

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Carbocisteine 375 mg Capsules, Hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 375 mg of Carbocisteine.

Excipient (s) with known effect: Lactose (each capsule contains 13.750 mg of Lactose monohydrate)

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsule, hard.

Golden yellow colored cap/ Golden yellow colored body, size “1” hard gelatin capsules imprinted “6C1” on cap and “375” on body with black ink, containing white to off white granular powder.

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

Posology

Adults including the elderly:

Dosage is based upon an initial daily dosage of 2250mg Carbocisteine in divided doses, reducing to 1500mg daily in divided doses when a satisfactory response is obtained e.g. two capsules three times a day reducing to one capsule four times a day.

Paediatric population:

This formulation is not recommended for children. It is recommended that syrup formulation of this drug be administered at a normal daily dose of 20 mg/kg body weight in divided doses.

Method of administration

Carbocisteine 375 mg Capsules are for oral use.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
- 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 gastro duodenal ulcers, or those taking concomitant medications known to cause gastrointestinal bleeding. If gastrointestinal bleeding occurs, patients should discontinue medication.
- Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

None stated.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no available data on carbocisteine use in pregnant women. No conclusions can be drawn regarding whether or not carbocisteine is safe for use during pregnancy. The use of carbocisteine in pregnant women is not recommended, especially during the first trimester.

Breast-feeding There are no available data on the presence of carbocisteine in human milk, milk production, or the effects on the breastfed infant. No conclusions can be drawn regarding whether or not carbocisteine is safe for use during breastfeeding. The use of carbocisteine in breastfeeding women is not recommended.

Fertility

There is no consistent evidence on the effects of this product on fertility in males or females.

4.7 Effects on ability to drive and use machines

Carbocisteine has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following CIOMS frequency rating is used, when applicable: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $\leq 1/100$); rare ($\geq 1/10,000$ to $\leq 1/1,000$); very rare ($\leq 1/10,000$); not known (cannot be estimated from the available data).

Immune System Disorders

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

Gastrointestinal disorders

There have been reports of diarrhoea, nausea, epigastric discomfort and 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 dermatitis bullous such as Stevens–Johnson syndrome and erythema multiforme have also been reported.

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 the national reporting system, Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Gastric lavage may be beneficial, followed by observation. Gastrointestinal disturbance is the most likely symptom of Carbocisteine Capsules overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: R05CB03

Mechanism of action

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 are known to be the initial response to irritation and will normally be followed by hyper secretion. 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 properties

Carbocisteine is rapidly absorbed from the gastrointestinal tract. In an 'in-house' study, at steady state (7 days) Carbocisteine 375 mg Capsules given as two capsules three times daily 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 _{1/2} (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

Derived Pharmacokinetic Parameters

*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 prescriber, which are additional to those already included in other sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:

Carbocisteine

Lactose monohydrate

Sodium Lauryl sulfate

Silica, colloidal anhydrous

Magnesium Stearate

Capsule Shell:

Gelatin

Sodium Lauryl sulfate

Size 1 golden yellow gelatin capsules containing iron oxide yellow (E172)

Titanium dioxide (E171)

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

Polypropylene container with polypropylene screw cap, containing 30 or 100 capsules.

PVC/PE/PVDC-Aluminium blister packs of 6, 18, 30 or 120 capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Brown & Burk UK Limited
5 Marryat Close, Hounslow West
Middlesex, TW4 5DQ
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 25298/0247

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/10/2019

10. DATE OF REVISION OF THE TEXT

30/10/2020