1. Name of the medicinal product

CARSTENE 2% (Carbocisteine Syrup 100mg/5ml)

2. Qualitative and quantitative composition

Each 5 ml contains:
Carbocisteine BP .....100 mg
Flavoured Syrupy Base .....Q.S.
Colour: Sunset Yellow FCF.
For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Oral syrup.

Orange coloured syrup

4. Clinical particulars

4.1 Therapeutic indications

Carbocisteine is a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterized by excessive, viscous mucus, including chronic obstructive airway disease

4.2 Posology and method of administration

The recommended dose for children 2-6 years is 2.5-5 ml syrup for children (half or one teaspoon), every 6 hours, for children 6-12 years 10 ml syrup for children (two teaspoons) every 8 hours. Duration of treatment usually does not exceed 8-10 days.

4.3 Contraindications

- Hypersensitivity to carbocisteine or to any of the excipients in anamnesis.
- Use in patients with active peptic ulceration.
- Children under 2 years old.

4.4 Special warnings and precautions for use

A productive cough must not be suppressed since this is a fundamental part of the bronchopulmonary defence mechanism.

It must be administered with caution to patients with severe respiratory insufficiency, as it could increase airway obstruction (see section 5.1).

The association of a bronchial mucus modifier with an antitussive and/or with a substance which dries the secretions (atropinic) is not advisable.

It must be administered with caution in patients with a history of peptic ulcer disease.

Management should be re-assessed if there are signs of pulmonary superinfection.

This medicinal product contains small amounts of ethanol (alcohol), 89.7 mg (i.e. less than 100 mg) per 15 ml dose (ethanol content: 0.8 % v/v).

This medicinal product contains 101 mg (about 0.1g) of sodium per 15 mL dose. To be taken into consideration by patients on a controlled sodium diet.

This medicine contains methyl parahydroxybenzoate (E218) which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction
Contraindications of concomitant use

No specific study for pharmacokinetic interaction has been conducted. Based on our knowledge of carbocisteine, no interactions are expected (see section 5.2).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of carbocisteine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity.
Carstene 2% is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding

There is insufficient information on the excretion of carbocisteine and/or its metabolites in human milk or in animal milk.
A risk to the newborns/infants cannot be excluded.
Therefore, Carstene 2% is not recommended during breast-feeding.

Fertility

Experimental data did not demonstrate any effect on male and female fertility in rat (see section 5.3).

4.7 Effects on ability to drive and use machines

Carstene 2% has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects are classified by their frequency, according to the following convention: very common (_1/10),common (_1/100 to <1/10), uncommon (_1/1000 to <1/100), rare (_1/10,000 to <1/1000), very rare (<1/10,000), not known (cannot be estimated from the available data). The incidence based on the MedDRA frequency convention and system organ class database is not known.

Body system	Adverse reactions (frequency not known)
Gastrointestinal disorders	Upper abdominal painNausea Vomiting Diarrhoea
Skin and subcutaneous tissue disorders	Allergic skin reactions, such as erythematous rash, pruritus, urticaria, angio-edema and fixed drug eruption.

4.9 Overdose

There is no experience on the poisoning following overdose. Due to the low toxicity of the product, it is unlikely that an overdose will have toxic effects.

Excessive doses could result most often in gastrointestinal disorder symptoms (nausea, vomiting, diarrhoea, stomach ache).

Treatment

In the event of a massive accidental ingestion, gastric lavage should be performed and symptomatic treatment administered.

There is no known antidote.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: MUCOLYTICS, ATC code: R05CB03 (R: respiratory system)

Carbocisteine (5-carboxymethyl L-cysteine) is a mucoregulator mucolytic-type that acts by altering the structure of the mucus. Carbocisteine stimulates sialomucin synthesis, and consequently modifies mucus composition, reduces mucus viscosity and facilitates expectoration.

Clinically, Carbocisteine treatment induces a decrease in sputum viscosity and an increase in sputum volume.

5.2 Pharmacokinetic properties

Absorption

After oral administration, carbocisteine is almost completely and rapidly absorbed from the gastrointestinal tract. Peak plasma concentration is reached 1 to 2 hours after dosing. After repeat-dose, no accumulation of carbocisteine is evidenced.

Distribution

The apparent volume of distribution of carbocisteine is approximately 60 litres. No information is available on the extent of protein binding.

Carbocisteine appears to penetrate into lung tissues and respiratory mucus, suggesting a local action.

Biotransformation

Acetylation, decarboxylation and sulfoxidation have been identified as the major metabolic pathways of carbocisteine.

Pronounced inter-individual variation in metabolic patterns has been observed.

Elimination

The plasma elimination half-life ranges between 1.5 and 2.1 hours.

Renal excretion is the principal route of elimination (96% of the administered dose after 168 hours), the dose being excreted as unchanged drug and metabolites.

5.3 Preclinical safety data
Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium methyl Hydroxyl benzoate BP
Sodium propyl Hydroxyl benzoate BP
Disodium Edetate BP
Sorbitol 70% BP
Citric acid monohydrate BP
Colour sunset yellow FCF IHS
Flavour raspberry IHS
Sucralose BP
Glycerin BP
Sodium hydroxide BP

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store below 300C. Protect from Light.

6.5 Nature and contents of container
Primary Packing: 100 ml clear glass bottles with PP cap and measuring cup.
Secondary Packing: 1 such bottle packed in a carton along with a package insert.

7. Marketing authorisation holder

GBGL Pharma Limited.