acetylcysteine - Drug Summary

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Related Drug Information

CLASSES

Antidotes, Systemic
Mucolytics

DEA CLASS

Rx

DESCRIPTION

N-acetyl derivative of L-cysteine
Used as an antidote for acetaminophen overdose, to reduce COPD exacerbations, may be effective in limiting nephrotoxicity due to radiographic-contrast agents, questionable efficacy as a mucolytic
Possesses a strong odor, often described as rotten eggs

COMMON BRAND NAMES

Acetadote, CETYLEV, Mucomyst, Mucosil Acetylcysteine

HOW SUPPLIED

Acetadote/Acetylcysteine Intravenous Inj Sol: 1mL, 200mg
Acetylcysteine/Mucomyst/Mucosil Acetylcysteine Oral Sol: 10%
Acetylcysteine/Mucomyst/Mucosil Acetylcysteine Respiratory (Inhalation) Sol: 10%, 20%
CETYLEV Oral Tab Effrv: 2.5g, 500mg

DOSAGE & INDICATIONS

For the prevention of hepatotoxicity after an acute acetaminophen overdose or repeated ingestion of supratherapeutic doses.

NOTE: The Rumack-Matthew nomogram should be used to estimate the hepatotoxicity potential from an acute acetaminophen (APAP) overdose in patients with a known APAP concentration, a known APAP ingestion time, and who present within 8 hours of the overdose. For patients whose serum APAP concentrations fall above the "possible" toxicity line on the nomogram, initiate treatment within 8 hours of suspected APAP ingestion for maximal protection against hepatic injury. Give activated charcoal as soon as possible after ingestion to prevent APAP absorption. For regular-release APAP overdoses, obtain serum drug concentration at least 4 hours post-ingestion; concentrations obtained earlier than 4 hours may not represent maximum APAP concentrations. For extended-release APAP overdoses, if the initial APAP serum concentration was below the possible toxicity line, obtain a second concentration 8 to 10 hours post-ingestion. The efficacy of acetylcysteine diminishes progressively after 8 hours post-ingestion. Beginning treatment 15 to 24 hours post-ingestion results in limited efficacy; however, it does not appear to worsen the condition and should not be withheld since the reported time of ingestion may not be correct. If the time of ingestion is unknown, or the serum APAP concentration is not available, cannot be interpreted, or is not available within 8 hours of APAP ingestion, acetylcysteine should be administered immediately regardless of the quantity reported to have been ingested. If greater than 24 hours has elapsed since the APAP ingestion, the clinician should determine the appropriateness of acetylcysteine administration based on the patients liver status and clinical presentation.

NOTE: The Rumack-Matthew nomogram is ineffective at predicting hepatotoxicity in patients who have ingested repeated supratherapeutic doses of acetaminophen over an extended period of time. In these patients, treatment should be guided by information obtained from laboratory tests, including: acetaminophen serum concentrations, liver function tests (LFTs), serum creatinine, BUN, electrolytes, bilirubin, blood glucose, and INR. Assistance may be obtained by contacting your regional poison control center at 1—800—222—1222 or the acetaminophen overdose center at 1—800—525—6115.

Intravenous dosage (21-hour regimen)

NOTE: Infusions beyond 21 hours should be considered when the absorption and/or half-life of acetaminophen (APAP) may be prolonged (e.g., suspected massive overdose, concurrent ingestion of other substances, patients with preexisting liver disease). In these cases, ALT/AST, INR, and APAP concentrations should be measured after the last maintenance dose. If the APAP concentration is still

detectable, ALT/AST are still increasing, or the INR remains elevated, the infusion may be continued. If the infusion is extended beyond 21 hours, the treating physician should contact either the US poison center (1-800-222-1222) or a special health professional assistance line for APAP overdose (1-800-525-6115) for assistance with dosing recommendations.

Adults, Adolescents, and Children weighing more than 40 kg

300 mg/kg total dose divided into 3 portions and given sequentially as a continuous infusion over a total of 21 hours with no significant time between portions. Divide the dose as follows: Loading Dose: 150 mg/kg (Max: 15,000 mg) in 200 mL of diluent infused IV over 1 hour; Second Dose: 50 mg/kg (Max: 5,000 mg) in 500 mL of diluent infused IV over 4 hours; Third Dose: 100 mg/kg (Max: 10,000 mg) in 1000 mL of diluent infused IV over 16 hours.

Children and Adolescents weighing 21 to 40 kg

300 mg/kg total dose divided into 3 portions and given sequentially as a continuous infusion over a total of 21 hours with no significant time between portions. Divide the dose as follows: Loading Dose: 150 mg/kg in 100 mL of diluent infused IV over 1 hour; Second Dose: 50 mg/kg in 250 mL of diluent infused IV over 4 hours; Third Dose: 100 mg/kg in 500 mL of diluent infused IV over 16 hours.

Infants and Children weighing 5 to 20 kg

300 mg/kg total dose divided into 3 portions and given sequentially as a continuous infusion over a total of 21 hours with no significant time between portions. Divide the dose as follows: Loading Dose: 150 mg/kg in 3 mL/kg of diluent infused IV over 1 hour; Second Dose: 50 mg/kg in 7 mL/kg of diluent infused IV over 4 hours; Third Dose: 100 mg/kg in 14 mL/kg of diluent infused IV over 16 hours.

Oral dosage (Nebulizer solution)

Adults, Adolescents, and Children

140 mg/kg PO as the loading dose, and then 70 mg/kg/dose PO every 4 hours for 17 doses starting 4 hours after loading dose. The manufacturer recommends lavage before administering acetylcysteine treatment if activated charcoal was administered; activated charcoal adsorbs acetylcysteine in vitro and may reduce its effectiveness. Any dose vomited within 1 hour of administration must be repeated.

Oral dosage (Effervescent tablet)

Adults, Adolescents, and Children weighing at least 100 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving six 2.5 gram tablets in 300 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for a total of 17 doses. Each maintenance dose is prepared by dissolving three 2.5 gram tablets in 300 mL of water. Any dose vomited within 1 hour of administration must be repeated. Of note, data are limited regarding dosing requirements for patients weighing more than 100 kg.

Adults, Adolescents, and Children weighing 90 to 99 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving five 2.5 gram tablets and three 500 mg tablets in 300 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving two 2.5 gram tablets and four 500 mg tablets in 300 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Adults, Adolescents, and Children weighing 80 to 89 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving five 2.5 gram tablets and one 500 mg tablet in 300 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving two 2.5 gram tablets and three 500 mg tablets in 300 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Adults, Adolescents, and Children weighing 70 to 79 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving four 2.5 gram tablets and two 500 mg tablets in 300 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving two 2.5 gram tablets and one 500 mg tablet in 300 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Adults, Adolescents, and Children weighing 60 to 69 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving four 2.5 gram tablets in 300 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving two 2.5 gram tablets in 300 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Adults, Adolescents, and Children weighing 50 to 59 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving three 2.5 gram tablets and one 500 mg tablet in 150 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving one 2.5 gram tablet and three 500 mg tablets in 150 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Adults, Adolescents, and Children weighing 40 to 49 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving two 2.5 gram tablets and four 500 mg tablets in 150 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving one 2.5 gram tablet and two 500 mg tablets in 150 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Adults, Adolescents, and Children weighing 30 to 39 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving two 2.5 gram tablets and two 500 mg tablets in 150 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving one 2.5 gram tablet and one 500 mg tablet in 150 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Children and Adolescents weighing 20 to 29 kg

140 mg/kg PO once as a loading dose. The loading dose is prepared by dissolving one 2.5 gram tablet and three 500 mg tablets in 150 mL of water. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. Each maintenance dose is prepared by dissolving four 500 mg tablets in 150 mL of water. Any dose vomited within 1 hour of administration must be repeated.

Infants and Children weighing 19 kg or less

140 mg/kg PO once as a loading dose. Starting 4 hours after the loading dose, give maintenance dose of 70 mg/kg/dose PO every 4 hours for 17 doses. The loading dose and each maintenance dose is prepared by dissolving two 2.5 gram tablets in 100 mL or water; the resulting solution has a concentration of 50 mg/mL. Any dose vomited within 1 hour of administration must be repeated.

For adjunctive treatment of chronic bronchopulmonary disorders such as chronic obstructive pulmonary disease (COPD), including chronic bronchitis, emphysema,

tuberculosis, bronchiectasis, and primary amyloidosis of the lung.

Nebulization dosage (using face mask, mouth piece, or tracheostomy)

NOTE: Administer a bronchodilator 10 to 15 minutes prior to dose.

Adults

3 to 5 mL of 20% solution or 6 to 10 mL of 10% solution inhaled via nebulization 3 to 4 times daily is the usual dosage for most patients. Dosage range: 1 to 10 mL of 20% solution or 2 to 20 mL of 10% solution via nebulization every 2 to 6 hours.

Direct intratracheal instillation dosage

Adults

1 to 2 mL of 10% or 20% solution, administered by direct instillation into the trachea as often as every hour. Tracheostomy patients, instill direct into the tracheostomy.

Oral dosage†

Adults

Not FDA approved. Dosages used include 200 mg PO 2 to 3 times daily; 300 mg PO twice daily; or 600 mg PO once daily, twice daily or three times per week.

For mucolysis of viscous or inspissated mucous secretions in patients with pulmonary conditions (e.g., pneumonia, bronchitis, cystic fibrosis, atelectasis due to mucous obstruction, and post-traumatic chest conditions) and for use during tracheostomy care, anaesthesia, and diagnostic bronchograms.

For diagnostic bronchial studies.

Endotracheal or Nebulization dosage

Infants, Children, and Adolescents

1 to 2 mL of 20% solution or 2 to 4 mL of 10% solution administered 2 to 3 times prior to the procedure via nebulization or by intratracheal instillation.

Nebulization dosage (using face mask, mouth piece, or tracheostomy)

Adults, Adolescents, Children, and Infants

3 to 5 mL of 20% solution or 6 to 10 mL of 10% solution, administered via nebulization 3 to 4 times daily is the recommended dosage for most patients; however, the dosage range is 1 to 10 mL of 20% solution or 2 to 20 mL of 10% solution administered every 2 to 6 hours. Dosages at the lower end of the range (e.g., 1 to 2 mL of 20% or 2 to 4 mL of 10%) may be most appropriate for infants. Administration of a bronchodilator 10 to 15 minutes prior to dose may reduce the incidence of bronchospasm.

Nebulization dosage (using tent or croupette)

Infants and Children

Specific dosage is dependent on the available equipment and patient need. Use a sufficient volume of 10% or 20% solution to provide a heavy mist for the desired period of time. Very large volumes (e.g., up to 300 mL) may be required. Intermittent or continuous administration for prolonged periods (e.g., overnight) may be desirable.

Direct intratracheal instillation dosage (general dosage)

Adults, Adolescents, Children, and Infants

1 to 2 mL of 10% or 20% solution administered by direct instillation into the trachea as often as every hour is the general dosing for direct instillation.

Direct intratracheal instillation dosage (for tracheostomy care)

Adults, Adolescents, Children, and Infants

1 to 2 mL of 10% or 20% solution directly into the tracheostomy every 1 to 4 hours for routine tracheostomy care. For instillation through percutaneous intratracheal catheter, 1 to 2 mL of 20% solution or 2 to 4 mL of 10% solution every 1 to 4 hours may be given by a syringe attached to the catheter.

Direct intratracheal instillation dosage (for introduction into a specific bronchopulmonary tree segment)

Adults, Adolescents, Children, and Infants

2 to 5 mL of 20% solution administered via a syringe connected to a small catheter that has been placed directly into the desired segment of the bronchopulmonary tree (under local anesthesia and direct vision).

For nephrotoxicity prophylaxis† against radiographic-contrast-induced reductions in renal function in those patients with preexisting renal insufficiency (SCr > 1.2mg/dl or CrCl < 60 ml/min) or who are otherwise at risk for radiocontrast-induced nephropathy.

Oral dosage

Adults

600 mg PO twice daily, given the day prior to and the day of administration of the contrast agent (i.e., for 2 days total) has been successful. Saline hydration is used concurrently in the 12 hours before and after contrast administration.

Intravenous dosage

Adults

150 mg/kg in 500 mL NS IV over 30 minutes immediately before contrast; then, 50 mg/kg in 500 mL NS IV over the next 4 hours has been studied in patients with stable renal dysfunction (CrCl < 50 mL/minute or SCr > 1.36 mg/dL) undergoing cardiac catheterization. In this rapid protocol comparing IV acetylcysteine (n = 41) to IV hydration (n = 39), 5% (n = 2) of patients in the IV acetylcysteine group compared to 21% (n = 8) of patients in the hydration group developed radiocontrast-induced nephropathy (increase in SCr of 25% at 2 or 4 days after contrast administration; p = 0.045; RR, 0.28; 95% CI, 0.08—0.98).

Oral and Intravenous dosage

Adults

In 354 patients with acute myocardial infarction undergoing angioplasty, a dose of 1200 mg IV bolus before angioplasty followed by 1200 mg PO twice daily for the 48 hours following angioplasty significantly reduced the incidence of contrast-induced nephropathy (defined as a 25% increase in creatinine over baseline within 72 hours after angioplasty) compared to a lower dose of acetylcysteine (600 mg IV bolus prior to angioplasty followed by 600 mg PO twice daily for 48 hours after angioplasty) or placebo. The incidence of acute renal failure was 8% in the high-dose acetylcysteine group, 15% in the low-dose acetylcysteine group, and 33% in patients receiving placebo (p < 0.001). Furthermore, the incidence of death, acute renal failure requiring temporary renal replacement therapy, and the need for mechanical ventilation was 5% in the high-dose group, 7% in the low-dose group, and 18% in

the placebo group (p = 0.002). In this study, patients received 0.9% sodium chloride at a rate of 1 mL/kg/hour for 12 hours after angioplasty; if the patients had overt heart failure, a lower rate of 0.5 mL/kg/hour for 12 hours was used.

For the treatment of giant papillary conjunctivitis (GPC)†.

Ophthalmic dosage†

Adults

A 1—2% solution can be prepared by mixing in artificial tears. Administer topically to the affected eye 4—6 times per day.

For the treatment of distal intestinal obstruction syndrome (DIOS)† (previously called meconium ileus equivalent).

Oral dosage

Children and Adolescents 10 years and older

Limited data are available; the ideal dosage has not been established. For the acute treatment of moderate DIOS episodes, some experts recommend a "Mucomyst cocktail", which consists of a phosphosoda enema followed by a clear liquid diet for 24 hours. During that 24-hour period, give 3 doses of 10% acetylcysteine 60 mL PO mixed with cold soda or orange juice. For recurrent DIOS, 10 mL of the 20% solution PO 4 times per day in combination with acetylcysteine enemas has also been used; most patients experienced some relief within 24 hours. For recurrent DIOS refractory to other therapies, 5 to 30 mL of the 10% solution PO 1 to 3 times daily may be used.

Children younger than 10 years

Limited data are available; the ideal dosage has not been established. For the acute treatment of moderate DIOS episodes, some experts recommend a "Mucomyst cocktail", which consists of a phosphosoda enema followed by a clear liquid diet for 24 hours. During that 24-hour period, give 3 doses of 10% acetylcysteine 30 mL PO mixed with 30 mL of cold soda or orange juice. For recurrent DIOS, 10 mL of the 20% solution PO 4 times per day in combination with acetylcysteine enemas has also been used; most patients experienced some relief within 24 hours. For recurrent DIOS refractory to other therapies, 5 to 30 mL of the 10% solution PO 1 to 3 times daily may be used.

Rectal dosage

Adolescents

Limited data are available; some experts consider rectal enemas of acetylcysteine to be ineffective. One study used 50 mL of the 20% solution mixed with 50 mL of water as an enema administered 1 to 4 times per day in combination with oral therapy.

†Indicates off-label use

MAXIMUM DOSAGE

NOTE: Maximum dosage may vary based upon indication and route of administration. Specific maximum dosage information is not available; however, commonly used maximum doses for IV acetylcysteine are 150 mg/kg (Max: 15,000 mg) for the loading dose, 50 mg/kg (Max: 5000 mg) for the second dose, and 100 mg/kg (Max: 10,000 mg) for the third dose. Specific maximum dosage information is not available for oral or inhalational dosing.

Adults

Maximum dosage is not well defined.

Geriatric

Maximum dosage is not well defined.

Adolescents

Maximum dosage is not well defined.

Children

Maximum dosage is not well defined.

DOSING CONSIDERATIONS

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available; it is not known if dosage adjustments are needed. Although there was a 3-fold increase in acetylcysteine plasma concentrations in patients with hepatic cirrhosis, the published medical literature does not indicate that the dose of acetylcysteine in patients with hepatic impairment should be reduced.

Renal Impairment

Specific guidelines for dosage adjustments in renal impairment are not available. Some experts have recommended the following adjustment for adult patients receiving systemic therapy of 140 mg/kg load then 70 mg/kg every 4 hours x 17 doses :
CrCl 10 ml/minute or greater or CRRT: no dosage adjustment
CrCl less than 10 ml/minute or peritoneal dialysis: 75% of recommended dose

ADMINISTRATION

For storage information, see specific product information within the How Supplied section.

NOTE: Three acetylcysteine formulations are commercially available in the US.
Mucomyst: solution available in teartop vials for oral or nebulizer administration; not FDA approved for parenteral injection.
Acetadote: solution available in sterile, single-dose vials for intravenous administration
Cetylev: available as 2.5 gram and 500 mg effervescent tablets for oral solution; not approved for use via parenteral injection, nebulizer, or intratracheal instillation.

Oral Administration

Oral Liquid Formulations

Oral solution (Mucomyst):
Not FDA approved for parenteral injection
It is recommended that the 10% or 20% solution be diluted to a 5% solution with diet cola or other diet soda to increase palatability and minimize the likelihood of vomiting. May administer with a straw to limit contact in mouth. The 20% solution is usually preferable to the 10% solution because a lower volume of drug is needed in the dilution, thereby increasing palatability.
If administered via a gastric tube, water may be used as the diluent.
Dilution of 10% solution: 1 mL of diluent for every 1 mL of solution.
Dilution of 20% solution: 3 mL of diluent for every 1 mL of solution.
The manufacturer provides a Dosage Guide and Preparation Chart in relation to body weight in the product label.
Use diluted solutions within 1 hour of preparation.

Effervescent tablet for oral solution (Cetylev):
For oral administration only; DO NOT administer via parenteral injection, nebulizer, or intratracheal instillation. Administration via a nasoduodenal tube may be considered for patients persistently unable to tolerate the orally administered dose.
Prepare only one dose at a time; each freshly prepared dose must be used within 2 hours.
Adults and pediatric patients weighing 20 kg or more: Use the patients weight and manufacturer provided dosing charts to calculate the number of 2.5 gram and 500 mg effervescent tablets required to make the 140 mg/kg loading dose and the 70 mg/kg maintenance doses.
Patients weighing 60 kg or more: Dissolve the required number of tablets in 300 mL of water. Note, data are limited regarding dosing requirements for patients weighing over 100 kg.
Patients weighing 20 to 59 kg: Dissolve the required number of tablets in 150 mL of water.
Pediatric patients weighing 19 kg or less: Dissolve two 2.5 gram tablets in 100 mL of water to create a 50 mg/mL solution.
Calculate the loading dose volume (mL): multiply patients weight (kg) by 140 mg/kg, then divide by 50 mg/mL (solution concentration).
Calculate the maintenance dose volume (mL): multiply patients weight (kg) by 70 mg/kg, then divide by 50 mg/mL (solution concentration).
Once tablets have dissolved in the required volume of water, administer solution immediately. If the patient vomits within 1 hour of oral administration, repeat that dose.
The solution produced by the effervescent tablets is interchangable with the 20% acetylcysteine solution, provided the effervescent tablet solution was appropriately prepared and diluted, and if the same acetylcysteine dosage is given.

Injectable Administration

For intravenous use only. Be sure to choose the correct product; the nebulizer solution should NOT be given intravenously.
The commercially available single-dose vial is sterile but preservative-free; discard any unused portion. Do not use if vial was previously opened.
Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

The IV formulation is hyperosmolar (2600 mOsm/L) and must be diluted prior to administration.
Acceptable diluents include: 5% Dextrose, 0.45% Sodium Chloride injection (1/2 Normal Saline), and Water for Injection. The volume of diluent to be used is dependent on patient weight (see Dosage).
Stability studies indicate that the diluted solution is stable for 24 hours at controlled room temperature.
The color of the IV formulation may turn from colorless to a slight pink or purple color after the stopper is punctured; however, the quality of the product is not affected.
Acetylcysteine reacts with certain materials (e.g., iron, nickel, copper, rubber); any part of the IV equipment that comes in contact with acetylcysteine should be made of plastic or glass.

Inhalation Administration

Solutions for inhalation are not FDA approved for parenteral injection.
The 10% solution may be administered undiluted.
The 20% solution may be administered undiluted or, if desired, may be diluted in sterile NS injection, sodium chloride for inhalation, or sterile water for injection or inhalation.
Acetylcysteine reacts with certain materials (e.g., iron, nickel, copper, rubber); therefore, any part of the nebulizer equipment that comes in contact with acetylcysteine should be made of plastic or glass.

Other Inhalation Administration

Nebulization Inhalation Administration
Ultrasonic or conventional nebulizers may be used. Hand-bulb nebulizers produce particles which are too large and the output is usually too small. Compressed air should be used to provide pressure.
Administer nebulized solution directly or using a plastic face mask, face tent, mouthpiece, oxygen tent, or head tent. The nebulizer may also be fitted onto intermittent positive pressure breathing (IPPB) machines. During administration, after 3/4 of the initial volume has been nebulized, dilute the remaining solution with an equal amount of NS or sterile water.
Immediately after administration, clean nebulizing equipment to prevent occlusion of fine orifices or corrosion of metal parts.

Other Administration Route(s)

Intratracheal Administration
Intratracheal instillation: Instill directly into the trachea or tracheostomy.
Percutaneous intratracheal catheter: Administer the solution via a syringe attached to the catheter.

STORAGE

Acetadote:
- Discard product if it contains particulate matter, is cloudy, or discolored
- Discard unused portion. Do not store for later use.
- Store at controlled room temperature (between 68 and 77 degrees F)

CETYLEV:
- Protect from moisture
- Store between 68 to 77 degrees F, excursions permitted 59 to 86 degrees F
- Store in original package until time of use

Mucomyst:
- Opened vials may be refrigerated (36 to 46 degress F)
- Store between 68 to 77 degrees F, excursions permitted 59 to 86 degrees F
- Store remaining undiluted portion of product in a refrigerator and use within 96 hours

Mucosil Acetylcysteine :
- Opened vials may be refrigerated (36 to 46 degress F)
- Store between 68 to 77 degrees F, excursions permitted 59 to 86 degrees F
- Store remaining undiluted portion of product in a refrigerator and use within 96 hours

CONTRAINDICATIONS / PRECAUTIONS

General Information

NOTE: When acetylcysteine is used for acetaminophen overdose, obtain APAP serum concentrations at least 4 hours post-ingestion of regular-release products or at least 8 hours post-ingestion of extended-release products. Predictors of liver injury include acetaminophen dose over 10 g, presentation more than 10 hours after the overdose and chronic ingestion of more than 80 g alcohol per day. Aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT), bilirubin, prothrombin time, creatinine, blood urea nitrogen (BUN), blood glucose, and electrolytes should be also determined at baseline in order to monitor hepatic and renal function and electrolyte and fluid balance in patients receiving acetylcysteine.

Acute bronchospasm, asthma, gag reflex depression, respiratory insufficiency

Intravenous acetylcysteine is contraindicated in patients who have had a previous anaphylactoid reaction to acetylcysteine, and acetylcysteine solution for oral use or inhalation is contraindicated in patients who have had any type of hypersensitivity reaction to the drug. Serious anaphylactoid reactions, including a fatality in a patient with asthma, have been reported in patients who received intravenous acetylcysteine (see Adverse Reactions). Intravenous and nebulized acetylcysteine should be used with caution in patients with asthma or a history of bronchospasm; when it is necessary to use these products in this population, careful monitoring is necessary. Intravenous administration or inhalation may result in acute bronchospasm or anaphylaxis. To minimize the risk of bronchospasm, inhaled acetylcysteine should be used with or after the administration of a

beta-agonist. Nebulized acetylcysteine should be used with caution in patients with respiratory insufficiency, an inadequate cough mechanism, or gag reflex depression. When administered into respiratory tract, either via inhalation or direct administration into a tracheostomy tube, acetylcysteine liquifies pulmonary secretions, and the increased volume produced can occlude the airway if the patient is unable to adequately clear the secretions. If the patient's cough is not adequate to keep the airway open, mechanical suction or endotracheal aspiration may be necessary.

Esophageal varices, GI bleeding, peptic ulcer disease, vomiting

Oral administration of acetylcysteine can exacerbate vomiting that is associated with acute acetaminophen overdose. In patients with esophageal varices or peptic ulcer disease, vomiting may increase the risk of upper GI bleeding or esophageal tears; thus, caution is advised when administering oral acetylcysteine to these patients. The acetylcysteine nebulizer solution has an unpleasant odor and when undiluted, has irritating and sclerosing properties on the GI mucosa. Acetylcysteine must be diluted with a proper solution to mask the odor and limit GI irritation prior to oral administration.

Children, infants, neonates

No pediatric-specific concerns have been identified with the use of acetylcysteine in infants or children; however, for any patients weighing < 40 kg or requiring fluid restriction, use caution to avoid fluid overload when administering IV acetylcysteine. To avoid fluid overload, the volume of diluent should be reduced compared to the standard preparation for adult patients (see Dosage). If the volume is not adjusted, fluid overload can occur, potentially resulting in hyponatremia, seizure, and death. Specific dosing recommendations are not available for neonates for any of the formulations; however, the manufacturer of IV acetylcysteine reports its use in 16 premature infants (gestational ages, 25—31 weeks) with no noted adverse effects (see Dosage).

Pregnancy

Adequate and well-controlled studies have not been performed in women receiving acetylcysteine during pregnancy; however, acetylcysteine does cross the placenta and has been detected in the cord blood of infants whose mothers received the drug at delivery. Four pregnant women with acetaminophen toxicity received oral or intravenous acetylcysteine at the time of delivery, and all of the women recovered. Three of the four neonates survived with no evidence of acetaminophen toxicity; one neonate (22 weeks gestational age) died shortly after delivery. Also, other limited case reports of pregnant women who received acetylcysteine during various trimesters have not reported adverse maternal, fetal, or neonatal outcomes. Of note, acetaminophen is also known to cross the placenta. Delaying treatment of pregnant women with acetaminophen overdose may increase the risk for maternal and fetal morbidity and mortality.

Breast-feeding

According to the manufacturer, it is not known whether acetylcysteine is distributed into human milk; use caution when acetylcysteine is administered to a nursing mother. Intravenous acetylcysteine is nearly completely eliminated within 30 hours after administration; therefore, mothers may consider reinitiating breast-feeding 30 hours after administration. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally administered drug, healthcare providers are encouraged to report the adverse effect to the FDA.

Heart failure, hypertension, renal disease

Use intravenous acetylcysteine cautiously in patients who require fluid restriction, such as patients with heart failure. The usual recommended administration technique for intravenous acetylcysteine (Acetadote) involves a significant amount of fluid and could result in volume overload and even hyponatremia, seizures, and death in extreme cases. For patients requiring fluid restriction, the volume of dilution should be reduced as clinically appropriate; however, carefully consider the osmolarity of the resultant solution and avoid infusion of a hyper- or hypo-osmolar solution. For specific treatment recommendations for patients requiring non-standard administration techniques clinicians can contact the US poison center (1—800—222—1222) or a special health professional assistance line for APAP overdose (1—800—525—6115) for assistance. Caution is advised when administering the acetylcysteine effervescent tablets to patients on a sodium restricted diet (i.e., patients with hypertension, heart failure, renal disease). Each 500 mg and 2.5 gram effervescent tablet contains 3.8 meq and 19 meq of sodium, respectively. At the recommended treatment dose, a 60 kg adult would receive 7 grams (304.3 meq) of sodium on day 1, 5.3 grams (230.4 meq) of sodium on day 2, and 4.4 grams (191.3 meq) of sodium on day 3.

ADVERSE REACTIONS

Severe

anaphylactoid reactions / Rapid / 7.9-17.0
bronchospasm / Rapid / Incidence not known

Moderate

sinus tachycardia / Rapid / 3.0-5.0
edema / Delayed / 1.2-1.6
hypotension / Rapid / 0.1-0.1
erythema / Early / Incidence not known
dyspnea / Early / Incidence not known
stomatitis / Delayed / Incidence not known
hemoptysis / Delayed / Incidence not known
wheezing / Rapid / Incidence not known

Mild

urticaria / Rapid / 6.1-7.6
flushing / Rapid / 6.1-7.6
pruritus / Rapid / 4.1-4.3
rash / Early / Incidence not known
rhinorrhea / Early / Incidence not known
pharyngitis / Delayed / Incidence not known
nausea / Early / Incidence not known
vomiting / Early / Incidence not known
dysgeusia / Early / Incidence not known
drowsiness / Early / Incidence not known
fever / Early / Incidence not known

DRUG INTERACTIONS

Charcoal: (Moderate) Administration of activated charcoal and oral acetylcysteine at the same time may cause a reduction in acetylcysteine (NAC) absorption. There are conflicting data as to whether the reduced bioavailability of NAC is clinically significant during the treatment of drug overdoses. In the case of a mixed drug overdose activated charcoal may be indicated for use along with NAC. However, if activated charcoal has been administered, lavage before administering oral NAC treatment. Activated charcoal adsorbs acetylcysteine in vitro and may do so in patients and thereby may reduce its effectiveness.

PREGNANCY AND LACTATION

Pregnancy

Adequate and well-controlled studies have not been performed in women receiving acetylcysteine during pregnancy; however, acetylcysteine does cross the placenta and has been detected in the cord blood of

infants whose mothers received the drug at delivery. Four pregnant women with acetaminophen toxicity received oral or intravenous acetylcysteine at the time of delivery, and all of the women recovered. Three of the four neonates survived with no evidence of acetaminophen toxicity; one neonate (22 weeks gestational age) died shortly after delivery. Also, other limited case reports of pregnant women who received acetylcysteine during various trimesters have not reported adverse maternal, fetal, or neonatal outcomes. Of note, acetaminophen is also known to cross the placenta. Delaying treatment of pregnant women with acetaminophen overdose may increase the risk for maternal and fetal morbidity and mortality.

According to the manufacturer, it is not known whether acetylcysteine is distributed into human milk; use caution when acetylcysteine is administered to a nursing mother. Intravenous acetylcysteine is nearly completely eliminated within 30 hours after administration; therefore, mothers may consider reinitiating breast-feeding 30 hours after administration. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally administered drug, healthcare providers are encouraged to report the adverse effect to the FDA.

MECHANISM OF ACTION

Mechanism of Action:•Antioxidant effects: Antioxidants such as acetylcysteine may prevent tissue damage to various organs by scavenging oxygen free radicals (e.g., superoxides) or by other poorly understood mechanisms, such as stabilization of cellular signal transduction systems and reduced apoptosis (programmed cell death). Acetylcysteine enhances the effects of nitric oxide (NO) by combining with NO to form S-nitrosothiol, a potent and biologically stable vasodilator. Acetylcysteine may thus compete with the superoxide radical for NO and thus prevent the formation of a damaging perioxinitrite free-radical. Thus, acetylcysteine exhibits multiple potential mechanisms of action that may limit ischemia and promote cellular repair and survival. Studies using acetylcysteine as an antioxidant for organ protection in settings of clinically-relevant heart, lung, liver, and renal ischemia are intriguing and continue to be pursued.•Mucolytic effects: As a mucolytic, it is believed that the free sulfhydryl groups in acetylcysteine react with the disulfide linkages of mucoproteins in bronchial secretions. This, in turn, acts to decrease the hypersecretion and viscosity of mucus secretions of the lungs and aids in the removal of these secretions through coughing, mechanical mechanisms, or postural drainage. Acetylcysteine does not depolymerize proteins and has no action on fibrin or living cells. In COPD, the use of oral acetylcysteine may also promote reductions in bacterial cell counts within the sputum, thus contributing to reduced exacerbation rates.•Prevention of hepatotoxicity secondary to acetaminophen (APAP) overdose: As an antidote, acetylcysteine is used to prevent hepatotoxicity after an acute overdose of acetaminophen. In this role, the sulfhydryl groups of acetylcysteine serve as a substrate for the toxic acetaminophen metabolite in place of glutathione in the liver. It is believed that acetaminophen is hepatotoxic due to the depletion of these glutathione residues. For acetylcysteine to be effective, it must be administered within several hours after the acute ingestion. Benefits are primarily seen in patients treated within 8—10 hours of the overdose.•Proposed prevention of nitrate tolerance: Sulfhydryl groups are also believed to be important in the response to vasodilator nitrates used in the treatment of ischemic heart disease. It is well known that tolerance to nitrates occurs after prolonged use. One proposed mechanism, based on in vitro data, is the decreased conversion of nitrates to nitric oxide, possibly due to depletion of sulfhydryl cofactors. In vivo data do not completely support this sulfhydryl-depletion hypothesis. While supplementation with acetylcysteine does augment nitrate effects in vivo, the mechanism of intracellular sulfhydryl group repletion is inadequate in explaining the reversal of nitrate tolerance; an extracellular thiol/nitrate interaction appears to enhance vasodilation. Acetylcysteine inhibits angiotensin converting enzyme (ACE) in vivo and acts as an antioxidant, two mechanisms that may preserve the function of nitroglycerin-derived nitric oxide (NO). These potential actions indicate that acetylcysteine may protect the neurohormonal or vasoconstrictive responses to nitrates, rather than act as a simple repeller of thiol stores.

PHARMACOKINETICS

Acetylcysteine is administered orally, intravenously, or by inhalation. Once in the systemic circulation, 66% to 87% of the drug is bound to plasma proteins. Any acetylcysteine that is absorbed systemically is deacetylated by the liver and intracellularly in most tissues to cysteine and disulfides. Cysteine is then further metabolized to glutathione, as well as other metabolites. Most of an acetylcysteine dose is expected to be metabolized and incorporated as cysteine into cellular pools. The mean terminal half-life of the intravenous solution is 5.6 hours, while the effervescent tablets have a reported mean terminal half-life of 18.1 hours. Renal clearance accounts for roughly 30% of total clearance. After 24 hours, 13% to 38% of a radioactive dose of S-acetylcysteine is excreted in the urine. No metabolites have been identified in the urine. Only about 3% of acetylcysteine is excreted in feces.

Affected cytochrome P450 isoenzymes: none

Oral Route

Acetylcysteine is rapidly absorbed with peak plasma concentrations reached approximately 2 hours (range, 1 to 3.5 hours) after oral administration; however, oral bioavailability is very low (approximately 9%).

Intravenous Route

The Vdss and protein binding for the IV formulation of acetylcysteine are reported to be 0.47 L/kg and 83%, respectively.

Inhalation Route

After oral inhalation, the majority of the administered dose undergoes a sulfhydryl-disulfide reaction; only a small portion of the dose is absorbed from the pulmonary epithelium.

Other Route(s)

Intratracheal Route
After intratracheal instillation, the majority of the administered dose undergoes a sulfhydryl-disulfide reaction; only a small portion of the dose is absorbed from the pulmonary epithelium.

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