SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Carbocisteine 375 mg Capsules, Hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 375mg of Carbocisteine.
Excipient(s) with known effect:
Each capsule contains 8.5mg of lactose monohydrate
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules, Hard (capsule)
Size “1” hard gelatin capsule having yellow cap & yellow body printed with “375” in black ink and containing a white to off white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Carbocisteine is a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterised by excessive or 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.

Children:

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

Method of administration

Carbocisteine 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 gastroduodenal ulcers, or those taking concomitant medications known to cause gastrointestinal bleeding. If gastrointestinal bleeding occurs, patients should discontinue medication.

Important information regarding the ingredients of this medicine

Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

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 (≥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 bullous dermatitis 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 Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mucolytic, 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
KEL (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

Plasma Determinations	Mean	Range
*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

Lactose Monohydrate
Colloidal Anhydrous Silica
Sodium Lauryl Sulfate
Magnesium stearate

Capsule Cap and Body
Iron Oxide Yellow (E172)
Titanium Dioxide (E171)
Sodium Lauryl Sulfate
Gelatin

Printing ink
Shellac

Strong Ammonia Solution
Black Iron Oxide (E172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container
Alu-PVC/PVDC blisters containing 6, 18, 30 or 120 capsules.
HDPE bottles containing 30 or 100 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0674

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/01/2019

10 DATE OF REVISION OF THE TEXT

07/05/2021