PROFESSIONAL INFORMATION

MUCOFIZZ 200

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

MUCOFIZZ 200 effervescent tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 200 mg acetylcysteine.

Sugar free.

Contains sweetener (saccharin sodium 20 mg).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Before reconstitution:

White to off white round, flat tablets.

After reconstitution:

Slightly opalescent, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MUCOFIZZ 200 is 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:

One (1) effervescent tablet two to three times daily (equivalent to 400 to 600 mg N-

acetylcysteine/day) for a maximum of 14 days.

Paediatric population

Children from 6 to 14 years of age:

One (1) effervescent tablet twice daily (equivalent to 400 mg N-acetylcysteine/day) for a maximum of 14 days.

Children from 2 to 5 years of age:

Half (½) an effervescent tablet two to three times daily (equivalent to 200 to 300 mg N-acetylcysteine/day) for a maximum of 14 days.

Method of administration

Oral use.

MUCOFIZZ 200 effervescent tablets 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

- Hypersensitivity to acetylcysteine or to any of the ingredients of MUCOFIZZ 200
- Pregnancy and lactation (see section 4.6)
- Children under the age of 2 years.

4.4 Special warnings and precautions for use

MUCOFIZZ 200 should be used with caution in asthmatic patients and elderly patients with respiratory insufficiency.

Patients with bronchial asthma should be closely monitored during therapy; if bronchospasm occurs, treatment with MUCOFIZZ 200 should be discontinued immediately.

Administration of acetylcysteine, as in MUCOFIZZ 200, 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.

MUCOFIZZ 200 may disrupt the gastric mucosal barrier, it should therefore be used with caution in patients with a history of peptic ulceration.

The total clearance of acetylcysteine in patients with cirrhosis was found to be markedly impaired, and the elimination half-life almost twice that of healthy patients. Since some of the more serious adverse effects of acetylcysteine occur when plasma concentrations are high, increased vigilance for untoward anaphylactoid reactions and other adverse effects may be necessary in patients with cirrhosis taking MUCOFIZZ 200.

Acetylcysteine, as in MUCOFIZZ 200, can cause interference with the colorimetric assay method for the determination of salicylates as well as with tests for ketones in urine.

4.5 Interaction with other medicines and other forms of interaction

Antitussive medicines and MUCOFIZZ 200 should not be administered concomitantly because reducing the cough reflex may lead to a build-up of bronchial secretions.

MUCOFIZZ 200 must be administered separately from tetracycline hydrochloride (with the exception of doxycycline) and other oral antibiotics, with an interval of at least 2 hours as there is a degree of antibiotic inactivation when taken together.

Activated charcoal may reduce the effect of acetylcysteine as in MUCOFIZZ 200.

Concurrent administration of nitro-glycerine (glyceryl trinitrate) and MUCOFIZZ 200

causes significant hypotension and leads to temporal artery dilation with possible onset of headache.

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If concurrent administration of nitro-glycerine (glyceryl trinitrate) and MUCOFIZZ 200 is required, patients should be monitored and warned for hypotension that can be severe and accompanied by a headache.

4.6 Fertility, pregnancy and lactation

Safety and efficacy during pregnancy and lactation have not been established.

Pregnancy

MUCOFIZZ 200 should not be used during pregnancy (see section 4.3).

Breastfeeding

It is not known whether acetylcysteine crosses into breastmilk. MUCOFIZZ 200 should not be taken when breastfeeding (see section 4.3).

Fertility

Fertility data are not 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. MUCOFIZZ 200 has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Tabulated summary of adverse reactions

System Organ Class	Frequency	Side effects
Immune system disorders	*Less frequent*	Hypersensitivity, anaphylactoid reaction/anaphylactic shock, angioedema
Metabolism and nutrition disorders	*Frequency unknown*	Acidosis
Nervous system disorders	*Less frequent* *Frequency unknown*	Headache Syncope, convulsions
Eye disorders	*Less frequent*	Blurred vision
Ear and labyrinth disorders	*Less frequent*	Tinnitus
Cardiac disorders	*Less frequent* *Frequency unknown*	Tachycardia Cardiac arrest
Vascular disorders	*Less frequent* *Frequency unknown*	Hypotension, haemorrhage Hypertension, flushing, sweating
Respiratory, thoracic and mediastinal disorders	*Less frequent* *Frequency unknown*	Dyspnoea, bronchospasm, rhinorrhoea Respiratory arrest, haemoptysis
Gastrointestinal disorders	*Less frequent*	Abdominal pain, diarrhoea, nausea, vomiting, stomatitis, heartburn
Hepato-biliary disorders	*Frequency unknown*	Disturbances in liver function
Skin and subcutaneous tissue disorders	*Less frequent* *Frequency unknown*	Urticaria, rash, pruritus, exanthema Oedema of the face
Musculoskeletal, connective tissue and bone disorders	*Frequency unknown*	Arthralgia
General disorders and administrative site conditions	*Less frequent*	Chills, fever

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 acetylcysteine, as in MUCOFIZZ 200. In most of these cases reported at least one other medicine was administered at the same time, which may have possibly enhanced the described mucocutaneous effects.

In case of recurrence skin and mucosal lesions, medical advice should be sought at once and the use of MUCOFIZZ 200 terminated immediately.

A decreased blood platelet aggregation in the presence of acetylcysteine, as in MUCOFIZZ 200, 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 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

Signs and symptoms:

An acute overdose of MUCOFIZZ 200, can cause gastrointestinal symptoms such as nausea, vomiting and diarrhoea.

Management of overdose:

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mucolytics

ATC code: R05CB01

Pharmacological classification:

A.10.3 Medicines acting on the respiratory system – others

Mechanism of action

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

5.2 Pharmacokinetic properties

Absorption

Acetylcysteine is rapidly absorbed and almost completely from the gastrointestinal tract with peak plasma concentrations achieved within 0,5 to 1 hour after oral doses of 200 to 600 mg.

Distribution

Acetylcysteine may be present in plasma and tissues as either the parent compound or as various metabolites such as cysteine, *N,N-diacetylcysteine*, and *N-acetylcysteine* either free or bound to plasma proteins. The protein binding of Acetylcysteine was determined to be about 50 %.

Biotransformation

Acetylcysteine is extensively metabolised in the gut wall and liver (high first-pass effect) and as a result has an oral bioavailability of approximately 10 %.

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

Renal clearance may account for 30 % of total body clearance. Following oral administration, the mean terminal half-life of acetylcysteine was calculated to be 6,25 hours.

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

Citric acid

Leucine

Maltodextrin

Orange flavour

Saccharin sodium

Sodium hydrogen carbonate

6.2 Incompatibilities

In the absence of compatibility studies, MUCOFIZZ 200 must not be mixed with other medicinal products.

6.3 Shelf life

36 months

In use: 3 months

After reconstitution, MUCOFIZZ 200 must be administered immediately.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture. Store in the original tube and keep the tube tightly closed when not in use.

6.5 Nature and contents of container

MUCOFIZZ 200 tablets are packed in a polypropylene tube closed with a polyethylene stopper equipped with silica gel. Each tube contains 10, 20 or 40 effervescent tablets and is packed in an outer carton.

Not all pack sizes are marketed in South Africa.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

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7945, South Africa

8. REGISTRATION NUMBER

A46/10.3/0384

9. DATE OF FIRST AUTHORISATION

November 2021

10. DATE OF REVISION OF THE TEXT

January 2022