MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

Stamp: Ministry of Health of Russia

INSTRUCTION LEAFLET
FOR MEDICAL USE OF THE MEDICINAL PRODUCT
ESPA-NAC®

Product licence number:

Brand name: ESPA-NAC®

Generic name: acetylcysteine

Chemical name: 2R) -2-Acetamido-3-sulfanylpropanoic acid

Pharmaceutical form: powder for oral solution

Product formulation:

1 sachet contains:

Active ingredients: acetylcysteine – 200,00 mg/600,00 mg;

Excipients: sucrose – 2744,10 mg/2344,10 mg, orange flavor – 50,00 mg, κ colloidal silicon dioxide – 3,00 mg, tartaric acid – 2,00 mg, sodium chloride – 0,90 mg.

Description: consistent powder of white to off-white color, without agglomerates and foreign particles, with a fruity smell.

Pharmacotherapeutic group: expectorant mucolytic agent.

ATC code: R05CB01

Pharmacological properties

Pharmacodynamic properties

Mucolytic agent, thins expectorations, increases their volume and facilitates the discharge of expectorations. The action is associated with the ability of free sulfhydryl groups of acetylcysteine to break intramolecular and intermolecular disulfide bonds of mucopolysaccharide chains, which leads to depolymeration of mucoproids and causes a decrease in expectorations viscosity (in some cases, it leads to a significant increase in expectorations volume, which requires aspiration of bronchial contents). It remains active with purulent expectorations. It does not affect immunity.

It increases the secretion of less viscous sialomucins by goblet cells and reduces the adhesion of bacteria to epithelial cells of the bronchial mucous membrane.

It stimulates the mucous cells of the bronchi, the secretion of which lyses fibrin.

It has a similar influence on the secretion formed in case of inflammatory diseases of the ENT-organs.

It has an antioxidant effect due to the presence of an SH-group capable of neutralizing electrophilic oxidative toxins.

It protects alpha-1-antitrypsin (elastase inhibitor) from the inactivating effect of HOC1, which is an oxidant produced by myeloperoxidase of active phagocytes.

It also has some anti-inflammatory effect (by suppressing the formation of free radicals and active oxygen-containing substances responsible for the inflammation progression in the lung tissue).

It leads to increased synthesis of glutathione, which explains the detoxifying effect in the event of paracetamol poisoning.

In case of the prophylactic use of acetylcysteine, a decrease in the frequency and severity of exacerbations has been observed in patients with chronic bronchitis and cystic fibrosis.

Pharmakokinetics

After oral administration, the absorption is high. The bioavailability is low: about 10% due to the presence of a strongly pronounced “first-pass” metabolism through the liver with the formation of a pharmacologically active metabolite - cysteine, as well as diacetylcystine and cystine.

The maximum concentration level (C_{max}) in plasma after oral administration is achieved in about 1-3 hours. The plasma protein binding is about 50%. It is excreted mainly by the kidneys in the form of inactive metabolites (inorganic sulfates, diacetylcystine), a small part is excreted unchanged with feces. The half-life ($T_{1/2}$) of acetylcysteine from plasma is about 1 hour. In case of impaired liver function, this value increases up to 8 hours.

It penetrates the placental barrier and accumulates in the amniotic fluid.

There are no data on penetration through the haematoencephalic barrier.

Indications

Diseases of the respiratory system, accompanied by the formation of viscous, difficult to separate expectorations:

- acute and chronic bronchitis, obstructive bronchitis;
- tracheitis, laryngotracheitis;
- pneumonia;
- bronchiectatic disease, bronchial asthma, chronic obstructive pulmonary disease (COPD), bronchiolitis;
- cystic fibrosis;

Acute and chronic sinusitis, inflammation of the middle ear (otitis media).

Contra-indications

- hypersensitivity to acetylcysteine or other components of the drug;
- gastric ulcer of the stomach and duodenal ulcer in the exacerbation phase;
- blood expectoration, pulmonary hemorrhage;
- sucrose/isomaltase deficiency, fructose intolerance, glucose-galactose malabsorption (the drug contains sucrose);

- pregnancy;
- period of breastfeeding;
- children's age up to 14 years *(for a dosage of 600 mg)*, children's age up to 2 years *(for a dosage of 200 mg)*;

Carefully: in past medical history of gastric ulcer and duodenal ulcer, esophageal varicose veins, bronchial asthma, obstructive bronchitis, adrenal diseases, hepatic and/or renal failure, arterial hypertension, histamine intolerance (prolonged use of the drug should be avoided, because acetylcysteine affects metabolism histamine and may lead to the occurrence of signs of intolerance, such as headache, vasomotor rhinitis, itching).

Administration during pregnancy and breast-feeding period

There is limited information on the use of acetylcysteine during pregnancy and breastfeeding, therefore the use of the drug is contraindicated during pregnancy. If it is necessary to use the drug during lactation, it is required to face up to the challenge to stop breastfeeding.

Posology and method of administration

ESPA-NAC® in the dose of 600 mg:

Adults and children over 14 years old: 1 sachet 2-3 times a day (400-600 mg).

Children of 6 to 14 years old: 1 sachet 2 times a day (400 mg).

Children of 2 to 6 years old: 1/2 sachet 2 -3 times a day (200-300 mg).

In cystic fibrosis:

Children of 2 to 6 years old: 1 sachet 2 times a day (400 mg).

Children up to 6 years old: 1 sachet 3 times a day (600 mg).

ESPA-NAC® in the dose of 200 mg:

Adults and children over 14 years old: 1 sachet once a day (600 mg).

In cystic fibrosis:

Children up to 6 years old: 1 sachet once a day (600 mg).

Additional fluid intake enhances the mucolytic effect of the drug. In short-term colds, the duration of admission is 5-7 days. In chronic bronchitis and cystic fibrosis, the drug should be administered for a longer time to prevent infections. In case of long-term illnesses, the duration of therapy should be determined by the attending physician.

Adverse drug reaction

According to the World Health Organization (WHO), unwanted effects are classified according to their frequency of development as follows: very often (≥ 1/10), often (≥ 1/100, <1/10), infrequently (≥ 1/1000, < 1/100), rarely (≥ 1/10000, <1/1000) and very rarely (< 1/10000); the frequency is unknown (the frequency of occurrence of the events cannot be determined from the available data).

Regarding the cardiovascular system:

rarely: decrease in blood pressure, increase in heart rate (tachycardia);

Regarding the respiratory system:

rarely: bronchial spasm (mainly in patients with a hyperreactive bronchial system in bronchial asthma), skin rash, itching and urticaria, exanthema, angioedema;

very rarely: anaphylactic reactions up to anaphylactic shock progression, Stevens-Johnson syndrome, toxic epidermal necrolysis.

Regarding the gastrointestinal tract:

rarely: stomatitis, abdominal pain, nausea, vomiting and diarrhea, heartburn, dyspepsia.

Regarding the sensory organs:

infrequently: ringing in the ears.

Others:

rarely: headache, fever, anecdotal reports of bleeding progression due to the presence of hypersensitivity reactions, decreased platelet aggregation.

Overdosage

In the event of oral administration of acetylcysteine for three months in a daily dose of up to 11,6 g, there were no life-threatening side effects. With oral administration of acetylcysteine at a dose of up to 500 mg/kg of body weight, no poisoning phenomena were observed.

Symptoms: heartburn and nausea, vomiting, diarrhea, stomach pain.

In newborns, there is a risk of hypersecretion occurrence.

Treatment: symptomatic therapy.

Interaction with other medicinal products

With the simultaneous use of acetylcysteine and *antitussic drugs*, a congestion of mucus may occur due to suppression of the cough reflex.

The simultaneous administration of acetylcysteine with *vasodilating agents* and *nitroglycerin* may lead to an increase in the vasorelaxant action of the latter.

It is pharmaceutically incompatible with antibiotics (penicillins, cephalosporins, erythromycin, tetracycline and amphotericin B) and *proteolytic enzymes*.

It reduces the absorption of penicillins, cephalosporins, tetracycline (they should be administered no earlier than 2 hours after intake of acetylcysteine).

Precaution

Patients with bronchial asthma and obstructive bronchitis should be prescribed acetylcysteine with caution under systematic monitoring of bronchial patency. When dissolving the drug, it is necessary to use glassware, avoid contact with metals, rubber (upon contact, sulfides with a characteristic odor are formed), oxygen and easily oxidized substances.

When treating diabetes mellitus patients, it is necessary to take into account that the preparation

contains sucrose (one 200/600 mg sachet contains 0.23/0.20 bread units, respectively).

Patients suffering from severe skin lesions - Stevens-Johnson syndrome or Lyell’s syndrome - may have fever, body pain, rhinitis, cough, and sore throat in the early phase. With symptomatic treatment, the erroneous prescription of mucolytic agents is possible. There are anecdotal reports (<1/10000) about the detection of Stevens-Johnson syndrome and Lyell's syndrome, which coincided with the prescription of the drug; however, there is no causal relationship with the drug intake. In case of occurrence of the above syndromes (sudden appearance of rashes and spots on the face and trunk, which can later spread to other parts of the body), it is recommended to stop treatment and seek immediate medical attention.

Effects on ability to drive and use machines

In therapeutic doses, it does not affect the ability to drive and use machines.

Pharmaceutical form and presentation

Powder for oral solution, 200 mg, 600 mg.

3.0 powder in a sachet of three-layer material (paper-aluminum-polyethylene).

20 sachets in a cardboard box along with instructions for use.

Storage conditions

Store at a temperature not higher than 25ºC.

Keep out of reach of young children.

Expiry date

4 years.

Do not use after the expiry date.

Dispensing requirements

No prescription.

Marketing authorization holder:

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