SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sodium Bicarbonate 8.4% w/v solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contain

Sodium bicarbonate	84.0 g

Electrolyte concentrations:

Na^+	1000 mmol/l
$HCO3^-$	1000 mmol/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
A clear, colourless aqueous solution

Theoretical osmolarity	2000 mOsm/l
pH	7.0 – 8.5

4.1. Therapeutic indications

- Correction of metabolic acidosis;
- Urine alkalinisation:
  - in the case of intoxication with weak organic acids, e. g. barbiturates or acetylsalicylic acid;
  - in order to improve the solubility of drug substances that are poorly soluble in neutral or acid medium, e. g. methotrexate, sulphonamides;
  - 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 x kg body weight x 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 body weight the base deficit is 5 mmol/l, then
5 x 70 x 0.2 = 70 mmol of sodium bicarbonate (70 ml of Sodium Bicarbonate 8.4% w/v) 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 newborns and children under 2 years: 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 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 and metabolic alkalosis
- Hypoventilation (risk of worsening acidosis)

- Hypernatraemia
- Hypokalaemia
- Excessive chloride loss

4.4 Special warnings and precautions for use

General

Sodium Bicarbonate should only be administered with particular caution in presence of the following conditions:

- 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.

It must be made absolutely sure that the solution is infused intravenously; accidental intra-arterial infusion may cause shock or loss of an extremity.

If infused undiluted or too rapidly into peripheral veins, 8.4 % w/v Sodium Bicarbonate Intravenous Infusion may cause vein irritation and consecutively phlebitis or thrombosis on account of its alkalinity and its high osmolarity.
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.

Potassium or calcium deficiencies 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
Newborns and children under 2 years: rapid infusion (10 ml/min) of hypertonic sodium bicarbonate solutions may produce hypernatraemia, a decrease in cerebrospinal fluid pressure and (in preterm infants) possible intracranial haemorrhage. Therefore, do not administer > 5 mmol per kg body weight per day (see also section 4.2).

4.5. Interactions with other medicinal products and other forms of interaction

Urine alkalinisation by sodium bicarbonate accelerates the elimination of acidic drug substances, e.g. acetylsalicylic acid, and delays the elimination 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 pre-eclampsia 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

Listing of 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

Paravenous administration may lead to tissue necrosis (see also section 4.4).

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms

Overdose may lead to alkalosis, hypernatraemia, serum hyperosmolarity or hyperhydration. When an acidosis is corrected too rapidly, esp. in the presence of respiratory disorders, the increased liberation of carbon dioxide may transiently aggravate cerebral acidosis.

Treatment

Therapy of alkalosis, depending on its severity: Infusion of physiological saline, substitution 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.

5.1. 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

Alterations in plasma bicarbonate levels can result in changes in the plasma potassium concentration. An increase in bicarbonate concentration causes a shift of

potassium into the cells, whereas a decrease has the opposite effect. This effect may aggravate existing hyperkalaemia or cause hypokalaemia.

An increase in pH due to increasing bicarbonate concentration, will also cause a decrease in the ionised calcium concentration. This is due to the increased binding of calcium to plasma proteins, especially albumin. This reduction of plasma calcium levels could contribute to the myocardial depressive effects of bicarbonate administration.

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 re-absorption is reduced under therapy with diuretics of the thiazide group or those acting on the loop of HENLE.

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 medicinal products. 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 of the container**

Not applicable. See section 6.6.

- **after dilution**

Not applicable. See section 6.6.

6.4 Special precautions for storage

Do not store above 25°C.
To avoid formation of crystals, do not refrigerate or freeze.

6.5 Nature and contents of container

Bottles of colourless glass type I (Ph. Eur.), sealed with rubber stoppers,
contents: 100 ml, 250 ml, 500 ml
supplied in packs of
1 × 100 ml, 10 × 100 ml
1 × 250 ml, 10 × 250 ml
1 × 500 ml, 10 × 500 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The containers are for single use only. Discard container and any unused content after use.

Only to be used if the solution is clear and colourless and if the bottle and its closure are undamaged.

This medicinal product is an almost saturated solution. 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.

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

7 MARKETING AUTHORISATION HOLDER

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