Gebrauchsinformation
Patient Information Leaflet
165 mm x 470 mm

Seite 1
Page 1

165 mm

470 mm

Natrapharm

Rx

Acetylcysteine

Pneumotyl®

200 mg Effervescent Tablet
600 mg Effervescent Tablet
Mucolytic

FORMULATION
Each effervescent tablet contains:
Acetylcysteine..... 200 mg or 600 mg

PHARMACEUTICAL FORM
White round effervescent tablets, faultless, scored on one side

CLINICAL PARTICULARS
Therapeutic indications
Secretolytic therapy in acute and chronic bronchopulmonary diseases accompanied by impaired formation and transport of mucus.

DOSAGE AND ADMINISTRATION
If not otherwise prescribed, the following dosage is recommended for acetylcysteine 200 mg effervescent tablets:

Adults and adolescents from 14 years of age
1 effervescent tablet 2-3 times daily (equivalent to 400 - 600 mg acetylcysteine per day)

Children and adolescents 6-14 years of age
1 effervescent tablet twice daily (equivalent to 400 mg acetylcysteine per day)

Children 2-5 years of age
½ effervescent tablet 2-3 times daily (equivalent to 200-300 mg acetylcysteine per day)

If not otherwise prescribed, the following dosage is recommended for acetylcysteine 600 mg effervescent tablets:

Adults and adolescents from 14 years of age
½ effervescent tablet twice daily or 1 effervescent tablet once daily (equivalent to 600 mg acetylcysteine per day)

Method of administration
The effervescent tablets are taken dissolved in a glass of water after meals.

Duration of use
Should not be taken for more than 4-5 days without medical advice.

CONTRAINDICATIONS
- Hypersensitivity to acetylcysteine or to any of the excipients
- Active peptic ulceration
- Children below 2 years of age

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Cave during use in patients with bronchial asthma and in patients with anamnestic ulcers.

The use of acetylcysteine, especially in early treatment can lead to liquefaction and thus to an increase in volume of bronchial secretions. If the patient is unable to expectorate (sufficiently expectorate), appropriate measures (such as drainage and aspiration) should be performed.

The occurrence of severe skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome has very rarely been reported in temporal connection with the use of acetylcysteine. If cutaneous and mucosal changes newly occur, medical advice should be sought without delay and use of acetylcysteine be terminated.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Combined administration of acetylcysteine with antitussives may cause a dangerous secretory congestion due to the reduced cough reflex, so that an especially careful diagnosis is required for this combination treatment.

Reports to date on an inactivation of antibiotics due to acetylcysteine exclusively refer to in vitro experiments in which the relevant substances were mixed directly. Nevertheless for safety reasons, oral antibiotics should be administered separately and at an interval of at least 2 hours. This does not apply to cefixime and loracarbef.

Acetylcysteine may potentiate the vasodilatory effect of nitroglycerin. Caution is advised.

PREGNANCY AND LACTATION
Pregnancy
No sufficient data on exposed pregnant women are available for acetylcysteine. Experimental animal studies do not suggest direct or indirect harmful effects on pregnancy, embryonal/foetal development, birth or postnatal development (see also Preclinical safety data). Acetylcysteine should be used during pregnancy after strict assessment of the benefit-risk ratio.

Lactation
No information is available regarding excretion into breast milk. Acetylcysteine should be used during lactation only after strict assessment of the benefit-risk ratio.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None known

Undesirable effects
The evaluation of adverse reactions is based on the following information on frequencies:

Very common:	(≥ 1/10)
Common:	(≥ 1/100 up to < 1/10)
Uncommon:	(≥ 1/1,000 up to < 1/100)
Rare:	(≥ 1/10,000 up to < 1/1,000)
Very rare:	(< 1/10,000)
Not known:	(cannot be estimated from the available data)

Immune system disorders

Uncommon:	Hypersensitivity reactions
Very rare:	Anaphylactic shock, anaphylactic/anaphylactoid reactions

Nervous system disorders

Uncommon:	Headache

Ear and labyrinth disorders

Uncommon:	Tinnitus

Cardiac disorders

Uncommon:	Tachycardia

Vascular disorders

Uncommon:	Hypotension
Very rare:	Hemorrhage

Respiratory, thoracic and mediastinal disorders

Rare:	Dyspnoea, bronchospasm

Gastrointestinal disorders

Uncommon:	Nausea, vomiting, diarrhoea, abdominal pain
Rare:	Dyspepsia

Skin and subcutaneous tissue disorders

Uncommon:	Urticaria, rash, angioedema, itching, exanthema

General disorders and administration site conditions

Uncommon:	Fever
Not known:	Facial edema

A decreased blood platelet aggregation in the presence of acetylcysteine has been confirmed by different studies. The clinical relevance has not yet been clarified to date.

Overdose
No case of toxic overdose has been observed to date in association with oral pharmaceutical forms of acetylcysteine. Volunteers were treated with a dose of 11.6 g acetylcysteine/day over 3 months without observing any severe side effects. Oral doses up to 500 mg acetylcysteine/kg BW were tolerated without any symptoms of intoxication.

Symptoms of intoxication
Overdoses may lead to gastrointestinal symptoms, such as nausea, vomiting and diarrhoea. Infants are at risk of hypersecretion.

Therapy of intoxication
If necessary, according to the symptoms.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: mucolytics
ATC Code: R05CB01

Acetylcysteine is a derivative of the amino acid cysteine. The efficacy of acetylcysteine is secretolytic and secretomotoric in the area of the respiratory tract. It is discussed that it splits off the interconnecting disulphide bonds between the mycopolysaccharide chains and that it has a depolymerizing effect on DNA-chains (in purulent mucus). Due to these mechanisms, the viscosity of mucus should be reduced.

An alternative mechanism of acetylcysteine is meant to be based on the capacity of its reactive SH group to bind chemical radicals and to detoxify them in this way.

Furthermore, acetylcysteine contributes to an increase in glutathione synthesis, which is important for the detoxification of noxae. This provides the explanation for its antidotal effect in paracetamol intoxication.

Pharmacokinetic properties
Absorption
Following oral administration, acetylcysteine is rapidly and almost completely absorbed and metabolized in the liver to cysteine, the pharmacologically active metabolite, as well as to diacetylcystine, cystine and further mixed disulphides.

Distribution
Due to the high first-pass effect, the bioavailability of orally administered acetylcysteine is very low (approx. 10%). In humans, maximum plasma concentrations are achieved after 1-3 hours with the maximum plasma concentration of the metabolite cysteine in the range of approx. 2 μmol/L. The protein binding of acetylcysteine was determined to be about 50%.

Biotransformation
Acetylcysteine and its metabolites occur in three different forms in the organism: partially in free form, partially bound to proteins via labile disulphide bonds and partially as incorporated amino acid. Acetylcysteine is excreted almost exclusively in the form of inactive metabolites (inorganic sulphates, diacetylcystine) via the kidneys. The plasma half-life of acetylcysteine is approximately 1 hour and is mainly determined by the rapid hepatic biotransformation. Impaired hepatic function therefore leads to prolonged plasma half-lives of up to 8 hours.

Elimination
Pharmacokinetic studies with intravenous administration of acetylcysteine revealed a distribution volume of 0.47 L/kg (in total) or 0.59 L/kg (reduced); the plasma clearance was determined to be 0.11 L/h/kg (in total) and 0.84 L/h/kg (reduced), respectively.

The elimination half-life after intravenous administration is 30-40 minutes while excretion follows three-phase kinetics (alpha, beta, and terminal gamma phase).

Acetylcysteine crosses the placenta and is detected in cord blood. No information is available regarding excretion into breast milk.

No knowledge is available concerning the behaviour of acetylcysteine at the blood-brain barrier in humans.

Preclinical safety data
Acute toxicity
The acute toxicity in animal experiments is low. For the treatment of overdoses, see Overdose.

Chronic toxicity
Studies in various animal species (rat, dog) with a duration of up to one year did not show any pathological alterations.

Tumorigenic and mutagenic potential
No mutagenic effects of acetylcysteine are to be expected. An in vitro test was negative.

No studies of a tumorigenic potential of acetylcysteine have been carried out.

Reproductive toxicology
No malformations were detected in embryotoxicity studies in rabbits and rats. Studies of fertility and perinatal or postnatal toxicity were negative.

Acetylcysteine passes the placenta in rats and was detected in amniotic fluid. The concentration of the metabolite L-cysteine is above the maternal plasma concentration in placenta and foetus for up to 8 hours after oral administration.

PHARMACEUTICAL PARTICULARS
Incompatibilities
Not applicable

Storage
Store at temperatures not exceeding 30°C.

Caution
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph
The patient is advised to seek IMMEDIATE medical attention at the first sign of adverse drug reaction.

AVAILABILITY
200 mg: Laminated aluminum foil strips x 2's (Box of 20's)
600 mg: Laminated aluminum-paper-foil x 2's (Box of 10's)

REGISTRATION NUMBER AND DATE OF FIRST AUTHORIZATION
PNEUMOTYL 200 mg Effervescent Tablet: DRP-7718-01 ; 09-2019
PNEUMOTYL 600 mg Effervescent Tablet: DRP-8201-01; 08-2019

DATE OF REVISION
January 2020
CDSv03

Manufactured by: **Hermes Arzneimittel GmbH**
Hans-Urmiller-Ring 52, 82515 Wolfratshausen, Germany

Imported by: **Sandoz Philippines Corporation**
5th and 6th Floor Ayala North Exchange Tower 1 (HQ), Ayala Ave.
cor. Salcedo and Amorsolo Sts., Brgy. San Lorenzo, Makati City

Distributed by: **Natrapharm, Inc.**
The Patriot Bldg., South Luzon Express Way, Parañaque, Metro Manila