

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Carbocisteine 375 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Carbocisteine 375 mg

Excipient(s) with known effect:

Each capsule contains 22.00 mg lactose monohydrate.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Capsule

Yellow size '1' hard gelatin capsules imprinted with 'C' on cap and '375mg' on body with black ink containing white to off white granular powder or friable plug.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Carbocisteine is a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterized 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. two capsules three times a day reducing to one capsule four times a day.

Children:

This formulation is not recommended for children.

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.

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 this product.

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 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 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: Cough and cold preparations, mucolytics.

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 375mg Capsules 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 _{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
<u>Derived Pharmacokinetic Parameters</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 prescriber, which are additional to those already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica (E551),

Lactose monohydrate,

Magnesium stearate (E572)

Size '1' dark yellow hard gelatin capsules containing sodium lauryl sulfate, iron oxide yellow (E172) and titanium dioxide (E171).

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package.

6.5 Nature and contents of container

Aluminium-PVC/PVDC (60 g/m²) white opaque blister packs of 6, 18, 30 and 120 capsules.

The blisters and leaflet are inserted into cardboard cartons.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Flamingo Pharma UK Ltd.

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11-15 Peterborough Road,

Harrow, Middlesex,
HA12AX, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 43461/0008

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

03/01/2017

10 DATE OF REVISION OF THE TEXT

17/03/2021