

1. NAME OF THE MEDICINAL PRODUCT

BRONCHOBOS[®] 250 mg/5 ml syrup
carbocisteine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of syrup contains: Carbocisteine 250 mg
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup (clear, slightly viscous solution with raspberry color and odor).

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

4.2. Posology and method of administration

Adults including the elderly:

Dosage is based upon an initial daily dosage of 2250 mg carbocisteine in divided doses, reducing to 1500 mg daily in divided doses when a satisfactory response is obtained e.g. 15 ml tds reducing to 10 ml tds.

Children:

BRONCHOBOS 250 mg/5 ml syrup is intended for children over 12 years of age, in doses recommended for adults.

BRONCHOBOS 125 mg/5 ml syrup is intended for children under 12 years of age.

Method of administration

BRONCHOBOS 250 mg/5 ml syrup is for oral use.

Note:

- For dosage of BRONCHOBOS 250 mg/5 ml syrup a 5 ml dosing spoon graduated at 2.5 ml and supplied in the box is used. Each dosing spoon of BRONCHOBOS 250 mg/5 ml syrup contains 250 mg carbocisteine.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Use in patients with active peptic ulceration.

4.4. Special warnings and precautions for use

- Caution is recommended in the elderly, in those with a history of gastroduodenal ulcers, or those taking concomitant medications known to cause gastrointestinal bleeding. If gastrointestinal bleeding occurs, patients should discontinue medication.
- BRONCHOBOS 250 mg/5 ml syrup contains ethanol 96% (alcohol). In keeping with the dosage instructions on every applications (15 ml) is supplied in the organism up to 375 mg of alcohol. This can be harmful for those suffering from alcoholism. It should also be taken into account in pregnant or breast-feeding women, children and high risk groups such as patients with liver disease or epilepsy.
- BRONCHOBOS 250 mg/5 ml syrup contains methylparahydroxybenzoate (E218) and propylparahydroxybenzoate (E216). Both of these ingredients may cause allergic reactions (possible delayed hypersensitivity reactions).
- BRONCHOBOS 250 mg/5 ml syrup contains cochineal red A (E124). It may cause allergic reaction.

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

None stated.

4.6. Pregnancy and lactation

Pregnancy

Although tests in mammalian species have revealed no teratogenic effects, carbocisteine is not recommended during the first trimester of pregnancy.

Lactation

Effects not known.

4.7. Effects on the ability to drive and use machines

None.

4.8. Adverse effects

Immune System Disorders

There have been reports of anaphylactic reactions and fixed drug eruption.

Gastrointestinal disorders

There have been reports of gastrointestinal bleeding occurring during treatment with carbocisteine. Frequency not known: vomiting, gastrointestinal bleeding.

Skin and subcutaneous tissue disorders

There have been reports of skin rashes and allergic skin eruptions. Isolated cases of bullous dermatitis such as Stevens–Johnson syndrome and erythema multiforme have also been reported.

4.9. Overdose

Gastric lavage may be beneficial, followed by observation. Gastrointestinal disturbance is the most likely symptom of carbocisteine overdosage.

5. PHARMACOLOGICAL CHARACTERISTICS

5.1. Pharmacodynamic characteristics

Pharmacotherapeutic group: Expectorants, excluding combinations with cough suppressant. Mucolytics with ATC cod R05CB03.

Carbocisteine (S-carboxymethyl L-cysteine) has been shown in normal and bronchitic animal models to affect the nature and amount of mucus glycoprotein which is secreted by the respiratory tract. An increase in the acid:neutral glycoprotein ratio of the mucus and a transformation of serous cells to mucus cells is known to be the initial response to irritation and will normally be followed by hypersecretion. The administration of Carbocisteine to animals exposed to irritants indicates that the glycoprotein that is secreted remains normal; administration after exposure indicates that return to the normal state is accelerated. Studies in humans have demonstrated that Carbocisteine reduces goblet cell hyperplasia. Carbocisteine can therefore be demonstrated to have a role in the management of disorders characterised by abnormal mucus.

5.2. Pharmacokinetic characteristics

Carbocisteine is rapidly absorbed from the GI tract. In an 'in-house' study, at steady state (7 days) carbocisteine capsules 375 mg given as 2 capsules t.d.s. to healthy volunteers gave the following pharmacokinetic parameters:

<u>Plasma Determinations</u>	<u>Mean</u>	<u>Range</u>
T Max (Hr)	2.0	1.0-3.0
T _½ (Hr)	1.87	1.4-2.5
K _{EL} (Hr ⁻¹)	0.387	0.28-0.50
AUC _{0-7.5} (mcg.Hr.ml ⁻¹)	39.26	26.0-62.4
<u>Derived Pharmacokinetic Parameters</u>	<u>Mean</u>	<u>Range</u>
*CL _S (L.Hr ⁻¹)	20.2	-
CL _S (ml.min ⁻¹)	331	-
V _D (L)	105.2	-
V _D (L.Kg ⁻¹)	1/75	-
*Calculated from dose for day 7 of study		

5.3. Preclinical safety data

There are no preclinical data of relevance to the precriber, which are additional to those already included in other sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Glycerol 85%

- Ethanol 96%
- Sodium hydroxide
- Carmellose sodium
- Citric acid monohydrate
- Methylparahydroxybenzoate (E218)
- Saccharin sodium
- Propylparahydroxybenzoate (E216)
- Aroma raspberry
- Cochineal red A (E124)
- Purified water

6.2. Incompatibilities

Mixture with linctus of pholcodine causes precipitation of carbocisteine from solution.

6.3. Shelf life

3 years.

After the first opening of BRONCHOBOS[®] 250 mg/5ml syrup, the shelf life is sixty days.

6.4. Special storage measures

Store at temperature up to 30°C. Do not freeze.

6.5. Nature and content of primary packaging material

BRONCHOBOS[®] 250 mg/5 ml syrup is packed in brown glass bottles of 250 mL containing 200 mL of syrup, child-resistant screw cap. Original pack includes measuring spoon graduated at 2.5 and 5 ml for correct use of medicament

6.6. Instructions on usage and handling and special measures for disposing of unused medicines or their waste

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

6.7. Issuing regime

Available without medical prescription.

7. MARKETING AUTHORISATION HOLDER

Bosnalijek, Pharmaceutical and Chemical Industry, Joint Stock Company, Jukićeva 53, Sarajevo, Bosnia and Herzegovina

7. NUMBER AND DATE OF AUTHORISATION

9. DATE OF REVISION OF THE TEXT

October, 2023.