For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

MUCOVISC

1. Generic Name

Acetylcysteine Effervescent Tablets 600 mg

2. Qualitative and quantitative composition

Each effervescent tablet contains:
Acetylcisteine B.P. ……600 mg
Excipients……q.s.
The excipients used are Ethyl cellulose, Methylene Dichloride, Sodium Bicarbonate, Anhydrous Citric Acid, Sodium Benzoate, Sodium Acetate, Sodium Chloride, Mannitol, Sucralose and Trusil Orange Flavour.

3. Dosage form and strength

Dosage form: Effervescent Tablets
Strength: 600 mg

4. Clinical particulars

4.1 Therapeutic indication

Acetylcysteine is indicated for use as a mucolytic in respiratory disorders such as in bronchitis, emphysema, mucoviscidoses and bronchiectasis. MUCOVISC tablets is indicated in adults only

4.2 Posology and method of administration

Posology
Adults

1 effervescent tablet of 600 mg once daily.

Paediatric population

Children older than 2 years of age and adolescents

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

Children under 2 years of age

The use of MUCOVISC is contraindicated in children under 2 years of age (see section 4.3).

Method of administration
Precautions to be taken before handling or administering the medicinal product.
For patients with a reduced cough reflex (elderly and weakened patients) are advised to take the effervescent tablet in the mornings.

Dissolve MUCOVISC in water (about 250 ml). This produces a solution that may be consumed immediately.

MUCOVISC are contraindicated in children under 2 years of age (see section 4.3). Other forms and strengths of Acetylcysteine are more suitable for are more suitable for children >2 and adolescents.

4.3 Contraindications

- Hypersensitivity to acetylcysteine or to any of the excipients.
- The tablets should not be used by children under 2 years of age.

4.4 Special warnings and precautions for use

Bronchospasms may occur with the use of acetylcysteine. If bronchospasm occur, the medicinal product should be discontinued immediately.
Caution is advised in patients with a history of peptic ulcer, especially when used concomitantly with other medicinal products known to irritate the mucous membrane of the gastrointestinal tract.

Serious skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome have very rarely been reported in temporal connection with the use of acetylcysteine. In most cases, at least one other suspect medicinal product, which was more likely the cause of the mucocutaneous syndrome could be identified. If cutaneous or mucosal alterations newly occur, immediate medical advice should be sought and the treatment with acetylcysteine should be discontinued immediately.

Bronchial secretions may become more fluid and increase in volume, in particular at the start of the treatment with acetylcysteine. When a patient is unable to cough up the secretions effectively, postural drainage and Broncho aspiration should be performed.

Paediatric population

Mucolytic drugs may obstruct the airways of children under 2 years of age, due to the physiological characteristics of the airways in this age group. The ability to cough up mucus may be limited. Therefore, mucolytic drugs should not be used in children under 2 years of age.

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

A mild sulfur odour does not indicate a change in the medicinal product, but is a property of the active substance itself.

Excipients

MUCOVISC contain sodium per dose in the form of sodium hydrogen carbonate. Caution is advised in patients on a sodium-restricted diet.

4.5 Drugs interactions

Interaction with other medicinal products
Simultaneous solution of MUCOVISC with other medicinal products is not recommended.

To date, the inactivation of antibiotics by acetylcysteine has been reported only in *in-vitro* tests, whereby the relevant substances were mixed directly with each other. However, if oral antibiotics are required, it is advised that these should be taken two hours before or after Acetylcysteine.

Acetylcysteine should not be administered concomitantly with antitussive medicinal products.

Acetylcysteine may enhance the vasodilatory effects of nitroglycerin. Caution is advised.

Activated charcoal can decrease the effect of acetylcysteine due to reduced absorption.

Interactions with laboratory tests

Acetylcysteine may have an effect on the values of salicylates by colorimetric analysis.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are limited data about the use of acetylcysteine in pregnant women. Animal studies do not indicate reproductive toxicity (see section 5.3). Acetylcysteine crosses the placenta. Available data do not indicate a risk to the child. If necessary, the use of MUCOVISC during pregnancy may be considered.

Breast-feeding

It is not known whether acetylcysteine passes into human milk, but at therapeutic doses no effects of acetylcysteine are expected on the infant. MUCOVISC may 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, however, not likely.

4.8 Undesirable effects

The table below lists the undesirable effects recorded after systemic use of oral acetylcysteine according to system/organ class.

System/organ class	**Undesirable effect**			
	Uncommon (≥1/1,000 to <1/100)	**Rare** (≥1/10.000 to <1/1,000)	**Very rare** (<1/10,000)	**Not known**
Immune system disorder	Hypersensitivity*		Anaphylactic shock, anaphylactic/anaphylactoid reactions	
Nervous system disorders	Headache			
Ear and labyrinth disorders	Tinnitus			
Vascular disorders			Haemorrhages	
Gastrointestinal disorders	Stomatitis, abdominal pain, nausea, vomiting, diarrhoea	Dyspepsia		
Skin and subcutaneous tissue disorders				Facial oedema

General disorders and administration site conditions	Pyrexia			
Investigations	Low blood pressure			

A decrease in platelet aggregation in the presence of acetylcysteine has been confirmed in various studies. The clinical significance of this has not been determined.

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

Acetylcysteine may have an undesirable effect on the gastric mucosa in patients with a history of peptic ulcer or peptic ulcer *[sic]*

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product 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 any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose

To date no toxic overdose has been observed for the oral pharmaceutical forms of acetylcysteine.

Voluntary study subjects were treated for three months with a dose of 11.6 acetylcysteine per day without any serious undesirable effects being observed.

Oral doses of up to 500 mg acetylcysteine per kg body weight are tolerated without any signs of poisoning.

Symptoms

Overdoses may lead to gastrointestinal effects such as nausea, vomiting and diarrhoea.

Treatment in the event of an overdose

Symptomatic treatment in the event of an overdose.

5. Pharmacological properties

5.1 Mechanism of Action

Acetylcysteine is a mucolytic.
The mucolytic action is mediated by a reduction in the viscosity of bronchial mucus. This is explained by the depolymerisation with the disulfide bridges between the macromolecules in the mucus being opened.

5.2 Pharmacodynamics properties

Pharmacotherapeutic group: Mucolytics ATC-code: R05C B01
Mechanism of action /Pharmacodynamic effects
Acetylcysteine is a mucolytic.

The mucolytic action is mediated by a reduction in the viscosity of bronchial mucus. This is explained by the depolymerisation with the disulfide bridges between the macromolecules in the mucus being opened.

In addition, acetylcysteine is a precursor of glutathione. Acetylcysteine is a derivative of the natural amino acid cysteine, which serves as a substrate for the synthesis of glutathione in the body.

Apart from the fact that acetylcysteine is able to normalise a state of glutathione depletion, it is able to conjugate with various toxic compounds.

5.3 Pharmacokinetic properties

Absorption / Distribution

Acetylcysteine is rapidly absorbed after oral administration and distributed throughout the organism. The highest tissue concentrations are reached in the liver, kidneys and lungs.

Biotransformation / Elimination

Acetylcysteine is mainly deacetylated to cysteine in the liver. Most of this is processed in the amino acid metabolism. Moreover, it forms reversible disulfide compounds with amino acids and proteins with free sulfydryl groups. Finally, high doses are largely converted into inorganic sulfate, which undergoes renal excretion.

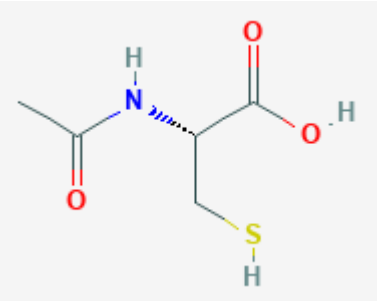
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Preclinical data of acetylcysteine based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction do not indicate a risk to humans.

7. Description

Acetylcisteine is also known as N-acetylcysteine or N-acetyl-L-cysteine or NAC. It is chemically (2R)-2-acetamido-3-sulfanylpropanoic acid having molecular weight of 163.2 and molecular formula of $C_5H_9NO_3S$. The chemical structure is:



Acetylcysteine Effervescent Tablets 600 mg are white colored, circular, flat, uncoated tablets, plain on both sides. The excipients used are Ethyl cellulose, Methylene Dichloride,

Sodium Bicarbonate, Anhydrous Citric Acid, Sodium Benzoate, Sodium Acetate, Sodium Chloride, Mannitol, Sucralose and Trusil Orange Flavour.

8. Pharmaceutical particulars

8.1 Incompatibilities

Acetylcysteine can react with rubber and metal (e.g. iron, nickel, copper). Use of glass and/or plastic delivery systems is recommended when administering via nasogastric or nasointestinal tube.

Do not mix antibiotics and acetylcysteine prior to administration, due to the possibility of *in-vitro* inactivation of the antibiotics (mainly β-lactam antibiotics).

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

MUCOVISC is available in pack of 10 tablets.

8.4 Storage and handing instructions

Store at a temperature not exceeding 25°C, Protected from light and moisture.

Keep medicines out of reach of children.

9. Patient Counselling Information

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet?

9.1 What MUCOVISC are **and what they are used for.**

Acetylcysteine breaks down and loosens thick phlegm, making it runny and easy to cough up. Acetylcysteine is used in the treatment of airway diseases such as bronchitis (inflammation of the mucous membrane in the airways), emphysema, mucoviscidosis (cystic fibrosis) and bronchiectasis (chronic widening of an airway passage). MUCOVISC is indicated only for adult**.**

9.2 What you need to know before you use MUCOVISC

Do not use MUCOVISC

- You are allergic to **MUCOVISC** or to any of the other ingredients of this medicine.
- Children under 2 years of age may not use this medicine.

Warning and Precautions
If you suffer of bronchial asthma then you should not take this medicine.

- If you have or have had a peptic ulcer, as MUCOVISC may irritate your gastric wall. In particular if you use other drugs known to irritate the gastric wall.

- There have been very rare reports of serious hypersensitivity reactions with (high) fever, skin redness, joint pains and/or eye infection (Stevens-Johnson syndrome), and acute hypersensitivity reactions accompanied by fever and blisters on the skin or peeling of the skin (Lyell syndrome) which were associated with the use of MUCOVISC . However, in most cases, at least one other medicine was used, which was most likely the cause for this reaction.

- If new changes to the skin or mucous membranes occur, you must immediately consult a doctor and stop using acetylcysteine. As the thick phlegm becomes more fluid, its volume will increase, especially at the beginning of the treatment. If you are unable to efficiently cough up this fluid phlegm, you must consult a doctor so that adequate measures can be taken to remove the phlegm.

- Medicines, such as MUCOVISC that dissolve phlegm (mucolytics) may block the airways of children under the age of 2, due to the characteristics of the airways in this age group. This may limit their ability to cough up phlegm. Therefore, MUCOVISC must not be used by children under the age of 2.

- MUCOVISC are not suitable for use in children and adolescent younger than 18.

- When opening the package you may perceive a mild sulfur odour (smell of rotten eggs). This is a property of the active ingredient and is normal. It does not indicate that the medicine has changed.

Other medicines and MUCOVISC
If you are using other medicines, do not dissolve them together with MUCOVISC. If you need to use medicines to control or prevent infections (antibiotics), you are advised to take these two hours before or after MUCOVISC. Cough suppressants should not be used at the same time as MUCOVISC, as you must be able to cough up the loosened phlegm. MUCOVISC may increase the blood pressure-lowering effect of nitroglycerin (a medicine used against tight painful feeling in the chest (angina pectoris)). Caution is advised. If you use activated charcoal (a medicine against traveller's diarrhoea), it may decrease the effect of MUCOVISC. Tell your doctor or pharmacist if you are taking or have recently taken any other medicines apart from MUCOVISC, including medicines obtained without a prescription.

Pregnancy and breast-feeding
Pregnancy

There is a limited amount of data from the use of acetylcysteine in pregnant women. Animal studies do not indicate direct or indirect harmful effects on the pregnancy, or the development of the child, before, during or after birth. Only use MUCOVISC after careful consideration of the benefits and risks during pregnancy.

Breast-feeding

It is not known whether acetylcysteine is excreted in breast milk. Only use Acetylcysteine

Alpex 600 mg effervescent tablets after careful consideration of the benefits and risks during breast-feeding. If you are pregnant or breast-feeding, contact your doctor or pharmacist before any medicine.

Driving and using machines

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

Ingredients of this medicine you should take into account this medicinal product contains sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

9.3 How to use MUCOVISC

Adults: 1 effervescent tablet once daily. Patients who have difficulty coughing up phlegm (elderly and weakened patients), are advised to take the effervescent tablet in the mornings. Dissolve the effervescent tablet in half a glass of water. Drink the solution immediately. Always use this medicine exactly as prescribed. Check with your doctor or pharmacist if you are not sure. Do not use this medicine for longer than 14 days without consulting a doctor.

If you use more MUCOVISC than you should Symptoms that may occur are: nausea, vomiting and diarrhoea. If you have used too many MUCOVISC, immediately contact your doctor or pharmacist. If you forget to take MUCOVISC if you have forgotten to take a dose and it is almost time for the next dose, do not take the 'forgotten' dose, but continue the schedule as given under "How to use MUCOVISC ". Do not take a double dose to make up for a forgotten dose.

If you use more MUCOVISC than you should

Symptoms that may occur are: nausea, vomiting and diarrhoea. If you have used too many MUCOVISC, immediately contact your doctor or pharmacist.

If you forget to take MUCOVISC

If you have forgotten to take a dose and it is almost time for the next dose, do not take the 'forgotten' dose, but continue the schedule as given under "How to use MUCOVISC “. Do not take a double dose to make up for a forgotten dose.

9.4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. If any of the following side effects occur, immediately stop using MUCOVISC and contact your doctor or go the emergency room of a nearby hospital.

- Shock (severe drop in blood pressure, paleness, restlessness, weak pulse, clammy skin, decreased consciousness) due to a sudden widening of the blood vessels as a result of severe hypersensitivity to certain ingredients (anaphylactic shock).
- Sudden fluid accumulation in the skin and mucous membranes (e.g. throat or tongue), breathing difficulties and/or itching and skin rash, often as a result of an allergic reaction (angioedema). The above mentioned reactions are very serious side effects. If you experience any of these reactions it is possible that you have a hypersensitivity reaction to MUCOVISC. You will require emergency medical care or need be admitted to the hospital. This very serious side effect is very rare (occurs in less than 1 in 10,000 users). Bleedings are also very rare. Inform you doctor if you experience any of the following side effects:
- Shortness of breath due to muscle cramping of the airways (bronchospasms).
- Difficulty breathing, shortness of breath or breathlessness (dyspnoea).

- Impaired digestion with symptoms of fullness in the upper abdomen, gastric pain, belching, nausea and heartburn (dyspepsia). These side effects are rare (occurring in 1 to 10 in every 10,000 users).
- Hypersensitivity this may manifests itself as bronchospasms and dyspnoea (see above) rapid heart rate (tachycardia), itching (pruritus), skin rash with severe itching and small bumps (urticaria) and angioedema.
- Headache
- Ringing in the ears (tinnitus)
- Inflammation of the oral mucous lining (stomatitis)
- Diarrhoea
- Fever (pyrexia)
- Low blood pressure
- Abdominal pain
- Nausea
- Vomiting

These side effects are uncommon (occurring in 1 to 10 in every 1,000 users). If you suffer from gastric or duodenal ulcers or have had these in the past, acetylcysteine may have an unfavourable effect on your gastrointestinal mucous membrane. If any of the side effects become serious, or you notice any side effects not mentioned in this leaflet, contact your doctor or pharmacist. Consult with your doctor or pharmacist if you notice that the effect of MUCOVISC is too strong or not strong enough.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store MUCOVISC

Store at a temperature not exceeding 25°C, Protected from light and moisture.

9.6 Contents of the pack and other information

MUCOVISC is available in pack of 10 tablets

10 Details of manufacturer

Manufactured by:
Swiss Garnier Genexiaa Sciences Private Limited.
(Unit II), Plot No. 568-569 & 576-579, Tarpin Block,
Rhenock, Rongli, East Sikkim – 737133.

11 Details of permission or licence number with date

Mfg Lic No. M/750/2016 issued on 28.03.2018

12 Date of revision

Not Applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/MUCOVISC 600 mg**/DEC-19/01/PI**