

# DRUG INFO



## N-ACETYLCYSTEINE (NAC)

UNIT FARMASI  
HOSPITAL KOTA MARUDU

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### INTRODUCTION

N-acetylcysteine (NAC), a sulfhydryl-containing compound and acetylated variant of the amino acid L-cysteine, with mucolytic properties is reported to be first used in medicine in 1967. It has been used clinically in cystic fibrosis since 1969. NAC's use has been expanded to acetaminophen toxicity and chronic obstructive lung disease since then.

### INDICATION

NAC is used to prevent or lessen hepatic injury after ingestion of a potentially hepatotoxic quantity of acetaminophen in patients with acute ingestion or from repeated suprathereapeutic ingestion.

### DOSAGE AND ADMINISTRATION

- 21-hour IV regimen approved by FDA for acetaminophen overdose treatment:
  - consists of 3 doses; total dose delivered: 300mg/kg in 21 hours

**Loading dose:** 150mg/kg IV (max: 15g) in 200ml over 60 minutes

**Second dose:** 50mg/kg IV (max: 5g) in 500ml over 4 hours

**Third dose:** 100mg/kg IV (max: 10g) in 1000ml over 16 hours

Note: the fluid volume should be reduced in **patients weighing  $\leq$  40kg or fluid restricted patients.**

Diluent: Dextrose 5%

- Treatment should be started within 8-10hr for maximum hepatoprotective effect. If the time of ingestion is unknown, initiate the treatment based on clinical evaluation.

### MODE OF ACTION

In acetaminophen toxicity where glucuronidation and sulfation pathways are saturated, more toxic metabolites are produced that depletes the glutathione reserves leading to accumulation. NAC acts as a hepatoprotective agent as it repletes glutathione reserves by providing cysteine, binds itself to the toxic metabolites and scavenges the free radicals. It also increases the oxygen delivery to tissues, mitochondrial ATP production and alters microvascular tone to increase blood flow and oxygen delivery to liver and other vital organs.

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## WARNING & PRECAUTIONS

- used with caution in patients with asthma, elderly and patients with severe respiratory insufficiency as the irritative effect that NAC produces on the mucosa may cause bronchospasm.
- used with caution in patients with history of peptic ulcer disease, as drug-induced nausea and vomiting may increase the risk of gastrointestinal bleeding in those patients.
- patients need to be monitored for occurrence of anaphylactoid reactions during IV NAC administration.
- IV NAC can also cause a false increase in INR which normalizes once infusion stops and a false-positive result for urine ketones.
- caution should be used in patients receiving nitroglycerin and related medications as NAC strongly potentiates the effect of these agents in whom it may cause hypotension.
- NAC should not be taken simultaneously with charcoal as it may cause a reduction in the absorption of NAC.
- the amount of diluent fluid used in IV NAC needs to be properly titrated in patients with tendency to develop fluid overload (cardiomyopathy or congestive heart failure) to prevent the occurrence of it.

## CLINICAL EFFICACY

In a retrospective study involving 98 patients and a small randomized, placebo-controlled trial involving 50 patients showed that treatment with acetylcysteine was associated with a 21% and 28% reduction in mortality respectively. The largest study (1976-1985) involving 2,023 patients to evaluate the efficacy of NAC was found that those patients treated within 8-10 hours of ingestion had a 6-8% incidence of hepatotoxicity compared to 26-34% in those treated 10-24 hours after ingestion. There were no acetaminophen-related hepatic failure deaths in those treated within 8-10 hours and only one death of a patient treated within 16 hours. The WHO Model List of Essential Medicines and Model Formulary of 2006, The United Kingdom National Health Service guideline and The American College of Emergency Physicians recommend acetylcysteine (NAC) as an antidote for acetaminophen (paracetamol) overdose.

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## ADVERSE EFFECTS

- Immunologic (> 10%): autoimmune disease
- Miscellaneous (>10%): anaphylactoid reaction
- Cardiovascular: flushing, tachycardia, oedema
- Dermatologic: urticaria, rash, pruritus
- Gastrointestinal: vomiting, nausea, diarrhoea
- Respiratory: pharyngitis, rhinorrhoea, rhonchi, throat tightness

## MONITORING PARAMETERS

- 1) Serum acetaminophen level
- 2) AST, ALT and bilirubin levels
- 3) INR and prothrombin time
- 4) Serum creatinine
- 5) BUN
- 6) Serum glucose
- 7) Haemoglobin (Hb) and haematocrit levels
- 8) Electrolytes

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