1.6 Product Information

1.6.1 Prescribing information (Summary of Product Characteristics)

1. Name of the Finished Pharmaceutical Product:

1.1 Product Name : SOBISIS

1.2 Strength : 500 mg

1.3 Pharmaceutical Form : Tablets

2. Qualitative and Quantitative Composition

2.1 Qualitative Declaration:

Each film coated tablet contains:
Sodium Bicarbonate USP …… 500 mg
Excipients .....q.s.
Color : Titanium dioxide USP

2.2 Quantitative Declaration:

Sr. No.	Name of Ingredient	Specification	Quantity (mg/ tablet)	Purpose of Ingredients
1.	Sodium Bicarbonate	USP	500 mg	Active material
2.	Microcrystalline Cellulose (PH 102)	BP	60 mg	Additive
3.	Microcrystalline Cellulose Plain	BP	103.2 mg	Additive and Disintegrating agent
4.	Pregelatinised Starch	BP	25 mg	Binding agent
5.	Iso Propyl Alcohol	BP	#1.572 mg(Eq. to 0.002 ml)	Solvent
6.	Purified Water	BP	18.00 mg(Eq. to 0.018 ml)	Solvent and moisturizing agent
7.	Purified Talc	BP	21.8 mg	Glidant
8.	Magnesium Stearate	BP	10 mg	Lubricant
9.	Hydroxypropylmethyl cellulose	BP	10.80 mg	Coating Material

Sr. No.	Name of Ingredient	Specification	Quantity (mg/ tablet)	Purpose of Ingredients
10.	Purified Talc	BP	3.6 mg	Glidant
11.	Titanium Dioxide	USP	1.8 mg	Opacifier
12.	Polyethylene Glycol (6000)	USNF	1.8 mg	Plasticizer
13.	Isopropyl Alcohol	BP	#105.0 mg(Eq. to 0.133 ml)	Solvent (Dissolving agent)
14.	Methylene Chloride	BP	#260.00mg (Eq. to 0.196 ml)	Solvent (Dissolving agent)

#: Quantity not included in the weight.

*** Standard quantity of Sodium Bicarbonate is calculated on the basis of 100 % assay and 0% LOD/water contents. Calculate actual quantity of the API on the basis of their actual assay and LOD/water content.**
**** Compensate extra quantity of API with Microcrystalline Cellulose (PH 102).**

3. Pharmaceutical Form: Tablets

4. Clinical Particulars

4.1 Therapeutic Indications

Sodium bicarbonate tablets are used for 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, and 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. It is also used in severe diarrhoea which is often accompanied by a significant loss of bicarbonate.

4.2 Posology and Method of Administration

Moderate metabolic acidosis: 325 to 2000 mg orally 1 to 4 times a day. One gram provides 11.9 mEq (mmoL) each of sodium and bicarbonate.

4.3 Contraindications

Sodium bicarbonate is contraindicated in patients with metabolic or respiratory alkalosis; in those who are losing chlorides by vomiting or from continuous GI suction; in those receiving diuretics known to produce hypochloremic alkalosis; and in patients with hypocalcemia in which alkalosis may produce tetany, hypertension, seizures, or heart failure. Orally administered sodium bicarbonate is contraindicated in patients with acute ingestion of strong mineral acids. Use extreme caution when giving drug to patients with heart failure, renal insufficiency, or other edematous or sodium-retaining conditions.

4.4 Special Warnings and Precautions for Use

Before taking sodium bicarbonate, consult your doctor if you have: a certain breathing problem (pulmonary edema), congestive heart failure, severe kidney disease (e.g., inability to make urine), severe liver disease (e.g., ascites, cirrhosis), high sodium levels, and swollen ankles/legs/feet due to retaining water (peripheral edema). Because this medication contains salt (sodium), do not use if you are on a salt-restricted diet. During pregnancy, this medication should be used only when clearly needed. This medication may worsen high blood pressure during pregnancy (toxemia of pregnancy). It is unknown if sodium bicarbonate tablets are excreted in breast milk. If you are or will be breast-feeding while you are using sodium bicarbonate tablets, check with your doctor or pharmacist to discuss the risks to your baby.

4.5 Interaction with other medicinal products and other forms of interaction

Some products that may interact with this drug include: aspirin and other salicylates (such as salsalate), barbiturates (such as phenobarbital), calcium supplements, corticosteroids (such as prednisone), memantine, medications with a special coating to protect the stomach (enteric coating), lithium, quinidine, "water pills" (thiazide diuretics such as hydrochlorothiazide).

4.6 Additional information on special populations

During pregnancy, this medication should be used only when clearly needed. This medication may worsen high blood pressure during pregnancy (toxemia of pregnancy). It is unknown if sodium bicarbonate tablets are excreted in breast milk. If you are or will be breast-feeding while you are using sodium bicarbonate tablets, check with your doctor or pharmacist to discuss the risks to your baby.

4.7 Paediatric population

There is no information available for effect of Sodium Bicarbonate on pediatric population.

4.8 Fertility, pregnancy and lactation

During pregnancy, this medication should be used only when clearly needed. This medication may worsen high blood pressure during pregnancy (toxemia of pregnancy). It is unknown if sodium bicarbonate tablets are excreted in breast milk. If you are or will be breast-feeding while you are using sodium bicarbonate tablets, check with your doctor or pharmacist to discuss the risks to your baby.

4.9 Effects on ability to drive and use machines

There is no information available for effect of Sodium Bicarbonate on ability to drive and use machine.

4.10 Undesirable effects:

Alkalosis and/or hypokalemia, cellulitis, with tissue necrosis or sloughing at the site of infiltration, Hyperirritability, Hypernatraemia, Hyperosmolality, chemical cellulitis, with tissue necrosis, tissue calcification, ulceration or sloughing at the site of infiltration. Hyperirritability, Cerebral oedema Hypercapnia.

4.11 Overdose:

Sodium bicarbonate should be stopped in alkalosis, manage the patient according to the degree of alkalosis present. 0.9% sodium chloride injection intravenous may be given; potassium chloride also may be indicated if there is hypokalemia. Severe alkalosis may be accompanied by hyperirritability or tetany and these symptoms may be controlled by calcium gluconate. An acidifying agent such as ammonium chloride may also be indicated in severe alkalosis

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

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

Alkalizer, systemic: Increases the plasma bicarbonate, buffers excess hydrogen ion concentration, and raises blood pH, thereby reversing the clinical manifestations of acidosis.

Alkalizer, urinary: Increases the excretion of free bicarbonate ions in the urine, thus effectively raising the urinary pH. By maintaining an alkaline urine, the actual dissolution of uric acid stones may be accomplished.

5.2 Pharmacokinetic Properties:

Absorption: Well absorbed after oral administration as sodium ion and bicarbonate.
Distribution: Occurs naturally and is confined to the systemic circulation.
Metabolism: None.
Excretion: Filtered and reabsorbed by the kidney; less than 1% of filtered bicarbonate is excreted.

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 (H2CO3), then to its volatile form, carbon dioxide (CO2) which is excreted by the lung. Normally, a ratio of 1:20 (carbonic acid: bicarbonate) is present in the extracellular fluid.

5.3 Preclinical Safety Data

Attached On Next Page

6.0 Pharmaceutical Particulars:

6.1 List of Excipients

Sr. No.	Name of Ingredient	Specification
1.	Microcrystalline Cellulose PH 102	BP
2.	Microcrystalline Cellulose plain	BP
3.	Pregelatinised Starch	BP
4.	Purified Water	BP
5.	Purified Talc	BP
6.	Magnesium Stearate	BP
7.	Hydroxylpropyl methyl cellulose	BP
8.	Titanium Dioxide	USP
9.	Polyethylene Glycol (6000)	US NF
10.	Isopropyl Alcohol	BP
11.	Methylene Chloride	BP

6.2 Incompatibilities:

Not Applicable

6.3 Shelf Life : 36 Month

Effect of Sodium Bicarbonate Preloading on Ischemic Renal Failure

Atkins J.L.
Department of Nephrology, Division of Medicine, Walter Reed Army Institute of Research, Washington, D.C., USA

Abstract

Rats pretreated with sodium bicarbonate were functionally protected from the damage of bilateral renal artery occlusion. The rise in serum creatinine (day 1 minus day 0) during the first 24 h after ischemia was 2.88 ± 0.28 mg% in the bicarbonate-loaded animals versus 3.90 ± 0.26 mg% in their matched controls ($p \leq 0.01$). Pretreatment with acetazolamide produced a similar alkaline urine as the bicarbonate loading (pH 8.3 vs. 7.0 in controls) and a similar degree of protection (delta creatinine 2.85 ± 0.41 vs. 4.23 ± 0.26 mg%; $p \leq 0.01$). A direct effect of sodium loading was excluded by comparing $NH4HCO_3$ with $NaHCO_3$ loading and observing no difference in delta creatinine levels after ischemia (3.39 ± 0.69 vs. 3.20 ± 0.61 mg%). These data indicate that $NaHCO_3$ protects in this model of acute renal failure and further suggest that the mechanism of protection is not related to either systemic alkalosis or sodium loading.

Counterproductive effects of sodium bicarbonate in diabetic ketoacidosis

Y Okuda
H J Adrogue
J B Field
H Nohara
K Yamashita
(1996) 81 (1): 314-320.

Although a growing body of evidence supports that alkali therapy in diabetic ketoacidosis (DKA) might be counterproductive, our knowledge about the consequences of this treatment on ketone metabolism is limited. Consequently, we performed clinical and animal studies to further examine this topic. The clinical studies assessed seven patients with DKA treated with continuous insulin infusion at a low dosage. Three of them also received sodium bicarbonate (NaHCO3), whereas the remaining four acted as controls. The group receiving NaHCO3 showed a 6-h delay in the improvement of ketosis as compared with controls. In addition, there was an increase in acetoacetate (AcAc) levels during alkali administration, followed by an increase in 3-hydroxybutyrate (3-OHB) level after its completion. Significant differences were not found between groups in the response of plasma glucose to the overall therapy. The animal study examined the effects of a NaHCO3-rich perfusate on the hepatic production of ketones with the in situ rat-liver preparation. Alkali loading resulted in an immediate increase in the AcAc level followed by increases in both the 3-OHB level and the 3-OHB/AcAc ratio after its completion. Hepatic ketogenesis increased even further, to about twice the basal level, after termination of the NaHCO3 loading. This investigation confirms that alkali administration augments ketone production and unravels an effect of bicarbonate infusion that promotes a selective build up of AcAc in body fluids. The data support that alkali therapy in DKA has nonsaltuary effects in the metabolism and plasma levels of ketones.

6.4 Special Precautions for Storage:

Store at a temperature not exceeding 30°C. Protect from light and moisture

6.5 Nature and contents of Container:

10 tablets in a blister, 10 such blisters are packed in a carton along with the pack Insert

6.6 Special Precautions for disposal and other handling: Not applicable

7 Marketing Authorization Holder and Manufacturing Site Addresses:

Marketing Authorization Holder:

Name	:	**LA RENON HEALTHCARE PRIVATE LIMITED**
Office Address:		207-208, ISCON Elegance, S. G. Highway, Circle-P, Prahlad Nagar Cross Roads, Ahmedabad-380015, Gujarat
Telephone	:	+91-79-3046-1000 (30 lines)
Fax	:	+91-79-3046-1001
Email	:	info@larenon.com

Manufacturing Site Addresses:
Stanford Laboratories Private Limited
(A subsidiary company of La Renon Healthcare Private Limited)
8 Industrial Area, Mehatpur,
Distt: Una, (H.P) 174 315, India

8 Marketing Authorization Number: MNB/08/695

9 Date of First Registration/Renewal of the Registration: Not Applicable

10 Date of Revision of the text: Not Applicable

11 Dosimetry (If Applicable) : Not Applicable

12 Instructions For Preparation Of Radiopharmaceuticals (If Applicable)

Not Applicable