SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sodium Bicarbonate 8.4%

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml of solution contain	
Sodium Hydrogen Carbonate	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

Theoretical osmolarity	2000 mOsm/l
pH	7.0 – 8.5

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Whenever a **rapid** alkalinising effect is desired, preference is to be given to sodium bicarbonate. The indications are as follows:
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. Treat metabolic acidosis in addition to measures designed to control the cause of the acidosis (e. g. insulin in uncomplicated diabetes, blood volume restoration in shock). Since an appreciable time interval may elapse before all ancillary effects occur bicarbonate therapy is indicated to minimize risks inherent to acidosis itself.
Urine alkalinisation (for example "sulphonamide nephrosis", salicylate or barbiturate intoxication).
Severe diarrhea.

4.2. Posology and method of administration

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:
ml of 1 M (8.4 % w/v) sodium bicarbonate solution = base deficit x kg b.w.
x 0.3

(The factor 0.3 corresponds to the proportion of the extracellular fluid in relation to total body fluid).

Example:
If in a patient of 70 kg b.w. the base deficit is 5 mmol/l, then 5 x 70 x 0.3 = 105 ml of 8.4 % w/v Sodium Bicarbonate Intravenous Infusion are to be given.

In neonates and infants the daily dose should not exceed 8 mmol/kg BW/day, administered by slow intravenous infusion, dosage and infusion rate should be controlled carefully.

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.

For urine alkalisation the dose is adjusted according to the desired pH of the urine and administration should be accompanied by monitoring of the acidbase balance and the water balance. Care should be taken not to exceed the maximum infusion rate stated below.

Maximum daily dose:

According to the correction requirements.

Flow rate:

Up to 1.5 mmol of sodium bicarbonate per kg body weight per hour, corresponding to 1.5 ml of 8.4 % w/v Sodium Bicarbonate Intravenous Infusion/kg bw/h.

Method of administration:

Intravenous use.

The solution must be infused into a central vein.

4.3. Contra-indications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

8.4 % Sodium Bicarbonate Intravenous Infusion must not be administered to patients with

- respiratory and metabolic alkalosis,
- hypernatraemia,
- hypokalaemia.

8.4 % w/v Sodium Bicarbonate Intravenous Infusion should only be administered with

particular caution in presence of the following conditions:

- hypoventilation,
- hypocalcaemia,
- increased serum osmolarity,
- further in all situations where sodium intake must be restricted like cardiac insufficiency, oedema, hypertension, eclampsia, severe kidney insufficiency.

4.4 Special warnings and precautions for use

Special warnings

Administration of 8.4 % w/v Sodium Bicarbonate Intravenous Infusion may lead to sodium and fluid overload.

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.

Neonates and children (< 2 years old): Rapid infusion (10ml/min) of hypertonic sodium bicarbonate solutions may produce hypernatraemia, a decrease in cerebrospinal fluid pressure and possible intracranial haemorrhage. Do not administer > 8 mmol/kg BW/day (cf. section 4.2 above).

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

Special precautions for use

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. Alkalisation 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.

4.5. Interactions with other medicaments and other forms of interaction

Urine alkalisation by sodium bicarbonate accelerates the elimination of acid 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. Pregnancy and lactation

As bicarbonate readily crosses the placental barrier, sodium bicarbonate solutions should only be given to pregnant women if clearly indicated.

Cave eclampsia!

4.7. Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Administration of 8.4 % w/v Sodium Bicarbonate Intravenous Infusion may lead to hypernatraemia, and serum hyperosmolarity.

Paravenous administration may lead to tissue necrosis.

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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form (https://sideeffects.health.gov.il)

4.9 Overdose

Symptoms

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

Emergency treatment, antidotes

Therapy of alkalosis, depending on its severity: Infusion of physiological saline, substitution of potassium; in marked alkalosis infusion of arginine hydrochloride or hydrochloric acid.

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

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
Carbon Dioxide

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:**

The expiry date of the product is indicated on the packaging materials.

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 glass type I (Ph. Eur.), sealed with rubber stoppers, contents: 100 ml
supplied in packs of
20 × 100 ml

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.

From a microbiological point of view, the solution should be administered immediately after connecting the container to the giving set. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 C°.

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

7 MANUFACTURER

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Carl-Braun-Straße 1
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Germany

8. REGISTRATION HOLDER

Lapidot Medical Import and Marketing Ltd.
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9. MARKETING AUTHORISATION NUMBER

055-42-26716-00

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