SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nephrotrans 500 mg gastro-resistant capsules, soft

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 500 mg sodium hydrogen carbonate.

Excipients with known effect: sorbitol and soya-bean oil.
Each capsule contains 50 mg sorbitol and 15 mg soya-bean oil.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Opaque, russet and white, elongated oval gastro-resistant capsule, soft with approximate size of 22 mm (length) and 7.8 mm (diameter).

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of metabolic acidosis and for maintenance treatment against recurrence of metabolic acidosis in adults with chronic renal impairment.

4.2 Posology and method of administration

Posology

The dosage depends on the severity of metabolic acidosis, based on the results of blood gas analysis or determination of serum bicarbonate.

The mean dosage is 3 to 5 g sodium hydrogen carbonate per day, equivalent to 40-65 mg sodium hydrogen carbonate per kg body weight per day.

The daily dose can be achieved by taking 6 to 10 capsules of Nephrotrans 500 mg.

Paediatric population
No data available. The safety and efficacy of Nephrotrans 500 mg in children and adolescents has not been established.

Method of administration
To be swallowed whole throughout the day with sufficient liquid.

This medicinal product should not be taken without medical supervision for prolonged periods, as there is a possibility for the development of hypernatremia or alkalosis.

Note: Patients with a blood pH level below 7.2 require the correction of acidosis by infusion.

4.3 Contraindications

- Hypersensitivity to the active substance, soya, peanuts, or to any of the excipients listed in section 6.1.
- metabolic alkalosis
- hypokalaemia
- hypernatraemia
- low sodium diet

4.4 Special warnings and precautions for use

The effect of Nephrotrans 500 mg should initially be monitored at intervals of at least one to two weeks (e.g. by pH measurement, standard bicarbonate, alkali reserve), especially at higher doses. Plasma electrolytes, especially sodium, potassium and calcium, should likewise be regularly monitored. These checks should also be performed regularly during long-term medication. Further dosing should be determined based on the outcome of these checks. Any possible hyperalkalinity can be corrected by a dose reduction.

Particular caution is required in the presence of hypoventilation, hypocalcaemia and hyperosmolar conditions.

This medicinal product contains 137 mg sodium per capsule, equivalent to approximately 7% of the WHO recommended maximum daily intake of 2 g sodium for an adult. The maximum daily dose of this product (10 capsules) is equivalent to 68% of the WHO recommended maximum daily intake for sodium. This should be particularly taken into account for those on a low salt diet.

Nephrotrans 500 mg contains 50 mg sorbitol in each capsule. Patients with rare hereditary problems of fructose intolerance (HFI) should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Due to the increase in pH levels in the stomach and intestines, absorption and excretion of weak acids and bases may be affected. This applies, for example, to sympathomimetics, anticholinergics, tricyclic antidepressants, barbiturates, H_2 antagonists, captopril and quinidine.

Functional interactions are possible with glucocorticoids and mineralocorticoids, androgens and potassium-depleting diuretics.

Vigilance is required for a possible effect on the solubility of medicines eliminated with the urine (e.g. ciprofloxacin).

4.6 Fertility, pregnancy and lactation

Pregnancy and breast-feeding
There is no experience with the use of Nephrotrans 500 mg in pregnancy and breast-feeding. In principle, there are no objections to the use of sodium hydrogen carbonate in the appropriate indication. However, it should be borne in mind that orally administered sodium hydrogen carbonate is well absorbed and readily crosses the placental barrier. Existing blood pressure dysregulation, such as the physiological respiratory alkalosis associated with pregnancy, may also be increased due to the sodium load.

Fertility
No data are available on the effect of Nephrotrans 500 mg on fertility.

4.7 Effects on ability to drive and use machines

Nephrotrans 500 mg has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following frequencies are used for the evaluation of adverse reactions:

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 (cannot be estimated from the available data)

Gastrointestinal disorders

Not known: flatulence and abdominal pain.

Renal and urinary disorders

Not known: promotion of calcium or magnesium phosphate nephrolithiasis in chronic use.

Musculoskeletal and connective tissue disorders

Not known: hypocalcaemic tetany (muscle hyperexcitability due to decreased calcium) if the dose is exceeded. In patients with pre-existing disorders of the gastrointestinal tract, e.g. diarrhoea, exacerbation of such disorders is possible.

Skin and subcutaneous tissue disorders

Very rare: allergic reactions due to soya oil.

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:

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In the event of an absolute or relative overdose (e.g. in renal impairment), even oral administration of sodium hydrogen carbonate can lead to alkalosis with dizziness, muscle weakness, fatigue, cyanosis, hypoventilation and symptoms of tetany. Apathy, confusion, ileus and circulatory collapse may subsequently follow. Treatment consists in correcting the fluid and electrolyte balance, particularly with the supply of calcium, potassium and, if necessary, chloride. In individual cases, symptoms of acute hypernatremia may also predominate, with confusion, increased excitability and even seizures and coma. In such cases, fluid administration (e.g. glucose solutions and hypo-osmolar electrolyte solutions) and diuretics are crucial.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antacids with sodium bicarbonate, ATC code: A02AH

Sodium hydrogen carbonate is a salt whose essential pharmacological properties result from its physiological role as a component of the HCO_3/CO_2 buffer. Sodium hydrogen carbonate leads to an increase in the body's pH level.

Sodium hydrogen carbonate in Nephrotrans 500 mg is provided in the form of gastro-resistant gelatin capsules, soft that are dissolvable in the small intestine, thereby avoiding gastric meteorism caused by the formation of carbon dioxide gas in the acidic environment of the stomach. The administered amount of bicarbonate available is similar to administration via sodium hydrogen carbonate infusions as the gastro-

resistant formulation prevents gastric bicarbonate degradation. There is a rise in the plasma carbonate level and correction of the bicarbonate deficit. Hence, it is possible to treat metabolic acidosis of various aetiology, provided the blood pH level is not below 7.2. Notwithstanding this, treatment of diabetic ketoacidosis has shown that, after correction of the pH level to 7.2, further use of insulin is more effective than treatment with buffer agents.

5.2 Pharmacokinetic properties

In one study, absorption of orally administered sodium hydrogen carbonate in the form of gastro-resistant capsules versus IV administration was studied by measuring the acid-base status and renal Na^+ elimination.

Based on this, absorption of sodium hydrogen carbonate from a total of 12 capsules of 0.5 g each sets in after about 2 hours, peak changes in the acid-base status are seen after approximately 5-8 hours and, in correlation to this, renal elimination of Na^+ and base equivalents is greatest at this time.

Overall, the changes in current and standard bicarbonate and base excess were significantly greater after oral administration than after IV administration. Although this indicates that a significant fraction of the oral sodium hydrogen carbonate dose is absorbed, it does not however allow any quantification of this amount. However, a rough estimate of the intestinally absorbed amount is possible by comparing the renally eliminated Na^+ amount after oral and intravenous administration, resulting in an absorption rate of 70%.

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

Yellow beeswax, hydrogenated soya-bean oil, partially hydrogenated soya-bean oil, refined rapeseed oil, soya lecithin, iron oxide (E172), titanium dioxide (E171), glycerol 85%, gelatin, partially dehydrated liquid sorbitol, hydrochloric acid 25%, triethyl citrate, methacrylic acid - ethyl acrylate copolymer (1:1), polysorbate 80, sodium laurilsulfate, glycerol monostearate, purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

Store in the original package in order to protect from light.

6.5 Nature and contents of container

Boxes containing capsules in PVC/PVDC clear blisters sealed to aluminium foil.

Packs with 100 gastro-resistant capsules, soft

Hospital packs with 500 gastro-resistant capsules, soft

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Medice Arzneimittel Pütter GmbH & Co. KG
Kuhloweg 37
58638 Iserlohn
Germany

8 MARKETING AUTHORISATION NUMBER(S)

PL 11243/0045

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/09/2024

10 DATE OF REVISION OF THE TEXT

25/09/2024