

# SUMMARY OF PRODUCT CHARACTERISTICS

## AMBROTON

Syrup 15mg/5ml

### 1. NAME OF THE MEDICINAL PRODUCT

Ambroton

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of syrup contains 3 mg ambroxol hydrochloride.

For a full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

Syrup

Ambroton syrup is a clear or almost clear, colourless or almost colourless, slightly viscous syrup.

### 4. CLINICAL PARTICULARS

#### **4.1 Therapeutic indication**

Acute and chronic respiratory diseases with the release of viscous mucus: acute and chronic bronchitis, pneumonia, chronic obstructive pulmonary disease, bronchial asthma with obstruction of sputum discharge, multiple bronchiectasis.

#### **4.2 Posology and method of administration**

For oral use, regardless of the meals.

Children 6-12 years: 5ml (15mg ambroxol) 2-3 times/day. The maximum dose - 45mg/day. After 2-3 days, if the child is getting better, the drug can be taken 2 times/day.

Children 2-5 years: 2.5ml (7.5mg ambroxol) 3 times/day; the maximum dose - 22.5mg/day. After 2-3 days, if the child is getting better, the drug can be taken 2 times/day.

Children under 2 years of age: the drug is contraindicated in children under 2 years of age.

*Patients with impaired renal and hepatic function:* Patients with impaired renal function or severe liver dysfunction should take the medication only as directed by a physician. Meanwhile the dose should be either reduced or the time between doses should be increased.

*Missed dose:* If the patient has forgotten to take medication or took an insufficient dose, he/she needs to continue taking the drug according to the dose regimen. If symptoms do not improve or worsen after 5 days of treatment, consult your doctor.

### **4.3 Contraindication**

Hypersensitivity to ambroxol or other components of the drug.

First trimester of pregnancy.

A rare hereditary intolerance to any component of Ambroton (see "Special precautions").

Children under 2 years of age.

*Use with caution* in II and III trimester of pregnancy, lactation, renal and/or hepatic insufficiency.

### **4.4 Special warnings and precautions for use**

During treatment, it is recommended to consume plenty of fluids (water, tea, juice) to enhance the mucolytic effect of the drug.

Very rare cases of severe skin lesions, including Stevens-Johnson syndrome and toxic epidermal necrolysis associated with the acquisition of mucolytics such as ambroxol hydrochloride were recorded. As a rule, these cases can be explained by the severity of the associated disease or concomitant use of other drugs. In addition, in the early stage of Stevens-Johnson and Lyell's syndrome, signs of nonspecific flu-like disease may start: fever, body ache, rhinitis, cough and sore throat. The appearance of these symptoms can lead to unnecessary symptomatic treatment by cough medications. Therefore, in the event of skin or mucosa lesions, immediately consult a doctor and, as a precautionary measure, discontinue the treatment by ambroxol hydrochloride.

In renal impairment or severe hepatic dysfunction medication should be taken only after consultation with doctor.

When prescribing this medication to children of 2-6 years of age, the risk/benefit ratio should be taken into account.

Patients with impaired bronchial motility and copious bronchial secretions (as for example, in a rare syndrome of primary ciliary dyskinesia), this drug should be used with caution because of the risk of a discharge of a large volume of sputum and bronchial obstruction.

AMBROTON syrup 5 ml contains 1.2 g sorbitol resulting in 7.2 g sorbitol per maximum recommended daily dose (30 ml). Patients with rare hereditary fructose intolerance should not take this medicine. It may also have a mild laxative effect.

### **4.5 Interactions with other medicinal products and other forms of interaction**

Ambroton is compatible with drugs inhibiting birth activity. Use with antitussives causes difficulty in sputum discharge along with reduced coughing. It increases concentration and penetration of amoxicillin, cefuroxime, and erythromycin in bronchial secretions.

#### **4.6 Pregnancy and lactation**

Preclinical studies and extensive clinical experience in the use of the drug showed no adverse effects of the drug during pregnancy. However, the general rules of drug prescription in pregnancy should be followed. The drug is not recommended during the first trimester of pregnancy. Ambroton passes into breast milk. Although adverse effects of ambroton in children are not expected, the drug is not recommended for use during breastfeeding.

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

There are no reported cases on the influence of the drug on the ability to drive and use machines. Relevant studies have not been conducted.

#### **4.8 Undesirable effects**

*Immune system:* anaphylactic reactions (including anaphylaxis) and other hypersensitivity reactions.

*CNS:* dysgeusia (*distortion of the sense of taste*).

*Respiratory system, the organs of the chest and mediastinum:* dysesthesia of the mouth and throat.

*GIT:* nausea, oral hypesthesia, vomiting, diarrhea, dyspepsia, abdominal pain, dry mouth, dry throat, heartburn, constipation, hypersalivation.

*Skin and subcutaneous tissues:* rash, urticaria, angioedema, pruritus.

*Urogenital system:* dysuria.

#### **4.9 Overdose**

Symptoms of overdose in humans have not been described. In case of an accidental overdose and / or cases of medical errors the observed symptoms are consistent with known side effects when taking Ambroton at recommended doses. *Possible side effects:* nausea, vomiting, diarrhea, dyspepsia. *Treatment:* induction of vomiting and gastric lavage during first 1-2 hours after taking the medicine, taking fat-containing food, symptomatic therapy.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

*Pharmacotherapeutic group:* Cough and cold preparations. Mucolytics. ATC code: R05CB06

Ambroxol has secretomotor, secretolytic and expectorant action. Stimulates serous cells of the bronchial mucosa glands, increases the amount of mucous secretion and release of surfactant in the alveoli and bronchi. It normalizes impaired ratio of serous and mucous components of sputum. Reduces the viscosity of sputum activating

hydrolases and increasing the release of lysosomes from the cells of Clara. Increases motor activity of the cilia of ciliated epithelium, increases mucociliary transport of sputum.

Local anesthetic effect was observed in *in vitro* studies due to the ability of ambroxol to block sodium channels. This process is reversible and concentration-dependent.

Clinical efficacy studies for the treatment with ambroxol of upper respiratory tract symptoms have shown rapid relief of pain and pain related discomfort in the ear-nose-trachea region upon inhalation.

It was also found that the release of cytokines from mononuclear and polymorphonuclear blood cells was significantly reduced.

### **5.2 Pharmacokinetic properties**

*Absorption:* absorption is high, maximum concentration is reached in 1-2.5h after oral administration.

*Distribution:* ambroxol hydrochloride distribution from blood into tissues is rapid and pronounced, and the highest concentration is observed in the lungs. The distribution volume after oral intake is 552 liters. Binding to plasma proteins is 90%. Ambroxol crosses brain-blood and placental barriers, and is excreted in the breast milk.

*Metabolism and excretion:* ambroxol is metabolized in the liver by conjugation, forms dibromanthranilic acid (about 10% of the dose), glucuronic conjugates and several secondary metabolites. Studies of human liver microsomes showed that CYP3F4 is a predominant enzyme responsible for the metabolism of ambroxol. About 30% of an oral dose is excreted as a result of first pass metabolism. Ambroxol hydrochloride has a half-life of 10 hours. The total clearance is within 660ml/min, renal clearance accounts for about 8% of the total clearance.

*Pharmacokinetics in special patient groups:* since the drug is metabolized in the liver and excreted by the kidneys, in case of severe renal dysfunction, accumulation of ambroxol metabolites formed in the liver may take place. In patients with impaired liver function elimination of ambroxol is decreased, leading to its increased level in the blood plasma 1.3-2 times.

Studies have shown that the pharmacokinetics of ambroxol is not sex- or age-dependent and does not require dose adjustments. Food intake has no effect on its bioavailability.

### **5.3 Preclinical safety data**

The acute oral, intravenous, subcutaneous and intraperitoneal toxicity of ambroxol in animals is low. It has a low index for acute toxicity. In repeat-dose studies, oral doses of 150 mg/kg/day (mouse, 4 weeks), 50 mg/kg/day (rat, 52 and 78 weeks) and 10 mg/kg/day (dog, 52 weeks) were the no-observed adverse effect level (NOAEL).

In vitro and in vivo studies did not reveal any mutagenic and tumorigenic potential. Ambroxol hydrochloride was neither embryotoxic nor teratogenic when tested at oral doses up to 3000 mg/kg/day in rats and up to 200 mg/kg/day in rabbits.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 *List of excipients:***

Benzoic acid (E210)

Hydroxyethyl cellulose

Acesulfame potassium (E950)

Sorbitol liquid non-crystallizing (E420)

Glycerol 99.5%

Flavor "raspberry flavoring"

Purified water

### **6.2 *Incompatibilities***

No information available.

### **6.3 *Proposed shelf life***

36 months from the date of manufacturing. 90 days after first opening. Do not use after expiration date mentioned in the package.

### **6.4 *Storage Conditions***

Store at temperature below 30°C, do not freeze. Keep out of reach of children.

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

100 ml of syrup in a dark glass bottle with a measuring spoon and patient information leaflet in a carton.

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

Non-prescription medicine.

## **7. MANUFACTURER**

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## **8. MARKETING AUTHORIZATION HOLDER**

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