Approved Proposed Professional Information for Medicines for Human Use:

AMUCO 600

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

AMUCO 600 effervescent tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 600 mg of acetylcysteine.

Excipients with known effect:

Contains sodium (146 mg per tablet) and sweetener (aspartame: 40 mg per tablet).

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablets.

White, round effervescent tablets, scored on one side with diameter of approximately 18,0 mm.

When a AMUCO 600 effervescent tablet is dissolved in water, the appearance of the solution is clear, colourless, with no particles and has a lemon smell.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AMUCO 600 effervescent tablets are used as a mucolytic in acute respiratory conditions.

4.2 Posology and method of administration

Posology

Adults and adolescents from 14 years of age:

½ effervescent tablet twice daily or 1 effervescent tablet once daily (equivalent to 600 mg acetylcysteine per day).

Method of administration

The effervescent tablets are taken dissolved in a glass of water after meals. Ingest the solution immediately.

Duration of use

AMUCO 600 effervescent tablets should not be taken for more than 14 days without medical advice.

Elderly and weakened patients:

Patients with a reduced cough reflex (elderly and weakened patients) should take AMUCO 600 preferably in the morning.

Paediatric patients

Due to the high content of active substance, acetylcysteine 600 mg should not be used in children less than 14 years of age.

4.3 Contraindications

- Hypersensitivity to acetylcysteine and/or to any of the excipients of AMUCO 600 listed in section 6.1.
- Safety in pregnancy has not been established. AMUCO 600 should not be used during pregnancy (see section 4.6).
- Active peptic ulceration.

4.4 Special warnings and precautions for use

Bronchospasms in asthmatic patients

AMUCO 600 should be used with caution in asthmatic patients. If bronchospasm occurs, AMUCO 600 should be discontinued immediately and appropriate treatment initiated.

Peptic ulcer

AMUCO 600 should be used with caution in patients with a history of peptic ulcer disease, both because drug-induced nausea and vomiting may increase the risk of gastrointestinal haemorrhage in patients predisposed to the condition, and because of a theoretical risk that mucolytics may disrupt the gastric mucosal barrier.

Bronchial secretions

The use of acetylcysteine, such as in AMUCO 600, especially in early treatment can lead to liquefaction and thus to an increase in volume of bronchial secretions. If the patient is unable to sufficiently expectorate, appropriate measures (such as drainage and aspiration) should be performed.

Skin reactions

The occurrence of severe skin reactions such as Stevens-Johnson syndrome and Lyell’s syndrome has very rarely been reported in temporal connection with the use of acetylcysteine. If cutaneous and mucosal changes occur, patients should consult their health care provider without delay and use of acetylcysteine should be terminated (see section 4.8).

Intolerance

Caution is advised in patients with histamine intolerance. Treatment with acetylcysteine for longer periods should be avoided in such patients, as acetylcysteine affects histamine metabolism and can result in symptoms of intolerance (e.g. headache, runny nose, itching).

Formulation

A mild sulphur odour does not indicate a change in the medicine but is a property of the active substance itself.

AMUCO 600 effervescent tablets should be dissolved fully before intake (section 4.2). Ingesting tablets which are not fully dissolved presents a risk of choking and aspiration, particularly to elderly patients.

Excipients

AMUCO 600 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.

AMUCO 600 contains aspartame.

Aspartame is a source of phenylalanine. It may be harmful for patients with phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

4.5 Interaction with other medicines and other forms of interaction

Antitussive medicines

Combined administration of AMUCO 600 with antitussives may cause a dangerous secretory congestion due to the reduced cough reflex, so that an especially careful diagnosis is required for this combination treatment.

Antibiotics

Tetracycline hydrochloride (with the exception of doxycycline) and other oral antibiotics must be administered separately from AMUCO 600 and with an interval of at least 2 hours.

Nitroglycerine

The concomitant administration of acetylcysteine can potentially result in an intensification of the vasodilatory and inhibition of platelet aggregation effects of glyceryl trinitrate (nitroglycerine).
If concomitant treatment with glyceryl trinitrate and acetylcysteine is considered necessary, patients should be monitored for the possible development of hypotension, which can be serious, and advised of the possibility of headaches.

Activated charcoal

Activated charcoal in high doses (as an antidote) can reduce the effectiveness of acetylcysteine.

Interactions with laboratory and urine tests

Acetylcysteine can affect the colorimetric determination of salicylates.
In urine tests, acetylcysteine can affect the results of determinations of ketone bodies.

Dissolution with other medicines

The dissolution of AMUCO 600 together with other medicines is not recommended.

4.6 Fertility, pregnancy and lactation

Safety and efficacy of acetylcysteine in pregnancy and lactation have not been established (see section 4.3).

Pregnancy

There are no adequate clinical data from the use of acetylcysteine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. AMUCO 600 should not be used during pregnancy.

Breastfeeding

No information is available regarding excretion of acetylcysteine or its metabolites into breast milk. A risk for the breast-fed child cannot be excluded. The use of acetylcysteine during breastfeeding is not recommended.

Fertility

Data concerning effects of acetylcysteine on human fertility are not available. In animal studies, no harmful effects on fertility were observed for therapy-relevant doses of acetylcysteine.

4.7 Effects on ability to drive and use machines

AMUCO 600 has no known effect on the ability to drive and use machines.

4.8 Undesirable effects

System Organ Class	**Less Frequent**	**Frequency unknown**
Immune system disorders	Hypersensitivity reactions	Anaphylactic shock, anaphylactic/ anaphylactoid reactions
Nervous system disorders	Headache, convulsions, syncope	
Eye disorders	Blurred vision	
Ear and labyrinth disorders	Tinnitus	
Cardiac disorders	Tachycardia	
Vascular disorders	Haemorrhage, hypertension	

Respiratory, thoracic and mediastinal disorders	Dyspnoea, bronchospasm - predominantly in patients with hyperactive reactive bronchial system in association with bronchial asthma	
Gastrointestinal disorders	Nausea, vomiting, diarrhoea, abdominal pain, stomatitis	Dyspepsia
Hepato-biliary disorders	Disturbances of the liver function, acidosis	
Skin and subcutaneous tissue disorders	*Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria, rash, angioedema, itching, exanthema, pruritus, flushing	
Musculoskeletal, connective tissue and bone disorders	Arthralgia	
General disorders and	Fever, hypotension	Facial oedema

administration site conditions		

*Severe skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in temporal association with the use of acetylcysteine.

If skin or mucous membrane abnormalities develop, the use of acetylcysteine must be discontinued immediately.

A decreased blood platelet aggregation in the presence of acetylcysteine has been confirmed by different studies. The clinical relevance has not yet been clarified to date.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Overdoses may lead to gastrointestinal symptoms such as nausea, vomiting and diarrhoea. Infants are at risk of hypersecretion.

Treatment of overdose is supportive and symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cough and cold preparations; Mucolytics

ATC Code: R05CB01

Acetylcysteine is a mucolytic agent that reduces the viscosity of non-infected bronchial secretions probably by the splitting of disulphide bonds in mucoproteins.
Acetylcysteine is a derivative of the amino acid cysteine. The efficacy of acetylcysteine is secretolytic and secretomotoric in the area of the respiratory tract. It splits off the interconnecting disulphide bonds between the mycopolysaccharide chains and that it has a depolymerising effect on DNA-chains (in purulent mucus).
This leads to a reduction in the viscosity of the mucus.

An alternative mechanism of acetylcysteine is meant to be based on the capacity of its reactive SH group to bind chemical radicals and to detoxify them in this way.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, acetylcysteine is rapidly and almost completely absorbed and metabolised in the liver to cysteine, the pharmacologically active metabolite, as well as to diacetylcystine, cysteine and further mixed disulphides.

Distribution

Due to the high first-pass effect, the bioavailability of orally administered acetylcysteine is very low (approx. 10 %). Maximum plasma concentrations are achieved after 1 to 3 hours. The protein binding of acetylcysteine is approximately 50 %.

Biotransformation

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

Elimination

Pharmacokinetic studies with intravenous administration of acetylcysteine revealed a distribution volume of 0,47 L/kg (in total) or 0,59 L/kg (reduced); the plasma clearance was determined to be 0,11 L/h/kg (in total) and 0,84 L/h/kg (reduced), respectively.

The elimination half-life after intravenous administration is 30 to 40 minutes while excretion follows three-phase kinetics (alpha, beta, and terminal gamma phase).

Acetylcysteine crosses the placenta and is detected in cord blood. No information is available regarding excretion into breast milk.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous citric acid

Sodium hydrogen carbonate

Aspartame

Povidone K-30

Sodium chloride

PEG 6000

Lemon flavour (contains corn maltodextrin, flavouring preparations, flavouring substances, natural flavouring substances and alpha-tocopherol (E307)).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

After first opening of the tube: 8 weeks

6.4 Special precautions for storage

Store at or below 25 °C in the original package in order to protect from moisture and light. Keep the container tightly closed.

For storage conditions after first opening of the medicine, see section 6.3.

6.5 Nature and contents of container

White, opaque polypropylene tablet container with polypropylene silica gel containing cap, in a carton box. Pack sizes of 10’s (1 container of 10 tablets) or 14’s (2 containers with 7 tablets each). Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

AMUCO 600: 47/10.3/0477

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03 May 2022

10. DATE OF REVISION OF THE TEXT