ACETYLCYSTEINE (Systemic)

Commonly used brand name(s):Mucomyst; Mucosil; Parvolex.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

Category

Antidote (to acetaminophen overdose)..

Indications

Accepted

Toxicity, acetaminophen (treatment)¾Acetylcysteine is indicated in the treatment of acetaminophen overdose to protect against hepatotoxicity 11, 12, 13.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Molecular weight¾163.19 9

Mechanism of action/Effect:

Acetylcysteine may protect against acetaminophen overdose-induced hepatotoxicity by maintaining or restoring hepatic concentrations of glutathione. Glutathione is required to inactivate an intermediate metabolite of acetaminophen that is thought to be hepatotoxic. In acetaminophen overdose, excessive quantities of this metabolite are formed because the primary metabolic (glucuronide and sulfate conjugation) pathways become saturated. Acetylcysteine may act by reducing the metabolite to the parent compound and/or by providing sulfhydryl for conjugation of the metabolite. Experimental evidence also suggests that a sulfhydryl-containing compound such as acetylcysteine may also directly inactivate the metabolite.

Biotransformation:

Deacetylated by the liver to cysteine and subsequently metabolized 1, 11.

Precautions to Consider

Carcinogenicity

Studies have not been done to determine the carcinogenic potential of acetylcysteine 1, 11.

Mutagenicity

In the Ames test, both with and without metabolic activation, acetylcysteine was not shown to be mutagenic 1, 11.

Pregnancy/Reproduction

Fertility¾Reproductive studies performed in rats given oral doses of up to 1000 mg per kg of body weight (mg/kg) of acetylcysteine per day showed a slight reduction in fertility with doses of 500 or 1000 mg/kg per day (2.6 and 5.2 times the human dose, respectively). Studies in rabbits given up to 500 mg/kg per day (2.6 times the human dose) revealed no evidence of impaired fertility. 11

Pregnancy¾Adequate and well-controlled studies in humans have not been done 11.

However, several reports have indicated that use of acetylcysteine to treat acetaminophen overdose in pregnant women is safe and effective, and may prevent hepatotoxicity in the fetus as well as in the mother 14.

Studies in rabbits given oral doses of 500 mg/kg per day on Day 6 through Day 16 of gestation and in rabbits given 10% acetylcysteine plus 0.5% isoproterenol by inhalation for 30 or 35 minutes twice a day on Day 16 through Day 18 of gestation showed no evidence of teratogenicity or harm to the fetus. Also, studies in rats administered acetylcysteine and isoproterenol by inhalation showed no evidence of teratogenicity or harm to the fetus. 11

FDA Pregnancy Category B 11.

Breast-feeding

It is not known whether acetylcysteine is distributed into breast milk 11.

However, problems in humans have not been documented.

Pediatrics

Appropriate studies on the relationship of age to the effects of acetylcysteine have not been performed in the pediatric population. However, no pediatrics-specific problems have been documented to date.

Geriatrics

No information is available on the relationship of age to the effects of acetylcysteine in geriatric patients being treated for acetaminophen overdose.

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist

Asthma, history of

(risk of bronchospastic reactions¾with intravenous administration)

Conditions predisposing to gastrointestinal hemorrhage, such as:

Esophageal varices

Peptic ulceration

(acetylcysteine-induced vomiting may increase the risk of hemorrhage)

Sensitivity to acetylcysteine

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Those indicating need for medical attention

Incidence rare

Bronchospastic allergic reaction (shortness of breath, troubled breathing, tightness in chest, or wheezing); dermatitis, allergic (skin rash or hives); facial edema

Note: Bronchospasm may also occur in conjunction with a generalized anaphylactoid reaction. These allergic reactions and facial edema have been reported only with intravenous administration. 12

Those indicating need for medical attention only if they continue or are bothersome

Drowsiness; fever; nausea or vomiting