluid. A membrane bound enzyme, sodium-potassium-activated adenosine triphosphatase ($\text{Na}^+\text{-K}^+\text{-ATPase}$), actively transports or pumps sodium out of, and potassium into, cells to maintain this concentration gradient.

Sodium has a primary role in regulating extracellular fluid volume. It controls water distribution, fluid and electrolyte balance and the osmotic pressure of body fluids. Sodium is also involved in nerve conduction, muscle contraction, acid-base balance and cell nutrient uptake.

Sodium homeostasis is complex, and is closely associated with fluid balance. Small changes in plasma sodium concentrations are corrected by alterations to the extracellular fluid volume. The secretion or suppression of anti-diuretic hormone (ADH) primarily controls water excretion by the kidney. Higher plasma sodium levels suppress ADH secretion and promote renal water loss, while an increase in ADH secretion increases water reabsorption by the renal distal tubules. Changes in extracellular volume will also affect ADH release, independently of osmolality. In addition, changes in extracellular volume modulate renal sodium excretion.

Total body sodium content is regulated by renal sodium excretion. Mechanisms involved include the renin-angiotensin system, glomerular filtration rate and natriuretic factors. A reduction in extracellular fluid volume leads to the production of angiotensin II, which stimulates aldosterone secretion. Aldosterone promotes sodium ion reabsorption by the distal tubules. Adrenal insufficiency or mineralocorticoid excess may disturb this mechanism.

Sodium acetate is metabolised in the liver to the bicarbonate. This has been shown to proceed readily, even in the presence of severe liver disease. Sodium acetate and other bicarbonate precursors are alkalinising agents, and can be used to correct metabolic acidosis, or for alkalinisation of the urine. Sodium acetate can be used to increase plasma bicarbonate concentration, help restore the plasma pH to within the normal range (7.37-7.42) and correct potassium imbalances in cases of acidosis. It can also be used to increase urinary pH in subjects with normal renal function. This can increase the solubility of certain weak acids, and can increase the ionisation and excretion of lipid soluble organic acids, such as phenobarbitone and salicylates.

In the absence of a plasma bicarbonate deficit, bicarbonate ions are excreted in the urine, making the urine alkaline. This is accompanied by diuresis.

5.2 Pharmacokinetic properties

Following administration, the acetate ion is metabolised in the liver to bicarbonate. Both the sodium and bicarbonate ions are excreted mainly in the urine. Some sodium is excreted in the faeces, and small amounts may also be excreted in saliva, sweat, bile and pancreatic secretions.

5.3 Preclinical safety data

Genotoxicity/Carcinogenicity

No information is available on the carcinogenicity or mutagenicity of sodium acetate.

Reproductive and developmental toxicity

There is also no information available on whether administration of sodium acetate would affect fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Water for injection

6.2 Incompatibilities

No data available.

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

DBL™ Sodium Acetate Concentrated Injection is available as follows:

Strength 1.64 grams/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

P O Box 3998

Auckland, New Zealand, 1140

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

09 Mar 1989

10. DATE OF REVISION OF THE TEXT

29 January 2019

Summary table of changes

Section changed	Summary of new information
All	Reformat to MedSafe Data Sheet guidance