1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Summary Product Characteristics (SPC)

Name of the medicinal product
Ambroxol Hydrochloride Syrup

Quantitative and qualitative composition
Ambroxol Hydrochloride
Each 5ml of oral solution contains 2.5 mg Ambroxol Hydrochloride.

Pharmaceutical form
Syrup

Clinical Particulars
Therapeutic indications
Productive cough Acute and chronic inflammatory disorders of respiratory tractsconcomitant with formation of viscous and hardly separated expectoration Acute and chronic inflammatory disease of rhinopharyngeal tract (laryngitis, pharyngitis, sinusitis and rhinitis) associated with viscid mucus
Asthmatic bronchitis, bronchial asthma with thick, hard expectoration
Bronchiectasis, Chronic pneumonia

Posology and route of administration
Posology
Syrup:
2-5 years old: 2.5 ml (1/2 teaspoonful), 2-3 times a day
5-10 years old: 5 ml (1 teaspoonful), 2-3 times a day
10 years old and adults: 10 ml (2 teaspoonful), 3 times a day
Method of administration
Oral use.
The dose can be taken preferably after meal.

Contraindications
First trimester of pregnancy, gastroduodenal ulcer, hypersensitivity to any component of the preparation.

Special warnings and precautions for use
Should be cautiously used in patients with increased sputum secretion and disorders of secretion discharge (such as the rare malignant cilia syndrome) due to a risk of airway obstruction because of impaired bronchi motor function and a large quantity of bronchial secretions.
In case of renal and/or liver disease the dose is reduced or the interval between the drug intakes is extended.
In case of severe renal insufficiency ambroxol metabolite accumulation is expected.
Should be used cautiously in patients with peptic ulcer disease history as mucolytic products may weaken gastric mucosal barrier.
There are very rare reports of severe skin reactions (e.g. Stevens-Johnson syndrome and Lyell's syndrome) occurrence during of Ambroxol administration. In case of changes of skin

and mucous membranes, Ambroxol administration should be immediately discontinued and the appropriate treatment should be carried out.

Interaction with other medicinal products and other forms of interaction
Ambroxol is not recommended for co-administration with expectorants (e.g, codeine), Cough reflex depression may occur due to excessive accumulation of sputum and threatening obstruction of respiratory tract.
Clinically significant adverse interactions with other drugs have not been observed.
The drug can be used simultaneously with antibiotics such as amoxicillin, cefuroxime, erythromycin and doxycycline, antibiotics penetration into lung tissues and their efficacy increase.

Pregnancy and lactation
Pregnancy
There was not detected a harmful effect on foetus development in animal studies. A potential risk to people is not known. Administration of the medicine is allowable only in cases when the expected benefit outweighs the potential risk.
Breast-feeding
Ambroxol penetrates into breast milk. It is not allowed to use during breastfeeding.

Effects on ability to drive and use machines
Drug administration has no influence on the ability to drive and use machines.

Undesirable effects
Like all medicines, Ambroxol can cause side effects, although not everybody gets them. Side effects are mainly dependent on the dose and different patients may have various side effects.
Classification of side effects frequency:
Very common: affect more than 1 in 10 treated patients
Common: affect less than 1 in 10, but more than 1 in 100 treated patients
Uncommon: affect less than 1 in 100, but more than 1 in 1,000 treated patients
Rare: affect less than 1 in 1,000 but more than 1 in 10,000 treated patients
Very rare: affect less than 1 in 10,000 treated patients including some case reports.
Side effects are observed if Ambroxol is used at high doses and for a long period.
Nervous system disorders: rare –headache.
Respiratory, thoracic and mediastinal disorders: rare - dry airways, increased nasal secretions.
Gastrointestinal disorders: rare - dry mouth, nausea, vomiting, diarrhea, epigastric pain, constipation.
Skin and subcutaneous tissue disorders: very rare, severe skin reactions such as Stevens-Johnson
syndrome and epidermal necrolysis.
General disorders and reactions in the place of administration: rare - hypersensitivity reactions (skin rash, facial swelling, shortness of breath, fever), fatigue. In case of hypersensitivity drug should be discontinued immediately and the appropriate treatment should be carried out.

Overdose

Ambroxol is low toxic, even at the dose 25 mg/kg of body weight a day. In case of overdose severe poisoning effects have been observed. *Symptoms:* the short-term anxiety, diarrhea, excessive saliva secretion, throat irritation, vomiting, and hypotension.
Events: gastric lavage (first 2 hours after ingestion) should be carried out only in case of a very high overdose. Patient should be observed and ensured symptomatic therapy.
There is no specific antidote.

Pharmacological Properties
Pharmacodynamic properties

Pharmacotherapeutic group: mucolytic agents.
ATC code: R05CB06.
The drug's active substance ambroxol (benzylamine derivative, bromhexine metabolite) is a direct action broncho-secretolytic or mucolytic agent with a strong expectorant effect. Ambroxol has secretolytic and secretomotoric effect. Ambroxol stimulates lysosomal enzymes release and hydrolytic enzymes activity in mucolytic cells that contribute to polysaccharide and protein cleavage in bronchial sputum. Ambroxol promote bronchial mucous glands serosa cells activity, thereby normalizing the serosa and mucous component of the relationship of bronchial secretions. As a result, sputum viscosity decreases. Ambroxol increases the amount of surfactant in the lungs, stimulating the synthesis and secretion in alveolar pneumocytes, promotes mucociliar transport facilitating the elimination of sputum from the bronchi.

Pharmacokinetic properties
The preparation is well absorbed from the gastrointestinal tract. Bioavailability is 70-80%. After intake of a single oral dose active substance peak plasma concentration is achieved after 2 hours. 80-90% of ambroxol bind to plasma proteins. Between dose and plasma concentration of the active substance is a linear relationship. 30% of ambroxol are metabolized, first passing through the liver (first pass metabolism). Ambroxol biotransformation occurs in the liver through
glucuronidation. Metabolites are not toxic. The average half-life after a single dose is approximately 1.3 hours, but after repeated dose - 80-10 hours. 90% of the dose is excreted from the body in the urine as metabolites, 10% -unchanged. Ambroxol crosses the blood-brain, placental barrier, excretes in breast milk.

Preclinical safety data
During acute and chronic toxicity, mutagenicity, carcinogenicity, genotoxicity studies in animals (mice, rats) that received oral ambroxol compared with a control group of animals substantial deviation have not been observed. Preclinical studies revealed no special hazard for humans.

Pharmaceuticals particulars
List of excipients

- Propylene Glycol
- Liquid sorbitol
- Glyrecol
- Citric Acid Monohydrate
- Sodium Citrate
- Saccharin Sodium

- Methyl Paraben
- Propyl Paraben
- Menthol
- Pineapple Flavor Liquid 17.92.0699
- D & C Yellow No. 10
- Purified Water

Incompatibilities
Not applicable.

Shelf life
Two (2) years.

Marketing authorization holder
Beximco Pharmaceuticals Ltd
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Marketing authorization number
DAR No: 186-391-031

Date of authorization
07.09.2004