SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Mucolit 375 Capsules
Mucolit Oral Solution 250 MG/ 5 ML
Mucolit 375 honey-lemon flavor lozenges
Tiptipot Mucolit

2. Qualitative and quantitative composition

Mucolit 375 Capsules
Each capsule contains 375 mg of Carbocysteine.

Mucolit Oral Solution 250 MG/ 5 ML
Each 5 ml of oral solution contains 250 mg of Carbocysteine.

Mucolit 375 honey-lemon flavor lozenges
Each lozenge contains 375 mg of Carbocysteine

Tiptipot Mucolit
Each ml contains 75mg of Carbocysteine.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Mucolit 375 Capsules:
Capsules.
Opaque blue cap and opaque yellow body, containing white to off-white powder.

Mucolit Oral Solution 250 mg/5 ml:
Oral Solution.
A clear, colorless to yellowish, slightly viscous and strawberry odor liquid.

Mucolit 375 honey-lemon flavor lozenges:
Lozenges.
Orange, round, flat lozenges, with a honey odor and honey-lemon flavor.

Tiptipot Mucolit:
Drops.
A slight yellowish to brownish liquid with a cream flavor.

4. Clinical particulars

4.1 Therapeutic indications

Treatment of disorders of the respiratory tract characterized by excessive or viscous mucus.

4.2 Posology and method of administration

Adults, including the elderly, and children over the age of 12:
Dosage is based upon an initial daily dosage of 2250mg Carbocysteine in divided doses, reducing to 1500mg daily in divided doses when a satisfactory response is

obtained e.g. two capsules/ lozenges three times a day reducing to one capsule/ lozenge four times a day or for oral solution 15ml three times a day reducing to 10ml three times a day.

Children:
Mucolit 375 Capsules and Mucolit 375 honey-lemon flavor lozenges are not recommended for children.
The normal daily dosage is 20mg-25/kg body weight in divided doses.
It is recommended that this is achieved with Mucolit Oral Solution or Tiptipot Mucolit only.

Oral Solution 250 mg/5 ml:
Children 2 – 5 years: The usual dose is 1.25 – 2.5 ml four times daily
Children 6– 12 years: The usual dose is 5 ml three times daily
It is recommended to wash the cup each time it is used.

Tiptipot Mucolit:
Children 2 – 5 years: 12-25 drops four times daily
Children 6– 12 years: The usual dose is 50 drops three times daily

Mucolit 375 Capsules, Mucolit 375 honey-lemon flavor lozenges, Mucolit oral solution, Tiptipot Mucolit are for oral use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Use in patients with active peptic ulceration.
- Use in children less than 2 years of age.

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.

- Excipients with known effect:
  <u>Mucolit Oral Solution 250 MG/ 5 ML</u>
  - This medicinal product contains Maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
  - This medicinal product contains 38 mg sodium per 5ml, equivalent to 1.9% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

  <u>Tiptipot Mucolit</u>
  - This medicinal product contains 15 mg sodium per 5ml, equivalent to 0.75% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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 Carbocysteine use in pregnant women. No conclusions can be drawn regarding whether or not Carbocysteine is safe for use during pregnancy. The use of Carbocysteine in pregnant women is not recommended, especially during the first trimester.

Breast-feeding
There are no available data on the presence of Carbocysteine in human milk, milk production, or the effects on the breastfed infant. No conclusions can be drawn regarding whether or not Carbocysteine is safe for use during breastfeeding. The use of Carbocysteine in breastfeeding women is not recommended.

4.7 Effects on ability to drive and use machines

Mucolit 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 Mucolit.
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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il/

4.9 Overdose

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC code: R05CB03

Carbocysteine (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 Carbocysteine 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 Carbocysteine reduces goblet cell hyperplasia. Carbocysteine can therefore be demonstrated to have a role in the management of disorders characterised by abnormal mucus.

5.2 Pharmacokinetic properties

Carbocysteine is rapidly absorbed from the GI tract. In a study conducted, at steady state (7 days) Carbocysteine 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
$AUG_{0.7.5}$ ($mcg.Hr.ml^{-1}$)	39.26	26.0-62.4

Derived Pharmacokinetic Parameters

CL_S ($L.Hr^{-1}$) - Calculated from dose for day 7 of study	20.2
CL_S ($ml.min^{-1}$)	331
V_D (L)	105.2
V_D ($L.Kg^{-1}$)	1/75

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

Mucolit 375 Capsules:
Microcrystalline Cellulose, Polyethylene Glycol 10000, Magnesium Stearate.
Capsule formula:
Iron yellow oxide, titanium dioxide, Brilliant blue FCF, Gelatin.

Mucolit Oral Solution:
Maltilol solution, sodium hydroxide, Sodium Citrate Dihydrate, Propylene Glycol, Hydroxyethyl Cellulose, Sodium Methyl Hydroxybenzoate, Strawberry flavor, Citric acid, Saccharin Sodium, Sodium Propyl Hydroxybenzoate.

Mucolit 375 honey-lemon flavor lozenges:
Xylitol, Sodium Starch Glycolate, Polyvinylpyrrolidone, Magnesium stearate, Microcrystalline Cellulose, Aspartame, Lemon Flavour, Honey Flavour, Quinoline yellow 70-E104, Sunset Yellow FCF E110.

Tiptipot Mucolit:
Sorbitol Solution 70%, Sodium Carbonate Decahydrate, Sodium Citrate, Sodium Methyl Hydroxybenzoate, Citric Acid, Cream essence, Saccharin Sodium, Disodium Edetate, Sodium Propyl Hydroxybenzoate, Purified water.

6.2 Incompatibilities
Mixture with linctus of pholcodine causes precipitation of Carbocysteine from solution.

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials.

Mucolit Oral Solution 250 MG/ 5 ML:
Discard 6 months after opening

Tiptipot Mucolit
Discard 2 months after opening

6.4 Special precautions for storage
Store below 25°C in original packaging. Do not freeze.

6.5 Special precautions for disposal and other handling
No special requirements.

7. Marketing authorisation holder
CTS Chemical industries Ltd.
3 Hakidma St.
Kiryat Malachi

8. Marketing authorisation number(s)
Mucolit 375 Capsules: 0633525396
Mucolit Oral Solution 250mg/ 5ml: 1574134597
Mucolit 375 honey-lemon flavor lozenges: 1420229736
Tiptipot Mucolit: 1225430239

9. Date of revision of the text:
Revised in 01/2021 according to the MOHs guidelines