SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Acetylcysteine 600 mg soluble tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soluble tablet contains 600 mg of acetylcysteine.

Excipient(s) with known effect
Each 600 mg soluble tablet contains 695 mg of sorbitol (E420) and 356.8 mg of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soluble tablet (tablets).
White, round, flat-faced tablets with bevelled edges

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acetylcysteine is a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterised by excessive, viscous mucus, including chronic obstructive airways disease.

4.2 Posology and method of administration

Posology

In general the usual recommended dosage is:

Adults including the elderly and adolescents over the age of 14
600 mg (1 soluble tablet) 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.

Hepatic and Renal Impairment

In patients with impaired kidney or liver impairment 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.

Paediatric population
Acetylcysteine 600 mg soluble tablets are contraindicated in children under the age of 14 years (see section 4.3).

Method of administration
For oral use

The soluble tablets should be dissolved completely in a glass of water before use and taken after food.

4.3 Contraindications

Hypersensitivity to acetylcysteine or to any of the excipients listed in section 6.1.

These tablets 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 this medicine 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 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 affects 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.

This medicinal product contains 356.8 mg sodium per dose, equivalent to 17.84% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

These tablets also contain sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Tablets in soluble formulations present a risk of choking and aspiration, particularly to elderly patients, if swallowed whole. This medicine should therefore be dissolved fully before intake.

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. Therefore, such combinations should be carefully considered.

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 soluble tablets 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 effects 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 colourmetric assay of salicylates. Acetylcysteine can influence results when measuring ketones in urine.

Other medications
It is not recommended to dissolve acetylcysteine preparations together with other medications.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no data from the use of acetylcysteine in pregnant women. Animal studies do not indicate any direct or indirect harmful effects on pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3).

Breast-feeding
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

The side effects are grouped according to their frequency as follows:
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)

System organ class	Adverse Reaction			
	Uncommon	**Rare**	**Very rare**	**Not known**
Immune system disorders	Hypersensitivity reactions		Anaphylactic shock / anaphylactic / anaphylactoid shock	
Nervous system disorders	Headache			
Ear and labyrinth disorders	Tinnitus			
Cardiac disorders	Tachycardia			
Vascular disorders			Haemorrhage	
Respiratory, thoracic and mediastinal disorders		Dyspnoea, bronchospasm		
Gastrointestinal disorders	Vomiting, diarrhoea, stomatitis, abdominal pain, nausea	Dyspepsia		
Skin and subcutaneous tissue disorders	Urticaria, rash, angioedema, pruritus,			
General disorders and administration site conditions	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 mucocutaneous 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 in blood platelet aggregation in the presence of acetylcysteine has been confirmed in various studies. The clinical significance of this has not yet been established.

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 Website: 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 11.6 g acetylcysteine per day. Oral doses of up to 500 mg/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: Mucolytics

ATC code: R05CB01

Acetylcysteine belongs to the group of acid cysteine derivative.

Mechanism of action
Acetylcysteine is believed to break the disulfide bonds in mucoproteins and it depolymerises 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 the 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 600 mg soluble tablets in the adolescent population. However, mild, moderate or severe adverse reactions have been reported with the use of IV acetylcysteine, including adolescent population.

5.2 Pharmacokinetic properties

Absorption and metabolism
Acetylcysteine is absorbed rapidly and almost completely after oral administration. It is metabolised 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 2 μmol/l and binding with proteins is about 50%.

No dosage adjustments are required in patients with impaired kidney or liver impairment.

Elimination
Acetylcysteine is excreted almost entirely as inactive metabolites (inorganic sulphates, diacetylcystine) through the renal route. The elimination half-life of the acetylcysteine is about 1 h, 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 administered 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 systemic exposure to acetylcysteine in the extreme case 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 sections 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

Repeat dose toxicity studies in various animals (rats and dogs) lasting up to one year showed no pathological changes.

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

Embryotoxicity studies in pregnant rabbits and rats during organogenesis 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

Ascorbic acid
Citric acid
Sodium hydrogen carbonate
Sodium carbonate
Sorbitol (E420)
Macrogol 6000
Sodium citrate
Sodium saccharine (E954)
Lemon flavour

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

2 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Keep the tablet tube tightly closed to protect from light and moisture.

6.5 Nature and contents of container

The packaging consists of a white polypropylene tube containing the tablets. Each tube is sealed with a tamper-evident polyethylene cap featuring, a calming spiral and desiccant compartment containing silica gel for moisture protection. The tube and patient leaflet are enclosed in a cardboard box.

Pack size: 30 (2x 15) tablets

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Ridge Pharma Limited
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Brunel Road
Theale, Reading
Berkshire, RG7 4AB
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 48804/0016

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

24/11/2025