PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S1

1. NAME OF THE MEDICINE

MUCO-ACYST 200 (effervescent tablet)

Acetylcysteine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MUCO-ACYST 200 effervescent tablets contain:

200.0 mg of acetylcysteine per effervescent tablet.

MUCO-ACYST 200 is sugar free.

MUCO-ACYST 200 contains sweetener: saccharin sodium 20.0 mg /effervescent tablet

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

MUCO-ACYST 200: White to off white round, flat tablets.

Upon dissolving in water: Slightly opalescent, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MUCO-ACYST 200 effervescent tablets are used as a mucolytic, of non-infective secretions in cystic fibrosis and in respiratory conditions.

4.2 Posology and method of administration

Posology

Children from 2 to 5 years of age:

½ (half) an effervescent tablet 2 to 3 times daily (equivalent to 200 to 300 mg acetylcysteine

/day).

Children from 6 to 14 years of age:

1 (one) effervescent tablet twice daily (equivalent to 400 mg acetylcysteine /day).

Adults and adolescents from 14 years of age:

1 (one) effervescent tablet 2 to 3 times daily (equivalent to 400 to 600 mg acetylcysteine /day).

Do not use continuously for more than 14 days without consulting a doctor.

Method of administration:

The effervescent tablet should be dissolved in a glass of water before use.

Do not to swallow the tablet whole.

4.3 Contraindications

MUCO-ACYST 200 is contraindicated in:

- patients known to be hypersensitive to acetylcysteine or any of the excipients listed in section 6.1.
- pregnancy and lactation
- in children below 2 years of age.

4.4 Special warnings and precautions for use

Asthmatic patients

MUCO-ACYST 200 should be used with caution in asthmatic patients.

Elderly patients

MUCO-ACYST 200 should be used with caution in elderly patients with respiratory insufficiency.

History of peptic ulceration

MUCO-ACYST 200 should be used with caution in patients with a history of peptic ulceration, since mucolytics may disrupt the gastric mucosal barrier.

Do not use continuously for more than 14 days without consulting a doctor.

4.5 Interaction with other medicinal products and other forms of interaction

Antibiotics

Tetracycline hydrochloride (with the exception of doxycycline) and other oral antibiotics must be administered separately from MUCO-ACYST 200, with an interval of at least 2 hours before or after acetylcysteine.

In vitro tests have shown that when cephalosporin antibiotics and acetylcysteine are mixed, there is a degree of antibiotic inactivation.

Thereby verifying the administration of oral antibiotics at least two hours before or after acetylcysteine.

Antitussive medicines

Antitussive medicines and MUCO-ACYST 200 should not be administered concomitantly because reducing the cough reflex may lead to a buildup of bronchial secretions.

Activated charcoal may reduce the effect of MUCO-ACYST 200.

Nitroglycerin

Concurrent administration of nitroglycerin and acetylcysteine causes significant hypotension and leads to temporal artery dilation with possible onset of headache.

If concurrent administration of nitroglycerin and MUCO-ACYST 200 is required, patients should be monitored and be cautioned about hypotension that can be severe and

accompanied by a headache.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety and/or efficacy has not been established, therefore the use of MUCO-ACYST 200 is contraindicated during pregnancy (see section 4.3).

Lactation

It is not known whether acetylcysteine crosses into breastmilk. Mothers on MUCO-ACYST 200 should not breastfeed their infants (see section 4.3).

Fertility

There are no data available on the effect of MUCO-ACYST 200 on fertility

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed.

MUCO-ACYST 200 has no known effect on the ability to drive and use machines.

4.8 Undesirable effects

The occurrence of serious skin reactions such as Stevens Johnson syndrome and toxic epidermal necrolysis have been reported in temporal association with the use of acetylcysteine. In most of these cases reported, at least one other medicine was administered at the same time, which may have possibly enhanced the described muco-cutaneous effects. In the case of recurrence of skin and mucosal lesions, medical advice should be sought immediately and the use of MUCO-ACYST 200 must be terminated.

Immune system disorders:

Less frequent:

hypersensitivity, anaphylactic shock and anaphylactic/anaphylactoid reaction.

Nervous system disorders

Less frequent:

headache.

Frequency unknown:

convulsions.

Eye disorders

Frequency unknown:

blurred vision.

Ear and labyrinth disorders:

Less frequent:

tinnitus.

Cardiac disorders

Less frequent:

tachycardia.

Frequency unknown:

cardiac arrest.

Vascular disorders

Less frequent:

hypotension and haemorrhage.

Frequency unknown:

flushing, syncope and sweating.

Respiratory, thoracic and mediastinal disorders:

Less frequent:

Dyspnoea, bronchospasm - predominantly in patients with hyper reactive bronchial system in association with bronchial asthma, and rhinorrhoea.

Frequency unknown:

respiratory arrest and haemoptysis.

Gastrointestinal disorders:

Less frequent:

stomatitis, abdominal pain, diarrhoea, vomiting, heartburn, nausea and dyspepsia.

MUCO-ACYST 200 should be used with caution in patients with recent gastro-duodenal ulceration (see section 4.4).

Hepato-biliary disorders

Frequency unknown:

disturbances of liver function.

Skin and subcutaneous tissue disorders:

Less frequent:

urticaria, rash, angioedema and pruritus.

Musculoskeletal, connective tissue and bone disorders

Frequency unknown:

arthralgia.

General disorders and administrative site conditions

Less frequent:

Fever, chills.

Frequency unknown:

acidosis.

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

Adverse reactions must also be reported to Unicorn Pharmaceuticals (Pty) Ltd to enquiries@unicornpharma.co.za

4.9 Overdose

Symptoms and signs

An acute overdose of acetylcysteine can cause gastrointestinal symptoms such as nausea, vomiting and diarrhoea.

Management of overdose

Treatment of overdose is to be symptomatic and supportive treatment as indicated by the patient's clinical condition.

5. PHARMACOLOGICAL PROPERTIES

CATEGORY AND CLASS:

A 10.3 Medicines acting on the respiratory system - other

5.1 Pharmacodynamic properties

Acetylcysteine is a mucolytic medicine that reduces the viscosity of non-infected secretions in the respiratory tract probably by splitting of disulphide bonds in mucoproteins.

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), diacetylcysteine, cysteine and further mixed disulphides.

Distribution

Due to the high first-pass effect, the bioavailability of orally administered acetylcysteine is very low (approximately 10 %). In humans, maximum plasma concentrations are achieved after 13 hours with the maximum plasma concentration of the metabolite cysteine in the range of approximately 2µmol/l. The protein binding of acetylcysteine is about 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, diacetylcysteine) 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 acetylcysteine), the plasma clearance was determined to be 0.11 l/h/kg (in total) and 0.84 l/h/kg (reduced acetylcysteine), respectively. The elimination half-life after intravenous administration is 30-40 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 in 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

Maltodextrin, citric acid anhydrous, sodium hydrogen carbonate, leucine and orange flavour.

MUCO-ACYST 200 contains sweetener: saccharin sodium

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 °C in a cool dry place. Protect from light.

Keep tablets in the tube until required for use.

KEEP THE TUBE TIGHTLY CLOSED.

Do not use the tablets after the expiry date printed on the container.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6.5 Nature and contents of container

Polypropylene tube closed with a polyethylene stoppers equipped with silica gel as drying agent. The tube is inserted into cardboard boxes with the leaflet.

Pack sizes

MUCO-ACYST 200:

Pack size:

- Cardboard box containing a tube of 10 tablets.
- Cardboard box containing one or two tubes of 20 tablets each.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Cnr. Searle & Pontac Streets,

Cape Town,

South Africa, 8001

8. REGISTRATION NUMBER(S)

MUCO-ACYST 200: 46/10.3/0386

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03 Aug 2021

10. DATE OF REVISION OF THE TEXT

Pending variation approval