AUSTRALIAN PRODUCT INFORMATION – DBL™ SODIUM ACETATE CONCENTRATED INJECTION (SODIUM ACETATE)

1. NAME OF THE MEDICINE

Sodium acetate

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. The strength supplied is 1.64 grams/10 mL in a glass ampoule.

For the full list of excipients, see **Section 6.1 List of excipients**.

3. PHARMACEUTICAL FORM

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.

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

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 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.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration

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 asymptomatically. 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, cardiac failure, eclampsia, hypertension or aldosteronismIt 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.

Solutions containing acetate ions should be used with great care in patients with metabolic or respiratory alkalosis. 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.Solutions containing acetate ions should be used with caution as excess administration may result in metabolic alkalosis

The intravenous administration of this solution (after appropriate dilution) can cause fluid and/or solute overloading resulting in dilution of other serum electrolyte concentrations, overhydration, congested states or pulmonary edema. Excessive administration of potassium free solutions may result in significant hypokalemia.

Use in renal impairment

Sodium acetate should be used with extreme caution in patients with renal function impairment. In patients with diminished renal function, administration of solutions containing sodium ions may result in sodium retention.

Use in the elderly

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.

Sodium ions are known to be substantially excreted by the kidney, and the risk of toxic reactions may be greater in patients with impaired renal function. Elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Paediatric use

Safety and effectiveness have been established in the age groups infant to adolescent.

Effects on laboratory tests

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

4.5 Interactions with Other Medicines and Other Forms of Interactions

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

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

Hypochloraemic 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.

4.6 Fertility, Pregnancy and Lactation

Effects on fertility

No data available.

Use in 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.

Use in 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 Machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse Effects (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 suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

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 Adverse effects**).

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 information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia). In New Zealand call 0800 764 766.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

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 (Na^+-K^+-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.

Clinical trials

No data available.

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

No data available.

Carcinogenicity

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Water for injections

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Store below 30°C

6.5 Nature and Contents of Container

DBL™ Sodium Acetate Concentrated Injection is supplied in glass ampoules as follows:

Strength: 1.64 grams/10 mL (cartons contain 10 and 50 ampoules)

Not all pack sizes may be marketed.

6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical Properties

The chemical formula of sodium acetate trihydrate is $CH_3COONa.3H_2O$. Its molecular weight is 136.1

Chemical structure

No data available.

CAS number

The CAS Registry number is 6131-90-4.

7. MEDICINE SCHEDULE (POISONS STANDARD)

Not scheduled.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

11 May 2007

10. DATE OF REVISION

17 June 2021

Summary Table of Changes

Section changed	Summary of new information
4.2	Addition of precaution relating to visual inspection for particulate matter and discolouration for parenteral drug products.
4.4	• Addition of extreme caution needed in patients with cardiac function and other sodium retaining states. • Addition precaution relating to solute overloading • Addition of precaution when used in the elderly • Addition of precaution when used in paedriatic population • Addition of precaution when used in patients with diminished renal function.