**Summary of Product Characteristics for Pharmaceutical Products**

## 1. Name of the medicinal product

ISOCET-P syrup

## 2. Qualitative and quantitative composition

Each 5 ml contains: Carbocisteine 100mg and
Promethazine hydrochloride 2.5mg

For the full list of excipients, see section 6.1.

## 3. Pharmaceutical form

Oral syrup
Orange colored syrup, free from visible impurities

## 4. Clinical particulars

### 4.1. Therapeutic indications

Symptomatic treatment of troublesome, non-productive cough, particularly occurring at night.

### 4.2 Posology and method of administration

Adults: 3 to 4 spoons (15 ml to 20 ml) three times a day.

Children: 2-5 years of age (2.5 ml to 5 ml) four times a day.
6-12 years of age 1½ to 2½ spoons (7.5 ml to 12.5 ml) three times a day. 12 -15 years of age 2½ to 3 spoons (12.5 ml to 15 ml) three times a day.

### 4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients
History of agranulocytosis
Risk of urinary retention related to urethro- prostatic disorders
Risk of angle-closure glaucoma
Children <2 years (due to the potential for fatal respiratory. depression).
Should NOT BE USED during pregnancy
Carbocisteine with Promethazine must generally not be used, unless otherwise indicated by the doctor, in combination with Sultopride.

### 4.4 Special warnings and precautions for use

This product contains promethazine hydrochloride. It should not be used in pediatric patients less than 2 years of age because of the potential for fatal respiratory depression.

To be used with caution and on physician advice in children 2 to 6 years of age.
Caution is recommended in the elderly, in patients with a history of gastroduodenal ulcers, and in those taking concomitant medications which may cause gastrointestinal bleeding.

If gastrointestinal bleeding occurs, patients should discontinue medication.
Monitoring (clinical and ECG where appropriate) should be increased in patients with epilepsy due to the possible lowering of the seizure threshold.
Should be used with caution in elderly subjects with:

- greater sensitivity to postural hypotension, dizziness and sedation
- chronic constipation (risk of paralytic

Should be used with caution in patients with certain cardiovascular diseases, due to the tachycardia- inducing and hypotensive effects of phenothiazines

Should be used with caution in patients with severe liver and/or kidney failure (due to the risk of accumulation)

Should be used with caution in case of concomitant use of CNS depressants (due to a risk of respiratory depression).

Concomitant use of promethazine and sodium oxybate is not recommended
In view of its H1-antihistamine sedating properties, promethazine should be used with caution due to its risk of sedation. Combination with other sedative medicinal products should be discouraged

Due to the anticholinergic properties of promethazine, the risk of severe constipation or even enterocolitis is increased when combined with other anticholinergic or neuroleptic medicinal products

This medicinal product contains 3 g of sucrose per measuring spoon and 9 g per tablespoon, which must be taken into account in the daily ration in case of a low sugar diet or diabetes mellitus.

In the event of long-standing disease of the liver or kidneys, consult the doctor for dosage adjustment. Refrain from alcoholic beverages or drugs containing alcohol throughout the duration of treatment.

Preferably avoid exposure to sunlight during the treatment.

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

Atropine-like medicinal products
It should be taken into account that atropine-like substances can have additive adverse effects and more easily lead to urinary retention, acute attacks of glaucoma, constipation, dry mouth, etc.
The various atropine-like medicinal products include imipramine antidepressants, most atropine-like H1- antihistamines, anticholinergic antiparkinsonians, atropine-like antispasmodics, disopyramide, phenothiazine neuroleptics and clozapine

Medications that lower the seizure threshold
The concomitant use of a pro-convulsant or medicinal products that lower the convulsive threshold should be carefully weighed because of the severity of the risk involved. These medicinal products include most antidepressants (imipramine agents, selective serotonin reuptake inhibitors), neuroleptics (phenothiazines and butyrophenones), mefloquine, chloroquine, bupropion and tramadol.

Sedative medicinal products
It should be taken into account that many medicinal products or substances can have additive depressant effects on the central nervous system and contribute to a decrease in alertness. These medicinal products include morphine derivatives (analgesics, antitussives and replacement therapies), neuroleptics, barbiturates, benzodiazepines, non-benzodiazepine anxiolytics (such as meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1- antihistamines, centrally-acting antihypertensives, baclofen and thalidomide.

Alcohol (beverage or excipients)
The sedative effect of promethazine is increased by alcohol. Impaired alertness may make driving vehicles and using machines dangerous.
The consumption of alcoholic beverages or medicinal products containing alcohol should be avoided.

Sodium oxybate
Increased CNS depression. Impaired alertness may make driving vehicles and using machines dangerous.

Combinations requiring precautions for use

With Topical agents for gastrointestinal use, antacids and adsorbents (charcoal):
Decreased gastrointestinal absorption of the active ingredients.Allow an interval (2 hours, if possible) between administration of topical gastrointestinal agents or antacids and phenothiazine neuroleptics.

With Lithium:
Risk of occurrence of neuropsychiatric signs suggestive of neuroleptic malignant syndrome or lithium intoxication. Regular clinical and laboratory monitoring is required, especially at the start of co-administration.

Combinations to be taken into consideration
With Anticholinesterases:
Risk of reduced efficacy of anticholinesterases via acetylcholine receptor antagonism due to the atropine.

With Other central nervous system depressants (sedative antidepressants, barbiturates, clonidine and related, hypnotics, morphine derivatives (analgesics and antitussives), methadone, neuroleptics, anxiolytics). Will lead to Increased CNS depression, change in alertness can make driving and using machines dangerous.

Other medicinal products that lower the convulsive threshold
Increased risk of convulsions.

Atropine-like medicinal products
(imipramine antidepressants, anticholinergic addition, atropine antispasmodics, disopyramide, phenothiazine neuroleptics)
Addition of atropine undesirable effects, such as urinary retention, constipation, dry mouth.

Other hypnotic agents
Increased CNS depression

Other sedative medicinal products
Increased CNS depression. Change in alertness can make driving and using machines dangerous.

Other Orthostatic Hypotension-inducing medicinal products
Risk of increased adverse effects, particularly dizziness or syncope.

Beta-blockers in heart failure
Vasodilator effect and risk of hypotension, particularly postural (additive effect).

Dapoxetine
Risk of increased adverse effects, particularly dizziness or syncope.

Blood pressure-lowering medicinal products
Risk of increased hypotension, especially orthostatic hypotension.

Opioids
Significant risk of colonic akinesia, with severe constipation.

Orlistat
Risk of treatment failure if administered concomitantly with orlistat.

## 4.6 Fertility, pregnancy, and lactation

**Pregnancy:**
Contraindicated
during pregnancy

**Lactation:** Carbocisteine with Promethazine is excreted in breast milk. Do not take this drug if breastfeeding.

## 4.7 Effects on ability to drive and use machines.

Attention, particularly which of drivers and machine users, is drawn to the possibility of drowsiness associated with the use of Carbocisteine with Promethazine. Patients should be advised that if they feel drowsy, they should not drive or operate heavy machinery.

## 4.8 Undesirable effects

Related to the carbocisteine content:

- Risk of bronchial congestion, especially in infants and certain patients unable to expectorateeffectively
- Allergic skin reactions such as pruritus, erythematous eruption, urticaria and angioedema.
- A few cases of fixed pigmented erythema have been reported.
- Gastrointestinal disorders (gastric pain, nausea, vomiting and diarrhea). If these occur, the doseshould be reduced.
- Gastrointestinal bleeding. Treatment should be discontinued.
- Isolated cases of bullous dermatoses, such as Stevens-Johnson syndrome and erythema multiforme Immune system disorders, Anaphylactic/ anaphylactoid reaction Skin and subcutaneous tissue disorders
- Severe cutaneous adverse reactions (SCAR) e.g. erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). In most of these cases reported at least one other drug was administered at the same time, which may have possibly enhanced the described mucocutaneous effects.

Related to the promethazine content:
The pharmacological characteristics of this compound can cause undesirable effects that vary in severity and may or may not be dose-dependent.

- Neurovegetative effects
  sedation or drowsiness, more significant at the start of treatment anticholinergic effects, such as dry mucous membranes, constipation, intestinal obstruction, ischemic colitis (see section, accommodation disorders, mydriasis, cardiac palpitations, risk of urinary retention, orthostatic hypotension
- balance disorders, dizziness, memory or concentration problems
- dyskinesia, tardive dyskinesia, abnormal movements, motor incoordination, tremor (more common in the elderly), akathisia
- mental confusion, hallucinations
- more rarely, effects such as excitement, agitation, nervousness, insomnia Respiratory effects: respiratory depression
- Sensitivity reactions
  erythema, eczema, pruritus, purpura, urticaria and possibly giant urticaria
  oedema, in rarer cases angioedema
  anaphylactic shock
- leucopenia, neutropenia and, exceptionally, agranulocytosis
- thrombocytopenia
- hemolytic anemia

**4.9 Overdose**

Gastrointestinal disturbance (gastralgias, nausea and vomiting) are the most likely symptoms of Carbocisteine overdosage.
Signs of promethazine overdose: seizures (especially in children), consciousness disorders, coma

**5.0 Pharmacological properties**

**5.1 Pharmacodynamic Properties**

Antihistamine for systemic use (Respiratory system, ATC code: R06AD02) Promethazine

Carbocisteine is a mucolytic agent which decreases the viscosity of the mucus, fluidizes it and facilitates its evacuation, thus promoting recovery. As a muco-regulatory agent, it helps regenerate the impaired bronchial mucosa. Promethazine, a phenothiazine derivative, is a sedating antihistamine with antimuscarinic, significant sedative, and some serotonin-antagonist properties. Promethazine hydrochloride is used for the symptomatic relief of allergic conditions including urticaria and angioedema, rhinitis and conjunctivitis, and in pruritic skin disorders.

**5.2 Pharmacokinetic properties**

Carbocisteine:
Orally administered carbocisteine is rapidly absorbed. Peak plasma concentrations are reached in two hours. Bioavailability is low (less than 10% of the administered dose), probably as a result of intraluminal metabolism and a marked liver first-pass effect. Elimination half-life is approximately two hours.
Carbocisteine and its metabolites are eliminated primarily in the kidneys.

Promethazine:
The bioavailability of promethazine is between 13 and 40%. Peak plasma concentrations are reached within 1.5 to 3 hours.
The volume of distribution is high due to the lipophilicity of the compound, approximately 15 L/kg. The drug is 75-80% plasma protein bound.
The half-life is between 10 and 15 hours.
Metabolism consists of sulfoxidation followed by demethylation.
Renal clearance represents less than 1% of total clearance and approximately 1% of administered promethazine is detected unchanged in the urine.
The metabolites found in the urine, particularly in sulfoxide form, represents approximately 20% of the dose.

## 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

# 6.0 Pharmaceutical particulars

## 6.1 List of excipients

- Sodium Hydroxide
- Sorbitol 70% liquid
- Sodium Methyl Paraben
- Sodium propyl Paraben
- Sodium saccharin
- Sodium citrate
- anhydrous Citric acid
- Honey flavour
- Sunset yellow colour
- Purified Water

## 6.2 Incompatibilities

Not applicable

**6.3 Shelf-life**

36 months

**6.4 Special precautions for storage**

Store in a dry place, below 30°C.Protected from direct sunlight Keep all medicines out of reach of children.

**6.5 Nature and contents of container**

100ml in a well labeled amber colored PET bottle in a unit box, with literature insert.

**6.6 Special precautions for disposal and other handling**

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

**7. Marketing authorization holder and manufacturing site addresses**

**Marketing authorization holder:**

Medcure Healthcare Limited, P.O Box 14609-00200, Kensia House, Muranga Road, Nairobi, Kenya.

**Manufacturing site address:**

Stedam Pharma Manufacturing Limited**,** P.O Box 35240-00200, North Airport Road, Plot no. 20753, Nairobi, Kenya.

**8. Marketing authorization number**

CTD9694

**9. Date of first registration**

29/05/2023

**10. Date of revision of the text:**

17/09/2023

**11. Dosimetry:**

Not Applicable

**12. Instructions for Preparation of Radiopharmaceuticals:**

Not Applicable