APPROVED
Order of Ministry of Healthcare of Ukraine
29.11.2017 № 1495
Registration certificate
№ UA/9928/01/01

INSTRUCTION
for medical use

ABROL®

Composition:
active substance: ambroxol hydrochloride*;*
1 tablet contains ambroxol hydrochloride 30 mg*;*
excipients: anhydrous colloidal silicon dioxide, croscarmellose sodium, microcrystalline cellulose, magnesium stearate.

Pharmaceutical form: Tablets.
Main physico-chemical properties: white round tablets with a break line on one side.

Pharmacotherapeutic group. Drugs used in cough and catarrhal diseases. Mucolytics. Code ATC R05C B06.

Pharmacological properties.
Pharmacodynamics.
Ambroxol hydrochloride is a substituted benzylamine and a metabolite of bromhexine. It has been shown that Ambroxol hydrochloride releases the secretion of the respiratory tract glands and amplifies the release of the lung surfactant by direct exposure to type II pneumocytes in alveoli and Clara cells in bronchioles. Ambroxol hydrochloride also stimulates ciliary activity, which facilitates mucus secretion and elimination (mucociliary clearance). Activation of fluid secretion and increase of mucociliary clearance facilitate pouring out mucus and facilitate coughing.
Ambroxol hydrochloride has a local anesthetic effect at the expense of reversible and dependent in the concentration unit of the neural sodium channels. It is also reported that ambroxol hydrochloride has an anti-inflammatory effect (due to significant reduced cytokine from the blood and tissue binding of mononuclear and polymorphonuclear cells).
In patients with pharyngitis, the use of ambroxol hydrochloride led to a significant reduction in pain and redness in the throat.
The use of ambroxol hydrochloride increases the concentration of antibiotics (amoxicillin, cefuroxime, erythromycin and doxycycline) in bronchopulmonary secretion and sputum.
Pharmacokinetics.
Absorption. Absorption of ambroxol hydrochloride of oral dosage forms is not prolonged fast and complete with linear dose dependence within therapeutic range. Maximum plasma level is reached after 1-2.5 hours following oral administration of immediate release dosage forms and on average after 6.5 hours following administration of sustained release dosage forms.
Distribution. At oral administration, the distribution of ambroxol hydrochloride from blood to tissues is rapid and pronounced, with the highest concentration of active substance in the lungs.

Expected volume of distribution at oral intake is 552 liters. In plasma, in the therapeutic range of doses, approximately 90% of the drug is bound to proteins.
Metabolism and withdrawal. Approximately 30% of the dose after oral administration is derived by presystemic metabolism. Ambroxol hydrochloride is metabolised mainly in the liver by glucuronidation and cleavage to dibromanthranilic acid (approximately 10% of the dose). Metabolism of ambroxol hydrochloride to dibromanthranilic acid occurs with CYP3A4. After 3 days of oral administration, about 6% of the dose is excreted unchanged in the urine, approximately 26% of the dose is in the conjugated form.
The half-life of the blood plasma is about 10 hours. Total clearance is within 660 ml / min. Renal clearance is approximately 83% of the total.
Pharmacokinetics in special populations of patients. In patients with impaired liver function, the elimination of ambroxol hydrochloride is reduced, which results in 1.3-2-fold higher plasma level. Since the therapeutic range of ambroxol hydrochloride is sufficiently wide, no dosage change is required.
Age and gender have no clinically significant effect on the pharmacokinetics of ambroxol hydrochloride, therefore no dose adjustment is required.
The intake of food does not affect the bioavailability of ambroxol hydrochloride.

Clinical characteristics.
Indication.
Secretolic therapy in acute and chronic bronchopulmonary diseases associated with bronchial secretion and mucus mellitus weakening.

Contraindication.
Abrol® should not be used in patients with known hypersensitivity to ambroxol hydrochloride or to other components of the drug.
Abrol®, 30 mg tablets, is not intended for use in children under the age of 6 due to the strength of the action. Children under the age of 6 years are recommended for the use of ambroxol in the appropriate dosage.

Interaction with other drugs and other types of interactions.
The simultaneous use of Abrol®, tablets and cough suppressants may lead to excessive accumulation of mucus as a result of inhibition of cough reflex. Therefore, such a combination is possible only after careful evaluation by the physician of the expected benefit ratio and possible risk of application.

Peculiarities of use.
There have been reports of severe skin lesions: erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalized exanthematosus pustulosis associated with the use of ambroxol hydrochloride. If there are signs or symptoms of skin rash progression (sometimes associated with the appearance of blistering or mucosal lesions), immediately stop treatment with amboxol hydrochloride and seek medical attention.
When violating bronchial motility and increased secretion of mucus (for example, with such a rare disease as primary ciliary dyskinesia), Abrol® should be used with caution, as ambroxol may increase mucus secretion.
Patients with impaired kidney function or severe hepatic insufficiency should only take Abrol® tablets, only after consulting their physician. When using ambroxol hydrochloride, as well as any active substance that is metabolized in the liver, and then excreted by the kidneys, there is accumulation of metabolites that are formed in the liver in patients with severe renal insufficiency.

Use during pregnancy or breastfeeding.
Pregnancy. Ambroxol hydrochloride penetrates the placental barrier.
The results of clinical data on the use of ambroxol hydrochloride after the 28th week of pregnancy showed no harmful effects on the fetus. However, you must adhere to the usual precautionary measures regarding the use of drugs during pregnancy. Especially in the first trimester of pregnancy it is not recommended to use the drug Abrol® tablets.
Breast-feeding. Ambroxol hydrochloride penetrates into breast milk. Abrol® tablets are not recommended for breastfeeding.
Fertility. Preclinical studies do not indicate direct or indirect harmful effects of ambroxol hydrochloride on fertility.

Effects on ability to drive and use machines.
There is no data about the influence on the velocity rate while driving a car or operating other machines. No appropriate studies were conducted.

Method of administration and dosage.
Unless otherwise specified, the recommended dosage of Abrol® tablets, as follows:
children aged 6 to 12 years: the dose is $^1/_2$ tablets 2-3 times a day (equivalent to 30-45 mg ambroxol hydrochloride per day);
adults and children aged 12 years and older: the dose is 1 tablet 3 times a day during the first 2-3 days (equivalent to 90 mg ambroxol hydrochloride per day). Treatment continues to use 1 tablet 2 times a day (equivalent to 60 mg ambroxol hydrochloride per day).
If it is necessary, the therapeutic effect for adults and children 12 years of age may be increased by the use of 2 tablets 2 times a day (equivalent to 120 mg ambroxol hydrochloride per day).
Pills should be swallowed whole with sufficient fluid (such as water, tea or fruit juice) regardless of food intake.
In general, there are no restrictions on the duration of use, but long-term therapy should be conducted under medical supervision.
Abrol® tablets should not be used for more than 4-5 days without consulting a physician.

Children.
Apply to children under the age of 6 years who do not tolerate to syrup.

Overdose
There are currently no reports of overdose cases. Symptoms known from rare reports of overdose and/or misdiagnosis are consistent with known side effects of ambroxol hydrochloride in recommended doses and require symptomatic treatment.

Adverse reactions.
Immune system and skin and subcutaneous tissue: itching, erythema, skin rash, urticaria, angioedema, anaphylactic reactions (including anaphylactic shock), other hypersensitivity reactions, severe skin disorders (Stevens-Johnson syndrome, toxic epidermal necrolysis (syndrome Lyell), acute generalized exanthematosus pustulosis).
Nervous system: dysgeusia (changes in taste).
Gastrointestinal tract: diarrhea, nausea, vomiting, dyspepsia, abdominal pain, dry mouth, heartburn, constipation, salivation, dryness in the throat.
Respiratory system, the thoracic and mediastinal organs: decreased sensitivity in the pharynx, dyspnea (including as a symptom of hypersensitivity reaction), bronchospasm, rhinorrhea, respiratory dryness.
Urinary system: dysuria.
General disorders: reactions from the mucous membranes, fever.

Shelf-life.
3 years.

Storage conditions.
Store at a temperature below 25°C in the original package.
Keep it out of reach of children.

Package.
10 tablets are in a blister; 2 blisters are in a carton package.

Conditions of supply.
Without prescription.

Manufacturer.
«KUSUM PHARM» LLC.

Address.
40020, Ukraine, Sumy oblast, Sumy, Skryabina Str., 54.

Last revision date.
29.11.2017 № 1495