SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Acetylcysteine 200 mg Powder for Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains Acetylcysteine 200 mg.

Excipients with known effect:
Sucrose: 2.742 g per sachet
Lactose: 23.25 mg per sachet

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution.

White to off white granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Mucolytic adjuvant in the therapy of respiratory disorders associated with thick, viscous, mucus hypersecretion.

4.2 Posology and method of administration

Posology

Adults and adolescents over the age of 12 years
200 mg (1 sachet) 3 times a day. Maximum recommended daily dose 600 mg/day.

The duration of therapy is dependent on the nature and severity of the illness and should be decided by the doctor treating the patient for adults and adolescents. Abundant fluid intake supports the mucolytic effect of acetylcysteine.

Method of administration

Empty the contents of one sachet into a glass containing 150 ml of water and stir using a teaspoon until it dissolves completely (within 5 minutes). It is important to **drink all** of the mixture.

4.3 Contraindications

Acetylcysteine 200 mg Powder for Oral Solution must not be used when:

- Hypersensitivity to the active substance, other chemically similar substance (for example carbocisteine, erdosteine or mecysteine) or to any of the excipients listed in section 6.1, is present.

4.4 Special warnings and precautions for use

Patients with bronchial asthma should be closely monitored during therapy; if bronchospasm occurs, treatment with Acetylcysteine 200 mg Powder for Oral Solution should be discontinued immediately.

Administration of acetylcysteine, 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.

There are no studies on the efficacy and safety of acetylcysteine 200 mg three times daily in adolescent population. However, mild to severe adverse reactions have been reported with the use of IV acetylcysteine in adults and adolescents.

This medicine contains sucrose and lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per, that is to say, essentially ‘sodium-free’.

Acetylcysteine can cause interference with the colorimetric assay method for the determination of salicylates.

Acetylcysteine can interfere with tests for ketones in urine.

Upon opening the sachet, the powder may smell of sulphur (rotten egg smell). This is a normal characteristic of the active substance.

Caution is recommended in the use of the product in patients with peptic ulcer or a history of peptic ulcer, especially in concomitant administration with other drugs with known effect of irritation of gastric mucosa. If the appearance of gastric discomfort is observed, the clinical situation should be reevaluated.

Acetylcysteine can affect histamine metabolism in a moderate way, therefore it should be administered with caution in long-term treatment in patients with histamine intolerance, since symptoms of intolerance (headache, vasomotor, rhinitis, pruritus) may occur.

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions

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

Activated charcoal may reduce the effect of acetylcysteine.

It is advisable not to mix Acetylcysteine 200 mg Powder for Oral Solution with other medicinal products.

Due to its possible chelating effect, it should be taken into account that acetylcysteine can reduce the bioavailability of the salts of some metals such as gold, calcium and iron. In this case it is recommended to space the doses at least 2 hours apart.

In vitro tests have shown that when cephalosporin antibiotics and acetylcysteine are mixed, there is a degree of antibiotic inactivation. It is precautionary to advise the administration of oral antibiotics at least two hours before or after acetylcysteine.

Concurrent administration of nitroglycerin and acetylcysteine causes significant hypotension and leads to temporal artery dilation with possible onset of headache.

If concurrent administration of nitroglycerin and acetylcysteine 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

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Acetylcysteine 200 mg Powder for Oral Solution during pregnancy.

Breastfeeding

There is insufficient information on the excretion of acetylcysteine in human milk. A risk to the newborns/infants cannot be excluded.

Fertility

The potential effect of acetylcysteine in fertility is unknown. Animal studies do not indicate deleterious effects on fertility in humans at recommended doses (see section 5.3).

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. Acetylcysteine 200 mg Powder for Oral Solution has no known effect on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency.

System Organ Class	**Frequency/Adverse Reactions**			
	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	Hypotension		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, pruritus			
General disorders and administration site conditions	Fever			Oedema of the face

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. 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.

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

A decreased blood platelet aggregation in the presence of acetylcysteine 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 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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or apple App Store.

4.9 Overdose

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

Treatment of Overdose

Treatment of overdose is to be symptomatic and supportive treatment as indicated by the patient's clinical condition.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mycolytics, ATC code: R05CB01

N-acetyl-L-cysteine (NAC), the active ingredient in Acetylcysteine 200 mg Powder for Oral Solution exerts an intense mucolytic-fluidizing 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 other secretions.

Furthermore, acetylcysteine exerts a direct antioxidant action, having a free thiol (-SH) nucleophilic group that is able to interact directly with electrophilic groups of oxidant radicals. Of particular interest is the recent finding that acetylcysteine protects α1-antitrypsin enzyme inhibiting elastase from inactivation by hypochlorous acid (HOCl), a powerful oxidant agent produced by the myeloperoxidase enzyme of activated phagocytes. Due to its molecular structure, acetylcysteine can readily cross cell membranes. Inside the cell, NAC is deacetylated to L-cysteine, an amino acid essential for 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. It is the most important protective intracellular mechanism against oxidant radicals, both exogenous and endogenous, as well as toward numerous cytotoxic substances.

These features make Acetylcysteine 200 mg Powder for Oral Solution particularly suitable for the treatment of acute and chronic affections of the respiratory system, characterised by thick, viscous mucous and mucopurulent secretions.

There is no evidence on the efficacy and safety of mucolytics including acetylcysteine in acute bronchitis.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, acetylcysteine is rapidly and almost completely absorbed and metabolised in the liver to cysteine (the pharmacologically active metabolite), diacetylcysteine, cysteine and further mixed disulphides.

Distribution

Due to the high first-pass effect, the bioavailability of orally administered acetylcysteine is very low (approximately 10%). In humans, maximum plasma concentrations are achieved after 1-3 hours with the maximum plasma concentration of the metabolite cysteine in the range of approximately 2 μmol/l. The protein binding of Acetylcysteine was determined to be about 50%.

Biotransformation
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
Pharmacokinetic studies with intravenous administration of acetylcysteine revealed a distribution volume of 0.47 l/kg (in total) or 0.59 l/kg (reduced acetylcysteine); the plasma clearance was determined to be 0.11 l/h/kg (in total) and 0.84 l/h/kg (reduced acetylcysteine), respectively. The elimination half-life after intravenous administration is 30-40 minutes while excretion follows three-phase kinetics (alpha, beta and terminal gamma phase).

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

5.3 Preclinical safety data

Acute toxicity studies in rats and mice, by oral, intraperitoneal and intravenous administration showed acetylcysteine to be of low toxicity. LD50 values greater than 7 g / kg in mice and 6 g / kg in rats have been reported.

Chronic toxicity studies with acetylcysteine in rats at doses up to 2000 mg / kg / day and dogs at doses up to 300 mg / kg / day for periods up to 52 weeks demonstrate that acetylcysteine is well tolerated, even at higher doses.

In reproductive toxicity studies in rats and rabbits, the oral administration of doses up to 2000 mg / kg / day did not show changes in reproductive capacity, teratogenic effects or peri/postnatal toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Ascorbic Acid
Saccharin Sodium
Orange flavour DM6024 (natural & nature identical & synthetic flavoring ingredients, lactose)

6.2 Incompatibilities

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

6.3 Shelf life

24 months

After reconstitution, the product must be administered immediately.

6.4 Special precautions for storage

Store in a cool, dry place and protect from light. Keep the sachets in the outer carton. This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container

4 ply laminate paper foil sachet containing 3 g powder for oral solution, packaged in a cardboard box, in packs of 30 sachets.

6.6 Special precautions for disposal

No special requirements for disposal. Any unused product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Waymade Plc T/A Sovereign Medical,
Sovereign House,
Miles Gray Road,
Basildon,
Essex
SS14 3FR
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 06464/3113

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30/03/2021

10 DATE OF REVISION OF THE TEXT

30/03/2021