SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Mucolight 600mg Effervescent Tablets
Acetylcysteine 600mg Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each effervescent tablet contains 600 mg acetylcysteine.
Excipient(s) with known effect:
Sorbitol (E420) 695 mg/tablet
Sodium content 356.8 mg/tablet

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Effervescent tablet.

White, round tablets with bevelled edges, 25mm in diameter

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Mucolight 600 mg effervescent tablet 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 elderly and adolescents 14 years: 600 mg (1 effervescent 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.

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

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.

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

Severe skin reactions such as Stevens Johnson syndrome and Lyell’s syndrome have very rarely been reported. In most cases at least one other drug was administered concomitantly.

If any skin or mucosal changes are seen seek immediate medical advice and stop taking these tablets (see section 4.8).

Use with caution in patients with asthma, a history of ulcers or intolerance to histamines. This medicinal product contains 356.8 mg sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

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

Hepatic and renal impairment can reduce clearance which may result in an increase in adverse drug reactions due to drug accumulation.

There are no studies on the efficacy and safety of once daily acetylcysteine 600 mg effervescent tablet in adolescent population. However, mild to severe adverse reactions have been reported with the use IV acetylcysteine in adults and adolescents.

Tablets in effervescent formulations present a risk of choking and aspiration, particularly to elderly patients, if swallowed whole. The tablet should therefore be dissolved fully before intake.
4.5 Interaction with other medicinal products and other forms of interaction

Antibiotics
Antibiotics should be administered separately and at an interval of at least 2 hours. In vitro experiments report an inactivation of certain antibiotics (tetracycline, aminoglycosides, cephalosporins, penicillins) due to acetylcysteine when the substances were directly mixed.

Antitussives
Combined use of antitussives (cough-relieving agents) with acetylcysteine may cause dangerous secretory congestion due to the reduced cough reflex.

Nitroglycerin
Administration of Mucolight Effervescent Tablets/Acetylcysteine Effervescent Tablets may lead to an increase in the vasodilatory and anti-platelet effect of glyceryl trinitrate. If the drugs are administered together the patient should be monitored for a hypotensive response.

Laboratory tests
Acetylcysteine may affect the colourmetric assay of salicyclates and the results of the determination of ketone bodies in urinalysis.

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of acetylcysteine in pregnancy has not been investigated. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development (see also 5.3). Prior to use in pregnancy, the potential risks should be balanced against the potential benefits.

Breast-feeding
No information is available on the excretion of the drug into breast milk. Breast-feeding is thus not advised during or immediately following the use of this drug.

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 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)
Unknown (frequency cannot be estimated from the available data)

<table>
<thead>
<tr>
<th>System/organ classes</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
<th>Not known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td></td>
<td>Hypersensitivity reactions</td>
<td>Anaphylactic shock, anaphylactic/ anaphylactoid reactions</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ear and labyrinth disorders</td>
<td></td>
<td>Tinnitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td>Tachycardia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular disease</td>
<td></td>
<td></td>
<td></td>
<td>Haemorrhage</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal</td>
<td></td>
<td></td>
<td>Bronchospasm, Dyspnoea</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Vomiting, diarrhoea, stomatitis, abdominal pain, nausea</td>
<td>Dyspepsia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diseases of the skin and subcutaneous tissue</td>
<td>Urticaria, rash, angioedema, pruritus, Exanthema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders</td>
<td>Fever</td>
<td></td>
<td></td>
<td>Facial oedema</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypotension</td>
</tr>
</tbody>
</table>

Incidents of severe skin reactions, such as Stevens Johnson syndrome and Lyell’s syndrome, with the use of acetylcysteine are very rare. In most cases at least one other drug was administered concomitantly, so the described muco-cutaneous effects could be exacerbated. Immediate medical advice should be sought in case of onset of skin or mucosal changes and the use of acetylcysteine should be discontinued.
Various studies confirmed a decrease in platelet aggregation during administration of acetylcysteine. The clinical significance of this is unclear.

**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.

4.9 Overdose

No cases of overdosage with oral dosage forms of acetylcysteine are known to be observed to date.

*a) Symptoms of overdose*

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

*b) Therapeutic interventions in overdose*

Treatment should be symptomatic.

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 600 mg effervescent tablet in adolescent population. However, mild, moderate or severe adverse reactions have been reported with the use of IV acetylcysteine including adolescents 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 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 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 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 (Vitamin C)
Citric acid
Sodium hydrogen carbonate
Sodium carbonate
Sorbitol (E420)
Macrogol 6000
Sodium citrate
Sodium saccharin
Flavour (Lemon)

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**
Tube packaging: 3 years.
Sachet packaging: 18 months

6.4 **Special precautions for storage**
Do not store above 25°C. For sachet packaging:
Store in the original package to protect from moisture and light.

For polypropylene tube packaging:

Keep the tube tightly closed. Store in the original package to protect from moisture and light.

Keep away from reach of infants and children.

6.5 **Nature and contents of container**
Tube packaging:
Purple and white polypropylene tube and white tamper evident polyethylene caps with inbuilt dessicant. Each tube contains 12 effervescent tablets and is packed in a carton.

Sachet packaging:
Each tablet is packaged into a sachet composed of one sided coated white paper 40g/m², 0.020μm aluminium foil, 20g/m² low density polyethylene and 30g/m² polyethylene. The sachets are packed in a carton having 10 or 20 effervescent tablets. Not all pack sizes may be marketed.

6.6 **Special precautions for disposal**
No special requirements.
7 MARKETING AUTHORISATION HOLDER
Ennogen Healthcare Limited
Unit G4 Riverside Industrial Estate, Riverside Way,
Dartford, Kent, DA1 5BS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 40739/0031

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
28/07/2016

10 DATE OF REVISION OF THE TEXT
28/07/2016