# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Acetylcysteine 600mg Capsules

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 600 mg acetylcysteine. For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Almost white, crystalline powder, filled in white hard gelatin 00 Capsule size.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Acetylcysteine 600mg Capsules are a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterized by excessive, viscous mucus, including chronic obstructive airways disease

### 4.2 Posology and method of administration

In general the usual recommended dosage is:

Adults including elderly and adolescents 14 years and older: 600 mg (1 capsule) once daily.

Duration of therapy: the duration of therapy is dependent on the nature and severity of the illness and should be decided by the doctor.

For oral use.

Swallow the capsule with a drink of water. The capsule should be taken after food.

Hepatic and Renal Impairment

In patients with impaired kidney or liver function there is insufficient data on whether dosage adjustments are required. Hepatic and renal impairment can reduce clearance which may result in an increase in adverse drug reactions due to drug accumulation.

## 4.3 Contraindications

Hypersensitivity to acetylcysteine or to any of the excipients listed in section 6.1. This medicine should not be used in children under 14 years of age.

## 4.4 Special warnings and precautions for use

Serious skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome have been reported whilst taking acetylcysteine, but these occur rarely. For this reason, medical advice should be sought immediately and the patient should stop taking acetylcysteine in the event of new-onset changes to the skin and mucous membranes. See also section 4.8.

There are no studies on the efficacy and safety of once daily acetylcysteine 600 mg capsule in the adolescent population. However, mild, moderate or severe adverse reactions have been reported with the use of IV acetylcysteine in the adolescent population.

This product should be used with caution by patients with bronchial asthma and patients with a history of peptic ulcer disease.

This product should be used with caution by patients with histamine intolerance. They should avoid long-term therapy because Acetylcysteine 600mg Capsules affect the metabolism of histamine and can lead to symptoms of intolerance (e.g. headaches, rhinitis, itching).

Acetylcysteine can, especially at the start of treatment, cause thinning and increased volume of bronchial secretions. If the patient is not able to expectorate this adequately, appropriate supportive measures should be implemented (such as postural drainage and suction removal).

No specific studies have been performed in patients with renal or hepatic impairment. Hepatic and renal impairment can reduce clearance and increase acetylcysteine plasma levels which may result in an increase in adverse drug reactions due to drug accumulation.

## 4.5 Interaction with other medicinal products and other forms of interaction

Analysis of interactions with other medicines has been performed only in adults.

Antitussives

If this product is used in combination with cough-relieving medicines (antitussives) the suppressed cough reflex may cause a dangerous build-up of secretions, which means that the indication for this combination treatment should be established particularly carfully.

Activated charcoal

Co-administration with activated charcoal can reduce the effectiveness of acetylcysteine.

Antibiotics

Reports of inactivation of antibiotics (aminoglycosides, penicillins, tetracycline) by acetylcysteine indicate that this inactivation occurs only when these substances are mixed directly together in vitro. Nevertheless, administration of oral doses of antibiotics and acetylcysteine capsules should be separated by minimum period of two hours. This does not apply to the antibiotics cefixime or loracarbef.

Acetylcysteine and glyceryl trinitrate

Simultaneous administration of these drugs may increase the vasodilatory and platelet aggregation-inhibiting effect of glyceryl trinitrate. If such combined treatment is considered necessary, the patient should be monitored for possible hypotension, which can be serious and may be indicated by headaches.

Interface with the measurement of laboratory parameters

Acetylcysteine can influence the colourimetric assay of salicylates.

Acetylcysteine can influence results when measuring ketones in urine.

## 4.6 Fertility, Pregnancy and lactation

Pregnancy

There are no data on the use of acetylcysteine in pregnant women. Animal studies do not indicate direct or indirect adverse effects on pregnancy, embryonic / fetal development, birth or postnatal development (see also section 5.3).

Lactation

There is insufficient information on the excretion of acetylcysteine or its metabolites in human milk. Use during pregnancy and while breast-feeding should be subject to careful consideration of the risk/benefit balance.

Fertility

No human data on the effect of acetylcysteine are available.

## 4.7 Effects on ability to drive and use machines

Acetylcysteine has no influence on the ability to drive and use machines.

## 4.8 Undesirable effects

In the evaluation of side effects, the following frequencies are defined as:

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 (frequency cannot be estimated from the available data).

| **System/organ classes** | **Adverse Reactions** | | | |
|---|---|---|---|---|
| | **Uncommon** | **Rare** | **Very rare** | **Not known** |
| Immune system disorders | Hypersensitivity reactions | | Anaphylactic shock, anaphylactic/ anaphylactoid reactions | |
| Nervous system disorders | Headache | | | |
| Ear and labyrinth disorders | Tinnitus | | | |
| Cardiac disorders | Tachycardia | | | |

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|---|---|---|---|---|
| Vascular disorders | | | Haemorrhage | |
| Respiratory , thoracic and mediastinal disorders | | Bronchospasm, dyspnoea | | |
| Gastrointestinal disorders | Vomiting, diarrhoea, stomatitis , abdominal pain, nausea | Dyspepsia | | |
| Skin and subcutaneous tissue disorders | Urticaria, rash, angioedema , pruritus, Exanthema | | | |
| General disorders | Fever | | | Facial oedema |
| Investigations | Hypotension | | | |

Serious skin reactions, such as Stevens-Johnson syndrome and Lyell‘s syndrome, have been reported whilst taking acetylcysteine, but these occur rarely. In most reported cases at least one further medicine was being taken simultaneously, so the described muco-cutaneous effects could be exacerbated. For this reason, in the event of new-onset changes of the skin and mucous membranes medical advice should be sought immediately and the patient should stop taking acetylcysteine.

A reduction of blood platelet aggregation in the presence of acetylcysteine has been confirmed by various studies. The clinical relevance is not yet understood.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

There have been no cases of toxic overdose observed with orally-dosed acetylcysteine. No serious undesirable effects were observed in volunteer test subjects dosed over a 3-month period with 11.6g acetylcysteine per day. Oral doses of up to 500mg/kg of acetylcysteine were tolerated without toxic effects.

*a) Symptoms of intoxication*

Overdoses can cause gastrointestinal symptoms such as nausea, vomiting and diarrhoea. In infants, there is a risk of hypersecretion.

*b ) Treatments for overdose*

Treat symptomatically if applicable.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mucolytic agent

ATC code: R05CB01

Acetylcysteine belongs to the group of amino acid cysteine derivate.

Mechanism of action

Acetylcysteine is believed to break the disulfide bonds in mucoproteins and it depolymerizes DNA strands in purulent mucus.

Pharmacodynamic effects

The effect of this activity is a reduction in the viscosity of mucous secretions. Another possible effect is detoxification of free radicals by interaction with the active sulfhydryl group of acetylcysteine.

In addition acetylcysteine increases synthesis of glutathione. Due to this mechanism of action, acetylcysteine is also indicated as a specific antidote in paracetamol poisoning.

There are no studies on the efficacy and safety of once daily acetylcysteine 600mg Capsules in the adolescent population. However mild, moderate or severe adverse reactions have been reported with the use of IV acetylcysteine including the adolescent population.

## 5.2 Pharmacokinetic properties

Absorption and metabolism

Acetylcysteine is absorbed rapidly and almost completely after oral administration. It is metabolized in the liver into a pharmaceutically active metabolite cysteine, inactive diacetylcystine and cystine and into the other

disulfides. Due to the high first pass effect, the bioavailability of orally administered acetylcysteine is very low (approximately 10%). In humans peak plasma levels of acetylcysteine are reached in approximately 1-3 hours after an oral dose. Plasma concentration of the active metabolite cysteine is about 2μmol/l and binding with proteins is about 50%.

Elimination

Acetylcysteine is excreted almost entirely as inactive metabolites (inorganic sulfates, diacetylcystine) through the renal route. The elimination half-life of the acetylcysteine is about 1h, which is primarily determined by the rapid biotransformation in the liver. In patients with liver dysfunction the elimination half-life of acetylcysteine increases to 8 h.

Distribution

In a pharmacokinetic study, intravenously administrated acetylcysteine in humans showed a distribution volume of 0.47 l/kg; the plasma clearance is 0.11 l/h/kg.

The elimination half-life after oral administration is 6.25 hours.

In a study with rats it was shown that acetylcysteine crosses the placenta.

There is no information on whether acetylcysteine crosses the blood-brain barrier in humans. There are no data on whether acetylcysteine is excreted in breast milk.

Hepatic and Renal impairment

There is evidence that clearance of acetylcysteine can be significantly reduced up to 90% in the subjects with end-stage renal disease. This could result in a marked increase in systematic exposure to acetylcysteine in extreme cases of patients with end-stage renal disease. It is not known to what extent the results can be extrapolated to the less severe forms of renal impairment that are more likely to be encountered during routine use of the proposed product (see section 4.2 and 4.4).

The elimination half-life of acetylcysteine was found to increase to eight hours in one study of patients with chronic liver disease. The total clearance of acetylcysteine was found to be significantly reduced following an intravenous dose of 600 mg over three minutes in nine subjects with hepatic cirrhosis.

## 5.3 Preclinical safety data

Repeated dose toxicity

Studies in various animals (rats and dogs) lasting up to one year showed no pathological changes.

Carcinogenesis and Mutagenicity

There are no studies on the tumorigenic effects of acetylcysteine. Bacteriological test did not show mutagenic effect.

Reproductive toxicity

Embryotoxicity studies on pregnant rabbits and rats during organogenesis were undertaken with orally administered acetylcysteine. The rabbits were dosed with 250, 500 and 750 mg/kg and the rats were dosed with 500, 1000 and 2000 mg/kg. Both tests did not show any developmental effects.

In fertility studies, peri- and postnatal study with rats no adverse effects on delivery and lactation or on physical development and maturation of the offspring were noted.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Crospovidone Cl-SF

Stearic acid

**Capsule shell contains:**

Gelatine

Titanium dioxide

## 6.2 Incompatibilities

This medicinal product must not be mixed with antibiotics (see section 4.5).

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

## 6.3 Shelf life

3 years.

### 6.4 Special precautions for storage

Store below 25°C.

### 6.5 Nature and contents of container

Pack size of 30.
Capsules are packed in PVC/PVDC blister packs. Blisters are place in carton boxes together with a patient leaflet.

### 6.6 Special precautions for disposal

No special requirements.

## 7 MARKETING AUTHORISATION HOLDER

Ennogen IP Ltd
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Dartford, DA1 5BS,
UK.

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 55612/0019

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/04/2025

## 10 DATE OF REVISION OF THE TEXT

16/04/2025