

# 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 carbocisteine

### Excipient(s) with known effect

Each Carbocisteine 375 mg Hard Capsule contains 22.5 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Capsule, hard

Yellow cap and yellow body, size '0' hard gelatine capsule, filled with white to off white granular powder imprinted with C on cap and 375 on body.

## 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 and 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.

##### *Paediatric population*

Carbocisteine 375 mg Capsules, hard are not recommended for children.

#### Method of administration

For oral use.

### 4.3 Contraindications

This medicine is contraindicated in case of:

- Hypersensitivity to the active substance 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, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

#### 4.5 Interaction with other medicinal products and other forms of interactions

None stated.

#### 4.6 Fertility, pregnancy and lactation

##### Pregnancy

Although tests in mammalian species have revealed no teratogenic effects, carbocisteine is not recommended during the pregnancy unless considered essential by the physician.

##### Breast-feeding

It is unknown whether carbocisteine and / or its metabolites are excreted in human milk.

A risk to the newborn or infant cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from carbocisteine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

##### 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

None stated.

#### 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  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); 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 and fixed drug eruption.

##### Gastrointestinal disorders

There have been reports of gastrointestinal bleeding occurring during treatment with carbocisteine, however the frequency is not known. Vomiting has also been observed, though the frequency of this occurrence is not known.

##### 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 HPRC Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.

Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

#### 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 375 mg given as 2 capsules 3 times a day to healthy volunteers gave the following pharmacokinetic parameters:

<u>Plasma Determinations</u>	<u>Mean</u>	<u>Range</u>
$T_{ams}$ (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:

Lactose monohydrate  
Povidone  
Sodium lauril sulfate  
Magnesium stearate

#### Capsule shell

Gelatin  
Iron oxide yellow  
titanium dioxide (E171).

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

2 years

#### **6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

#### **6.5 Nature and contents of container**

The capsules are packaged in clear or opaque Alu-PVC blister packs.

Blister packs of 6, 18, 30 or 120 capsules.

Not all pack sizes may be marketed.

#### **6.6 Special precautions for disposal**

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

### **7 MARKETING AUTHORISATION HOLDER**

Key Pharmaceuticals Ltd.  
Galen House  
83 High Street, Somersham  
Cambridgeshire  
PE28 3JB  
United Kingdom

### **8 MARKETING AUTHORISATION NUMBER**

PA0343/008/001

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

Date of first authorisation: 6<sup>th</sup> March 2020

### **10 DATE OF REVISION OF THE TEXT**