Patient Information Leaflet (For SINGAPORE market only)

mentopin®
Acetylcysteine 600

EFFERVESCENT TABLET

Active substance: ACETYLCYSTEINE

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

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
- You must talk to a doctor if you do not feel better or if you feel worse after 4-5 days.

What is in this leaflet

1. WHAT MENTOPIN ACETYLCYSTEINE 600 IS AND WHAT IT IS USED FOR

It is used to make mucus thinner and easier to cough up in bronchitis associated with the common cold. MENTOPIN Acetylcysteine 600 is a medicine that is used to make sticky mucus in the airways thinner.

Therapeutic indications

To loosen mucus and make it easier to cough up in respiratory tract conditions associated with sticky mucus. You must talk to a doctor if you do not feel better or if you feel worse after 4-5 days.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE MENTOPIN ACETYLCYSTEINE 600

Do not take MENTOPIN Acetylcysteine 600

- if you are allergic to Acetylcysteine or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- There have been very rare reports of the occurrence of severe skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis in temporal association with the use of Acetylcysteine. Therefore, if you develop any new skin and mucosal changes, you should seek medical advice and stop using Acetylcysteine straight away.
- Caution should be exercised if you have bronchial asthma or have ever had or have a stomach or intestinal ulcer.
- Caution should be exercised in patients with histamine intolerance. Prolonged treatment should be avoided in these patients because MENTOPIN Acetylcysteine 600 interferes with histamine metabolism and may lead to intolerance symptoms (e.g. headache, rhinitis, itching).
- The use of MENTOPIN Acetylcysteine 600, particularly when administration is first started, can thin bronchial secretions, resulting in an increase in the volume of these secretions. If you are not able to adequately expectorate this increase volume of secretions, appropriate measures will be performed by your doctor.

Children and adolescents

MENTOPIN Acetylcysteine 600 must not be used in children under 14 years of age because of its high active substance content.

Other medicines and MENTOPIN Acetylcysteine 600:

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

Cough suppressants/antitussives

When MENTOPIN Acetylcysteine 600 is used in combination with cough suppressants (antitussives), the reduced cough reflex may lead to dangerous stasis of secretions. Particular caution should therefore be exercised when using this combination. Therefore, be sure to consult your doctor prior to combined use.

Antibiotics

There is evidence from experimental studies to suggest that Acetylcysteine decreases the effect of antibiotics (tetracycline, aminoglycosides, penicillins). For safety considerations, antibiotics should therefore be taken separately and at least two hours apart from Acetylcysteine.

Activated charcoal

The use of activated charcoal may reduce the effect of acetylcysteine.

Glyceryl trinitrate

Enhanced dilation of blood vessels and decreased blood platelet effects have been reported when using glyceryl trinitrate and acetylcysteine at the same time. Your doctor will monitor you for reduced blood pressure, which could be serious and may be indicated by headache.

Dissolving acetylcysteine preparations concurrently with other medicinal products is not recommended.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

As no adequate experience with the use of Acetylcysteine in pregnant women is available, you should not use MENTOPIN Acetylcysteine 600 during pregnancy unless your treating doctor considers this absolutely necessary.

Breast-feeding

No information is available on the excretion of Acetylcysteine in breast milk. Therefore, you should not use MENTOPIN Acetylcysteine 600 whilst breast-feeding unless your treating doctor considers this absolutely necessary.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Driving and using machines

No special precautions need to be taken into consideration.

MENTOPIN Acetylcysteine 600 contains sodium, lactose and sorbitol

Each effervescent tablet contains 6 mmol (138.8 mg) sodium. To be taken into consideration by patients on a controlled sodium diet. This medicine contains lactose and sorbitol. Therefore, if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking MENTOPIN Acetylcysteine 600.

3. HOW TO TAKE MENTOPIN ACETYLCYSTEINE 600

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is:

Age	Total daily dose (effervescent tablets)
Adolescents over 14 years of age and adults	1 effervescent tablet once daily

Method of administration and total duration of use

If your condition gets worse or does not get better after 4-5 days, you should see a doctor.

Take MENTOPIN Acetylcysteine 600 after meals.

Please dissolve the MENTOPIN Acetylcysteine 600 in a glass of drinking water and drink all of the solution in the glass.

Note:
You may notice a smell of sulphur.

If you take more MENTOPIN Acetylcysteine 600 than you should

An overdose may cause symptoms of irritation in the gastrointestinal tract (e.g. abdominal pain, nausea, vomiting, diarrhoea). Serious side effects or symptoms of poisoning have not yet been observed even after massive overdoses of Acetylcysteine tablets. You should still notify your doctor if you suspect an overdose with MENTOPIN Acetylcysteine 600.

If you forget to take MENTOPIN Acetylcysteine 600

Do not take a double dose to make up for a forgotten dose.

If you stop taking MENTOPIN Acetylcysteine 600

Please do not stop taking MENTOPIN Acetylcysteine 600 without consulting your doctor first. If you do, your condition might get worse.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Significant side effects and signs you should pay attention for and measures, if you are affected:

Stop taking MENTOPIN Acetylcysteine 600 and contact your doctor immediately, if you experience any of the following side effects:

Uncommon (affects 1 to 10 users in 1,000):

- Allergic reactions (such as itching, formation of hives, skin rash, shortness of breath, swelling of the skin and mucous membranes, especially in the face, accelerated heart beat and blood pressure reduction)

Very rare (affects less than 1 user in 10,000):

- Severe allergic reactions, up to and including shock
- Serious skin reactions, such as Stevens-Johnson syndrome and Lyell's syndrome

Other possible side effects

Uncommon (affects 1 to 10 users in 1,000):

- Headache
- Inflammation of the oral mucous
- Abdominal pain
- Nausea
- Vomiting
- Diarrhoea
- Fever

Rare (affects 1 to 10 users in 10,000):

- Shortness of breath
- Bronchospasms - predominantly in patients with a hyper reactive bronchial system associated with asthma
- Digestive disorders (dyspepsia)

There have been very rare (affects less than 1 user in 10,000) reports of bleeding associated with the administration of Acetylcysteine, and some of these bleeding episodes occurred as part of hypersensitivity reactions.

Countermeasures

MENTOPIN Acetylcysteine 600 must not be taken again after the first signs of a hypersensitivity reaction (see above). If this happens, please contact a doctor.

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

5. HOW TO STORE MENTOPIN ACETYLCYSTEINE 600

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and foil strip after <Exp. Date:>. The expiry date refers to the last day of that month.

Store below 30°C in a dry place away from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What MENTOPIN Acetylcysteine 600 contains:

The active substance is: Acetylcysteine

The other ingredients are:

Citric acid, Ascorbic acid, Sodium hydrogen carbonate, Sodium carbonate, Mannitol, Lactose, Sodium cyclamate, Saccharin sodium, Sodium citrate, Flavour Lemon "AU", code 132 (contains sorbitol).

What MENTOPIN Acetylcysteine 600 Effervescent Tablet looks like and contents of the pack:

White, round tablets with a score line on one side.

MENTOPIN Acetylcysteine 600 are available in packs of 10 and 20 effervescent tablets.

Product Owner
HERMES ARZNEIMITTEL GMBH
Georg-Kalb-Str. 5 - 8
82049 Pullach I. Isartal
Germany

Manufacturer
HERMES PHARMA GMBH
Hans-Urmiller-Ring 52
82515 Wolfratshausen
Germany

Marketing Authorisation Holder & Distributor
MEDICELL PHARMACEUTICAL(S) PTE LTD
12 Tannery Rd #03-02/03 HB Centre 1
Singapore 347722

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PACKAGE INSERT

mentopin®

Acetylcysteine 600

EFFERVESCENT TABLET

Brand or Product Name
Mentopin Acetylcysteine 600mg Effervescent Tablet

Name and Strength of Active Substance(s)
Mentopin Acetylcysteine 600mg Effervescent Tablet contains 600mg acetylcysteine.

Product Description
Round, white tablets with a smooth and faultless surface and a break-mark on one side.

Pharmacodynamics
Pharmacotherapeutic group: mucolytics
ATC code: R05CB01

Mechanism of action
Acetylcysteine is a derivative of the amino acid cysteine. Acetylcysteine has a secretolytic and secretomotoric effect in the area of the bronchial tract. It is discussed that acetylcysteine breaks the disulfide bonds between the mucopolysaccharide fibres and has a depolymerising effect on DNA fibres (in purulent mucus). This mechanism is thought to decrease the viscosity of the mucus.

An alternative mechanism of acetylcysteine is meant to be based on the ability of its reactive SH group to bind – and hence detoxify – chemical radicals.

Furthermore, acetylcysteine contributes to an increased glutathione synthesis, which is an important endocellular mechanism against oxidant radicals, either of external or internal nature, as well as towards numerous cytotoxic substances. This explains its effect as an antidote in paracetamol intoxication.

Pharmacokinetics
Following oral administration, acetylcysteine is rapidly and almost completely absorbed and metabolized in the liver to cysteine, the pharmacologically active metabolite, as well as diacetylcystine, cystine and other mixed disulfides. Due to the high first-pass effect, the bioavailability of orally administered acetylcysteine is very low (approx. 10 %). In humans, maximum plasma concentrations are reached after 1 - 3 hours, whereby the maximum plasma concentration of the metabolite cysteine is in the range of approx. 2 µmol/l. Protein binding of acetylcysteine has been determined to be approx. 50 %.

Acetylcysteine and its metabolites occur in three different forms in the organism: partially in free form, partially bound to protein via labile disulfide bonds and partially as incorporated amino acid. Acetylcysteine is excreted almost exclusively in the form of inactive metabolites (inorganic sulphates, diacetylcystine) via the kidneys. The plasma half-life of acetylcysteine is approximately 1 hour and is mainly determined by its rapid hepatic biotransformation.

Impairment of hepatic function therefore leads to prolonged plasma half-lives of up to 8 hours.

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

N-acetylcysteine crosses the placenta and is detected in umbilical cord blood. There is no information available on the excretion into breast milk.
No knowledge is available concerning the behaviour of acetylcysteine at the blood-brain barrier in humans.

Indication
Treatment of respiratory affections characterized by thick & viscous hypersecretions: Acute bronchitis, chronic bronchitis and its exacerbations, pulmonary emphysema, mucoviscidosis & bronchiectasis.

Recommended Dosage
Adults and adolescents over 14 years of age: take 1 effervescent tablet once daily
Dissolve content of an effervescent tablet in a glass of water and drink immediately

Mode of Administration
Oral

Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in this package insert.
Due to the high amount of active substance it contains, Mentopin must not be used in children aged under 14.

Warnings and Precautions
Very rarely, severe skin reactions such as Stevens-Johnson syndrome and Lyell's syndrome have been reported in temporal association with the use of acetylcysteine. In most of these reported cases, at least one further medicinal product was administered which is presumed to be far more likely to cause the mucocutaneous symptoms. Should any new skin or mucosal changes occur, medical advice should therefore be sought immediately, and the patient should stop taking acetylcysteine.

The product should be used with caution in patients with asthma and patients with a history of ulcers.

Caution is required in patients with histamine intolerance. Long-term use should be avoided in patients with histamine intolerance, as acetylcysteine affects histamine metabolism and can produce symptoms of intolerance (e.g. headaches, runny nose, itching).

Administration of acetylcysteine, particularly when administration is first started, can thin bronchial secretions, resulting in an increase in the volume of these secretions. If the patient is unable to adequately expectorate this increased volume of secretions, appropriate procedures (e.g. postural drainage and suction) should be performed.

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

This medicinal product contains 138.8 mg sodium per effervescent tablet, equivalent to 7 % of the WHO recommended maximum daily dietary intake of 2 g sodium for an adult.

Interactions with other Medicaments
Cough suppressants (Antitussives)
Combined use of acetylcysteine with antitussives (cough suppressants) may cause a dangerous secretory congestion due to the reduced cough reflex. Hence, particular care is required when determining whether there is an indication for treatment with this combination.

Antibiotics
Up to now, reports on inactivation of antibiotics (tetracycline, aminoglycosides, penicillins) by acetylcysteine have only emerged from in vitro trials, in which the substances concerned were mixed directly. For safety considerations, oral administration of antibiotics should therefore be taken separately with an interval of at least 2 hours.
This does not apply to loracarbef.

Activated charcoal
The use of activated charcoal may reduce the effect of acetylcysteine.

Glyceryl trinitrate (nitroglycerin)
Co-administration of acetylcysteine can result in an enhancement of vasodilatory and antiplatelet effects of glyceryl trinitrate (nitroglycerin). If a common treatment with nitroglycerin and acetylcysteine is considered necessary, the patient should be monitored for a potential hypotension, which could be serious and may be indicated by headache.
Dissolution of acetylcysteine formulations concomitantly with other drugs is not recommended.

Statement on usage during pregnancy and lactation
Pregnancy
No sufficient clinical data on exposed pregnant women are available for acetylcysteine.

Experimental animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Breastfeeding
There is no information available on the excretion into breast milk.
The use of acetylcysteine in pregnancy and lactation should follow a strict assessment of benefit-risk ratio.

Fertility
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Adverse Effects / Undesirable Effects
The frequency of undesirable effects is based on the following categories:

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
Not known	Cannot be estimated from the available data

Immune system disorders

Uncommon:	Allergic reactions (such as pruritus, urticaria, rash, bronchospasm, angioedema, tachycardia and hypotension)
Very rare:	Anaphylactic/anaphylactoid reactions with shock in extreme cases

Nervous system disorders

Uncommon:	Headache

Gastrointestinal disorders

Uncommon:	Stomatitis, abdominal pain, nausea, vomiting and diarrhoea
Rare:	Dyspepsia

Respiratory, thoracic and mediastinal disorders

Rare:	Dyspnoea, bronchospasm – predominantly in patients with a hyperreactive bronchial system associated with asthma

General disorders and administration site conditions

Uncommon:	Fever

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. Should any new skin or mucosal changes occur, medical advice should therefore be sought immediately, and the patient should stop taking acetylcysteine.

Furthermore, bleeding has been reported very rarely in association with the administration of acetylcysteine, in some cases as part of hypersensitivity reactions. A decrease in blood platelet aggregation in the presence of acetylcysteine has been confirmed by various studies. To date, the clinical relevance of this has not yet been clarified.

Overdose and Treatment
There is no specific antidote for acetylcysteine and treatment is symptomatic. General supportive measures should be carried out and if necessary, according to the symptoms.

List of Excipients
Citric acid, sodium hydrogen carbonate, sodium carbonate, ascorbic acid, mannitol, lactose, lemon flavour (contains sorbitol [Ph. Eur.]), sodium cyclamate, saccharin sodium, sodium citrate.

Storage Conditions
Store below 30°C

Dosage Forms and Packaging
Mentopin Acetylcysteine 600mg Effervescent Tablet: Pack in aluminium seal foil (pack of 2 x 5's, 2 x 10's).

Name and Address of Manufacturer
Hermes Pharma GmbH
Hans-Urmiller-Ring 52,
82515 Wolfrathausen,
Germany.

Date of Revision of Package Insert
July 2021