1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

TUSSMUCO 200 mg effervescent tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet of TUSSMUCO contains 200 mg N-acetylcysteine.

Contains sugar: Glucose liquid 113 mg and mannitol 190 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablets

TUSSMUCO is a round, white to off white, mottled, flat tablet plain on one side and a break line on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

TUSSMUCO 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

Adults and adolescents from 14 years of age:

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

Paediatric population

Children from 6 to 14 years of age:

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

Children from 2 to 5 years of age:

½ (half) an effervescent tablet 2 to 3 times daily (equivalent to 200 to 300 mg N-acetylcysteine/day).

Method of administration

For oral administration.

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

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

4.3. Contraindications

TUSSMUCO is contraindicated in:

- Patients with hypersensitivity to N-acetylcysteine or to any excipients in TUSSMUCO (see section 6.1).
- In children below 2 years of age.
- Safety in pregnancy has not been established. TUSSMUCO effervescent tablets should not be used during pregnancy (see section 4.6).
- Active peptic ulceration.

4.4. Special warnings and precautions for use

TUSSMUCO should be used with caution in asthmatic patients (see section 4.8).

Since mucolytics, such as TUSSMUCO may disrupt the gastric mucosal barrier, TUSSMUCO should be used with caution in patients with a history of peptic ulceration (see section 4.3).

Administration of TUSSMUCO, especially at the beginning of treatment, may liquefy bronchial secretions and, at the same time, increase their volume. If the patient is unable to expectorate efficiently, to avoid retention of secretions, postural drainage and tracheal suction should be used.

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 as contained in TUSSMUCO. If cutaneous and mucosal changes occur, the patient should seek medical advice without delay and the use of TUSSMUCO should be terminated (see section 4.8).

Caution is advised in patients with histamine intolerance. Treatment with TUSSMUCO for longer periods should be avoided in such patients as TUSSMUCO affects histamine metabolism and can result in symptoms of intolerance (e.g. headache, runny nose and itching) (see section 4.8).

Do not use TUSSMUCO continuously for more than 14 days without consulting a doctor (see section 4.2).

Children and adolescents

Mucolytics, such as TUSSMUCO, can result in blockage of the respiratory tract in children under 2 years of age due to the characteristics of their respiratory tract and their limited ability to cough up mucus. Therefore, TUSSMUCO must not be used in children under 2 years of age (see section 4.3).

Excipients

Patients with rare glucose-galactose malabsorption should not take this medicine.

4.5. Interaction with other medicines and other forms of interaction

Tetracycline hydrochloride (with the exception of doxycycline) and other oral antibiotics such as cephalosporin cause a degree of antibiotic inactivation and must be administered separately from TUSSMUCO and with an interval of at least 2 hours.

Antitussive medicines and TUSSMUCO should not be administered concomitantly because reducing the cough reflex may lead to a build-up of bronchial secretions.

Activated charcoal may reduce the effect of TUSSMUCO.

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

If concurrent administration of nitroglycerin and TUSSMUCO is required, patients should be monitored and warned for hypotension that can be severe and accompanied by a headache.

TUSSMUCO can affect the colometric determination of salicylates.
In urine tests, TUSSMUCO can affect the results of determination of ketone bodies.
The dissolution (mixing) of TUSSMUCO together with other medicines is not recommended.

4.6. Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy has not been established (see section 4.3).

Breastfeeding

Safety has not been established.
There is insufficient information on the excretion of N-acetylcysteine in human milk. A risk to the newborns/infants cannot be excluded.

Fertility

No data available

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

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that TUSSMUCO do not adversely affect their ability to do so safely (see section 4.8).

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Immune system disorders		Anaphylactic reactions up to shock, hypersensitivity (allergic reactions), anaphylactic/anaphylactoid reaction	
Nervous system disorders		Headache	
Ear and labyrinth disorders		Tinnitus	
Cardiac disorders		Tachycardia	
Vascular disorders		Haemorrhage, hypotension,	
Respiratory, thoracic and mediastinal disorders		Dyspnoea, bronchospasm - predominantly in patients with hyper reactive bronchial system in association with bronchial asthma	
Gastrointestinal disorders		Stomatitis, abdominal pain, diarrhoea, vomiting, heartburn, nausea, dyspepsia	
Skin and subcutaneous tissue disorders		Pruritus, urticaria, exanthema, rash, angioedema, Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN).	
General disorders and administrative site conditions		Fever	Oedema of the face

b) Description of selected adverse reactions

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 N-acetylcysteine, as contained in TUSSMUCO.

In case of recurrent skin and mucosal lesions, medical advice should be sought at once and the use of N-acetylcysteine terminated immediately.

A decreased blood platelet aggregation in the presence of N-acetylcysteine has been confirmed by various 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 providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/health-products-vigilance/

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

Small children are at risk of hypersecretion (see section 4.8).

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

Treatment

Treatment would be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

A 10.3 Medicines acting on the respiratory system – other

Pharmacotherapeutic group: Mucolytics

ATC code: R05CB01

Mechanism of action

N-acetyl-L-cysteine (NAC) exerts an intense mucolytic fluidising action on mucous and mucopurulent secretions by depolymerising the mucoproteic complexes and the nucleic acids which confer viscosity to the vitreous and purulent component of the sputum and other secretions.

5.2. Pharmacokinetic properties

Absorption

Following oral administration, N-acetylcysteine is rapidly and almost completely absorbed and metabolised in the liver to cysteine (the pharmacologically active metabolite), diN-acetylcysteine, cysteine and further mixed disulphides.

Distribution

Due to the high first-pass effect, the bioavailability of orally administered N-acetylcysteine is very low (approximately 10 %). In humans, maximum plasma concentrations are achieved after 1 to 3 hours with the maximum plasma concentration of the metabolite cysteine in the range of approximately 2 µmol/L. The protein binding of N-acetylcysteine was determined to be about 50 %.

Biotransformation

N-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. N-acetylcysteine is excreted almost exclusively in the form of inactive metabolites (inorganic sulphates, di-acetylcysteine) via the kidneys. The plasma half-life of N-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 N-acetylcysteine revealed a distribution volume of 0,47 L/kg (in total) or 0,59 L/kg (reduced N-acetylcysteine); the plasma clearance was determined to be 0,11 L/h/kg (in total) and 0,84 L/h/kg (reduced N-acetylcysteine), 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).

N-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 N-acetylcysteine at the blood-brain barrier in humans.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Ascorbic acid, citric acid anhydrous, glucose liquid, lemon flavour, mannitol, sodium benzoate, sodium bicarbonate, sodium citrate, tartaric acid.

Lemon flavour consists of: acacia gum 414, ascorbic acid 300, corn maltodextrin, flavouring preparation, natural flavouring substance.

6.2. Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C.

6.5. Nature and contents of container

15 or 20 or 25 or 40 (2 x 20's) tablets are packed into a polypropylene tube with a white LDPE cap with a tamper seal and desiccant. The tube is packed into a cardboard carton.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

54/10.3/0854

9. DATE OF FIRST AUTHORISATION

17 November 2020

10. DATE OF REVISION OF TEXT

10 June 2022

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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