1. NAME OF THE MEDICINAL PRODUCT

Carbocisteine 250 mg/5 ml Adult Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of oral solution contains 250 mg of Carbocisteine. Also contains 0.5g of alcohol, 33mg of sodium and 2.5 g of liquid maltitol

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

Carbocisteine Syrup is clear pale yellow syrup with caramel odour

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.

This medicine is not recommended for use in children and adolescents under the age of 18 years due to the alcohol content.

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. for normal syrup 15ml tds reducing to 10ml tds.

Paediatric population:
This medicine is not recommended for use in children and adolescents under the age of 18 years due to alcohol content.

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 gastroduodenal 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 fructose intolerance, the lapp lactase deficiency or glucose-galactase malabsorption should not take this medicine.

Carbocisteine syrup is contraindicated for use in children less than 2 years of age.

Carbocisteine Syrup contains approximately 11.9 % ethanol (alcohol). A 15 ml dose of this medicine contains upto 1.5 g of ethanol; this is about the same amount of alcohol as 35.6 ml of beer or 14.8 ml of wine (i.e. 1/10 glass of wine) per dose. This can be harmful for those suffering from alcoholism. It should be taken into account in pregnant or breast feeding women and high risk groups such as patients with liver disease or fits (epilepsy).

This medicinal product contains 33 mg sodium per 5 ml, equivalent to 1.65 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Precautions for use

This medicine contains maltitol liquid, may have a mild laxative effect

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 known data available on the effects of this product on fertility in males or females.

4.7 Effects on ability to drive and use machines

Carbocisteine Syrup 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 Syrup.

Frequency not know: 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 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 Syrup overdosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: 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 properties

Carbocisteine is rapidly absorbed from the GI tract. In an 'in-house' study, at steady state (7 days) Carbocisteine capsules 375mg 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 section of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xanthan gum,
Sodium saccharin,
Liquid maltitol,
Ethanol 96%,
Sodium hydroxide,
Caramel flavouring agent*,
Purified water.

* Composition of caramel flavouring agent IFF SC227828 :
Diacetyl,
Propylene glycol,
Butyric acid,
Methylcyclopentenolone,
Maltol,
4-hydroxy-2,5-dimethyl-3(2H)-furanone,
piperonal and
Vanillin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Before opening: 36 months.
After the bottle has been opened: 15 days

6.4 Special precautions for storage

Do not store above 25 °C
Store in the original container and keep the bottle in outer carton in order to protect from light.

6.5 Nature and contents of container

Type III amber glass bottles closed with a polypropylene cap equipped with a low density polyethylene plug/seal. A polypropylene measuring cup is supplied with each bottle.
Pack sizes: 200 ml, 250 ml, 300 ml

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 Ltd
5 Marryat Close
Hounslow West
Middlesex
TW4 5DQ
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 25298/0082

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/02/2019

10. DATE OF REVISION OF THE TEXT

23/12/2020