

# Mucomist<sup>®</sup> Respirator Solution,

Acetylcysteine USP 200 mg/ ml

Solution for inhalation (not for injection)

## DESCRIPTION

Mucomist<sup>®</sup> Respirator Solution is a derivative of the amino acid, cysteine. It acts mostly on the mucoproteins, through its free sulphhydryl groups, to open disulphide bonds and lower the viscosity of the mucus. Furthermore, acetylcysteine exerts an antioxidant action by interacting directly with the oxidant radicals. The action of acetylcysteine in limiting hepatotoxicity after paracetamol (acetaminophen) overdose is probably due to the replenishing of hepatic stores of glutathione.

## INDICATIONS

Mucomist<sup>®</sup> is indicated as adjuvant therapy for patients with abnormal, viscid, or inspissated mucus secretions in such conditions as:

- Chronic bronchopulmonary disease (chronic emphysema, emphysema with bronchitis, chronic asthmatic bronchitis, tuberculosis, bronchiectasis, and primary amyloidosis of the lungs)
- Acute bronchopulmonary disease (pneumonia, bronchitis, tracheobronchitis)
- Pulmonary complications of cystic fibrosis
- Tracheostomy care
- Pulmonary complications associated with surgery
- Use during anaesthesia
- Post-traumatic chest conditions
- Atelectasis due to mucus obstruction
- Diagnostic bronchial studies (bronchograms, bronchspirometry, and bronchial wedge catheterization)

## As an Antidote for Acetaminophen Overdose

Acetylcysteine, administered orally, is indicated as an antidote to prevent or lessen hepatic injury, which may occur following the ingestion of a potentially hepatotoxic quantity of acetaminophen. It is essential to initiate treatment as soon as possible after the overdose and, in any case, within 24 hours of ingestion.

## DOSAGE AND ADMINISTRATION

### As a Mucolytic Agent

The 20% solution may be diluted to a lesser concentration with either Sodium Chloride for Injection, Sodium Chloride for Inhalation, Sterile Water for Injection, or Sterile Water for Inhalation. Acetylcysteine may be administered using conventional nebulizers made of plastic or glass. Certain materials used in the nebulization equipment react with acetylcysteine. The most reactive of these are certain metals (notably iron and copper) and rubber. Acetylcysteine should not be placed directly into the chamber of a heated (hot pot) nebulizer.

### **Nebulization (Face Mask, Mouthpiece, Tracheostomy)**

When nebulized into a face mask, mouthpiece, or tracheostomy, 1–10 mL of the 20% solution may be given every 2–6 hours. The recommended dose for most patients is 3–5 mL of the 20% solution, 3–4 times a day.

### **Nebulization Tent or Croupette**

Under special circumstances, it may be necessary to nebulize into a tent or croupette, and this method of use must be individualized to take into account the available equipment and the patient's particular needs. This form of administration requires very large volumes of the solution, occasionally as much as 300 mL during a single treatment period. If a tent or croupette must be used, the recommended dose is the volume of acetylcysteine (using 20%) that will maintain a very heavy mist in the tent or croupette for the desired period. Administration for intermittent or continuous prolonged periods, including overnight, may be desirable.

### **Direct Instillation**

When used by direct instillation, 1–2 mL of a 20% solution may be given as often as every hour. When used for the routine nursing care of patients with tracheostomy, 1–2 mL of a 20% solution may be given every 1–4 hours by instillation into the tracheostomy.

Acetylcysteine may be introduced directly into a particular segment of the bronchopulmonary tree by inserting (under local anaesthesia and direct vision) a small plastic catheter into the trachea. Then, 2–5 mL of the 20% solution may be instilled by means of a syringe connected to the catheter. Acetylcysteine may also be given through a percutaneous intratracheal catheter. Here, 1–2 mL of the 20% solution, every 1–4 hours, may be given via a syringe attached to the catheter.

### **Diagnostic Bronchograms**

For diagnostic bronchial studies, two to three administrations of 1–2 mL of the 20% solution should be given by nebulization or by instillation intratracheally, prior to the procedure.

### **As an Antidote for Acetaminophen Overdose**

Regardless of the overdose of acetaminophen ingested, administer acetylcysteine immediately if 24 hours or less have elapsed from the reported time of ingestion. Do not wait for the results of the assays for acetaminophen before initiating treatment with acetylcysteine.

The stomach should be emptied promptly by lavage or by inducing emesis with syrup of ipecac. In the case of mixed drug overdose, activated charcoal may be indicated. However, if activated charcoal has been administered, lavage before administering acetylcysteine treatment.

Administer the loading dose of acetylcysteine at 140 mg per kg of body weight. Then, 4 hours after the loading dose, administer the first maintenance dose (70 mg of acetylcysteine per kg of body weight). The maintenance dose should then be repeated at 4-hour intervals for totally 17 doses, unless the acetaminophen assay reveals a non-toxic level as discussed below.

If the patient vomits the loading dose or any maintenance dose within 1 hour of administration, repeat that dose.

In the occasional instances where the patient is persistently unable to retain the orally administered acetylcysteine, the antidote may be administered to duodenal intubation.

### **Preparation of Acetylcysteine for Oral Administration**

Oral administration requires dilution of the 20% solution with diet cola or other diet soft drinks, to a final concentration of 5%. If administered via a gastric tube or a Miller-Abbott tube, water

may be used as the diluent. The dilutions should be freshly prepared and utilized within 1 hour. The remaining undiluted solutions in the opened vials can be stored in the refrigerator up to 96 hours.

***Dosage Guide and Preparation***

<b>Doses in Relation to Body Weight</b>					
<b>Body Weight (kg)</b>	<b>Body Weight (lb)</b>	<b>Grams Acetyl-cysteine</b>	<b>Loading Dose of Acetylcysteine</b>		
			<b>mL of 20% Acetylcysteine</b>	<b>mL of Diluent</b>	<b>Total mL of 5% Solution</b>
100–109	220–240	15	75	225	300
90–99	198–218	14	70	210	280
80–89	176–196	13	65	195	260
70–79	154–174	11	55	165	220
60–69	132–152	10	50	150	200
50–59	110–130	8	40	120	160
40–49	88–108	7	35	105	140
30–39	66–86	6	30	90	120
20–29	44–64	4	20	60	80
<b>(kg)</b>	<b>(lb)</b>	<b>Maintenance Dose **</b>			
100–109	220–240	7.5	37	113	150
90–99	198–218	7	35	105	140
80–89	176–196	6.5	33	97	130
70–79	154–174	5.5	28	82	110
60–69	132–152	5	25	75	100
50–59	110–130	4	20	60	80
40–49	88–108	3.5	18	52	70
30–39	66–86	3	15	45	60
20–29	44–64	2	10	30	40

\*\* If a patient weighs less than 20 kg (usually, patients younger than 6 years of age), calculate the dose of acetylcysteine. Each mL of 20% solution contains 200 mg of acetylcysteine. The loading dose is 140 mg/kg of body weight. The maintenance dose is 70 mg/kg. To each mL of 20% acetylcysteine, 3mL of diluent should be added. Do not decrease the proportion of diluent.

**CLINICAL PHARMACOLOGY**

### ***As a Mucolytic Agent***

The viscosity of pulmonary mucus secretions depends on the concentrations of mucoprotein and, to a lesser extent, deoxyribonucleic acid (DNA). The latter increases with increasing purulence owing to the presence of cellular debris. The mucolytic action of acetylcysteine is related to the sulphhydryl group in the molecule. This group probably “opens” disulphide linkages in the mucus, thereby lowering the viscosity. Acetylcysteine undergoes rapid deacetylation *in vivo* to yield cysteine, or oxidation to yield diacetylcystine.

### ***As an Antidote for Acetaminophen Overdose***

Acetaminophen is rapidly absorbed from the upper gastrointestinal tract, with peak plasma levels occurring 30–60 minutes after therapeutic doses and usually within 4 hours following an overdose. Acetylcysteine has been shown to reduce the extent of liver injury following acetaminophen overdose. Its effectiveness depends on early oral administration, with benefits seen principally in patients treated within 16 hours of the overdose. Acetylcysteine probably protects the liver by maintaining or restoring the glutathione levels, or by acting as an alternate substrate for conjugation with the reactive metabolite and, therefore, resultant detoxification.

### **CONTRAINDICATIONS**

Hypersensitivity to acetylcysteine, its derivatives, or any of the components in the preparation.

### **WARNINGS AND PRECAUTIONS**

After proper administration of acetylcysteine, an increased volume of liquefied bronchial secretions may occur. When cough is inadequate, the airway must be maintained open by mechanical suction if necessary. When there is a mechanical block due to foreign body or local accumulation, the airway should be cleared by endotracheal aspiration, with or without bronchoscopy. Asthmatics under treatment with acetylcysteine should be watched carefully. Most patients with bronchospasm are quickly relieved by the use of a bronchodilator given by nebulization. If bronchospasm progresses, the medication should be discontinued immediately. With the administration of acetylcysteine, the patient may observe, initially, a slight disagreeable odour that soon becomes unnoticeable. With a face mask, there may be stickiness on the face after nebulization. This is easily removed by washing with water.

Under certain conditions, a color change may occur in acetylcysteine in the opened bottle. The light purple color is the result of a chemical reaction which does not significantly affect safety or mucolytic effectiveness of acetylcysteine.

Dilution of acetylcysteine minimizes the propensity of oral acetylcysteine to aggravate vomiting.

### **Drug Interactions**

It is preferable not to mix other drugs with the **Mucomist® Respirator Solution**. Drug stability and safety of acetylcysteine when mixed with other drugs have not been established. Acetylcysteine should not be mixed with certain antibiotics. For example, antibiotics like tetracycline hydrochloride, oxytetracycline hydrochloride, and erythromycin lactobionate were found to be incompatible when mixed in the same solution. These agents may be administered from separate solutions if administration of these agents is desirable.

**Hepatic Impairment**

There are no data indicating that acetylcysteine influences hepatic failure, but this remains a theoretical possibility.

**Pregnancy**

*Pregnancy Category B.* There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies may not always be predictive of human responses, **Mucomist® Respirator Solution** should be administered to pregnant women only if clearly needed.

**Lactation**

It is not known if this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **Mucomist® Respirator Solution** are administered to nursing mothers.

**UNDESIRABLE EFFECTS**

Adverse effects have included stomatitis, nausea, vomiting, fever, rhinorrhoea, drowsiness, clamminess, chest tightness, and bronchoconstriction. Clinically overt acetylcysteine-induced bronchospasm occurs infrequently and unpredictably, even in patients with asthmatic bronchitis or bronchitis complicating bronchial asthma. Acquired sensitization to acetylcysteine has been reported rarely. Reports of irritation to the tracheal and bronchial tracts have been received and, although, haemoptysis has occurred in patients receiving acetylcysteine, such findings are not uncommon in patients with bronchopulmonary disease and a causal relationship has not been established. Oral administration of acetylcysteine, especially in the large doses needed to treat acetaminophen overdose, may result in nausea, vomiting and other gastrointestinal symptoms. Rash, with or without mild fever, has been observed rarely.

**OVERDOSAGE**

No particular symptoms have been observed in patients accidentally taking high doses of **Mucomist® Respirator Solution**. However, in cases of overdose, treatment should be symptomatic and supportive.

**PHARMACEUTICAL PRECAUTION**

The physical and chemical compatibility of acetylcysteine solutions with certain other drugs that might be concomitantly administered by nebulization, direct instillation, or topical application has been studied. Acetylcysteine should not be mixed with certain antibiotics. For example, antibiotics like tetracycline hydrochloride, oxytetracycline hydrochloride, and erythromycin lactobionate were found to be incompatible when mixed in the same solution. These agents may be administered from separate solutions if administration of these agents is desirable. If it is deemed advisable to prepare an admixture, it should be administered as soon as possible after preparation. Do not store unused mixtures.

**SHELF-LIFE:** 2 years

**STORAGE AND HANDLING INSTRUCTIONS**

**Mucomist® Respirator Solution** do not contain an antimicrobial agent; hence, care must be taken to minimize contamination of the sterile solution. If only a portion of the solution is used, store the remainder in a refrigerator and use only for inhalation within 96 hours. Store in a cool. Protect from light.

**PACKAGING INFORMATION: Mucomist® 200 Respiratory Solution 3 ml** Available in pack of 5 ampoules