Acetylcysteine Injection

Initial U.S. Approval 2004

**DOSAGE AND ADMINISTRATION**

*Pregnancy:* This drug should be used during pregnancy only if clearly needed (8.1).

To report SUSPECTED ADVERSE REACTIONS, contact Perrigo at 1-800-328-5113 or FDA at www.fda.gov/medwatch.

**WARNINGS AND PRECAUTIONS**

- **Anaphylactoid reactions** have been reported following the administration of Acetylcysteine Injection.
- **Hypersensitivity** reactions may occur, including urticaria, facial swelling, angioedema, rash, or other skin reactions.
- **Carcinogenesis, Mutagenesis, Impairment of Fertility**
- **Reproductive and Developmental Toxicology**
- **Overdosage**
- **Acetaminophen Assays Interpretation and Methodology – Acute Ingestion**
- **Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion**

**FULL PRESCRIBING INFORMATION:**

1 **INDICATIONS AND USAGE**

1.1 Acetylcysteine Assay Interpretation and Methodology – Acute Ingestion

1.2 Acetylcysteine Assay Interpretation and Methodology – Repeated Supratherapeutic Ingestion

2 **DOSAGE AND ADMINISTRATION**

2.1 Administration Instructions (Three-Bag Method: Loading, Second and Third dose)

2.2 Loading Dose: 150 mg/kg in 3 mL/kg of body weight of diluent administered over 60 min

2.3 Dose 1: 100 mg/kg in 500 mL of diluent administered over 4 hr

2.4 Dose 2: 100 mg/kg in 1000 mL of diluent administered over 16 hr

2.5 Dose 3: 50 mg/kg in 7 mL/kg of body weight of diluent administered over 4 hr

2.6 Dose 4: 10 mg/kg in 14 mL/kg of body weight of diluent administered over 16 hr

2.7 DOSAGE FORMS AND STRENGTHS

Vials: 200 mg/vial (100 mg/mL)

Syringes: 20 mg/vial (20 mg/mL)

Intravenous Pumps: 100 mg/mL

3 **CONTRAINDICATIONS**

3.1 Patients with previous anaphylactic reaction to acetylcysteine

3.2 Patients who are under 18 years of age

3.3 Patients with a known or suspected history of renal failure

3.4 Patients with a known or suspected history of hepatic failure

4 **WARNINGS AND PRECAUTIONS**

4.1 Monitoring of serum acetaminophen levels

4.2 Monitoring of plasma or serum total bilirubin levels

4.3 Monitoring of plasma or serum glutamic oxaloacetic transaminase (AST) and glutamic pyruvic transaminase (ALT)

5 **ADVERSE REACTIONS**

5.1 Acute hepatic injury

5.2 Patients with previous anaphylactoid reaction to acetylcysteine

5.3 Patients with asthma or where there is a history of bronchospasm

6 **CLINICAL PHARMACOLOGY**

6.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

6.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

7 **DRUG INTERACTIONS**

7.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

7.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

8 **CLINICAL STUDIES**

8.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

8.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

9 **REPRODUCIBILITY**

9.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

9.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

10 **OVERDOSAGE**

10.1 Recommendations for managing Repeated Supratherapeutic Ingestion

11 **CLINICAL PHARMACOLOGY**

11.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

11.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

12 **CLINICAL PHARMACOLOGY**

12.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

12.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

13 **CLINICAL STUDIES**

13.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

13.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

14 **HOW SUPPLIED/STORAGE AND HANDLING**

14.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

14.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

15 **PATIENT COUNSELING INFORMATION**

15.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

15.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

16 **FULL PRESCRIBING INFORMATION:**

16.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

16.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

17 **ADVERSE REACTIONS:**

17.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

17.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

18 **USRX PHARMACOECONOMICS**

18.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

18.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

19 **RECOMMENDATIONS FOR MANAGING REPEATED SUPERTHERAPEUTIC INGESTION:**

19.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

19.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

20 **REFERENCES:**

20.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

20.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

21 **FULL PRESCRIPTION INFORMATION:**

21.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

21.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion

22 **FULL PRESCRIPTION INFORMATION:**

22.1 Acetaminophen Assays Interpretation and Methodology – Acute Ingestion

22.2 Acetaminophen Assays Interpretation and Methodology – Repeated Supratherapeutic Ingestion
Acetylcysteine injection is an intravenous (I.V.) medication for the treatment of acetaminophen overdose. Acetylcysteine is the nonproprietary name for the N-acetyl derivative of the naturally occurring compound cysteine, which is involved in the synthesis of the sulfur-containing amino acids methionine, cysteine, and glutathione. Acetylcysteine is a strong donor of sulfur atoms, and is used in the therapy of acetaminophen overdose. It is metabolized in the liver to form principally the sulfate and glucuronide conjugates.

5 CLINICAL PHARMACOLOGY

5.1 Mechanism of Action

Acetylcysteine is derived from the upper gastrointestinal tract with peak plasma levels occurring 30 to 60 minutes following an intravenous loading dose. Acetylcysteine is metabolized in the liver to form principally the sulfate and glucuronide conjugates and is eliminated in urine. The toxic metabolite in the hepatocyte resulting in cellular necrosis.

5.1.1 Acetaminophen Poisoning

Acetylcysteine is effective in the treatment of acetaminophen overdose. I.V. acetylcysteine was administered to the patients falling in the 16-40 year old age bracket. A total of 399 patients received acetylcysteine or placebo. The loading dose was 150 mg/kg followed by 100 mg/kg/hour. I.V. acetylcysteine has been studied in over 2500 patients with acetaminophen overdose. Of the 23 patients who received I.V. acetylcysteine treatment, 3 patients (13%) had hepatotoxicity that reached Grade 3 or 4. The stopper in the Acetylcysteine Injection vial is formulated with a synthetic base-polymer and is compatible with 5% Dextrose (D5W), 0.9% Normal saline (0.9% NaCl), Inositol (0.5% Inositol), and Water for Injection (WFI). Acetylcysteine Injection is hyperosmolar (2600 mOsm/L) and is compatible with 5% Dextrose (D5W), 0.9% Normal saline (0.9% NaCl), Inositol (0.5% Inositol), and Water for Injection (WFI). Acetylcysteine Injection should be used with caution in patients with asthma, or where there is a history of anaphylactoid reactions to another drug and may not reflect the rates observed in practice.

5.3.1 Reproduction Studies

Acetylcysteine was not genotoxic in the Ames test or the in vitro micronucleus test. It was, however, positive in the in vitro micronucletest [17)]. For forward mutation test (SGT) it was positive at concentrations of 5, 10, and 25 μg/ml. In vitro micronucleus test, the recommended human dose of 500 mg/kg did not affect the fertility or general reproductive performance.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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