

PACKAGE INSERT

ALPAC Effervescent Tablet 600mg

1. NAME OF THE MEDICINAL PRODUCT

ALPAC Effervescent Tablet 600mg.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ALPAC Effervescent Tablet 600mg contains 600 mg of N-Acetylcysteine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablet.

Round, flat, white to yellowish effervescent tablet (1500 mg/tablet; ~ 17 x 4.25mm). Clear with air bubbles after dissolve in water

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

All respiratory tract diseases leading to the formation of thick secretions difficult to be expectorated, such as acute and chronic bronchitis, laryngitis, sinusitis, tracheitis, influenza, bronchial asthma and (as complementary treatment) mucoviscidosis

4.2 Posology and method of administration

Posology

Adults

1 effervescent tablet of 600 mg once daily.

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 ALPAC Effervescent Tablet 600mg in a glass of water. This produces a solution that may be consumed immediately.

ALPAC Effervescent Tablet 600mg are contraindicated in children under 2 years of age (see section 4.3). Other forms and strengths of N-Acetylcysteine are more suitable for are more suitable for children >2 and adolescents.

4.3 Contraindications

- Hypersensitivity to N-Acetylcysteine or to any of the excipients listed in section 6.1.
- 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 N-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 N-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 N-Acetylcysteine should be discontinued immediately.

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

ALPAC Effervescent Tablet 600mg may cause severe allergy and serious skin reactions. Stop using ALPAC Effervescent Tablet 600mg and seek medical assistance immediately if you experience any of the following symptoms:

Severe allergy

Breathing difficulties, light headedness, skin swellings or rash.

Severe skin reaction

Skin reddening, blisters, rash, fever, sore throat or eye irritation.

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

ALPAC Effervescent Tablet 600mg contain 115 mg of sodium per dose in the form of sodium hydrogen carbonate. Caution is advised in patients on a sodium-restricted diet.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction with other medicinal products

Simultaneous solution of ALPAC Effervescent Tablet 600mg with other medicinal products is not recommended.

To date, the inactivation of antibiotics by N-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 N-Acetylcysteine.

N-Acetylcysteine should not be administered concomitantly with antitussive medicinal products.

N-Acetylcysteine may enhance the vasodilatory effects of nitroglycerin. Caution is advised. Activated charcoal can decrease the effect of N-Acetylcysteine due to reduced absorption.

Interactions with laboratory tests

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

Incompatibilities

N-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 N-Acetylcysteine prior to administration, due to the possibility of *in-vitro* inactivation of the antibiotics (mainly β -lactam antibiotics).

4.6 Pregnancy, lactation and fertility

Pregnancy

There are limited data about the use of N-Acetylcysteine in pregnant women. Animal studies do not indicate reproductive toxicity (see section 5.3). N-Acetylcysteine crosses the placenta. Available data do not indicate a risk to the child. If necessary, the use ALPAC Effervescent Tablet 600mg during pregnancy may be considered.

Breast-feeding

It is not known whether N-Acetylcysteine passes into human milk, but at therapeutic doses no effects of N-Acetylcysteine are expected on the infant. ALPAC Effervescent Tablet 600mg may be used during breastfeeding.

Fertility

Based on available preclinical experience, there are no indications for possible effects of the use of N-Acetylcysteine on fertility.

4.7 Effects on ability to drive and use machines

There are no data on the effect of N-Acetylcysteine on the ability to drive. An effect is, however, not likely.

4.8 Undesirable effects

Immune System Disorders

Anaphylactic / anaphylactoid reaction

Skin and Subcutaneous Tissue Disorders

Severe cutaneous adverse reactions (SCAR) e.g. erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). In most of these cases reported at least one other drug was administered at the same time, which may have possibly enhanced the described mucocutaneous effects.

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

System/organ class	Undesirable effect			
	Uncommon ($\geq 1/1,000$ to <1/100)	Rare ($\geq 1/10,000$ 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 N-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.

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

Preclinical safety data

Preclinical data of N-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.

4.9 Overdose

To date no toxic overdose has been observed for the oral pharmaceutical forms of N-Acetylcysteine.

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

Oral doses of up to 500 mg N-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 Pharmacodynamic properties

Pharmacotherapeutic group: Mucolytics ATC-code: R05C B01

Mechanism of action / Pharmacodynamic effects

N-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, N-Acetylcysteine is a precursor of glutathione. N-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 N-Acetylcysteine is able to normalise a state of glutathione depletion, it is able to conjugate with various toxic compounds.

5.2 Pharmacokinetic properties

Absorption / Distribution

N-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

N-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 sulfhydryl groups. Finally, high doses are largely converted into inorganic sulfate, which undergoes renal excretion.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Bicarbonate

Citric Acid

Orange Flavour

Sucralose

6.2 Shelf life

2 years

Shelf life after first opening: the product may be stored for a maximum of 90 days in tube with 10 effervescent tablets

6.3 Special precautions for storage

Store in the original package to protect against moisture.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.4 Nature and contents of container

The tablet container(s) are packaged in cardboard boxes. The box contains 10 effervescent tablets.

The effervescent tablets are packaged in a propylene tube with a polyethylene cap and a desiccant.

6.5 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Malaysia

Mansa Healthcare Sdn Bhd, E-3A-11 Starparc Point, Jalan Ibu Kota, Setapak, 53300
Kuala Lumpur, Malaysia

Singapore

Mansa Healthcare Pte Ltd, 3 Shenton Way, #07-05 Shenton House, Singapore 068805

8. MARKETING AUTHORISATION NUMBER(S)**Malaysia**

ALPAC Effervescent Tablet 600mg: MALXXXXX

Singapore

ALPAC Effervescent Tablet 600mg: SINXXXXX

9. MANUFACTURER

Alpex Pharma AS

Via Cantonale, 6805 Mezzovico – Vira

Switzerland

10. DATE OF REVISION OF THE TEXT

15 June 2021