

AUSTRALIAN PRODUCT INFORMATION – SODIUM BICARBONATE 8.4% (SODIUM BICARBONATE) Injection BP

1. NAME OF THE MEDICINE

Sodium bicarbonate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

A sterile, hypertonic, preservative-free solution containing sodium bicarbonate 8.4 g/100 mL.

Each mL of solution contains 1 mmol each of sodium and bicarbonate ions.

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

3. PHARMACEUTICAL FORM

Injection for intravenous infusion.

A clear, colourless solution, free from visible impurities.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Metabolic acidosis in severe renal disease, uncontrolled diabetes, circulatory insufficiency due to shock or severe dehydration, extracorporeal circulation of blood, cardiac arrest and severe primary lactic acidosis where a rapid increase in plasma total CO₂ content is crucial. Treatment of metabolic acidosis should be concurrent with measures designed to control the cause of the acidosis.

Urinary alkalinisation in the treatment of certain drug intoxications (i.e. barbiturates, salicylates, lithium, methyl alcohol) and in the haemolytic reactions requiring alkalinisation of the urine to diminish nephrotoxicity of blood pigments.

Urinary alkalinisation is also used in methotrexate therapy to prevent nephrotoxicity.

Severe diarrhoea which is often accompanied by a significant loss of bicarbonate.

4.2 Dose and Method of Administration

Dosage

In cardiac arrest

Administration is determined based on the results of arterial blood pH, PaCO₂ and calculation of base deficit. For adults, an initial dose of 1 mmol/kg followed by 0.5 mmol/kg every 10 minutes of arrest, depending on arterial blood gases. In cardiac arrest, the risks from acidosis exceed those of hypernatraemia.

In mild conditions of metabolic acidosis

Sodium Bicarbonate Intravenous Infusion may be admixed with other intravenous fluids if compatibility is proven.

The amount of bicarbonate to be given to older children and adults over a 4 to 8 hour period is approximately 2 to 5 mmol/kg, depending upon the severity of the acidosis as judged by the lowering of total CO₂ content, blood pH and clinical condition of the patient. Initially, an infusion of 2 to 5 mmol/kg over 4 to 8 hours will produce improvement in the acid-base status of the blood.

Therapy should be planned in a step by step method as the degree of response from a given dose is not precisely predictable.

In general it is unwise to try and fully correct a low total CO₂ content during the first 24 hours of therapy. This may be accompanied by unrecognised alkalosis due to a delay in the readjustment of normal ventilation.

Children and adolescents

Children: The usual dose is 1 mmol/kg (1 mL/kg) given by slow intravenous injection.

For infants up to 2 years of age: A 4.2% solution is recommended at a rate not exceeding 8 mmol/kg/day. This will minimise the risk of the possibility of hypernatraemia, decreasing cerebrospinal fluid pressure and intracranial haemorrhage. Diluents may be sterile, physiological solution, glucose 5%, or other standard electrolyte solutions but each should be tested for compatibility.

Method of Administration

Sodium Bicarbonate Intravenous Infusion is administered intravenously preferably into a large vein.

4.3 Contraindications

- renal failure
- metabolic alkalosis
- respiratory alkalosis
- hypertension
- oedema
- congestive heart failure
- a history of urinary calculi and coexistent potassium depletion or hypocalcaemia
- hypernatraemia, hypoventilation or chloride depletion
- in patients at risk of developing diuretic induced hypochloraemic alkalosis
- eclampsia, aldosteronism.

It is also generally contraindicated in patients with excessive chloride loss from vomiting or continuous gastrointestinal suctioning and in patients at risk of developing diuretic induced hypochloraemic alkalosis.

4.4 Special Warnings and Precautions for Use

- Whenever respiratory acidosis is concomitant with metabolic acidosis, both pulmonary ventilation and perfusion must be adequately supported to get rid of excess carbon dioxide.
- To minimise the risks of pre-existing hypokalaemia and/or hypocalcaemia, these electrolyte disturbances should be corrected prior to initiation of, or concomitantly with, sodium bicarbonate therapy.
- Arterial blood gas analysis, in particular, arterial/venous blood pH and carbon dioxide levels should be performed during the course of sodium bicarbonate treatment to minimise the possibility of overdosage and resultant alkalosis.
- Accidental extravasation of hypertonic solutions may cause cellulitis, tissue necrosis, ulceration, vascular irritation and sloughing. The use of scalp veins should be avoided. Prompt elevation of the affected area, warmth and local injection of lignocaine or hyaluronidase are recommended to prevent sloughing.
- Whenever respiratory acidosis is present with metabolic acidosis both pulmonary ventilation and perfusion must be adequately supported in order to eliminate excess CO₂.
- Solutions containing sodium may cause fluid and/or solute overload, resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary oedema. Extravascular infiltration should be avoided (see Section 4.8 Adverse Effects (Undesirable Effects)).
- Sodium bicarbonate should be used with caution in patients with cirrhosis.
- Excessively elevated plasma sodium concentrations may cause dehydration of the brain, resulting in somnolence and confusion, which may progress to convulsions, coma, respiratory failure and ultimately death.
- Bicarbonate should be given with caution to patients with type A lactic acidosis (tissue hypoxia). Administration of bicarbonate may limit the available oxygen, increase lactate production, thus, worsen the acidosis.
- Sodium bicarbonate should not be used in the treatment of diabetic ketoacidosis with pH between 6.90 and 7.10.
- Do not use the injection if it contains precipitate. Do not use unless the solution is clear and the container and seal are intact. Discard any unused portion.
- The aim of all bicarbonate therapy is to produce a substantial correction of the low total CO₂ content and blood pH, but the risks of overdosage and alkalosis should be avoided. Hence, repeated fractional doses and periodic monitoring by appropriate laboratory tests are recommended to minimise the possibility of overdosage.

Use in Renal Impairment

Sodium retention and oedema may occur during sodium bicarbonate therapy, especially when the drug is given in large doses or to patients with renal insufficiency, congestive heart failure or those predisposed to sodium retention and oedema. Sodium and water overload may result in hypernatraemia and hyperosmolality. Severe hyperosmolal states may develop during cardiopulmonary resuscitation when excessive doses of sodium bicarbonate are administered. Serum potassium may decrease during sodium bicarbonate therapy leading to hypokalaemia.

Sodium bicarbonate should be used with extreme caution in patients with in patients with renal insufficiency or other oedematous or sodium retaining conditions; especially those with severe insufficiency such as oliguria or anuria; and in patients receiving corticosteroids or corticotropin, since each gram of sodium bicarbonate contains 12 mEq of sodium.

Use in the Elderly

Clinical studies of sodium bicarbonate injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the 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.

Paediatric use

Rapid injections (10 mL/min) of hypertonic sodium bicarbonate solutions to neonates and children under 2 years of age may produce hypernatraemia, a decrease in cerebrospinal fluid pressure and possible intracranial haemorrhage. Do not administer more than 8 mmol/kg/day.

In emergency situations, such as cardiac arrest, the risk of rapid infusion of the drug must be weighed against the potential for death from acidosis. Also, administration of this drug to children undergoing cardiopulmonary resuscitation may worsen respiratory acidosis.

Effects on Laboratory Tests

The high urinary alkalinity sometimes produced by sodium bicarbonate may cause a false positive Labistix test for urinary protein.

4.5 Interactions with Other Medicines and Other Forms of Interactions

- Urinary alkalinisation will increase the renal clearance of tetracyclines, especially doxycycline, but it will increase the half life and duration of action of basic drugs such as quinidine, amphetamines, ephedrine and pseudoephedrine.
- The addition of sodium bicarbonate to solutions containing calcium should be avoided except where compatibility has been shown. Solutions turning hazy as a result of sodium bicarbonate-calcium admixtures should be discarded.
- Use caution when giving parenteral fluids, especially those containing sodium ions, to patients receiving corticosteroids or corticotrophin.
- Hypochloraemic alkalosis may occur if sodium bicarbonate 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 concentration by promoting an intracellular ion shift. Potassium depletion may predispose to metabolic alkalosis and coexistent hypocalcaemia may be associated with carpopedal spasm as the plasma pH rises. These dangers can be minimised if such electrolyte imbalances are appropriately treated prior to or concomitantly with bicarbonate infusion.

- Alkalinisation of the urine leads to increased renal clearance of acidic drugs such as salicylates, tetracyclines, (especially doxycycline), barbiturates and tricyclic antidepressants. Conversely, it prolongs the half-life and duration of basic drugs such as quinidine, amphetamines, ephedrine and pseudoephedrine and may result in toxicity.
- Sodium bicarbonate enhances lithium excretion.
- Solutions containing sodium ions should be used with great care, if at all, in patients receiving corticosteroids or corticotropin.
- The following drug may have enhanced or prolonged effects due to concomitant administration with sodium bicarbonate: flecainide.
- The following drugs may have decreased effectiveness due to concomitant administration with sodium bicarbonate: aspirin and other salicylates, barbiturates and lithium.
- The following drugs have been reported to be susceptible to inactivation on mixing with sodium bicarbonate solution: adrenaline HCl, benzylpenicillin potassium, carmustine, glycopyrrolate, isoprenaline HCl and suxamethonium chloride.
- Additives may be incompatible with the product; noradrenaline (norepinephrine) and dobutamine are incompatible with sodium bicarbonate solution. When introducing additives, use aseptic technique, mix thoroughly and do not store the resultant solution.

4.6 Fertility, Pregnancy and Lactation

Effects on Fertility

No data available

Use in Pregnancy

Animal reproduction studies have not been performed with sodium bicarbonate. It is also not known whether sodium bicarbonate can cause foetal harm when administered to pregnant women. Sodium bicarbonate should be used during pregnancy only when clearly needed and the benefits of therapy outweigh the potential risks.

Use in Lactation

It is not known whether sodium bicarbonate is excreted in breast milk. However, problems in humans have not been reported.

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)

- Alkalosis and/or hypokalaemia may result from prolonged use or overcorrection of the bicarbonate deficit, especially in patients with impaired renal function (see Section 4.9 Overdose).
- Hyperirritability or tetany may occur caused by rapid shifts of free ionised calcium or due to serum protein alterations arising from the pH changes. Metabolic alkalosis may be accompanied by compensatory hyperventilation, paradoxical acidosis of the cerebrospinal fluid, severe hypokalaemia, hyperirritability or tetany.
- Hypernatraemia has been reported with sodium bicarbonate use, especially in patients with renal disease.
- Hyperosmolality has also been associated with sodium bicarbonate use.
- Accidental extravasation of intravenous hypertonic solutions of sodium bicarbonate has been reported to cause chemical cellulitis, with tissue necrosis, tissue calcification, ulceration or sloughing at the site of infiltration. Hyperirritability or tetany may occur, caused by rapid shifts of free ionised calcium or due to serum protein alterations arising from the pH changes.
- Cerebral oedema has occurred with sodium bicarbonate use and a possibility of intracranial haemorrhage exists.
- Hypercapnia has occurred in patients receiving sodium bicarbonate and with fixed ventilation.

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

Alkalosis is a direct result of overdosage. Excessive administration of bicarbonate may lead to hypokalaemia and metabolic alkalosis, especially in patients with impaired renal function. Symptoms include mood changes (hyperirritability), tiredness, shortness of breath, muscle weakness and irregular heartbeat. Muscle hypertonicity, twitching and tetany may develop, especially in hypocalcaemic patients.

Treatment

Administration of sodium bicarbonate should be immediately discontinued. In order to control the symptoms of alkalosis, the patient should rebreath expired air, and the patient treated with intravenous sodium chloride 0.9% and potassium chloride if hypokalaemia is present.

Any accompanying hyperirritability or tetany can be controlled with calcium gluconate. Ammonium chloride may be indicated in severe cases (except in patients with pre-existing hepatic disease).

Treatment of hypernatraemia usually requires water replacement. In some cases, restricted sodium intake and oral water may be sufficient. If more severe, glucose 5% may be administered by slow intravenous infusion. If total body sodium is too high, loop diuretics combined with an infusion of 5% glucose and potassium supplementation may be necessary.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Mechanism of Action

Sodium bicarbonate is a systemic alkalinising agent which, when given intravenously will increase plasma bicarbonate, buffers excess hydrogen ion concentration, raises blood pH and reverses the clinical manifestations of acidosis.

Clinical Trials

No data available

5.2 Pharmacokinetic Properties

Sodium bicarbonate dissociates in water to provide sodium (Na^+) and bicarbonate (HCO_3^-) ions. Sodium is the principal cation of the extracellular fluid. Bicarbonate is a normal constituent of body fluids and the normal plasma level ranges from 24 to 31 mmol/L. Plasma concentration is regulated by the kidney. The bicarbonate anion, at the correct concentration of hydrogen ion (H^+) may be converted to carbonic acid (H_2CO_3), then to its volatile form, carbon dioxide (CO_2) which is excreted by the lung. Normally, a ratio of 1:20 (carbonic acid: bicarbonate) is present in the extracellular fluid.

Excretion

In a healthy adult with normal kidney function, practically all the glomerular filtered bicarbonate ion is reabsorbed and less than 1% is excreted in the urine.

5.3 Preclinical Safety Data

Genotoxicity

No data available

Carcinogenicity

No data available

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Disodium Edetate

Water for Injections

6.2 Incompatibilities

See Section 4.5 Interactions with Other Medicines and Other Forms of Interactions.

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. Single use only. Discard any unused portion.

6.5 Nature and Contents of Container

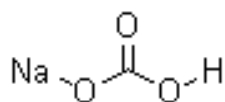
A 100 mL glass vial with a grey halobutyl siliconised rubber stopper. Each carton contains 10 vials.

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

Chemical structure



Molecular Formula: NaHCO_3

CAS Number

144-55-8

7. MEDICINE SCHEDULE (POISONS STANDARD)

Australia - Unscheduled.

8. SPONSOR

Manufacturer

Pfizer (Perth) Pty Limited
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15 Brodie Hall Drive,
Bentley WA 6102 Australia

Sponsor

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9. DATE OF FIRST APPROVAL

09 July 1991

10. DATE OF REVISION

09 February 2021

Summary Table of Changes

Section changed	Summary of new information
2	Minor edits.
3	Minor edits.
4.2	Correction of spelling.
4.4	Further information on fluid overload. Addition of information to prevent overdosage. Addition of information on the use in the elderly.
4.5	Addition of information on potassium deletion. Deletion of duplicate text. Addition of information on additives.
4.8	Deletion of duplicate text.
4.9	Correction of spelling.
6.5	Minor edit.