mentopin®
Acetylcysteine 600
EFFERVESCENT TABLET

Brand or Product Name
Mentopin Acetylcysteine 600mg Effervescent Tablet

Name and Strength of Active Substance(s)
Mentopin Acetylcysteine 600mg Effervescent Tablet contains 600mg acetylcysteine.

Product Description
Round, white tablets with a smooth and faultless surface and a break-mark on one side.

Pharmacodynamics
Pharmacotherapeutic group: mucolytics
ATC code: R05CB01

Mechanism of action
Acetylcysteine is a derivative of the amino acid cysteine. Acetylcysteine has a secretolytic and secretomotoric effect in the area of the bronchial tract. It is discussed that acetylcysteine breaks the disulfide bonds between the mucopolysaccharide fibres and has a depolymerising effect on
DNA fibres (in purulent mucus). This mechanism is thought to decrease the viscosity of the mucus. An alternative mechanism of acetylcysteine is meant to be based on the ability of its reactive SH group to bind - and hence detoxify - chemical radicals.

Furthermore, acetylcysteine contributes to an increased glutathione synthesis, which is important for the detoxification of noxae. This explains its effect as an antidote in paracetamol intoxication.

A protective effect on the frequency and severity of bacterial exacerbations in patients with chronic bronchitis/cystic fibrosis has been described when acetylcysteine is given prophylactically.

Pharmacokinetics
Following oral administration, acetylcysteine is rapidly and almost completely absorbed and metabolized in the liver to cysteine, the pharmacologically active metabolite, as well as diacetylcystine, cystine and other mixed disulfides. Due to the high first-pass effect, the bioavailability of orally administered acetylcysteine is very low (approx. 10 %). In humans, maximum plasma concentrations are reached after 1 - 3 hours, whereby the maximum plasma concentration of the metabolite cysteine is in the range of approx. 2 µmol/l. Protein binding of acetylcysteine has been determined to be approx. 50 %.

Acetylcysteine and its metabolites occur in three different forms in the organism: partially in free form, partially bound to protein via labile disulfide 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 its rapid hepatic biotransformation.
Impairment of hepatic function therefore leads to prolonged plasma half-lives of up to 8 hours.

Pharmacokinetic studies with intravenous administration of acetylcysteine have shown a distribution volume of 0.47 l/kg (in total) and 0.59 l/kg (reduced); plasma clearance was determined to be 0.11 l/h/kg (in total) and 0.84 l/h/kg (reduced). The elimination half-life after intravenous administration is 30 - 40 minutes, whereby elimination follows three-phase kinetics (alpha, beta and terminal gamma phase).

N-acetylcysteine crosses the placenta and is detected in umbilical cord blood. There is no information available on the excretion into breast milk.

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

Indication
Treatment of respiratory affections characterized by thick & viscous hypersecretions: Acute bronchitis, chronic bronchitis and its exacerbations, pulmonary emphysema, mucoviscidosis & bronchiectasis.

Recommended Dosage

Adults and adolescents over 14 years of age: take 1 effervescent tablet once daily

Dissolve content of an effervescent tablet in a glass of water and drink immediately.

Mode of Administration
Oral

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in this package insert.
Due to the high amount of active substance it contains, Mentopin must not be used in children aged under 14.

Warnings and Precautions
Very rarely, severe skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome have been reported in temporal association with the use of acetylcysteine. In most of these reported cases, at least one further medicinal product was administered which is presumed to be far more likely to cause the mucocutaneous symptoms. Should any new skin or mucosal changes occur, medical advice should therefore be sought immediately, and the patient should stop taking acetylcysteine.

The product should be used with caution in patients with asthma and patients with a history of ulcers.

Caution is required in patients with histamine intolerance. Long-term use should be avoided in patients with histamine intolerance, as acetylcysteine affects histamine metabolism and can produce symptoms of intolerance (e.g. headaches, runny nose, itching).

Administration of acetylcysteine, particularly when administration is first started, can thin bronchial secretions, resulting in an increase in the volume of these secretions. If the patient is unable to adequately expectorate this increased volume of secretions, appropriate procedures (e.g. postural drainage and suction) should be performed.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicinal product contains 138.8 mg sodium per effervescent tablet, equivalent to 7 % of the WHO recommended maximum daily dietary intake of 2 g sodium for an adult.

Interactions with other Medicaments
Cough suppressants (Antitussives)
Combined use of acetylcysteine with antitussives (cough suppressants) may cause a dangerous secretory congestion due to the reduced cough reflex. Hence, particular care is required when determining whether there is an indication for treatment with this combination.

Antibiotics
Up to now, reports on inactivation of antibiotics (tetracycline, aminoglycosides, penicillins) by acetylcysteine have only emerged from in vitro trials, in which the substances concerned were mixed directly. For safety considerations, oral administration of antibiotics should therefore be taken separately with an interval of at least 2 hours.
This does not apply to loracarbef.

Activated charcoal
The use of activated charcoal may reduce the effect of acetylcysteine.

Glyceryl trinitrate (nitroglycerin)
Co-administration of acetylcysteine can result in an enhancement of vasodilatory and antiplatelet effects of glyceryl trinitrate (nitroglycerin). If a common treatment with nitroglycerin and acetylcysteine is considered necessary, the patient should be monitored for a potential hypotension, which could be serious and may be indicated by headache.

Statement on usage during pregnancy and lactation
Pregnancy
No sufficient clinical data on exposed pregnant women are available for acetylcysteine.
Experimental animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Breastfeeding
There is no information available on the excretion into breast milk.

The use of acetylcysteine in pregnancy and lactation should follow a strict assessment of benefit-risk ratio.

Fertility
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Adverse Effects / Undesirable Effects

The frequency of undesirable effects is based on the following categories:

Very common	≥ 1/10
Common	≥ 1/100 to < 1/10
Uncommon	≥ 1/1,000 to < 1/100
Rare	≥ 1/10,000 to < 1/1,000
Very rare	< 1/10,000

Not known	Cannot be estimated from the available data

Immune system disorders

Uncommon:	Allergic reactions (such as pruritus, urticaria, rash, bronchospasm, angioedema, tachycardia and hypotension)
Very rare:	Anaphylactic /anaphylactoid reactions with shock in extreme cases

Nervous system disorders

Uncommon:	Headache

Gastrointestinal disorders

Uncommon:	Stomatitis, abdominal pain, nausea, vomiting and diarrhoea
Rare:	Dyspepsia

Respiratory, thoracic and mediastinal disorders

Rare:	Dyspnoea, bronchospasm – predominantly in patients with a hyperreactive bronchial system associated with asthma

General disorders and administration site conditions

Uncommon:	Fever

Skin and Subcutaneous Tissue Disorders

Severe cutaneous adverse reactions (SCAR) e.g. erythema multiforme, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). In most of these cases reported at least one other drug was administered at the same time, which may have possibly enhanced the described mucocutaneous effects. Should any new skin or mucosal changes occur, medical advice should therefore be sought immediately, and the patient should stop taking acetylcysteine.

Furthermore, bleeding has been reported very rarely in association with the administration of acetylcysteine, in some cases as part of hypersensitivity reactions. A decrease in blood platelet aggregation in the presence of acetylcysteine has been confirmed by various studies. To date, the clinical relevance of this has not yet been clarified.

Overdose and Treatment

There is no specific antidote for acetylcysteine and treatment is symptomatic. General supportive measures should be carried out and if necessary, according to the symptoms.

List of Excipients

Citric acid, sodium hydrogen carbonate, sodium carbonate, ascorbic acid, mannitol, lactose, lemon flavour (contains sorbitol [Ph. Eur.]), sodium cyclamate, saccharin sodium, sodium citrate.

Storage Conditions

Store below 30°C

Dosage Forms and Packaging

Mentopin Acetylcysteine 600mg Effervescent Tablet: Pack in aluminium seal foil (pack of 2 x 5's, 2 x 10's).

Name and Address of Manufacturer

Hermes Pharma GmbH
Hans-Urmiller-Ring 52,
82515 Wolfrathausen,
Germany.

Date of Revision of Package Insert

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