APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

SODIUM BICARBONATE 4 % INJECTION FRESENIUS

SODIUM BICARBONATE 8,5 % INJECTION FRESENIUS

Solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 50 ml contains:

	4 % *m/v*	8,5 % *m/v*
Sodium bicarbonate	2 g	4,25 g

Sugar free.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the correction of metabolic acidosis.

4.2 Posology and method of administration

Posology

Dilute before use: The dose must be found in an empirical fashion. If possible, small doses should be used initially so as not to overtreat. SODIUM BICARBONATE INJECTION FRESENIUS is incompatible with acids, acidic salts, many alkaloidal salts, aspirin and with bismuth salicylate.

Solutions up to 4,2 % (0,5 mmol per ml) of SODIUM BICARBONATE INJECTION FRESENIUS are administered intravenously for the rapid correction of acidosis. Solutions containing up to 8,4 % (1 mmol per ml) are used for the initial treatment of metabolic acidosis caused by cardiac arrest.

When used in the treatment of persistent metabolic acidosis in neonates the SODIUM BICARBONATE INJECTION FRESENIUS should be given slowly as a dilute (M/4) solution to prevent intraventricular haemorrhage.

Method of administration

For intravenous administration only.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Conditions where sodium intake is restricted (e.g., renal failure, hypertension, oedema, congestive heart failure).
- Patients with hypoventilation (risk of worsening of acidosis).
- Metabolic or respiratory alkalosis.
- Patients with a history of urinary calculi.
- Patients with coexistent potassium depletion or chloride depletion, hypocalcaemia and hypernatraemia.
- Patients who are losing chloride by vomiting or from continuous gastrointestinal suction.

- Hypochlorhydria.
- Patients receiving diuretics known to produce hypochloraemic alkalosis.

4.4 Special warnings and precautions for use

SODIUM BICARBONATE INJECTION FRESENIUS should be used extremely cautiously in patients with impaired renal function, in toxaemia of pregnancy, aldosteronism and oliguria or anuria.

In patients with diminished renal function, administration of SODIUM BICARBONATE INJECTION FRESENIUS may result in sodium retention.

The intravenous administration of SODIUM BICARBONATE INJECTION FRESENIUS can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary oedema (see section 4.8).

The risk of dilutional states is inversely proportional to the electrolyte concentrations of administered parenteral solutions. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of such solutions.

Whenever SODIUM BICARBONATE INJECTION FRESENIUS is used intravenously, arterial blood gas analyses, in particular arterial/venous blood pH and carbon dioxide levels, should be performed before and during the course of treatment to minimise the possibility of overdosage and resultant alkalosis.

Inadvertent extravasation of intravenously administered hypertonic solutions of SODIUM BICARBONATE INJECTION FRESENIUS have been reported to cause chemical cellulitis because of their alkalinity, with tissue necrosis, ulceration or sloughing at the site of infiltration (see section 4.4). Prompt elevation of the part, warmth and local injection of lidocaine or

hyaluronidase are recommended to prevent sloughing of extravasated intravenous infusions. The use of scalp veins should be avoided.

Whenever respiratory acidosis is concomitant with metabolic acidosis, both pulmonary ventilation and perfusion must be adequately supported to get rid of excess CO_2.

Administration of sodium bicarbonate to a patient with inadequate minute ventilation can cause worsening of the acidosis.

The treatment of metabolic acidosis must, if possible, be combined with concurrent treatment to combat the primary cause of the acidosis, for example the administration of insulin in uncomplicated diabetes, or blood volume restoration in shock.
During treatment of acidosis, frequent monitoring of serum-electrolyte concentrations and acid-base status is essential. Alkalinisation of the urine by bicarbonates or bicarbonate precursors leads to increased renal clearance of acidic medicines. If this feature is being used to eliminate medicines such as salicylates or barbiturates, then it is essential to maintain a high urine output. Conversely, urinary alkalinisation prolongs the half-life of basic medicines and may result in toxicity.

In long-term therapy, care is essential to prevent the risk of overdose and alkalosis (see section 4.9). Therefore, repeat administrations of fractional doses, or an infusion, should be given while regularly monitoring the acid-base balance and electrolytes. As soon as the most severe symptoms are under control, the dose and frequency of administration must be reduced until normal values have been restored.

There is no evidence to support the use of bicarbonate therapy in the treatment of hypoperfusion-induced lactic acidaemia associated with sepsis.

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 administration of SODIUM BICARBONATE INJECTION FRESENIUS.

SODIUM BICARBONATE INJECTION FRESENIUS contains sodium:

SODIUM BICARBONATE 4 % INJECTION FRESENIUS contains 10,95 mg sodium per ml, equivalent to 0,55 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

SODIUM BICARBONATE 8,5 % INJECTION FRESENIUS contains 23,27 mg sodium per ml, equivalent to 1,16 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Paediatric population

Rapid injection (10 ml/min) of hypertonic SODIUM BICARBONATE INJECTION FRESENIUS into neonates and children under two years of age may produce hypernatraemia, a decrease in cerebrospinal fluid pressure and possible intracranial haemorrhage. The rate of administration in such patients should therefore be limited to no more than 8 mmol (mEq)/kg/day. A 4,2 % solution may be preferred for such slow administration. In emergencies such as cardiac arrest, the risk of rapid infusion must be weighed against the potential for fatality due to acidosis (see section 4.8).

4.5 Interaction with other medicines and other forms of interaction

Caution should be used when administering SODIUM BICARBONATE INJECTION FRESENIUS to patients receiving corticosteroids or corticotrophin.

Urinary alkalisation will increase the renal clearance of medicines which are acid in nature e.g., tetracyclines, especially doxycycline, acetylsalicylic acid, chlorpropamide, lithium, methenamine. It increases the half-life and duration of action of basic medicines such as quinidine, amphetamines, ephedrine, pseudoephedrine, memantine and flecainide. SODIUM BICARBONATE INJECTION FRESENIUS increases renal tubular reabsorption of mecamylamine causing hypotension.

Hypochloraemic alkalosis may occur if SODIUM BICARBONATE INJECTION FRESENIUS is used in conjunction with potassium depleting diuretics such as bumetamide, ethacrynic acid, furosemide, and thiazides.

Concurrent use in patients taking potassium supplements may reduce serum potassium concentration by promoting an intracellular ion shift.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established (see section 4.4).

4.7 Effects on ability to drive and use machines

Not applicable. SODIUM BICARBONATE INJECTION FRESENIUS is intended for use only in emergencies.

4.8 Undesirable effects

a. Summary of the safety profile

Excessive administration of bicarbonate may lead to metabolic alkalosis, especially in patients with impaired renal function. Symptoms may include shortness of breath and muscle weakness (associated with potassium depletion). Muscle hypertonicity, twitching, and tetany may develop, especially in hypocalcaemic patients.

Seizures may be exacerbated or precipitated in epileptic patients.

Excessive doses of sodium salts may also lead to sodium overloading and hyperosmolality.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Metabolism and nutrition disorders	Frequency unknown	Metabolic alkalosis, hypokalaemia, sodium overloading/hypernatraemia, hyperosmolality, hypocalcaemia, hypoglycaemia, paradoxical intracellular acidosis
Nervous system disorders	Frequency unknown	Intracranial haemorrhage (in neonates), hyperirritability, tetany, seizures
Cardiac disorders	Frequency unknown	Deterioration of hemodynamic status associated with volume overload
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Shortness of breath
Musculoskeletal and connective tissue disorders	Frequency unknown	Muscle weakness, muscle hypertonicity, twitching
General disorders and administration site conditions	Frequency unknown	Extravasation, tissue necrosis from incorrect administration (intra-arterial, paravenous), chemical cellulitis, ulceration, sloughing

c. Description of selected adverse reactions

Inadvertent extravasation of intravenously administered hypertonic solutions of SODIUM BICARBONATE INJECTION FRESENIUS have been reported to cause chemical cellulitis

because of their alkalinity, with tissue necrosis, ulceration or sloughing at the site of infiltration (see section 4.4).

d. Paediatric population

Rapid injection (10 ml/min) of hypertonic SODIUM BICARBONATE INJECTION FRESENIUS into neonates and children under two years of age may produce hypernatraemia, a decrease in cerebrospinal fluid pressure and possible intracranial haemorrhage (see section 4.4).

Reporting of suspected adverse reactions

Health care providers are asked to report any suspected adverse drug reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

Reporting suspected adverse reactions after authorisation of SODIUM BICARBONATE INJECTION FRESENIUS is important. It allows continued monitoring of the benefit/risk balance of SODIUM BICARBONATE INJECTION FRESENIUS. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms of hypernatraemia may include hypotension, oliguria, restlessness, weakness, thirst, reduced salivation and lacrimation, swollen tongue, tachycardia, flushing of the skin, pyrexia, dizziness, headache, delirium, hyperpnoea and respiratory arrest. Retention of sodium leads to the accumulation of fluid with cerebral oedema and peripheral and pulmonary oedema.

Treatment is symptomatic and supportive.

Symptoms of metabolic alkalosis may include compensatory hyperventilation, paradoxical acidosis of the cerebrospinal fluid, severe hypokalaemia, hyperirritability and tetany (see section 4.8).

Treatment of metabolic alkalosis associated with bicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance as does the treatment of any hypernatraemia associated with excessive intake of sodium salts. Replacement of calcium, chloride, and potassium ions may be of particular importance.

Discontinue the administration of SODIUM BICARBONATE INJECTION FRESENIUS, rebreathe expired air or, if more severe, administer calcium gluconate especially if tetany is present. In severe alkalosis, an infusion of 2,14 % ammonium chloride is recommended, except in patients with pre-existing hepatic disease. If hypokalaemia is present administer potassium chloride.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 24 Mineral substitutes, electrolytes.

Pharmacotherapeutic group: Electrolyte solutions.

ATC code: B05XA02.

Mechanism of action

Electrolyte solution for intravenous use, after dilution, especially for restoring the balance of the bicarbonate-carbonic acid systems. The bicarbonate-carbonic acid system is the major buffer system in the body that is subject to compensatory physiological regulation. Following any alteration in this system, every other buffer pair defines and in turn is defined by the pH. Thus, any alteration in the bicarbonate-carbonic acid system achieved by the lungs and

kidneys brings into play the buffer systems in the body fluids. The ratio of the bicarbonate-carbonic acid system at a pH of 7,4 is 20:1.

5.2 Pharmacokinetic properties

Sodium bicarbonate is eliminated principally in the urine and effectively alkalises the urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate

Carbon dioxide (for pH-adjustment)

Water for injection.

6.2 Incompatibilities

SODIUM BICARBONATE INJECTION FRESENIUS is incompatible with acids, acidic salts, many alkaloidal salts, aspirin and with bismuth salicylate.

In the absence of other compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

12 months.

In-use shelf life: Use immediately after opening.

6.4 Special precautions for storage

Store at or below 25 °C.

Any unused portion should be discarded.

For storage of the opened product, see section 6.3.

6.5 Nature and contents of container

50 ml solution for injection in 50 ml “Alka” bags. Each bag is labelled and overpouched with a silica coated flow wrap. The overwrapped Alka bags are packed into corrugated cardboard shipper boxes.

Pack sizes of 10, 50 or 60.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7 HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten 6020

Gqeberha

South Africa

8 REGISTRATION NUMBER(S)

SODIUM BICARBONATE 4 % INJECTION FRESENIUS: U/24/234

SODIUM BICARBONATE 8,5 % INJECTION FRESENIUS: U/24/235

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 January 1988

10 DATE OF REVISION OF THE TEXT

05 October 2022