Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

8.4% w/v Sodium Bicarbonate Intravenous Infusion BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml of solution contains:

Active ingredient:
Sodium Hydrogen Carbonate (Sodium Bicarbonate) 8.4 g

Electrolyte concentrations:	*mmol/100 ml*
Na^+	100
HCO_3^-	100

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for infusion (Infusion)
A clear, colourless, sterile aqueous solution.

Theoretical osmolarity:	2000 mOsm/l
pH	7.0-8.5

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

- Correction of metabolic acidosis.
- Urine alkalinisation:
  - as part of the management strategy for enhanced elimination in the case of intoxication with weak organic acids, e.g. phenobarbital or acetylsalicylic acid (depending on the clinical condition, time course of intoxication and type of poison other options to enhance elimination (e.g. dialysis, hemoperfusion, single-dose or repeated-dose activated charcoal) might be considered as well);
  - in order to improve the solubility of drug substances that are poorly soluble in neutral or acid medium, e.g. methotrexate, sulfadiazine;
  - in the case of haemolysis.

4.2 Posology and method of administration

Posology
Correction of metabolic acidosis
Correction of metabolic acidosis should not be effected too rapidly. It is advisable to start administering only half of the calculated dose and adjust further doses according to the actual results of blood gas analysis.

The dose depends on the degree of the disorder of the acid-base status.

According to the blood gas values the amount to be administered is calculated applying the following formula:

$^{\#}$mmol sodium bicarbonate = base deficit × kg body weight × 0.2**

[**](The factor 0.2 corresponds to the proportion of the extracellular fluid in relation to total body weight.).

Example:
If in a patient of 70 kg bodyweight the base deficit is 5 mmol/l, then
5 x 70 x 0.23 = 70mmol of sodium bicarbonate (≙ 70 ml of 8.4 % w/v Sodium Bicarbonate Intravenous Infusion BP) are to be given.

Maximum daily dose:
According to the correction requirements.

Maximum infusion rate:
Up to 1.5 mmol of sodium bicarbonate per kg body weight per hour.

Paediatric population
The dosage has to be adjusted individually. The first dose can be up to 1 mmol/kg body weight, administered by slow intravenous infusion.
In infants (including newborn infants) and toddlers, the daily dose should not exceed 5 mmol per kg body weight per day, administered by slow intravenous infusion. 4.2% w/v (or less concentrated) sodium bicarbonate solutions should be preferred (see also section 4.4).

Urine alkalinisation
For urine alkalinisation the dose is adjusted according to the desired pH of the urine and administration should be accompanied by monitoring of the acid-base balance, the water balance and the electrolyte balance. Care should be taken not to exceed the maximum infusion rate stated above. In haemodynamically stable adults and children urine alkalinisation may be achieved with a bolus of 1-2 mmol sodium bicarbonate per kg body weight, followed by an infusion of 132 mmol sodium bicarbonate in 1 litre of glucose 5% in water, with a flow rate of 1.5-2 times the maintenance fluid rate. Urine pH should not exceed 8.5.

Method and route of administration
Intravenous use. For central venous infusion only.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Respiratory or metabolic alkalosis
- Hypoventilation
- Hypernatraemia
- Hypokalaemia
- Excessive chloride loss

4.4 Special warnings and precautions for use

General

Sodium Bicarbonate should not be administered in the following situations unless it has been established that its expected benefits clearly outweigh potential risks:
- respiratory acidosis
- hypocalcaemia
- increased serum osmolarity,
- further in all situations where sodium intake must be restricted like cardiac insufficiency, oedema, hypertension, eclampsia, severe kidney insufficiency.

When respiratory acidosis is concomitant with metabolic acidosis, both pulmonary ventilation and perfusion must be adequately supported to ensure adequate elimination of excess CO_2.

Administration of Sodium Bicarbonate may lead to sodium and fluid overload.

Accidental paravenous administration may lead to tissue necrosis.

Patient monitoring should include regular checks of the acid-base balance, the serum electrolyte concentrations and the water balance.

Correction of the acid-base status is always associated with shifts of the electrolyte balance. In particular, the potassium balance is affected. Alkalinisation or correction of acidosis promote the potassium influx into cells and may therefore lead to hypokalaemia.

Hypokalaemia or hypocalcaemia should be corrected before beginning of the alkalinising therapy.

The effects of bicarbonate on organ function, complication rates and survival in diabetic ketoacidosis, cardiac arrest and lactic acidosis have not been investigated sufficiently. Caution is advised when using sodium bicarbonate in these conditions.

Paediatric population

Newborn infants, infants and toddlers: Rapid infusion of hypertonic sodium bicarbonate solutions may produce hypernatraemia, a decrease in cerebrospinal fluid pressure and (in preterm infants) possible intracranial haemorrhage. Do not administer > 5 mmol per kg body weight per day (see also section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

Urine alkalinisation by sodium bicarbonate increases the elimination rates of acidic drug substances, e.g. acetylsalicylic acid, and decreases the elimination rates of basic drug substances.
Sodium bicarbonate may interact with gluco- and mineralocorticoids, androgens and diuretics increasing the potassium excretion.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of sodium bicarbonate in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3.). Sodium bicarbonate should not be used during pregnancy unless the clinical condition of the woman requires treatment with sodium bicarbonate. Bicarbonate readily crosses the placental barrier.

Caution should be exercised in toxaemia of pregnancy due to the high sodium level of the medicinal product (see section 4.4).

Breast-feeding
It is unknown whether sodium bicarbonate/metabolites are excreted in human milk. During breast-feeding the solution should only be given if the benefits clearly outweigh the risks.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Sodium Bicarbonate has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects are listed according to their frequencies as follows:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (frequency cannot be estimated from the available data)

Metabolism and nutrition disorders
Not known: Hypernatraemia, serum hyperosmolarity

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

4.9.1. Symptoms
Overdose may lead to alkalosis, hypernatraemia, serum hyperosmolarity or hyperhydration. When an acidosis is corrected too rapidly, especially in cases of concomitant ventilatory disorders, the increased liberation of carbon dioxide may transiently aggravate cerebral acidosis.

4.9.2. Emergency treatment, antidotes
Therapy of alkalosis, depending on its severity: Infusion of physiological saline, correction of potassium; in marked alkalosis infusion of arginine hydrochloride or hydrochloric acid. In general the patient should be treated symptomatically and electrolytes and acid-base balance should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: IV solutions, solutions affecting the electrolyte balance, electrolytes
ATC-Code: B05B B01

Mechanism of action
The pharmacological properties of sodium bicarbonate result from its physiological role in the HCO_3^-/CO_2 buffer system.

Pharmacodynamic effects
Exogenously administered sodium bicarbonate rapidly absorbs hydrogen ions from the extracellular space and thus leads to a rise of the pH in the organism.

Secondary pharmacodynamic effects
By this buffering process carbon dioxide is produced which is subsequently eliminated via the lungs. Therefore lung function should be unimpaired. Otherwise a marked rise of the pCO_2 will cause an aggravation of intracellular acidosis.

The raise of the blood pH also affects the electrolyte balance. The cellular potassium uptake is increased so hypokalaemia may be provoked or an existing hypokalaemia may be aggravated. The binding of calcium to plasma proteins is increased so hypocalcaemia may be provoked or an existing hypocalcaemia may be aggravated.

5.2 Pharmacokinetic properties

Distribution
Bicarbonate readily passes across the placental barrier but it passes only slowly across the blood-brain barrier.

Elimination
In the kidneys, bicarbonate is filtered in the glomeruli and the major proportion of it is re-absorbed in the tubules. When plasma bicarbonate concentrations rise to above 24 mmol/l, bicarbonate is excreted by the kidneys. Renal bicarbonate reabsorption is reduced under therapy with diuretics of the thiazide group or those acting on the loop of Henle's.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Water for injections

6.2 Incompatibilities

Due to their alkaline pH, sodium bicarbonate solutions are incompatible with most medicaments. In particular, they must not be administered simultaneously with solutions containing calcium, magnesium or phosphate because of the possibility of precipitation.

6.3 Shelf life

Unopened: 2 years.

After first opening:
Not applicable, see section 6.6.

After dilution:
Not applicable, see section 6

6.4 Special precautions for storage

Do not store above 25^{o}C.
To avoid formation of crystals, do not refrigerate or freeze.

6.5 Nature and contents of container

Infusion bottle of colourless glass (type I according to Ph. Eur.) sealed with an EPDM or bromobutyl rubber stopper.

Contents: 100 ml.

supplied in packs of

20 × 100 ml

6.6 Special precautions for disposal and other handling

No special requirements for disposal.
Single-dose container. Discard container and any unused content after use.
Only to be used if solution is clear, colourless, free from visible particles and the bottle or its closure are undamaged.
This medicinal product is an almost saturated solution, and should therefore not be stored below normal room temperature. Crystals which may possibly have developed during storage can be dissolved by simply warming the bottle. As an additional safety measure against crystals that might be inadvertently infused with the solution, it is recommended to use an infusion set fitted with an integral fluid filter.

The solution should be administered immediately after connecting the container to the giving set.

7 MARKETING AUTHORISATION HOLDER

B. Braun Medical Ltd.
3 Naas Road Industrial Park
Dublin 12
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0179/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st April 1983

Date of last renewal: 1st April 2008

10 DATE OF REVISION OF THE TEXT

August 2017