SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Carbocisteine 750 mg Capsules, Hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 750 mg of Carbocisteine.
Excipient (s) with known effect: Lactose (each capsule contains 27.50 mg of Lactose monohydrate)
For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsule, hard.

Turmeric yellow coloured cap/ Turmeric yellow coloured body, size "00" hard gelatin capsules imprinted "6C2" on cap and "750" 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 2250 mg Carbocisteine in divided doses, reducing to 1500 mg daily in divided doses when a satisfactory response is obtained e.g. one capsules three times a day reducing to one capsule two times a day.

Paediatric population:

This formulation is not recommended for children. The normal daily dosage is 20 mg/kg body weight in divided doses. It is recommended that this is achieved with carbocisteine paediatric syrup.

Method of administration

Carbocisteine 750 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
Experimental data did not demonstrate any effect on male and female fertility in rat.

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 (≥ 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).

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 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 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 properties

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:

Plasma Determinations	Mean	Range
T Max (Hr)	2.0	1.0-3.0
T½ (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 Laurilsulfate
Silica, colloidal anhydrous
Magnesium Stearate

Capsule Shell:
Gelatin
Sodium Laurilsulfate
Iron oxide yellow
Titanium dioxide

Printing Ink:
Shellac
Isopropyl alcohol
Butyl alcohol
Dehydrated alcohol
Propylene glycol
Strong Ammonium solution
Black Iron Oxide
Potassium hydroxide

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

PVC/PE/PVdC-Aluminium blister packs of 30 or 60 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 25298/0226

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/04/2020

10. DATE OF REVISION OF THE TEXT

09/07/2021