NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Acetylcysteine 200mg/mL Injection (Martindale)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Acetylcysteine 20% w/v or 200 milligrams in 1 mL.

Each 10 mL ampoule contains 2 g acetylcysteine.

For the full list of excipients, see *section 6.1*.

3. PHARMACEUTICAL FORM

Infusion concentrate

4. CLINICAL PARTICULARS

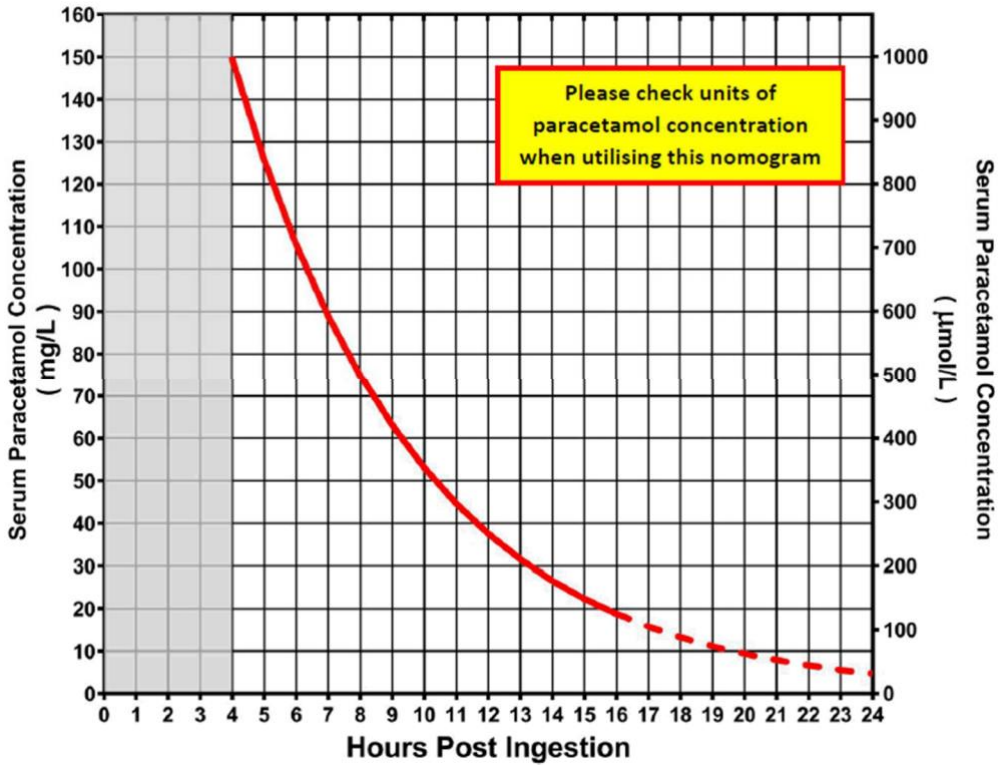
4.1 Therapeutic indications

N-acetylcysteine is indicated for the treatment of paracetamol overdose in patients:

- who present within 8 hours after an acute overdose of immediate-release paracetamol with a serum paracetamol level on or over the nomogram line. or
- who present more than 8 hours after an acute overdose of immediate-release paracetamol. or
- who have ingested ≥200 milligrams/kg or ≥10 g (whichever is less) of modified-release paracetamol. or
- who have ingested <200 milligrams/kg and <10 g of modified-release paracetamol, with serum paracetamol level over the nomogram line. or
- who have ingested ≥200 milligrams/kg or ≥10 g (whichever is less) of paracetamol over a single 24 hour period, and have an ALT ≥50 U/L or serum paracetamol concentration ≥20 milligrams/L (132 μmol/L). or
- who have ingested ≥300 milligrams/kg or ≥12 g (whichever is less) of paracetamol over a single 48 hour period, and have an ALT ≥50 U/L or serum paracetamol concentration ≥20 milligrams/L (132 μmol/L). or
- who have ingested the equivalent or more of a daily therapeutic dose of paracetamol per day for more than 48 hours and also have abdominal pain or nausea or vomiting, and have an ALT ≥50 U/L or serum paracetamol concentration ≥20 milligrams/L (132 μmol/L). or
- where there is any doubt over the time of an acute overdose, irrespective of serum paracetamol level. or

- where serum paracetamol concentration is ≥150 milligrams/L 4 hours post-ingestion in children less than 6 years of age.

Figure 1. Paracetamol Treatment Nomogram (Rumack-Matthew Nomogram)



*Note: µmol/L = micromol/L = nmol/mL

4.2 Dose and method of administration

Acetylcysteine should be administered by intravenous infusion preferably using 5% glucose as the infusion fluid. 0.9% sodium chloride solution may be used if 5% glucose is not suitable.

The majority of patients should be treated with the two infusion schedule. However some patients may require prolonged treatment.

Dose in Adults (age ≥14 years)

Acetylcysteine 200 milligrams/mL Injection is infused in two intravenous infusions containing different doses.

INITIAL INFUSION: An initial dose of 200 milligrams/kg (maximum 22 g) of acetylcysteine diluted in 500 mL of 5% glucose or 0.9% sodium chloride and infused intravenously over 4 hours i.e. an infusion rate of 50 milligrams/kg/hour of acetylcysteine for 4 hours.

SECOND INFUSION*: The initial infusion is followed by a continuous intravenous infusion of 100 milligrams/kg (maximum 11 g) of acetylcysteine in 1000 mL of 5% glucose or 0.9% sodium chloride over 16 hours i.e. an infusion rate of 6.25 milligrams/kg/hour of acetylcysteine for 16 hours.

* If the initial serum paracetamol concentration was more than double the nomogram line (refer to Figure 1) following an acute ingestion of paracetamol, increase acetylcysteine dose to 200 milligrams/kg (maximum 22 g) diluted in 1000 mL of 5% glucose or 0.9% sodium chloride intravenously, over 16 hours. i.e. an infusion rate of 12.5

milligrams/kg/hour of acetylcysteine for 16 hours.

The dose **should be calculated using the patient's actual body weight** rounded to the nearest 10 kg, with a ceiling of 110 kg.

Table 1. Dose and Volume of Acetylcysteine to be Used for Each Infusion in Adults

PATIENT'S BODY WEIGHT (kg)	**BAG 1: INITIAL INFUSION** (200 milligrams/kg (maximum 22 g) of acetylcysteine to be added to 500 mL of 5% glucose or 0.9% sodium chloride)		**BAG 2: SECOND INFUSION*** (100 milligrams/kg (maximum 11 g) of acetylcysteine to be added to 1000 mL of 5% glucose or 0.9% sodium chloride)	
	Dose (g) of Acetylcysteine	Volume (mL) of Acetylcysteine	Dose (g) of Acetylcysteine	Volume (mL) of Acetylcysteine
50	10 g	50 mL	5 g	25 mL
60	12 g	60 mL	6 g	30 mL
70	14 g	70 mL	7 g	35 mL
80	16 g	80 mL	8 g	40 mL
90	18 g	90 mL	9 g	45 mL
100	20 g	100 mL	10 g	50 mL
110 **(maximum dose)**	22 g	110 mL	11 g	55 mL

* Note: If the serum paracetamol concentration was more than double the nomogram line, increase acetylcysteine dose to 200 milligrams/kg.

Dose in Children (age <14 years)

Children should be treated with the same doses (milligrams/kg) and regimens as adults; however the quantity of intravenous fluid used must be modified to take into account age and weight as fluid overload is a potential danger in children.

The full course of treatment with acetylcysteine includes two consecutive intravenous infusions.

INITIAL INFUSION: An initial dose of 200 milligrams/kg (maximum 22 g) of acetylcysteine diluted in 7 mL/kg up to 500 mL of 5% glucose or 0.9% sodium chloride and infused intravenously over 4 hours i.e. an infusion rate of 50 milligrams/kg/hour of acetylcysteine for 4 hours.

SECOND INFUSION*: The initial infusion is followed by a continuous intravenous infusion of 100 milligrams/kg (maximum 11 g) of acetylcysteine in 14 mL/kg up to 1000 mL of 5% glucose or 0.9% sodium chloride over 16 hours i.e. an infusion rate of 6.25 milligrams/kg/hour of acetylcysteine for 16 hours.

The dose **should be calculated using the patient's actual body weight**. Determine the total volume of solution needed from the table.

Table 2. Dose and Volume of Acetylcysteine & Volume of Diluent to be Used for Each Infusion in Children

PATIENT'S BODY WEIGHT (kg)[#] (examples)	**BAG 1: INITIAL INFUSION** (200 milligrams/kg (maximum 22 g) of acetylcysteine to be added to 7 mL/kg up to 500 mL of 5% glucose or 0.9% sodium chloride)			**BAG 2: SECOND INFUSION*** (100 milligrams/kg (maximum 11 g) of acetylcysteine to be added to 14 mL/kg up to 1000 mL of 5% glucose or 0.9% sodium chloride)		
	Dose (g) of Acetylcysteine	Volume (mL) of Acetylcysteine	Volume (mL) of Diluent	Dose (g) of Acetylcysteine	Volume (mL) of Acetylcysteine	Volume (mL) of Diluent
15	3 g	15 mL	105 mL	1.5 g	7.5 mL	210 mL
20	4 g	20 mL	140 mL	2 g	10 mL	280 mL
25	5 g	25 mL	175 mL	2.5 g	12.5 mL	350 mL

[#] Use actual body weight.
[*] Note: If the serum paracetamol concentration was more than double the nomogram line, increase acetylcysteine dose to 200 milligrams/kg

Method of Administration

To be most effective in protecting against liver injury, therapy with acetylcysteine should be started within 8 hours of paracetamol ingestion.

Management of Paracetamol Overdose with Acetylcysteine

The paracetamol treatment nomogram is used to decide whether to start or continue acetylcysteine infusion. The dosing depends on the time since paracetamol ingestion, formulation of paracetamol, dose ingested, serum paracetamol concentration (early), and presence of clinical and laboratory features suggesting acute liver injury.

It should be noted that, after an ingestion of a potentially fatal dose of paracetamol, the patient may appear relatively well initially and may even continue normal activities for a day or two before the onset of hepatic failure. Liver injury is more likely to occur with a lower dosage of paracetamol in patients who have a history of chronic alcohol use or enzyme-inducing drug ingestion (e.g. isoniazid, rifampicin, anticonvulsants including carbamazepine, phenytoin, phenobarbitone, primidone, sodium valproate).

Patients are notoriously unreliable as to the amount ingested and the time of ingestion. Hepatic necrosis is preventable if treatment can be instituted within 8 hours of ingestion.

Note: Liver injury may not be clinically or biochemically apparent for up to 24 hours after ingestion.

Hepatic necrosis has been seen with 6 grams of paracetamol, and death with 15 grams.

The following A-C sections are applicable to both adults and children, for both solid and liquid paracetamol ingestion.

A. Acute Ingestion of Immediate-Release Paracetamol

- In patients who present within 8 hours after an overdose, with a serum paracetamol concentration on or over the nomogram line, commence acetylcysteine infusion.*

- In patients who present more than 8 to 24 hours after an overdose, commence acetylcysteine infusion immediately. Measure serum paracetamol concentration and alanine aminotransferase (ALT). For patients who have serum paracetamol concentration on or over the nomogram line and/or ALT >50 U/L, continue the rest of the treatment (otherwise no further treatment is required).*

** For patients who have serum paracetamol concentration double the nomogram line, complete acetylcysteine infusion with double dose of the second bag (200 milligrams/kg over 16 hours).*

- In patients who present more than 24 hours after an overdose, commence acetylcysteine infusion immediately. Measure serum paracetamol concentration and ALT. If serum paracetamol concentration is ≥10 milligrams/L (66 µmol/L) and/or ALT >50 U/L, continue the rest of the treatment (otherwise no further treatment required).

- In patients whose time of ingestion is not known, follow the advice above for more than 8 to 24 hours after an overdose, commence acetylcysteine immediately. Measure serum paracetamol concentration and ALT. If the serum paracetamol concentration is ≥10 milligrams/L (66 µmol/L) and/or the ALT is >50 U/L, continue the rest of the treatment (otherwise no further treatment required).

Two hours before the completion of acetylcysteine infusion, ALT measurement should be repeated in all patients. For those with an initial serum paracetamol concentration double the nomogram line, a serum paracetamol concentration should also be repeated. Acetylcysteine treatment should be continued if the serum paracetamol concentration is >10 milligrams/L (66 µmol/L), or ALT is elevated (>50 U/L) and increasing (if baseline ALT >50 U/L).

B. Acute Ingestion of Modified-Release (MR) Paracetamol

- In patients who ingested MR paracetamol dose of <10 grams AND <200 milligrams/kg, measure 2 serum paracetamol concentrations at least 4 hours post-ingestion and 4 hours apart. If either serum paracetamol concentration is over the nomogram treatment line, commence acetylcysteine infusion.*

- In patients who ingested MR paracetamol dose of ≥10 grams or ≥200 milligrams/kg (whichever is less) and present more than 4 hours post-ingestion, commence acetylcysteine infusion immediately.

    - If dose ingested is ≥30 grams or ≥500 milligrams/kg (whichever is less), complete acetylcysteine infusion with double dose of the second bag (200 milligrams/kg over 16 hours).

    - If dose ingested is NOT ≥30 grams or NOT ≥500 milligrams/kg, measure 2 serum paracetamol concentrations at least 4 hours post-ingestion and 4 hours apart, and if either serum paracetamol concentration is more than double the nomogram treatment line, acetylcysteine treatment should be continued.*

** For patients with either of the two serum paracetamol concentration more than double the nomogram line, complete acetylcysteine infusion with double dose of the second bag (200 milligrams/kg over 16 hours).*

Measure serum paracetamol concentration and ALT for all patients before ceasing acetylcysteine infusion. Acetylcysteine treatment should be continued if serum paracetamol concentration is >10 milligrams/L (66 µmol/L), or ALT is elevated (>50 U/L) and increasing (if baseline ALT >50 U/L).

C. Repeated Supratherapeutic Ingestion (RSTI) of Paracetamol

Patients who ingest excessive paracetamol for a therapeutic purpose (e.g. pain, viral infection) or ingest therapeutic doses of paracetamol and have symptoms of acute liver injury (e.g. abdominal pain, nausea and vomiting) are managed as RSTI. If the ingestion is deliberate/intentional they should be managed as per acute intentional ingestion.

- In patients who ingested paracetamol dose of ≥10 grams or ≥200 milligrams/kg (whichever is less) over a single 24 hour period, and have an ALT ≥50 U/L or serum paracetamol concentration ≥20 milligrams/L (132 μmol/L), commence acetylcysteine infusion.

- In patients who ingested paracetamol dose of ≥12 grams or ≥300 milligrams/kg (whichever is less) over a single 48 hour period, and have an ALT ≥50 U/L or serum paracetamol concentration ≥20 milligrams/L (132 μmol/L), commence acetylcysteine infusion.

- In patients who ingested a daily therapeutic dose per day for more than 48 hours in those who also have abdominal pain or nausea or vomiting, and have an ALT ≥50 U/L or serum paracetamol concentration ≥20 milligrams/L (132 μmol/L), commence acetylcysteine infusion.

Repeat serum paracetamol concentration and ALT, 8 hours after the previous concentration sampling. If ALT ≥50 U/L or serum paracetamol concentration ≥10 milligrams/L (66 μmol/L), continue acetylcysteine infusion and check ALT at 12 hourly intervals.

D. Paediatric (<6 years) liquid paracetamol ingestion

In children less than 6 years of age, where ingestion of greater than 200 milligrams/kg of liquid paracetamol is suspected, a serum paracetamol concentration should be measured at least 2 hours post-ingestion. If the 2-hour post-ingestion serum paracetamol concentration is greater than 150 milligrams/L (1000 μmol/L), this should be repeated 4 hours post-ingestion and acetylcysteine commenced if this is ≥150 milligrams/L (1000 μmol/L). Further, for those children who present later than 4 hours post-ingestion or in children older than 6 years of age, treatment is as per the adult acute paracetamol exposure guideline.

E. General Management

Acetylcysteine should be administered if appropriate (see above). Acetylcysteine should be diluted in 5% glucose or 0.9% sodium chloride solution, and administered by intravenous infusion. Nausea should be treated.

Measurements of plasma hepatic enzymes and blood bilirubin, and coagulation tests, should be performed as soon as possible after admission.

Daily liver function tests, and measurements of blood urea, blood electrolytes, blood glucose, blood gases, haemoglobin, white blood cell counts, platelets and prothrombin time should be conducted . An electrocardiogram (ECG) should also be performed. Patients should be monitored for coagulopathy, hepatic encephalopathy, renal failure and cardiotoxicity (minor ST changes are common). There is usually a metabolic acidosis. Hepatic encephalopathy is likely if bilirubin is above 60 millimoles /L on days 3 to 5, or if the prothrombin time is prolonged.

If ongoing acetylcysteine treatment is required, continue at the rate of the second infusion (e.g. 100 milligrams/kg over 16 hours i.e. 6.25 milligrams/kg/hour). Higher ongoing infusion rates

(e.g. 200 milligrams/kg over 16 hours i.e. 12.5 milligrams/kg/hour) may be required for massive paracetamol ingestions and a clinical toxicologist should be consulted.

4.3 Contraindications

There are no contraindications to the treatment of paracetamol overdose with acetylcysteine.

4.4 Special warnings and precautions for use

Acetylcysteine should be used with caution in asthma or where there is a history of bronchospasm. It should also be used with caution with patients with a past history of oesophageal varices and peptic ulcer (acetylcysteine-induced vomiting may increase the risk of haemorrhage).

Acetylcysteine is not compatible with rubber and some metals, particularly, iron, copper and nickel. Acetylcysteine 200mg/mL Injection can be used satisfactorily with silicone rubber and plastic.

Anaphylactoid Reactions

Anaphylactoid hypersensitivity reactions can occur with acetylcysteine. The patient should be carefully observed for signs of an anaphylactoid reaction. Nausea, vomiting, flushing, skin rash, pruritus and urticaria are the most common features, but more serious anaphylactoid reactions have been reported where the patient develops angioedema, bronchospasm, respiratory distress, tachycardia and hypotension. In very rare cases these reactions have been fatal. There is some evidence that patients with a history of atopy and asthma may be at increased risk of developing an anaphylactoid reaction.

Most anaphylactoid reactions can be managed by temporally suspending the acetylcysteine infusion, administering appropriate supportive care, antihistamines and bronchodilators and restarting at a lower infusion rate. Once an anaphylactoid reaction is under control, the infusion can normally be restarted at an infusion rate of 50 milligrams/kg/hour over 4 hours (i.e. 12.5 milligrams/kg/hour), followed by the final 16 hour infusion (100 milligrams/kg over 16 hours i.e. 6.25 milligrams/kg/hour).

In patients who have previously experienced an anaphylactoid reaction with acetylcysteine consideration should be given to pre-treatment with an IV antihistamine 15 minutes before starting the acetylcysteine infusion.

Coagulation

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. An isolated increase in prothrombin time up to 1.3 at the end of a 21 hour course of acetylcysteine without an elevated transaminase activity does not require further monitoring or treatment with acetylcysteine.

Fluid and Electrolytes

Use with caution in children, patients requiring fluid restriction or those who weigh less than <40 kg because of the risk of fluid overload which may result in hyponatraemia and seizures which may be life threatening (see *section 4.2*).

Each 10 mL ampoule of the infusion concentrate contains 322.6 milligrams sodium. To be taken into consideration with patients on a controlled sodium diet.

Use in Renal/Hepatic Impairment

Caution should be taken when administering acetylcysteine in patients with hepatic or renal failure, since there is little data relating to the effects of acetylcysteine in abnormal renal and/or hepatic function. The decision to administer should be based on a risk/benefit assessment for the individual subject.

In the presence of hepatic failure due to paracetamol overdose the degree of existing liver injury and the possible risk associated with the administration of acetylcysteine should be considered.

Paediatric use

The safety and effectiveness of acetylcysteine in children has not been established.

No paediatric-specific adverse effects have been documented.

Use of acetylcysteine in paediatric patients is based on clinical practice (see *section 4.2*).

Effects on Laboratory Tests

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

4.5 Interaction with other medicines and other forms of interaction

There are no known interactions.

4.6 Fertility, pregnancy and lactation

Fertility

There was evidence of effects on fertility in male rats given acetylcysteine at doses up to 60% of the maximum clinical dose, on a body surface area basis. No effects were observed at doses 15% the maximum clinical dose, on a body surface area basis (see *section 5.3*).

Pregnancy

Category B2 [1]

There was no evidence of teratogenicity in limited studies in rats and rabbits following administration of acetylcysteine during the period of gestation at doses up to 1.2 times the maximum clinical dose, on a body surface area basis. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage. There are no well-controlled studies in pregnant women but experience does not include any

[1] *Category B2: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed*

positive evidence of adverse effects to the fetus.

Lactation

There was no evidence of adverse effects in a limited study in rats following administration of acetylcysteine during late gestation and lactation at 60% of the maximum clinical dose, on a body surface area basis. It is not known whether acetylcysteine and/or its metabolites are excreted in milk. There are no data on the use of acetylcysteine in lactating women and therefore breastfeeding is not recommended during treatment.

4.7 Effects on ability to drive and use machinery

Acetylcysteine is presumed to be safe since it is unlikely to produce an effect that may impair the patient's ability to concentrate and react and therefore not constitute a risk in the ability to drive and use machines.

4.8 Undesirable effects

Intravenous administration of acetylcysteine, especially in the large doses needed to treat paracetamol overdose, may result in nausea, vomiting and other gastrointestinal symptoms.

Anaphylactoid reactions have been reported following intravenous administration of acetylcysteine. Bronchospasm may occur in conjunction with a generalised anaphylactic reaction. Other symptoms include airway obstruction (bronchospasm), angioedema, dyspnoea, hypotension, shock, tachycardia, urticaria, and injection site reaction (including rash). These reactions were particularly observed in a regimen no longer in use and usually occurred following the loading dose, therefore appeared to be dose related. Careful monitoring is recommended.

There have been rare instances of death.

The following adverse effects have been reported:

Blood and lymphatic system disorders: Thrombocytopenia

Immune system disorders: Anaphylactoid reaction

Metabolism and nutrition disorders: Acidosis

Psychiatric disorders: Anxiety

Nervous system disorders: Syncope, seizure

Eye disorders: Blurred vision, eye pain

Cardiac disorders: Cyanosis, tachycardia, bradycardia, cardiac arrest, extrasystoles

Vascular disorders: Flushing, hypotension, hypertension, vasodilation

Respiratory, thoracic and mediastinal disorders: Dyspnoea, respiratory arrest, bronchospasm, cough, stridor

Gastrointestinal disorders: Vomiting, nausea

Hepatobiliary disorders: Hepatic function abnormal

Skin and subcutaneous tissue disorders: Angioedema, urticaria, rash (erythematous and maculopapular), hyperhidrosis, oedema periorbital

Musculoskeletal and connective tissue disorders: Arthralgia

General disorders and administration site conditions: Malaise, chills, injection site reaction, chest pain, facial pain, face oedema

Investigations: Body temperature increased, changes in prothrombin time (INR) (usually increased).

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Symptoms

Symptoms following overdose with acetylcysteine have been similar to those of anaphylactoid reactions noted under *section 4.8*, but they may be more severe. Hypotension appears to be especially prominent. There is also a theoretical risk of hepatic encephalopathy.

Treatment

There is no specific treatment. General supportive measures should be carried out. It has been suggested that generalised reactions to acetylcysteine can be treated with intravenous injection of an antihistamine, and infusion of acetylcysteine should be temporarily stopped but can be restarted at the correct rate without further reaction.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidotes, ATC Code: V03AB23

Mechanism of action

Paracetamol is metabolised in the liver, mainly by conjugation with glucuronide and sulphate. It is also metabolised by cytochrome P450 to form a reactive, potentially toxic metabolite. This

metabolite is normally detoxified by conjugation with hepatic glutathione, to form non- toxic derivatives. In paracetamol overdosage, the glucuronide and sulphate conjugation pathways are saturated, so that more of the toxic metabolite is formed. As hepatic glutathione stores are depleted, this toxic metabolite may bind to hepatocyte proteins, leading to liver cell damage and necrosis. Acetylcysteine is a sulphydryl (SH) group donor, and may protect the liver from damage by restoring depleted hepatic-reduced glutathione levels, or by acting as an alternative substrate for conjugation with, and thus detoxification of, the toxic paracetamol metabolite.

5.2 Pharmacokinetic properties

Distribution

The parent compound and metabolites may be present in the plasma either free or protein bound.

Metabolism

Acetylcysteine is the N-acetyl derivative of the naturally occurring amino acid, L-cysteine, and is deacetylated in the liver to cysteine, or oxidised to other metabolites such as N- acetylcystine or N,N-diacetylcystine.

Excretion

Renal clearance accounts for about 30% of total body clearance. Following intravenous administration, mean terminal half lives have been calculated to be 1.95 and 5.58 hours respectively for reduced and total acetylcysteine.

5.3 Preclinical safety data

Genotoxicity

No evidence of mutagenicity was obtained in limited gene mutation assays with Acetylcysteine. The potential for acetylcysteine to cause chromosomal damage has not been investigated.

Carcinogenicity

Carcinogenicity assays have not been performed with acetylcysteine. In rats, no evidence of carcinogenicity was reported following 18 months of daily dietary administration of acetylcysteine at 60% of the maximum clinical dose, on a body surface area basis.

Reproductive and developmental toxicity

There was evidence of effects on fertility in male rats given acetylcysteine at doses up to 60% of the maximum clinical dose, on a body surface area basis. No effects were observed at doses 15% the maximum clinical dose, on a body surface area basis.

6. PHARMACEUTICAL PARTICUALRS

6.1 List of excipients

Sodium hydroxide (for pH adjustment)
Disodium edetate
Water for injections.

6.2 Incompatibilities

No data available.

6.3 Shelf life

24 months

Once diluted according to directions (see *section 4.2*), start using within 3 hours.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

10 mL Type I clear glass ampoules, in packs of 10 ampoules.

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

Max Health Ltd
PO Box 44452 Pt Chevalier
Auckland 1246
Telephone: (09) 815 2664.

9. DATE OF FIRST APPROVAL

30 October 2008

10. DATE OF REVISION OF THE TEXT

1 September 2026

Summary table of changes

Section changed	Summary of new information
Throughout	MedDRA term corrections.
4.1	Indications updated for different paracetamol overdose scenarios (presentation/ingestions times, dosage forms, amount ingested).
4.2	Update from three to two infusion dosage schedule for adults and children. Change in infusion fluid quantities used in preparation of the infusion solution. Relocate text 'Management of Paracetamol Overdose with Acetylcysteine' from 4.4 to 4.2. More information has been added on management of paracetamol ingestion in different scenarios.
4.4	Addition of statement on caution in asthma and if history of bronchospasm or oesophageal varices and peptic ulcers. Moved statement on compatibility with rubbers and metals from 4.2 to 4.4. Under Anaphylactoid Reactions hourly dosages added. Add subsection Paediatric use.
4.6	Added the statement under Pregnancy '*Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.'*
4.8	Added statement that the anaphylactoid reactions were particularly observed in a regimen no longer in use.
5.2	Added headings -Distribution, Metabolism, Excretion.