SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

AceCil 600 mg Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 600 mg acetylcysteine.

Excipient(s) with known effect: contains sodium (146 mg per tablet) and aspartame (20 mg per tablet, equal to 11 mg phenylalanine).

For the full list of excipients, see section 6.1.
Thickness: 4.95 mm; diameter: 18.0 mm.

3 PHARMACEUTICAL FORM

Effervescent tablet.

White, round and smooth effervescent tablets.
Thickness: 4.95 mm; diameter: 18.0 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acetylcysteine is indicated for pulmonary conditions, requiring viscosity reduction of the bronchial secretion to facilitate productive coughing, such as in bronchitis, emphysema, mucoviscidose, and bronchiectasis.

AceCil 600 mg Effervescent Tablets is indicated in adults *only*.

4.2 Posology and method of administration

Posology

Adults
600 mg (1 effervescent tablet) once daily.

Paediatric population
Children under 2 years of age
AceCil 600 mg Effervescent Tablets is contraindicated for use in children under 2 years of age (see section 4.3).

Children 2 years of age and older, and adolescents
The safety and efficacy is not established in children aged 2 years and older and adolescents. Other forms and strengths of acetylcysteine are more suitable for these patient groups.

Method of administration

Administer the required dose by dissolving an effervescent tablet in half a glass of water, to obtain a solution which can be ingested directly.

Patients with a muffled cough reflex (elderly and debilitated patients) are advised to take the tablet in the morning.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
The tablets should not be used in children under 2 years of age.
The tablets should not be used in children and pregnant women with phenylketonuria.

4.4 Special warnings and precautions for use

Bronchospasms may occur with the use of acetylcysteine. If bronchospasms occur, the medicinal product should be discontinued immediately.

Caution is advised in patients with peptic ulcer disease in their history, especially when using concomitantly other medicines known to irritate the gastrointestinal tract mucous.

In very rare cases, the occurrence of serious skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome have been reported when acetylcysteine was used in the same time period. In most cases at least one co suspected drug could be identified, which was more likely the cause of the mucocutaneous syndrome. If new skin or mucosal changes are seen immediate medical advice should be sought and treatment with acetylcysteine should be discontinued.

Mainly at the beginning of the treatment with acetylcysteine bronchial secretion can become fluid and increase in volume. When a patient is unable

to effectively cough up the secretions, postural drainage and broncho-aspiration have to be performed.

AceCil 600 mg Effervescent Tablets are sugar-free and can therefore be used by diabetics.

This medicinal product contains 146 mg of sodium per effervescent tablet, equivalent to 7.3% of the WHO recommended maximum daily intake of 2 g sodium for an adult. Caution is advised in patients on a controlled sodium diet.

In homozygous patients with phenylketonuria the amount of phenylalanine supplied by aspartame in this product should be taken into account in their dietary prescription.

Paediatric population
Mucolytics can block the airways of children under the age of 2 due to physiological characteristics of the respiratory system in this age group. The ability to cough up mucus may be limited. Therefore mucolytics should not be used in children younger than 2 years.

The safety and efficacy is not established in children aged 2 years and older and in adolescents.

The effervescent tablets should be dissolved fully before intake (section 4.2). Not fully dissolved tablets present a risk of choking and aspiration, particularly to elderly patients.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction with other medicinal products
Simultaneous dissolution of AceCil 600 mg Effervescent Tablets with other medicines is not recommended.

The inactivation of antibiotics by acetylcysteine has so far only been reported in *in vitro* tests, in which the relevant substances are directly mixed. Nevertheless, when oral antibiotics are required it is advisable to take these two hours before or after acetylcysteine.

Acetylcysteine should not be administered concomitantly with antitussive medicinal products.

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

Activated charcoal may decrease the effect of the acetylcysteine associated with reduced absorption.

Interaction with laboratory tests
Acetylcysteine may affect the result for colorimetric salicylate determinations.

4.6 Fertility, pregnancy and lactation

Pregnancy

Acetylcysteine effervescent tablets are contraindicated in pregnant women with phenylketonuria due to the aspartame content.

There is a limited amount from data on the use of acetylcysteine in pregnant women. Animal studies do not indicate reproductive toxicity (see section 5.3). Acetylcysteine passes the placenta. Available data do not indicate a risk for the child. The use of AceCil 600 mg Effervescent Tablets during pregnancy should be considered if necessary.

Breastfeeding

It is unknown whether acetylcysteine is excreted in breast milk, but in therapeutic doses of AceCil 600 mg Effervescent Tablets no effects on breast-fed infants are anticipated. AceCil 600 mg Effervescent Tablets can be used during breastfeeding.

Fertility

Based on available preclinical experience, there are no indications for possible effects of the use of acetylcysteine on fertility.

4.7 Effects on ability to drive and use machines

There are no data on the effect of acetylcysteine on the ability to drive. An effect is not likely.

4.8 Undesirable effects

In below table adverse effects after systemic use of oral acetylcysteine are indicated according to organ class.

Organ class	**Adverse effect**			
	Uncommon (≥1/1000 to <1/100)	**Rare** (≥1/10.000 to <1/1000)	**Very rare** (<1/10.000)	**Not known**
Immune system disorders	Hypersensitivity reactions*		Anaphylactic shock, anaphylactic/ anaphylatoid reactions	
Nervous system disorders	Headache			
Ear and labyrinth disorders	Tinnitus			

Vascular disease			Haemorrhage	
Gastrointestinal disorders	Stomatitis, abdominal pain, nausea, vomiting, diarrhoea	Dyspepsia		
Skin and subcutaneous tissue disorders				Facial oedema
General disorders and administration site disorders	Pyrexia			
Investigations	Hypotension			

* Hypersensitivity reactions include bronchospasm, dyspnoea, pruritus, urticarial, rash, angioedema and tachycardia.

A decrease in platelet aggregation in the presence of acetylcysteine is confirmed in several studies. The clinical significance of this is not yet established.

In patients with peptic ulcer or peptic ulcer history acetylcysteine may have an unfavourable effect on the gastric mucosa.

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

To date no toxic overdose has been reported for the oral pharmaceutical forms of acetylcysteine.
Voluntary test subjects are treated for three months with a dose of 11.6 mg acetylcysteine per day without observation of any serious side effects.
Oral doses up to 500 mg acetylcysteine per kg body weight have been toleraed with no signs of intoxication.

Symptoms
Overdoses may cause gastrointestinal symptoms such as nausea, vomiting and diarrhea.

Treatment in case of overdose
Symptomatic treatment if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: mucolytics, ATC code: R05C B01

Acetylcysteine is a mucolytic.
The mucolytic action is caused by decrease in viscosity of the bronchial mucous. This is explained by depolymerisation, in which the disulphide bonds in macro molecules present in mucous are opened.

In addition, acetylcysteine is a precursor of glutathione. Acetylcysteine is a derivative of the natural amino acid cysteine, which in the body serves as a substrate for the synthesis of glutathione.
In addition to the fact that acetylcysteine is able to normalize a state of glutathione depletion it can conjugate with different toxic compounds.

5.2 Pharmacokinetic properties

Acetylcysteine is rapidly absorbed after oral administration and is distributed over the entire organism. The highest tissue levels are achieved in the liver, kidney and lungs. Acetylcysteine is mostly de-acetylated to cysteine in the liver. This will mainly be processed in the amino acid metabolism. Also reversible disulphide compounds are formed with amino acids and proteins with free sulfhydryl groups. Finally, high doses are mostly converted in inorganic sulphate and renally excreted.

5.3 Preclinical safety data

Preclinical data based on conventional studies regarding safety pharmacology, repeat dose toxicity, genotoxicity, carcinogenic potency and reproductive toxicity do no indicate a risk of acetylcysteine in humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid (E330), Sodium hydrogen carbonate (E500 ii), Aspartame (E951), Povidone K-30 (E1201), Sodium chloride, PEG 6000, Lemon flavour (contains corn maltodextrin, flavouring preparations, flavouring substances, natural flavouring substances and alpha-tocopherol (E307)).

6.2 Incompatibilities

Acetylcysteine is known to affect rubber and metal (amongst others iron, nickel, copper). It is recommended to use a glass and / or plastic delivery system, when administered via nasogastric or naso-intestinal tube.

The mixing of antibiotics with acetylcysteine before administration should be avoided in relation to possible in-vitro inactivation of the antibiotic (in particular of β-lactam antibiotics). Taking in succession is allowed.

6.3 Shelf life

2 years
After first opening of the tube: 8 weeks

6.4 Special precautions for storage

Store in the original pacakge in order to protect from moisture and light. Keep the container tightly closed.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Polypropylene (PP) tablet container with silica gel containing PP cap in a carton box: 2x10 or 3x10 effervescent tablets per box.

6.6 Special precautions for disposal

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Essential-Healthcare Ltd. 249 – Ongar Road,
Brentwood, Essex, CM15 9DZ, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

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