Package Leaflet

Fluimucil®

For oral use

PHARMACOLOGICAL PROPERTIES

Acetylcysteine (NAC), the active ingredient of FLUIMUCIL®, exerts an intense mucolytic-fluidifying action on mucous and mucopurulent secretions, by depolymerizing the mucoproteic complexes and the nucleic acids which confer viscosity to the vitreous and purulent component of the sputum and of other secretions.

Additional properties are: reduction of induced hyperplasia of mucous cells, increase in surfactant production by stimulation of type II pneumocytes, stimulation of mucociliary activity, leading to improved mucociliary clearance.

Furthermore, NAC, exerts a direct antioxidant action, being provided with a free thiol (-SH nucleophilic) group, which is able to interact directly with the electrophilic groups of the oxidant radicals. Of particular interest is the finding that NAC protects the ∝-1-antitrypsin, enzyme inhibitor of elastase, from the inactivation due to the action of hypochlorous acid (HOCl), a powerful oxidant agent produced by the myeloperoxidase enzyme of activated phagocytes. Furthermore, Acetylcysteine exerts in addition an indirect antioxidant effect through its role as GSH precursor. Inside the cell, NAC is deacetylized, forming L-cysteine, an amino acid indispensable for the glutathione synthesis (GSH). GSH is a highly reactive tripeptide, found ubiquitously in the various tissues of animals and is essential for the maintenance of functional capacity as well as cellular morphological integrity, as it represents the most important protective, endocellular mechanism against oxidant radicals, either of external or internal nature as well as towards numerous cytotoxic substances. NAC plays a role of primary importance in the maintenance of adequate GSH levels thus contributing to the cellular protections from harmful agents which, through progressive GSH depletion, would be able to express their cytotoxic actions, as in the case of acetaminophen poisoning. Due to this mechanism of action, NAC is also indicated as a specific antidote in acetaminophen poisoning. In the course of a cyclophosphamide treatment and in haemorrhagic cystitis, (in the latter case it provides SH-groups necessary to inactivate acrolein, a toxic metabolite that affects the urinary mucosa, whilst not interfering with chemotherapy).

INDICATIONS

FLUIMUCIL® is indicated as an adjuvant treatment in certain clinical condition characterized by the presence of thick and viscous mucoid or mucopurulent secretions such as:

- Chronic bronchopulmonary diseases (chronic obstructive pulmonary disease, emphysema with bronchitis, chronic asthmatic bronchitis, bronchiectasis);
- Acute bronchopulmonary diseases (asthma with bronchial mucus plugging, bronchitis, bronchopneumonia, tracheobronchitis, bronchiolitis, pulmonary complications of cystic fibrosis, pulmonary complications associated with surgery).

CONTRAINDICATIONS
Known hypersensitivity to acetylcysteine or to any of the excipients (please see below the section Warning and Precautions)
Children under 2 years of age.

POSOLOGY
Adults and children above 6 years
– 1 sachet FLUIMUCIL® 200mg or 2 sachets FLUIMUCIL® 100mg, 2-3 times a day;
Children (2-6 years of age)
– 1 sachet FLUIMUCIL® 100 mg from 2 to 4 times a day, according to the age.

The duration of treatment should be 5 to 10 days in the acute treatment, whereas it may be continued in the chronic states for several months, according to the advice of the physician.

MODALITY OF USE
Dissolve the contents of the sachets in a glass containing a small quantity of water, mixing it, if necessary, with a spoon. A palatable solution is thus obtained, to be drunk immediately.

WARNING AND PRECAUTIONS
Mucolytic agents can induce respiratory obstruction in children under 2 years of age. Due to the physiological characteristics of the airways in this age group, the ability to expectorate may be limited. Therefore mucolytic agents should not be used in children under 2 years of age (see paragraph Contraindications)

Caution should be taken in patients suffering from or with a history of peptic ulcer, especially in the case of concomitant administration of other medicines with a known irritating effect on the gastric mucosa.

Patients suffering from bronchial asthma must be strictly controlled during the therapy; should bronchospasm occur, the treatment must immediately be suspended.

The administration of acetylcysteine, mainly at treatment start, might fluidify bronchial secretion and increase their volume. If the patient is not able to effectively expectorate, postural drainage and bronchoaspiration should be performed.

Acetylcysteine may moderately affect histamine metabolism, therefore caution should be used when administering the product for long-term therapy in patients with histamine intolerance, since symptoms of intolerance can occur (headache, vasomotor rhinitis, itching)

The possible presence of a sulphureous odour does not indicate an alteration of the product but is a characteristic of the active ingredient contained in this preparation.
FLUIMUCIL® contains Sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking FLUIMUCIL®. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
FLUIMUCIL® contains colouring agent E110: it may cause allergic reactions

INTERACTION WITH OTHER MEDICINAL PRODUCTS

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Drug-drug interaction

Interaction studies have only been performed in adults.

Antitussive drugs and mucolytic agents, like acetylcysteine, should not be concurrently administered, because the reduction in cough reflex could lead to accumulation of bronchial secretions.

Activated charcoal may reduce the effect of acetylcysteine.

Dissolution of acetylcysteine formulations concomitantly with other drugs is not recommended.

Reports of an inactivation of antibiotics resulting from acetylcysteine so far only relate to in-vitro tests in which the relevant substances were mixed directly. Nevertheless, when other oral drugs or antibiotics are required, it is advisable to administer them 2 hours apart from acetylcysteine. This does not relate to loracarbef.

Concurrent administration of nitroglycerin and acetylcysteine has been shown to cause significant hypotension and enhance temporal artery dilation. If concurrent nitroglycerin and acetylcysteine therapy is necessary, patients should be monitored for hypotension, which can be severe, and warned of the possibility of headaches.

Concurrent use of acetylcysteine and carbamazepine may result in subtherapeutic carbamazepine levels.

Drug-Lab modifications

Acetylcysteine may cause interference with colorimetric assay method for salicylate measurement.

Acetylcysteine may interfere with urine ketone test.

FERTILITY, PREGNANCY AND LACTATION

Pregnancy

There are limited 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. As a precautionary measure, it is preferable to avoid the use of FLUIMUCIL® during pregnancy. Prior to use in pregnancy, the potential risks should be balanced against the potential benefits.

Lactation

It is unknown whether acetylcysteine/metabolites are excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from FLUIMUCIL® therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility
No data are available on the effect of acetylcysteine on human fertility. Animal studies do not indicate harmful effects with respect to fertility for humans at the recommended doses.
If you are pregnant or breastfeeding, ask your doctor or pharmacist for the advice before taking this medicine.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Acetylcysteine has no known influence on the ability to drive and use machines.

OVERDOSE
Healthy volunteers received 11.2 g acetylcysteine daily for three months without any serious undesirable effects. Oral doses of up to 500 mg acetylcysteine/kg body weight were tolerated without any symptoms of poisoning.

If you have taken more Fluimucil® than you should, you might experience nausea, vomit or diarrhoea. Contact your doctor.

Treatment
There is no specific antidote for acetylcysteine and treatment is symptomatic.

SIDE EFFECTS
The most frequent adverse events associated with the oral administration of acetylcysteine are gastrointestinal in nature. Hypersensitivity reactions including anaphylactic shock, anaphylactic/anaphylactoid reaction, bronchospasm, angioedema, rash and pruritus have been reported less frequently.

In the table below adverse reactions are listed by system organ class and frequency (very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System-organ class	**Undesirable effects**			
	Uncommon (≥1/1,000; <1/100)	**Rare (≥1/10,000; <1/1,000)**	**Very rare (<1/10,000)**	**Not known**
Immune system disorders	Hypersensitivity		Anaphylactic shock, anaphylactic/ anaphylactoid reaction	
Nervous system disorders	Headache			
Ear and labyrinth disorders	Tinnitus			
Cardiac disorders	Tachycardia			
Vascular disorders			Haemorrhage	

Respiratory, thoracic and mediastinal disorders		Bronchospasm, dyspnoea		
Gastrointestinal disorders	Vomiting, diarrhoea, stomatitis, abdominal pain, nausea	Dyspepsia		
Skin and subcutaneous tissue disorders	Urticaria, rash, angioedema, itching			
General disorders and administration site conditions	Fever			Face oedema
Investigations	Reduced arterial pressure			

In very rare cases, the occurrence of severe skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome has been reported in temporal connection with the administration of acetylcysteine. In most cases at least one co-suspect drug more probably involved in triggering the reported mucocutaneous syndrome could be identified. Because of this, medical advice should be sought straight away if any new changes to the skin or mucous membranes occur, and acetylcysteine should be stopped immediately.

A decrease in platelet aggregation in the presence of acetylcysteine has been confirmed by various investigations. The clinical significance has not yet been established.

If you get any side effects, talk to your doctor or pharmacist.

PHARMACEUTICAL PARTICULARS

LIST OF EXCIPIENTS of Fluimucil® (100mg granules for oral solution)
Sucrose, Colouring agent E 110, excipient q.s. to 5 grams

LIST OF EXCIPIENTS of Fluimucil® (200mg granules for oral solution)
Sucrose, Colouring agent E 110, excipient q.s. to 3 grams

INCOMPATIBILITIES
Fluimucil® must not be mixed with other medicinal products.

SHELF LIFE
3 years

SPECIAL PRECAUTIONS FOR STORAGE
Store below 25°C. Protect from heat and humidity.

PACKAGING

- FLUIMUCIL® 100mg - 30 sachets of 100 mg acetylcysteine.
- FLUIMUCIL® 200mg – 60 sachets of 200 mg acetylcysteine.

MARKETING AUTHORISATION HOLDER

United Italian Trading Corporation (Pte) Ltd

MANUFACTURED BY
Zambon Switzerland Ltd.
6814 Cadempino (Switzerland)

KEEP OUT OF SIGHT AND REACH OF CHILDREN.