PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Acetylcysteine Injection

200 mg / mL

Sterile Solution for Injection

House Standard

Antidote for Acetaminophen Poisoning

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Canada.

Date of Preparation:
June 20, 2022.

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Acetylcysteine Injection

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Nonmedicinal Ingredients
Intravenous	Sterile solution for injection / 200 mg / mL	Edetate Disodium, Sodium Hydroxide and Water for Injection

INDICATIONS AND CLINICAL USE

Acetylcysteine Injection (acetylcysteine) administered intravenously is indicated as an antidote to prevent or lessen hepatic injury which may occur following the ingestion of a potentially hepatotoxic quantity of acetaminophen.

CONTRAINDICATIONS

Acetylcysteine Injection is contraindicated in those patients who are sensitive to the drug or to any of the inactive ingredients. There are no contraindications to oral or intravenous administration of acetylcysteine in the treatment of acetaminophen overdose.

WARNINGS AND PRECAUTIONS

General

Acetylcysteine Injection is not compatible with rubber and metals, particularly iron, copper and nickel. Silicone and lacquered rubber and plastic are satisfactory for use with Acetylcysteine Injection.

The colour of the acetylcysteine solution may change to a light purple colour once the stopper is punctured. The colour change is the result of a chemical reaction which does not significantly impair the safety of acetylcysteine.

Fluid overload

Intravenous administration of Acetylcysteine Injection can cause fluid overload, potentially resulting in hyponatraemia, seizure and death. Use with caution in children, patients requiring fluid restriction or those who weigh less than 40 kg because of the risk of fluid overload. To avoid fluid overload, use the recommended dilution shown in Table 1 (see DOSAGE AND ADMINISTRATION).

Gastrointestinal

Occasionally severe and persistent vomiting occurs as a symptom of acute acetaminophen overdose. Patients at risk of gastric hemorrhage (e.g. esophageal varices, peptic ulcers, etc.) should be evaluated concerning the risk of upper gastrointestinal hemorrhage versus the risk of developing hepatic toxicity, and treatment with Acetylcysteine Injection given accordingly.

Hematologic
Changes in haemostatic parameters have been observed in association with acetylcysteine treatment, some leading to decreased prothrombin time, but most leading to a small increase in prothrombin time. Administer Vitamin K if prothrombin time ratio exceeds 1.5 or with fresh frozen plasma if the prothrombin time ratio exceeds 3.0.

Hepatic
If encephalopathy due to hepatic failure is evident, Acetylcysteine Injection treatment should be discontinued to avoid further administration of nitrogenous substances. There is no data indicating acetylcysteine adversely influences hepatic failure; however, this remains a theoretical possibility.

Hypersensitivity
Serious acute hypersensitivity reactions including rash, hypotension, wheezing, and/or shortness of breath have been observed in patients receiving intravenous acetylcysteine for acetaminophen overdose and occurred soon after initiation of the infusion. If a severe hypersensitivity reaction occurs, immediately stop the infusion of Acetylcysteine Injection and initiate appropriate treatment.

Hypersensitivity reactions following the intravenous administration of acetylcysteine have been reported. If a severe hypersensitivity reaction occurs, immediately stop the infusion of Acetylcysteine Injection and initiate appropriate treatment.

Generalized urticaria has been observed rarely in patients receiving oral acetylcysteine for acetaminophen overdose. If this occurs and other allergic symptoms appear, treatment with Acetylcysteine Injection should be discontinued unless it is deemed essential and the allergic symptoms cannot be otherwise controlled.

Acute flushing and erythema of the skin may occur in patients receiving Acetylcysteine Injection. These reactions usually occur 30 to 60 minutes after initiating the infusion and often resolve spontaneously despite continued infusion of acetylcysteine. If a reaction to Acetylcysteine Injection involves more than simply flushing and erythema of the skin, it should be treated as a hypersensitivity reaction.

Management of less severe hypersensitivity reactions should be based upon the severity of the reaction and include temporary interruption of the infusion and/or administration of antihistaminic drugs. The acetylcysteine infusion may be carefully restarted after treatment of the hypersensitivity symptoms has been initiated; however, if the hypersensitivity reaction returns upon re-initiation of treatment or increases in severity, Acetylcysteine Injection should be discontinued and alternative patient management should be considered.

Special Populations

Pregnant Women and Nursing Women
Prior to use in pregnancy, the potential risks should be balanced against the potential benefits. The safety of N-acetylcysteine in pregnancy has not been investigated in formal prospective clinical trials. However, clinical experience indicates that use of N-acetylcysteine in pregnancy for the treatment of acetaminophen overdose is effective.

No information is available on the excretion of the drug into breast milk. Breast-feeding is thus not advised during or immediately following the use of this drug.

Disease-Associated Maternal and/or Embryo/Fetal Risk

Acetaminophen and acetylcysteine cross the placenta. Delaying treatment in pregnant women with acetaminophen overdose and potentially toxic acetaminophen plasma levels may increase the risk of maternal and fetal morbidity and mortality.

Monitoring and Laboratory Tests

The plasma or serum levels of acetaminophen of patients being treated for ingestion of a potentially hepatotoxic quantity of acetaminophen should be obtained at least 4 hours after ingestion and throughout treatment with Acetylcysteine Injection. In addition, laboratory tests to monitor hepatic and renal function and electrolyte and fluid balance should be obtained prior to and throughout treatment with Acetylcysteine Injection (see DOSAGE AND ADMINISTRATION – As an antidote for acetaminophen poisoning, Dosing Considerations).

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Intravenous administration of acetylcysteine, especially in large doses needed to treat acetaminophen overdose, in order of frequency may result in: nausea, vomiting and other gastrointestinal symptoms.

Hypersensitivity reactions following the intravenous administration of acetylcysteine have been reported. Symptoms include acute flushing and erythema of the skin angioedema, tachycardia or hypertension, rashes, pruritus, facial edema, urticaria, hypotension and bronchospasm / respiratory distress.

Other reported adverse reactions include: injection site reactions, cough, chest tightness or pain, puffy eyes, sweating, malaise, raised temperature, vasodilation, blurred vision, bradycardia, facial or eye pain, syncope, acidosis, thrombocytopenia, respiratory or cardiac arrest, stridor, anxiety, extravasation, arthropathy, arthralgia, deterioration of liver function, generalised seizure, cyanosis, lowered blood urea.

Hypokalaemia and ECG changes have been noted in patients with acetaminophen poisoning irrespective of the treatment given. Monitoring of plasma potassium concentration is therefore recommended.

DRUG INTERACTIONS

Drug-Drug Interactions

No relevant drug-drug interaction studies have been assessed by Health Canada

Drug-Laboratory Interactions

Acetylcysteine may cause a false-positive reaction with reagent dipstick tests for urinary ketones.

DOSAGE AND ADMINISTRATION

Dosing Considerations

In the case of an overdosage of acetaminophen, Acetylcysteine Injection should be administered immediately if 24 hours or less have elapsed from the reported time of ingestion. To be effective in protecting against severe liver damage, therapy with Acetylcysteine Injection must be started within 10 hours of acetaminophen ingestion. There is some evidence of progressively diminished efficacy

thereafter, possibly lasting up to 24 hours. However, if the time of acute acetaminophen ingestion is unknown, Acetylcysteine Injection should be administered immediately.

It should be borne in mind that after a toxic dose of acetaminophen, the patient may appear relatively well initially and may even continue normal activities for a day or two before the onset of hepatic failure.

The following procedure is recommended:

1. The stomach should be emptied promptly by lavage.

2. In the case of a mixed drug overdose activated charcoal may be indicated. Activated charcoal will absorb acetylcysteine and reduce its effectiveness. Therefore, if activated charcoal has been administered, intravenous administration of Acetylcysteine Injection is recommended.

3. Obtain a plasma or serum sample to assay for acetaminophen concentration at least 4 hours after acute acetaminophen ingestion. Acetaminophen concentrations obtained earlier than 4 hours post-ingestion may be misleading as they may not represent maximum acetaminophen concentrations. The acetaminophen assay provides a reliable prognostic indication of potential hepatotoxicity and serves as a basis for determining the need for continuing with the maintenance doses of acetylcysteine treatment (See DOSAGE AND ADMINISTRATION- Interpretation of Acetaminophen Assays).

4. Obtain the following blood laboratory measurements to monitor hepatic and renal function and electrolyte and fluid balance: AST, ALT, bilirubin, prothrombin time, international normalized ratio (INR), creatinine, BUN, blood sugar and electrolytes.

5. Administer the **loading dose** of acetylcysteine **immediately** as outlined in Table 1 according to the route of administration employed. **Do not** wait for blood and laboratory tests to start administration of Acetylcysteine Injection.

6. **Maintenance doses** should be administered following the loading dose as detailed below and outlined in Table 1. Determine the need for continued treatment with Acetylcysteine Injection after the loading dose based on the plasma acetaminophen concentration and the possible toxicity line in the nomogram (See DOSAGE AND ADMINISTRATION - Interpretation of Acetaminophen Assays, Figure 1).

7. Repeat AST, ALT, bilirubin, prothrombin time, creatinine, BUN, blood sugar and electrolytes daily if acetaminophen plasma level is in the potentially toxic range as discussed below. The tests may be repeated regularly to monitor hepatic function even after the acetaminophen plasma levels are below the toxic level and/or after the last maintenance dose to determine the need for continued treatment with Acetylcysteine Injection.

Recommended Dose and Dosage Adjustment

Dosage and Preparation of Acetylcysteine Injection for Intravenous Administration:
Following acetaminophen overdose, Acetylcysteine Injection may be used for intravenous administration according to the Dosage Guide in Table 1. Dilutions recommended should be prepared with 5% dextrose in water as appropriate.

Acetylcysteine Injection for intravenous use should be considered as a single-use container.

Solutions recommended under each column in Table 1 should be freshly prepared and used only over times stated.

Adults and Pediatrics: The full course of treatment with acetylcysteine comprises 3 intravenous infusions as detailed in Table 1.

Table 1: Dosage Guide and Preparation for Intravenous Administration

Infusion	Initial Infusion (in 5% dextrose over 15 minutes)		2nd Infusion (in 500 ml 5% dextrose over 4 hours)	3rd Infusion (in 1 litre 5% dextrose over 16 hours)
Body Weight (kg)	Acetylcysteine (mL)	5% Dextrose (mL)	Acetylcysteine (mL)	Acetylcysteine (mL)
10-15	11.25	40	3.75	7.5
15-20	15	50	5	10
20-25	18.75	75	6.25	12.5
25-30	22.5	75	7.5	15
30-40	30	100	10	20
40-50	37.5	200	12.5	25
50-60	45	200	15	30
60-70	52.5	200	17.5	35
70-80	60	200	20	40
80-90	67.5	200	22.5	45
90-100	75	200	25	50
100-110	82.5	200	27.5	55

The volumes and rates of infusion for children suggested in Table 1 must be adjusted according to the medical circumstances. Restrictions in the volume of parenteral fluids administered and the state of hydration and serum electrolytes for each patient must be monitored closely.

Interpretation of Acetaminophen Assays

The acute ingestion of acetaminophen in quantities of 150 mg / kg or greater may result in hepatic toxicity. However, the reported history of the quantity of a drug ingested as an overdose is often inaccurate and is not a reliable guide to therapy of the overdose. **THEREFORE, PLASMA OR SERUM ACETAMINOPHEN CONCENTRATIONS, DETERMINED AS EARLY AS POSSIBLE, BUT NO SOONER THAN FOUR HOURS FOLLOWING AN ACUTE OVERDOSE, ARE ESSENTIAL IN ASSESSING THE POTENTIAL RISK OF HEPATOTOXICITY.** (DO NOT WAIT FOR ASSAY RESULTS TO BEGIN ACETYLCYSTEINE TREATMENT).

Nomogram (Rumack-Matthew) for Estimating Potential for Hepatotoxicity from Acute Acetaminophen Ingestion

The Rumack-Matthew nomogram, Figure 1, should be used to estimate the probability that plasma acetaminophen levels in relation to intervals post-ingestion will result in hepatotoxicity.

When results of the plasma acetaminophen assay are available refer to the nomogram (Figure 1) to determine if plasma concentration is in the potentially toxic range. Values above the solid line connecting 200 mcg / mL at 4 hours with 50 mcg / mL at 12 hours are associated with a possibility of hepatic toxicity if an antidote is not administered.

1. If the plasma acetaminophen level is above the broken line continue with maintenance doses of acetylcysteine. It is better to err on the safe side and thus the broken line is plotted 25% below the solid line which defines possible toxicity.

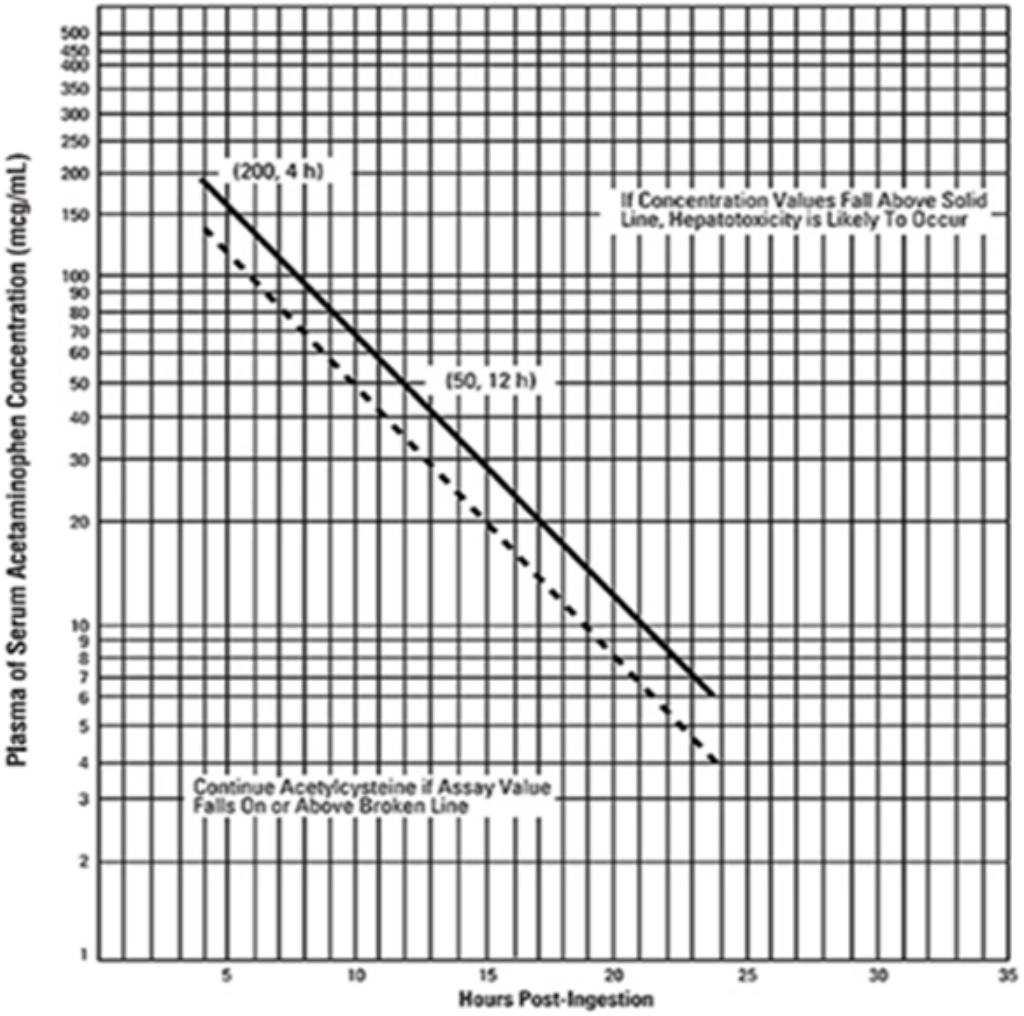
2. If the plasma acetaminophen level is below the broken line described above, there is minimal risk of hepatic toxicity and acetylcysteine treatment can be discontinued. However, continued monitoring of serum AST and ALT, prothrombin time and INR are recommended and continued treatment with maintenance doses may be required if AST and ALT are still increasing or the INR remains elevated.

3. Acetaminophen levels and AST, ALT, prothrombin time and INR should be checked after the last maintenance dose to determine the need for continued treatment with Acetylcysteine Injection.

Considerations

1. The recommendations for treatment based on this nomogram do not apply to patients who have ingested acetaminophen at dosages higher than those recommended for extended periods of time. The acetylcysteine treatment for these patients should be guided by acetaminophen serum and plasma concentrations and laboratory tests to monitor hepatic and renal function and electrolyte and fluid balance.
2. Chronic alcohol ingestion and/or concomitant barbiturate therapy, malnutrition, or CYP450 enzyme inducing drugs may induce a greater formation of the hepatotoxic metabolite (NAPQI) for any given dose of acetaminophen. The nomogram may underestimate the hepatotoxicity risk and consideration should be given to treating these patients even if the acetaminophen concentrations are not in the non-toxic range.

FIGURE 1: Nomogram: Plasma or Serum Acetaminophen Concentration vs. Time Post Acetaminophen Ingestion



Acetaminophen Assay Methodology
Assay procedures most suitable for determining acetaminophen concentrations utilize high pressure liquid chromatography (HPLC) or gas liquid chromatography (GLC). The assay should measure only parent acetaminophen and not conjugated.

Supportive Treatment of Acetaminophen Overdose:
1. Maintain fluid and electrolyte balance based on clinical evaluation of state of hydration and serum electrolytes.
2. Treat as necessary for hypoglycemia.
3. Administer Vitamin K if prothrombin time ratio exceeds 1.5 or fresh frozen plasma if the prothrombin time ratio exceeds 3.0.
4. Diuretics and forced diuresis should be avoided. Hemodialysis or peritoneal dialysis has not been found helpful.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Overdosage of acetylcysteine has been reported to be associated with effects similar to the hypersensitivity reactions (See WARNINGS AND PRECAUTIONS), but they may be more severe. General supportive measures should be carried out.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Acetaminophen is rapidly absorbed from the upper gastrointestinal tract following ingestion with peak plasma levels occurring between 30 and 60 minutes after therapeutic doses and usually within 4 hours following an overdose. The parent compound, which is non-toxic, is extensively metabolized in the liver to form principally the sulfate and glucuronide conjugates which are also non-toxic and are rapidly excreted in the urine.

A small fraction of the ingested dose is metabolized in the liver via oxidation by the cytochrome P-450 enzyme pathway, primarily CYP2E1, to form a reactive, potentially toxic, intermediate metabolite (N-acetyl-p-benzoquinone imine or NAPQI). NAPQI undergoes rapid conjugation with hepatic glutathione to form the non-toxic cysteine and mercapturic acid derivatives which are then excreted by the kidney.
Therapeutic doses of acetaminophen do not saturate the glucuronide and sulfate conjugation pathways and do not result in formation of sufficient reactive metabolite to deplete glutathione stores.

However, following ingestion of a large overdose (150 mg / kg or greater) of acetaminophen the glucuronide and sulfate conjugation pathways are saturated resulting in a larger fraction of the drug being metabolized via the P-450 pathway. The increased formation of NAPQI may deplete the hepatic stores of glutathione with subsequent binding of the metabolite to protein molecules within the hepatocyte resulting in cellular necrosis.

Acetylcysteine probably protects the liver by maintaining or restoring the glutathione levels, or by acting as an alternate substrate for conjugation with and thus detoxification of the reactive metabolite of acetaminophen, NAPQI.

STORAGE AND STABILITY

Acetylcysteine Injection is not compatible with rubber and metals, particularly iron, copper and nickel.

Store unopened vials between 15 and 30°C. Protect from light. The colour of the acetylcysteine solution may change to a light purple colour once the stopper is punctured. The colour change is the result of a chemical reaction which does not significantly impair the safety of acetylcysteine.

Do not use if solution shows haziness, particulate matter, discolouration, or leakage.

Storage of Diluted Solution for IV

Acetylcysteine Injection: Dilutions should be freshly prepared and used only over times stated (See DOSAGE AND ADMINISTRATION - Dosage and Preparation of Acetylcysteine Injection for Intravenous Administration). Discard unused portions.

SPECIAL HANDLING INSTRUCTIONS

Do not use previously opened vials for intravenous administration.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Acetylcysteine Injection is available in 10 glass vials of 30 mL in boxes of 1.

Each mL contains acetylcysteine 200 mg, Edetate Disodium 0.5 mg and Sodium Hydroxide to adjust pH and water for injection.

The vial stopper is not made with natural rubber latex.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

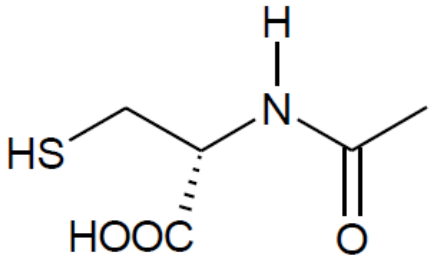
Drug Substance

Proper name: Acetylcysteine

Chemical name: (2R)-2-Acetamido-3-sulfanylpropanoic acid; N-Acetyl-L-Cysteine; L-cysteine; N-acetyl.

Molecular formula and molecular mass: $C_5H_9NO_3S$; 163.2 g / mol

Structural formula:



Appearance: White, crystalline powder.

DETAILED PHARMACOLOGY

Animal studies

Acetylcysteine is efficacious in preventing lethality from acute acetaminophen overdosage in CF-1 mice, even when therapy is delayed 4½ hours after dosing with acetaminophen. This time frame is especially noteworthy, since unprotected mice become debilitated by 1½ hours, have liver involvement by 3½ hours and die as early as 4 to 5 hours post-overdose.

The protective effect of acetylcysteine in preventing lethality was accompanied by marked hepatoprotection, which was closely reflected by the alanine transaminase (ALT) when the antidote was administered early. However, ALT levels were found to be poor prognostic indicators of survival in late acetylcysteine administration.

Parallel comparisons with reference compounds indicate that acetylcysteine is more efficacious than cysteamine in both overall survival rate and effectiveness on late administration (4½ hours after acetaminophen dosing). Similar studies with methionine indicate that both acetylcysteine and methionine show high efficacy, but that methionine produces a bell-shaped rather than a linear dose response pattern on late administration, i.e., the higher as well as the lower doses resulted in lower survival rates that the mid-range doses. A highly lethal acetaminophen challenge dose was used (1500 mg / kg) resulting in a 7% survival rate in the untreated mice.

The effects of delayed administration after a less severe challenge (1200 mg / kg) were examined. The survival rate in the untreated mice was 70%. Treatment was initiated 9 hours after overdosing. When acetylcysteine was administered at this time which coincided with peak acetaminophen-induced liver insult, slight protection rather than-exacerbation of toxicity occurred. In this experiment the reference compound, methionine, showed a similar pattern. Cysteamine, in contrast, showed a tendency to worsen the overall condition of animals if treatment was instituted as early as 4½ hours after dosing with 1200 mg / kg of acetaminophen.

Safety assessment of acutely administered acetylcysteine to normal CF-1 mice indicates that it is well tolerated by both oral and intravenous routes.

TOXICOLOGY

Acute toxicity studies conducted in various animal species show that acetylcysteine has low toxicity. The oral LD_{50} of acetylcysteine was greater than 1000 mg / kg in dogs, greater than 3000 mg / kg in mice and 6000 mg / kg in rats. With parenteral administration (intravenous or intraperitoneal) to the same three species and to guinea pigs, the LD_{50} ranged between 700 mg / kg for the dog and 2650 mg / kg for the rat.

Gross and microscopic studies performed at autopsy on rats and dogs, treated with very large oral doses of acetylcysteine for 8 weeks, revealed no pathologic abnormalities in either species attributable to the administration of the agent. During administration of the test doses, growth and body weights of the animals were not deleteriously affected. Hemograms and liver function studies revealed no abnormalities attributable to the drug.

Histologic studies were done in guinea pigs exposed to aerosol sprays of 3% and 18% solutions of acetylcysteine for 15 minutes daily for 8 weeks. The histologic sections of the lungs, trachea, bronchi and larynx of these animals were not different from those of the control group exposed to normal saline. The mortality and morbidity rates in the two groups were not significantly different.

Other groups of guinea pigs were exposed to nebulization of the 3% and 18% solutions of acetylcysteine daily for three weeks, rested for two weeks, and then re-exposed for three days. These studies revealed no evidence of sensitization.

Dogs, rabbits and rats were exposed to a chamber atmosphere produced by 30 second nebulization of a 20% solution of acetylcysteine; these test animals remained in the atmosphere for an additional 15 minutes. Exposure was done twice daily for 35 consecutive days. Other groups of rabbits, rats and guinea pigs were exposed to a chamber atmosphere produced by continuous nebulization of a 20% solution of acetylcysteine for 1 hour a day 5 days a week for 12 weeks. No clinical or histopathological changes were found that could be attributed to acetylcysteine.

No evidence of local irritation was observed with acetylcysteine injected intracutaneously in guinea pigs. Ciliary activity in excised rat trachea was not inhibited by topical application of acetylcysteine.

Toxicology mechanism studies indicated that the antidotal profile of acetylcysteine is not related to facilitated plasma or urinary clearance of acetaminophen or acetaminophen metabolites, nor to cleavage of covalent bonds or significant tissue re-distribution of acetaminophen or its metabolites. Acetylcysteine antidotal therapy was associated with increased mercapturate conjugate in the urine, suggesting that acetylcysteine, like endogenous glutathione, may be serving as a substrate for the detoxification of the reactive metabolite of acetaminophen.

REFERENCES

1. WellSpring Pharmaceutical Canada Corp. Product Monograph: MUCOMYST. Control number 075829. Date of revision: January 29, 2002.

2. Sandoz Canada Inc. Product Monograph: ACETYLCYSTEINE SOLUTION. Control number 233514. Date of revision: February 10, 2020.

3. Product Monograph for ACETYLCYSTEINE SOLUTION USP (200 mg / mL), TELIP, LLC, a subsidiary of Teligent, Inc., Submission Control Number: 251092, Date of Revision: August 31, 2021.

PATIENT MEDICATION INFORMATION
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Acetylcysteine Injection

Read this carefully before you start taking **Acetylcysteine Injection** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Acetylcysteine Injection**.

What is Acetylcysteine Injection used for?
Acetylcysteine Injection is used to:

- Treat or prevent damage to your liver which may occur after you have taken too much acetaminophen (overdose).

How does Acetylcysteine Injection work?
Acetylcysteine Injection works:

- By protecting your liver after you have taken too much acetaminophen. It may do this by:
  - restoring and keeping the right levels of a naturally occurring substance in your liver or
  - lowering the amount of harmful substances in your liver

What are the ingredients in Acetylcysteine Injection?
Medicinal ingredient: Acetylcysteine
Non-medicinal ingredients: Edetate Disodium, Sodium Hydroxide and water for Injection.

Acetylcysteine Injection comes in the following dosage forms:
Sterile solution for injection: 200 mg / mL.

Do not use Acetylcysteine Injection if:

- You are allergic to acetylcysteine or to any of the other ingredients in Acetylcysteine Injection.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Acetylcysteine Injection. Talk about any health conditions or problems you may have, including if you:

- have had a serious allergic reaction in the past such as a rash, low blood pressure, wheezing and/ or shortness of breath.
- are pregnant or planning on becoming pregnant
- breastfeeding or planning on breastfeeding
- have brain damage caused by liver failure and are taking this drug as intravenously (I.V).

Other warnings you should know about:

<u>To treat acetaminophen poisoning:</u>

General:

- **Acetylcysteine Injection is not compatible with rubber and metals, particularly iron, copper and nickel.**
- If the vial is left punctured/open, the solution may change to a light purple colour. This

colour change does not significantly impair the safety of the acetylcysteine solution.
- Your doctor will take samples of your blood after an overdose. This is to monitor the levels of acetaminophen in your body. Your doctor will also monitor your liver and kidney function, the levels of electrolytes and fluid in your body.

When taken as an Intravenous Injection:
- **The contents of the vial are to be used only once. Throw away the rest. Do not use the contents in a vial if it has been previously opened.**
- Taking Acetylcysteine Injection as an injection can cause your body to hold on to excess fluid. This may cause hyponatremia. This is a condition that occurs when the level of sodium in your blood becomes too low. It may also cause seizures and can lead to death. You should be careful if you are taking this drug and you weigh less than 40 kilograms or you are giving this drug as an injection to a child.
- You may notice that your face or skin becomes hot and red (flush). This usually happens 30 to 60 minutes after you start taking the drug. It usually goes away on its own. If it gets worse or does not go away, tell your doctor.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Acetylcysteine Injection:
Acetylcysteine Injection is not compatible with rubber and metals, particularly iron, copper and nickel.

How to take Acetylcysteine Injection:
Acetylcysteine Injection can be taken intravenously (IV). Your doctor will determine the amount of Acetylcysteine Injection you will receive based on your condition and your weight.

Overdose:

If you think you, or a person you are caring for, have taken too much Acetylcysteine Injection, contact a healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Signs of an overdose include those that are similar to an allergic reaction but may be more severe such as:
- rash
- difficulty breathing
- shortness of breath
- swelling of the face, eyes, lips, tongue or throat

What are possible side effects from using Acetylcysteine Injection?
These are not all the possible side effects you may feel when taking Acetylcysteine Injection. If you experience any side effects not listed here, contact your healthcare professional.
Side effects include:
- swelling in the mouth or a sore mouth
- nausea
- vomiting
- runny nose
- cough
- a feeling of tightness in the chest or chest pain

- puffy eyes and/or blurred vision
- sweating
- generally feeling unwell
- fever
- a slow heart rate
- pain in your eyes or your face
- a condition called acidosis which may cause weariness, vomiting, thirst or feeling restless
- feeling anxious
- pain, stiffness, swelling and redness in your joints.
- bluish skin

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNKNOWN **Allergic reaction:** sudden wheeziness, chest pain or tightness, swelling of face, eyelids, tongue, lips or throat and a skin rash anywhere on the body (hives)			√
Bronchospasm: sudden worsening of shortness of breath, trouble breathing and wheezing after inhalation.			√
High blood pressure: rapid heart rate	√		
Low blood pressure: dizziness		√	
Injection site reaction: irritation at the site of injection		√	
Thrombocytopenia: increased risk of bleeding or bruising after injury		√	
Respiratory arrest (stop breathing)			√
Cardiac arrest (heart stops beating)			√
Decreased liver function: yellowing of the skin, feeling tired, nausea, vomiting		√	
Seizures			√
Low blood potassium: Muscle weakness and spasms		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

- You can report any suspected side effects associated with the use of health products to Health Canada by: Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at room temperature (15-30˚C). Protect the vials from light.

For intravenous (IV) use:
Use the contents of the vial only **once** (single use). Throw away the rest. **Do not use the contents of the vial if it has been previously opened**.

For Solutions that have been diluted for intravenous (IV) use:
Solutions should be prepared as needed and used over specific times.

Keep out of reach and sight of children.

If you want more information about Acetylcysteine Injection:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.auropharma.ca, or by calling 1-855-648-6681.

This leaflet was prepared by:

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