

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fluifort 90 mg/ml syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml syrup contains:

active ingredient: carbocysteine monohydrate lysine salt equivalent to 9 g carbocysteine lysine salt

For the excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Mucolytic, fluidifying agent in the acute and chronic diseases of the respiratory system.

4.2 Posology and method of administration

A measuring cup is enclosed in the package.

To open the bottle press the cap and turn counterclockwise.

Adults:

15 ml 2-3 times a day or according to medical prescription.

The maximum duration of therapy is up to 14 days. However, carbocysteine monohydrate lysine salt can also be used for prolonged periods, according to the doctor's judgment.

Children:

- older than 5 years of age: 5 ml 2-3 times a day or according to medical prescription
- 2 to 5 years of age: 2.5 ml 2-3 times a day or according to medical prescription

The maximum duration of therapy is up to 7 days. However, carbocysteine monohydrate lysine salt can also be used for prolonged periods, according to the doctor's judgment.

Patients with liver or kidney impairment:

The normal dosage can be used.

4.3 Contraindications

Hypersensitivity to the active ingredient or to any of the excipients. Gastric-duodenal ulcer. Pregnancy and lactation. This product is contraindicated in children below 2 years.

4.4 Special warnings and precautions for use

Mucolytic agents could induce bronchial obstruction in children below 2 years. Indeed bronchial mucus drainage capability is limited in this age, because of the physiologic features of the respiratory tract.

They should not be used in children below 2 years (see Section 4.3).

Gastrointestinal bleeding

Cases of gastrointestinal bleeding have been reported with the use of carbocysteine. Caution is recommended in the elderly, in patients with a history of gastroduodenal ulcers or in patients taking concomitant medications known to increase the risk of gastrointestinal bleeding. In case of gastrointestinal bleeding, the patient should discontinue carbocysteine treatment.

Asthmatic and debilitated patients:

Specific precautions are recommended in patients with severe respiratory insufficiency, in patients with asthma and a history of bronchospasm, as well as in debilitated patients. The use of carbocysteine causes a decrease in mucus viscosity and an increase in mucus clearance, both through the ciliary activity of the epithelium and through the cough reflex. Therefore, an increase in cough and sputum is expected. The use of antitussive medicines inhibits the cough reflex and increases the risk of airway obstruction, due to increased accumulation of mucus in the airways. Concomitant use of this medicine with antitussive medicines and/or medicines that inhibit bronchial secretion (e.g. anti-muscarinic medicines) is not recommended.

No tolerance or dependence phenomena are known.

This product should not be administered to patients with rare inherited problems of glucose intolerance, glucose-galactose malabsorption or insufficiency of the saccharose-isomaltase enzyme.

The product contains methyl-para-hydroxybenzoate, known to possibly cause urticaria. Para-hydroxybenzoates may generally cause delayed reactions, such as contact dermatitis, and they may rarely cause immediate reactions with manifestations of urticaria and bronchospasm.

Fluifort 90 mg/ml syrup does not contain gluten; therefore, it may be administered to patients suffering from celiac disease.

Fluifort 90 mg/ml syrup does not contain aspartame; therefore, it may be administered to patients suffering from phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

In controlled clinical trials, no interactions with the most commonly used drugs for the treatment of upper and lower airways disorders nor with food and laboratory tests have been observed.

4.6 Pregnancy and lactation

Although the active ingredient is neither teratogenic nor mutagenic and has not shown any negative effect on the reproductive function in animals, Fluifort should not be administered during pregnancy (see 4.3). As no data are available concerning the excretion of carbocysteine monohydrate lysine salt in breast milk, use of the medicinal product during lactation is contraindicated (see 4.3).

4.7 Effects on ability to drive and use machines

No negative effects of the drug on the ability to drive or use machines have been reported or can be assumed.

4.8 Undesirable effects

Undesirable effects are described according to MedDRA system organ class and based on frequency estimated from post-marketing experience.

Frequencies are defined as follows: very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon: ($\geq 1/1,000$, $< 1/100$); rare ($\geq 1/10,000$, $< 1/1,000$); very rare ($< 1/10,000$); not known (frequency cannot be estimated from the available data).

Classification	Frequency	Adverse reaction
Skin, subcutaneous tissue	Not known	Skin rash, urticaria, erythema, exanthema, exanthema/erythema bullous, pruritus, angioedema, dermatitis, Stevens-Johnson Syndrome, bullous dermatitis, erythema multiforme, toxic skin eruption.
Gastrointestinal system	Not known	Abdominal pain, nausea, vomiting, diarrhea, gastrointestinal bleeding
Nervous system	Not known	Vertigo
Respiratory system	Not known	Dyspnea
Cardiovascular system	Not known	Flushing

Bronchial obstruction may occur after oral and rectal use of mucolytic agents (unknown frequency).

The medicine contains methyl-p-hydroxybenzoate, known for the possibility of causing urticaria. In general the para-hydroxybenzoates may cause delayed reactions, such as contact dermatitis, and rarely immediate reactions with manifestations of urticaria and bronchospasm.

4.9 Overdose

Very rare cases of adverse reactions occurring in patients treated with doses of Fluifort 2-3 times higher than the recommended doses have been reported. Reactions were never severe. The symptoms reported in these cases mainly included skin reactions, with two single cases of gastrointestinal events and alterations of sensory systems, respectively.

Furthermore, a case of a 9-year-old boy treated with a dosage inadequate for his age (2.7 g/day per single administration) has been reported. Immediately after the intake, the patient has repeatedly experienced vomiting.

No specific antidote exists; gastric lavage followed by a specific support therapy is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Preparations for cough and cold diseases; expectorants except for the combinations with cough sedatives, mucolytics.

ATC code: R05CB03

Carbocysteine monohydrate lysine salt restores in a dose-dependent manner the viscosity and elasticity of the mucous secretions at the level of the upper and lower airways. The drug efficacy in normalizing the mucous secretions seems to be due to the capacity of increasing the synthesis of sialomucins thus restoring the equilibrium between sialo- and fuco-mucins, a fundamental element that contributes to the fluidity of mucus.

Moreover, carbocysteine monohydrate lysine salt stimulates the secretion of chloride ions in the epithelium of the airways, a phenomenon which is associated with the transport of water

and, thus, with the fluidification of mucus. In the rabbit, oral administration of carbocysteine monohydrate lysine salt prevents the reduction of mucociliary transport determined by the intratracheal instillation of exogenous elastase.

Carbocysteine monohydrate lysine salt increases in a dose-dependent manner the concentration of lactoferrin, lysozyme and alpha1-antichymotrypsin, indicating a functional resumption of the serum cells of peribronchial glands and of their mechanisms of proteic synthesis.

Carbocysteine monohydrate lysine salt has demonstrated a positive effect on the production of nasal secretory and tracheobronchial IgA.

Furthermore, carbocysteine monohydrate lysine salt improves the mucociliary clearance and the diffusibility of the antibiotic.

5.2 Pharmacokinetic properties

After oral administration, carbocysteine monohydrate lysine salt is quite completely and rapidly absorbed. The absorption peak occurs in 1.5-2 hours. The plasma half-life is about 1.5 hours. The elimination of carbocysteine monohydrate lysine salt and of its metabolites mainly occurs through the kidney. The product is excreted unchanged in the urines for 30-60% of the administered dose; the remainder is excreted in the form of various metabolites. As for all derivatives with a blocked thiolytic group, carbocysteine monohydrate lysine salt specifically fixes to the bronchopulmonary tissue. The drug achieves median concentrations of 3.5 µg/ml in the mucus, with a half-time of about 1.8 hours (2 g/day dose).

The bioavailability of carbocysteine is not affected by the different pharmaceutical forms.

5.3 Preclinical safety data

The acute, subacute and chronic toxicity studies have not evidenced the occurrence of any toxicity at dosages that were remarkably higher than those therapeutically recommended (DL₅₀ in mg/kg: mouse and rat i.p. > 5760; mouse and rat orally > 13500. Non toxic doses in chronic studies: 3 months oral study in dogs = 300 mg/kg/day; 6 months oral study in rats = 500 mg/kg/day).

Teratogenic studies conducted in two animal species (rat and rabbit) have not shown organogenetic anomalies. Reproductive toxicity studies conducted in the rat demonstrated that carbocysteine monohydrate lysine salt does not interfere with the fertility, reproduction, embryo-fetal and post-natal development.

The product is not chemically related with cancerogenic compounds and has been shown not to be mutagenic in “in vitro” and “in vivo” genotoxicity tests.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Saccharose, natural cherry flavour, methyl-para-hydroxybenzoate, caramel, purified water.

6.2 Incompatibilities

None

6.3 Shelf life

Two years

The expiry date refers to the product in the original package and correctly stored.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Fluifort Syrup is a clear, brilliant, yellowish brown liquid.

Each bottle along with instructions for the application is packaged in a cardboard box containing a spoon or cup.

Children's packing: 40 ml in bottle along with spoon.

Packaging for adults: 120 ml in bottle with measuring cup.

6.6 Special precaution for disposal

No special requirements

7. MARKETING AUTHORIZATION HOLDER

Eurodrug Laboratories S.A.
Kortrijksesteenweg 214
9830 Sint-Martens-Latem
Belgium

8. MARKETING AUTHORIZATION NUMBER

9. DATE OF REVISION OF THE TEXT

June 2023