Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nacsys 600 mg Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 600 mg of acetylcysteine.

Excipient(s) with known effect: contains sodium hydrogen bicarbonate (E500) (equivalent to 115 mg of sodium).

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).

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acetylcysteine is indicated for use as a mucolytic in respiratory disorders such as in bronchitis, emphysema, mucoviscidoses and bronchiectasis. NACSYS 600 mg effervescent 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 NACSYS 600 mg effervescent tablets 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 NACSYS 600 mg effervescent tablets in half a glass of water. This produces a solution that may be consumed immediately.

NACSYS 600 mg effervescent tablets 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 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 acetylcysteine especially in patients with asthma. If bronchospasms 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 bronchoaspiration 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 in 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
This medicinal product contains 115 mg sodium per effervescent tablet equivalent to 5.75% of the WHO recommended maximum daily intake of 2g for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction with other medicinal products
Simultaneous dissolution of NACSYS 600 mg effervescent tablets 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 Fertility, pregnancy and lactation

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 NACSYS 600 mg effervescent tablets 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. NACSYS 600 mg effervescent tablets 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, unlikely.

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.

In patients with a peptic ulcer or peptic ulcer history, acetylcysteine may have an unfavourable effect on the gastric mucosa.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2 Tel: +353 1 6764971 - Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

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 Pharmacodynamic 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.

5.2 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.

5.3 Preclinical safety data

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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydrogen carbonate (E500)
Citric acid (E330)
Sucralose (E955)
Orange flavour (contains Orange Essential Oil, Orange Essential Oil Terpenless, Gum Arabic (E414), butylhydroxyanisole (E320), Citric acid monohydrate (E330) and Maltodextrin (DE19))

6.2 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).

6.3 Shelf life

3 years
Shelf life after first opening: the product may be stored for a maximum of 10 days in tube with 10 effervescent tablets or 20 days in tube with 20 effervescent tablets.

6.4 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.

6.5 Nature and contents of container

The effervescent tablets are packaged in propylene tubes with a polyethylene cap and a desiccant. Each tube contains 6, 10 or 20 tablets.

The tube(s)are packaged in cardboard cartons containing6, 2x6, 10, 2x10, 20 or 3x10 effervescent tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Alpex Pharma (Irl) Limited
Stradbrook House
Stradbrook Road
Blackrock
Co. Dublin
A94 X9A2
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2166/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 2nd June 2017
Date of last renewal: 29th October 2019

10 DATE OF REVISION OF THE TEXT

July 2023