

PACKAGE INSERT TEMPLATE FOR ACETYLCYSTEINE GRANULES

Brand or Product Name

[Product name] Granules

Name and Strength of Active Substance(s)

...mg equivalent to ...mg

Product Description

[Visual description of the appearance of the product (eg colour, markings etc)]

eg Yellow granules with a characteristic orange, slightly sulphurous odour

Pharmacodynamics

Acetylcysteine exerts its mucolytic action through its free sulfhydryl group, which opens the disulfide bonds and lowers mucus viscosity. This action increases with increasing pH and is most significant at pH 7 to 9. The mucolytic action of acetylcysteine is not affected by the presence of DNA. N-acetylcysteine has been demonstrated to cause a decrease in sputum consistency, to facilitate easier expectoration, and to increase sputum volume. Bronchial mucus is composed of over 95% water; however, the physical characteristics of the mucus are due to glycoproteins. These glycoproteins bind to each other by way of disulfide bonds and give the mucus viscosity. N-acetylcysteine ruptures these disulfide bonds causing depolymerization and a rapid decrease in mucus viscosity. It also produces an irritative bronchorrheic effect on the mucosa, stimulating mucociliary clearance; this irritative effect may cause bronchospasm, thus acetylcysteine is not recommended in asthmatics.

Pharmacokinetics

Absorption

Absorption of acetylcysteine is rapid following oral administration, but the bioavailability is only 6-10% due to extensive first pass metabolism.

Oral bioavailability is similar for a single 600-mg dose and three 200-mg doses

Peak plasma levels of acetylcysteine occur approximately one hour following oral administration.

Distribution

Acetylcysteine may be present in plasma as the parent compound or as various oxidised metabolites such as N-acetylcystine, N,N-diacetylcystine, and cysteine either free or bound to

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plasma proteins by labile disulfide bonds or as a fraction incorporated into protein peptide chains.

Following a 100-mg oral dose, 48% was present in lung tissue

Metabolism

Acetylcysteine undergoes extensive metabolism in the liver and intestinal wall.

Acetylcysteine undergoes rapid deacetylation in vivo to yield cysteine or oxidation to yield diacetylcystine . Following deacetylation in the liver, it enters the normal metabolic pathway of the amino acid cysteine . An appreciable elevation in total serum sulfhydryl concentration occurs.

Elimination

Renal Excretion: 22% to 30%

Faeces: 3%

Total Body Clearance: 6.5 L/hr (healthy subjects)

The mean terminal half-life is approximately 6 hours.

Indication

Indicated as secretolytic/mucolytic therapy in acute & chronic bronchopulmonary diseases associated with abnormal mucus secretion & impaired mucus transport.

Recommended Dosage

Adults:

600 mg daily as a single dose or in divided doses (200mg 2 - 3 times a day)

Children:

- 2 to 7 years 200mg twice daily.
- 8 years and over: Adult dose

*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.

*Dissolve content of a sachet in a glass of water and drink immediately.

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Mode of Administration

Oral

Contraindications

It is contraindicated in patients with hypersensitivity to acetylcysteine, or any of the excipients.

Contraindicated in children under 2 years of age

Warnings and Precautions

Acetylcysteine should be used with caution in asthmatic patients, elderly or debilitated patients with severe respiratory insufficiency. It should also be used with caution in patients with a history of peptic ulcer disease, both because drug-induced nausea and vomiting may increase the risk of gastrointestinal haemorrhage in patients predisposed to the condition, and because of a theoretical risk that mucolytics may disrupt the gastric mucosal barrier.

Allergic symptoms including generalized urticaria have been reported; discontinue acetylcysteine if symptoms appear and cannot be medically managed

Encephalopathy due to hepatic failure; discontinue acetylcysteine therapy to avoid further administration of nitrogenous substances

Interactions with Other Medicaments

Acetylcysteine should not be taken simultaneously with charcoal as it may cause a reduction in the absorption of acetylcysteine.

Statement on Usage During Pregnancy and Lactation*Pregnancy*

No adequate and well-controlled studies have been done in pregnant women. Therefore, acetylcysteine should be used during pregnancy only when clearly needed.

Lactation

It is not known whether or not acetylcysteine passes into breast milk. Until more data is available, use caution when considering the use of acetylcysteine in lactating women.

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Adverse Effects / Undesirable Effects

Hypersensitivity reactions have been reported in patients receiving acetylcysteine, including bronchospasm, angioedema, rashes and pruritus; hypotension, or occasionally hypertension, may occur. Other adverse effects reported with acetylcysteine include flushing, nausea and vomiting, fever, syncope, sweating, arthralgia, blurred vision, disturbances of liver function, acidosis, convulsions, and cardiac or respiratory arrest.

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.

Storage Conditions

[eg Store below.... °C]

Dosage Forms and Packaging Available

[Packaging type & pack size]

Name and Address of Manufacturer

[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder

[Name & full address of marketing authorization holder]

Date of Revision of Package Insert

[day/month/year]

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