IV Acetylcysteine (NAC) Protocol for Acetaminophen Poisoning

Overview for Frontline Providers

March & April 2026

Ontario Poison Centre | Centre antipoison de l'Ontario

OPC has a revised IV acetylcysteine (NAC) protocol for acetaminophen poisoning.

*Launch date: **April 1 at 0700 ET**

You have a patient with suspected acetaminophen toxicity.

What next?

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Ontario: 1 (800) 268-9017
Manitoba: 1 (855) 776-4766
Nunavut: 1 (866) 913-7897

Session Overview

We will **briefly** review:

Baseline bloodwork and monitoring frequency

IV NAC dosing under the revised protocol (1- bag)

NAC stopping criteria

Patient Care Resources

Q & A

**Note: we will not review site-specific pump programming or EMR workflows.*

Where can I find Patient Care Resources?

ontariopoisoncentre.ca

manitobapoison.ca

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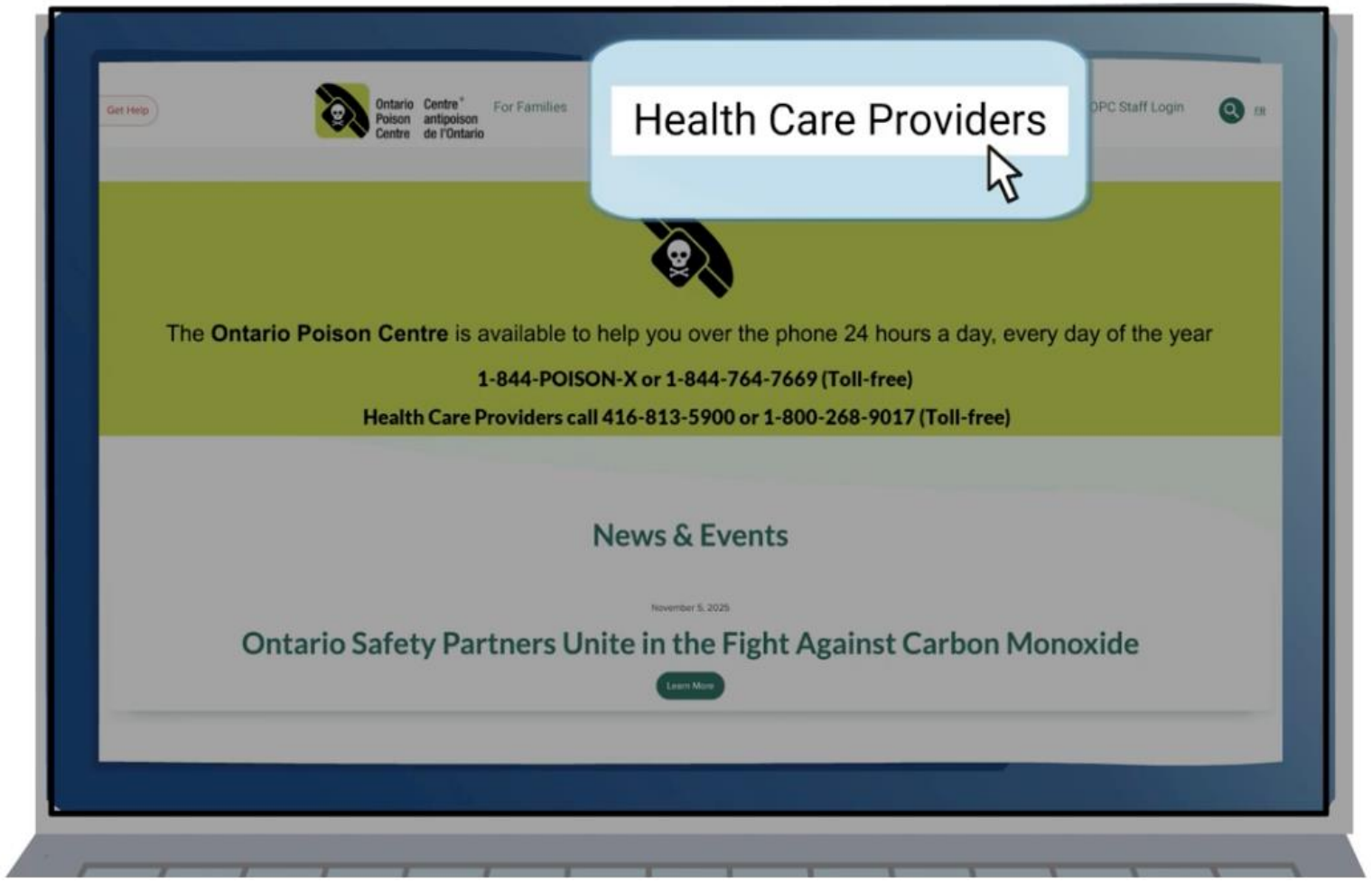
Click on “Health Care Providers”



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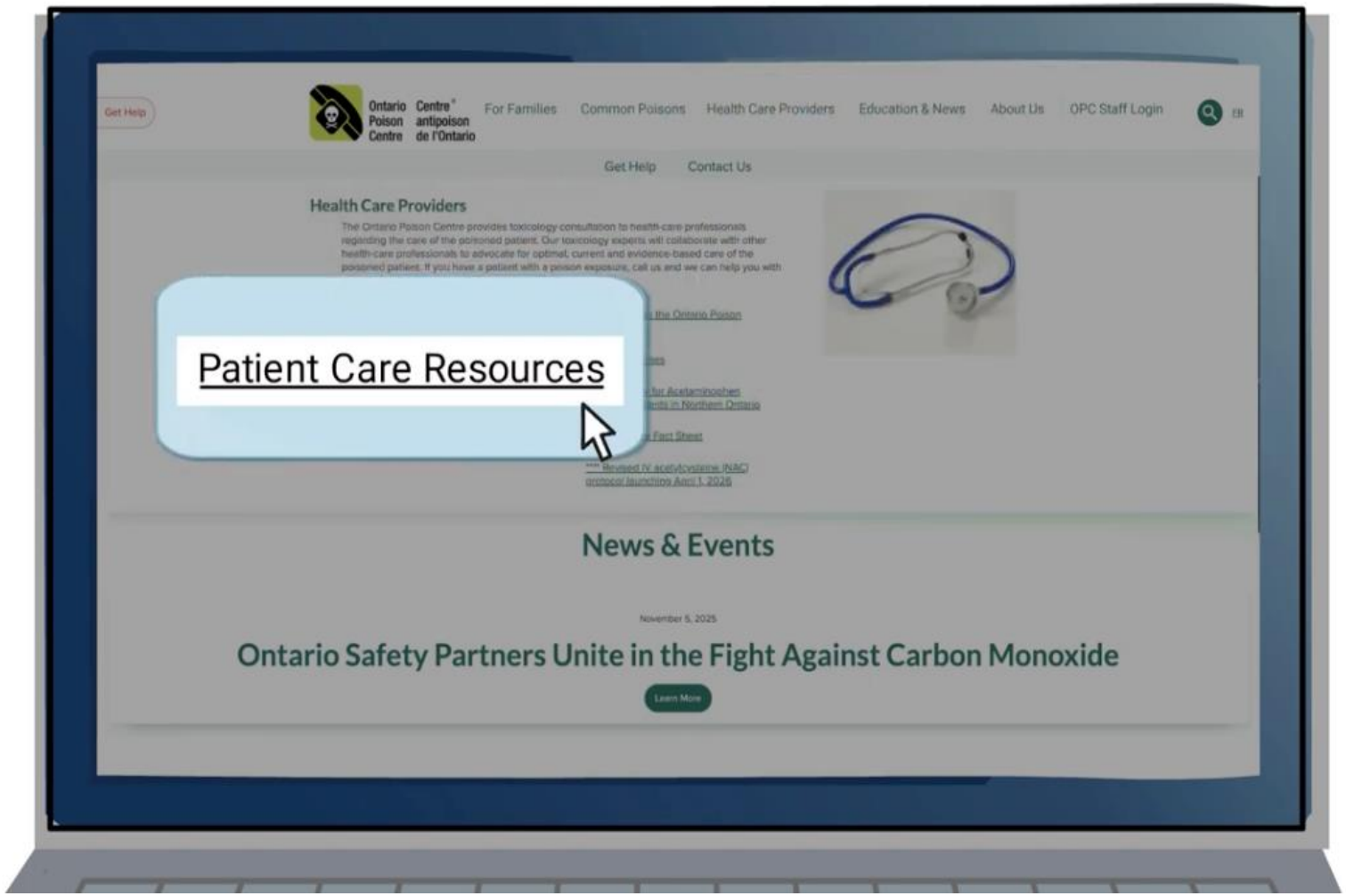
Click on “Patient Care Resources”



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Patient Care Resources

IV Acetylcysteine (NAC)

- Dosing
  - Pre-April 1, 2026 protocol
  - April 1, 2026 protocol (NEW)
- Preparation
  - 3% NAC solution
- Monitoring & Discontinuation
  - Recommended Bloodwork
  - NAC Stopping Criteria
- Adverse Effects
  - NAAR Management (Non-Allergic Anaphylactoid Reaction)
- Other Management Resources
  - Oral Acetylcysteine (NAC)
  - Fomepizole

Ontario & Nunavut

Manitoba

Case: Acute Ingestion

21:00 local time

80 kg

35-year-old female presents to emergency dept

Ingested 30 x 500mg tablets of acetaminophen at 1400 (7 hours ago)

Vitals signs normal, GCS 15, c/o nausea

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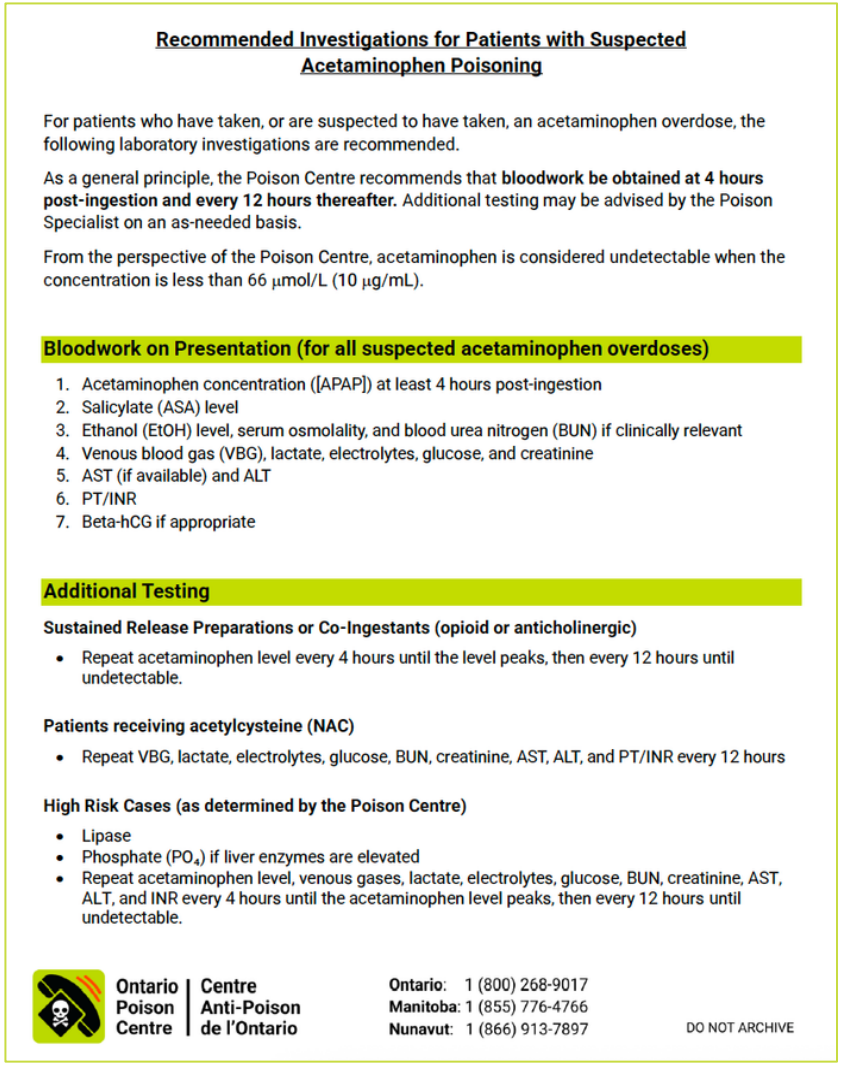
Patient Care Resources

IV Acetylcysteine (NAC)

- Monitoring & Discontinuation
  - Recommended Bloodwork
  - NAC Stopping Criteria



Recommended Investigations for Patients with Suspected Acetaminophen Poisoning

For patients who have taken, or are suspected to have taken, an acetaminophen overdose, the following laboratory investigations are recommended.

As a general principle, the Poison Centre recommends that **bloodwork be obtained at 4 hours post-ingestion and every 12 hours thereafter.** Additional testing may be advised by the Poison Specialist on an as-needed basis.

From the perspective of the Poison Centre, acetaminophen is considered undetectable when the concentration is less than 66 μmol/L (10 μg/mL).

Bloodwork on Presentation (for all suspected acetaminophen overdoses)

1. Acetaminophen concentration ([APAP]) at least 4 hours post-ingestion
2. Salicylate (ASA) level
3. Ethanol (EtOH) level, serum osmolality, and blood urea nitrogen (BUN) if clinically relevant
4. Venous blood gas (VBG), lactate, electrolytes, glucose, and creatinine
5. AST (if available) and ALT
6. PT/INR
7. Beta-hCG if appropriate

Additional Testing

Sustained Release Preparations or Co-Ingestants (opioid or anticholinergic)

- Repeat acetaminophen level every 4 hours until the level peaks, then every 12 hours until undetectable.

Patients receiving acetylcysteine (NAC)

- Repeat VBG, lactate, electrolytes, glucose, BUN, creatinine, AST, ALT, and PT/INR every 12 hours

High Risk Cases (as determined by the Poison Centre)

- Lipase
- Phosphate (PO_4) if liver enzymes are elevated
- Repeat acetaminophen level, venous gases, lactate, electrolytes, glucose, BUN, creatinine, AST, ALT, and INR every 4 hours until the acetaminophen level peaks, then every 12 hours until undetectable.

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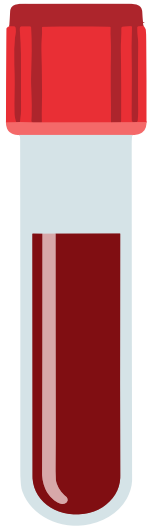
DO NOT ARCHIVE

Bloodwork on Presentation



Acetaminophen (APAP) level **at least 4 hours** post-ingestion

Salicylate (ASA) level

VBG, lactate, electrolytes, glucose, and creatinine

AST (if available) and ALT

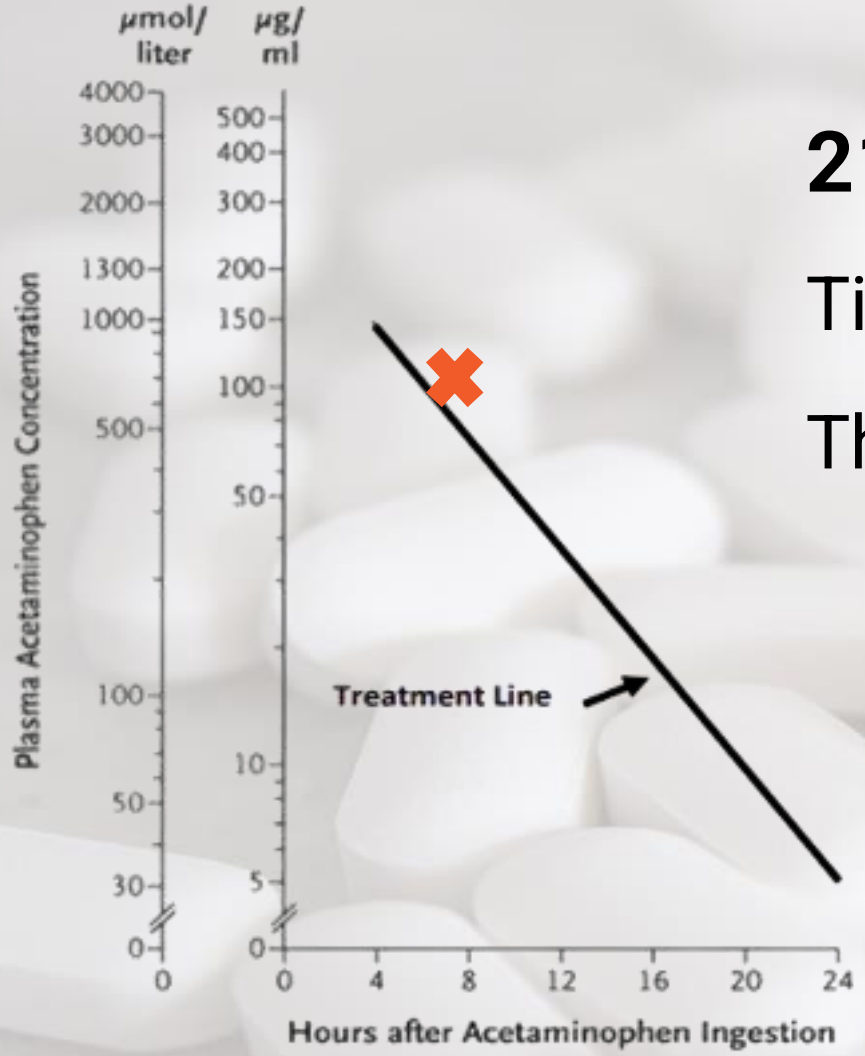
PT/INR

If clinically relevant: ethanol (EtOH) level, serum osmolality, and blood urea nitrogen (BUN)

For patients receiving acetylcysteine (NAC), **repeat bloodwork every 12 hours.**

OPC will advise if additional labs or more frequent monitoring is required.

Case: Acute Ingestion



21:00 APAP: 742 μmol/L (112 mg/L)

Time of ingestion: **14:00** (7 hours ago)

This plots **above** the treatment line.

Patient needs NAC.

*Other baseline labs “normal”

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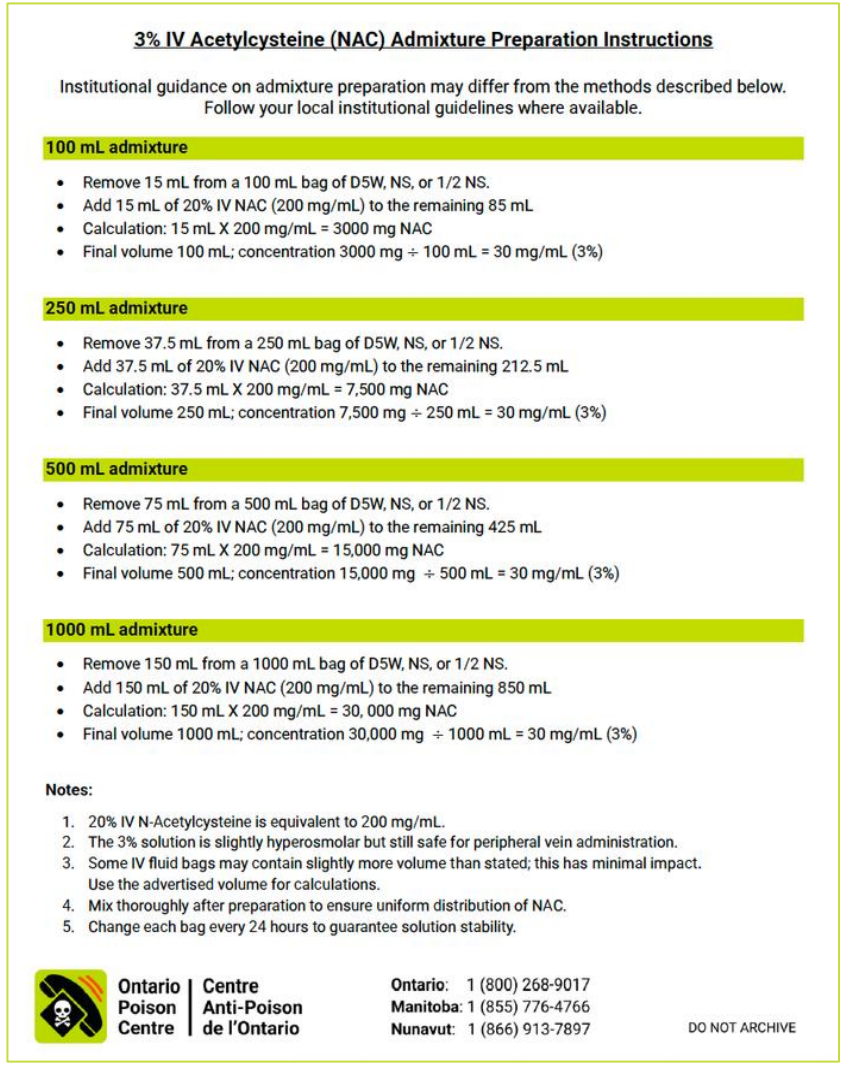
Patient Care Resources

IV Acetylcysteine (NAC)

- Preparation
  - 3% NAC solution



3% IV Acetylcysteine (NAC) Admixture Preparation Instructions

Institutional guidance on admixture preparation may differ from the methods described below. Follow your local institutional guidelines where available.

100 mL admixture

- Remove 15 mL from a 100 mL bag of D5W, NS, or 1/2 NS.
- Add 15 mL of 20% IV NAC (200 mg/mL) to the remaining 85 mL
- Calculation: 15 mL X 200 mg/mL = 3000 mg NAC
- Final volume 100 mL; concentration 3000 mg ÷ 100 mL = 30 mg/mL (3%)

250 mL admixture

- Remove 37.5 mL from a 250 mL bag of D5W, NS, or 1/2 NS.
- Add 37.5 mL of 20% IV NAC (200 mg/mL) to the remaining 212.5 mL
- Calculation: 37.5 mL X 200 mg/mL = 7,500 mg NAC
- Final volume 250 mL; concentration 7,500 mg ÷ 250 mL = 30 mg/mL (3%)

500 mL admixture

- Remove 75 mL from a 500 mL bag of D5W, NS, or 1/2 NS.
- Add 75 mL of 20% IV NAC (200 mg/mL) to the remaining 425 mL
- Calculation: 75 mL X 200 mg/mL = 15,000 mg NAC
- Final volume 500 mL; concentration 15,000 mg ÷ 500 mL = 30 mg/mL (3%)

1000 mL admixture

- Remove 150 mL from a 1000 mL bag of D5W, NS, or 1/2 NS.
- Add 150 mL of 20% IV NAC (200 mg/mL) to the remaining 850 mL
- Calculation: 150 mL X 200 mg/mL = 30, 000 mg NAC
- Final volume 1000 mL; concentration 30,000 mg ÷ 1000 mL = 30 mg/mL (3%)

Notes:

1. 20% IV N-Acetylcysteine is equivalent to 200 mg/mL.
2. The 3% solution is slightly hyperosmolar but still safe for peripheral vein administration.
3. Some IV fluid bags may contain slightly more volume than stated; this has minimal impact. Use the advertised volume for calculations.
4. Mix thoroughly after preparation to ensure uniform distribution of NAC.
5. Change each bag every 24 hours to guarantee solution stability.

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DO NOT ARCHIVE

Institutional guidance on preparing a **3% NAC** solution may differ from our Patient Care Resource.

Follow local institutional guidelines where available.

Multiple diluent options:

D5W, NS, ½ NS

Choice of diluent will be determined by prescriber.

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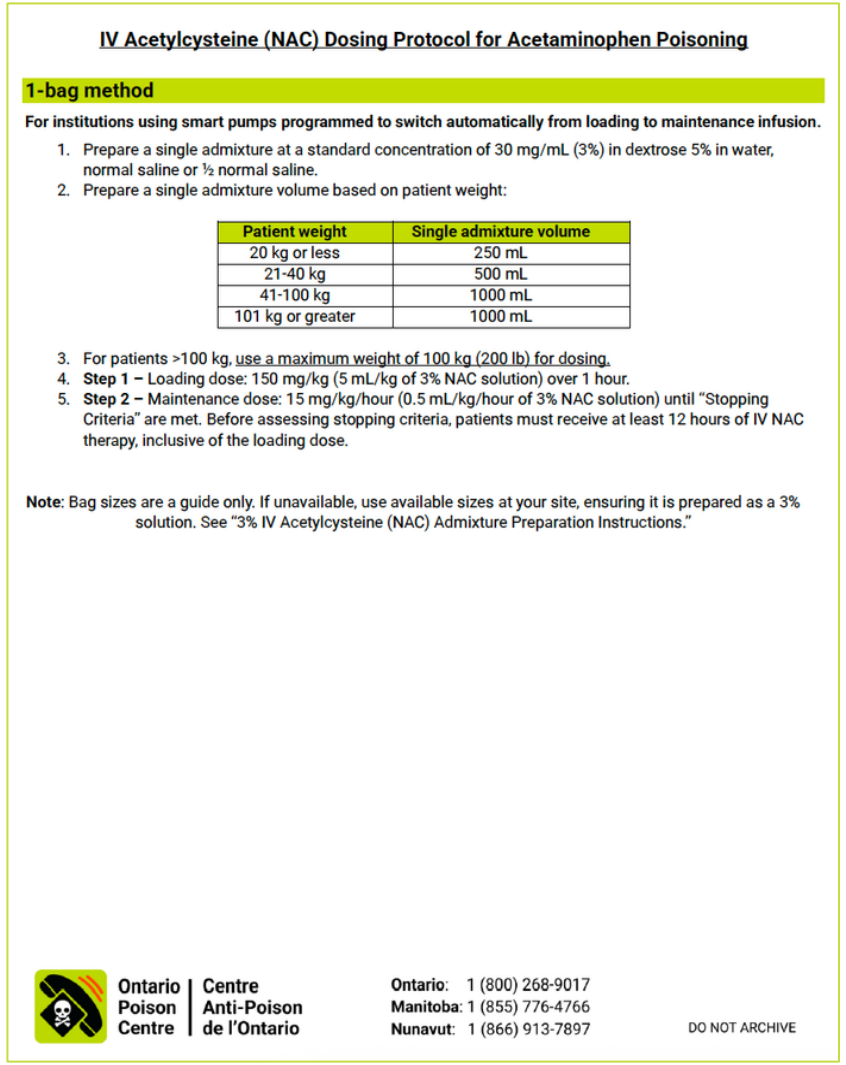
Patient Care Resources

IV Acetylcysteine (NAC)

- Dosing
  - 1-bag method
  - 2-bag method
  - 1 & 2-bag method (combined resource)



IV Acetylcysteine (NAC) Dosing Protocol for Acetaminophen Poisoning

1-bag method

For institutions using smart pumps programmed to switch automatically from loading to maintenance infusion.

1. Prepare a single admixture at a standard concentration of 30 mg/mL (3%) in dextrose 5% in water, normal saline or ½ normal saline.
2. Prepare a single admixture volume based on patient weight:

Patient weight	Single admixture volume
20 kg or less	250 mL
21-40 kg	500 mL
41-100 kg	1000 mL
101 kg or greater	1000 mL

3. For patients >100 kg, use a maximum weight of 100 kg (200 lb) for dosing.
4. **Step 1 –** Loading dose: 150 mg/kg (5 mL/kg of 3% NAC solution) over 1 hour.
5. **Step 2 –** Maintenance dose: 15 mg/kg/hour (0.5 mL/kg/hour of 3% NAC solution) until "Stopping Criteria" are met. Before assessing stopping criteria, patients must receive at least 12 hours of IV NAC therapy, inclusive of the loading dose.

Note: Bag sizes are a guide only. If unavailable, use available sizes at your site, ensuring it is prepared as a 3% solution. See "3% IV Acetylcysteine (NAC) Admixture Preparation Instructions."

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IV NAC Protocol: 2-Step Infusion

⟶ **Loading dose**:
150 mg/kg over 1 hour

⟶ **Maintenance infusion**:
15 mg/kg/hour until stopping criteria are met

No change in dosing if patient is undergoing dialysis or presents with severely elevated [APAP] (i.e. there is **no "high dose"** protocol)

IV NAC Protocol: 2-Step Infusion

⟶ **Loading dose**:

150 mg/kg over 1 hour

***Cap dosing weight at 100 kg**

⟶ **Maintenance infusion**:

15 mg/kg/hour until stopping criteria are met

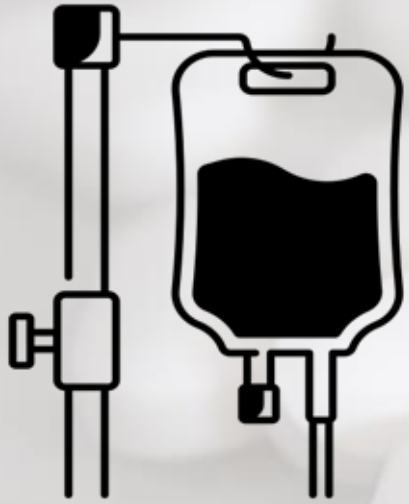
*i.e. Use 100 kg for patients > 100 kg

Maximum loading dose= 15000 mg

Maximum maintenance infusion rate= 1500 mg/h

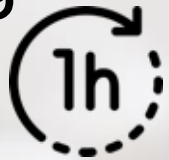
Case: Acute Ingestion

80 kg



1000 mL

IV NAC loading dose: 150 mg/kg

150 x 80 kg = 12000 mg over 

1 hour passes…

Loading dose completed.

Rate change.

IV NAC maintenance infusion: 15 mg/kg/hour

15 x 80 kg = 1200 mg/hour

Case: Acute Ingestion

80 kg

21:30 **IV NAC** 12000 mg over 1 hour

22:30 **IV NAC** 1200 mg/hour

Next labs ordered for **09:30**

APAP **74** µmol/L (**11** mg/L)

AST **106**, ALT 92

VBG, lactate, electrolytes, creatinine, PT, INR

→ *within normal reference range*

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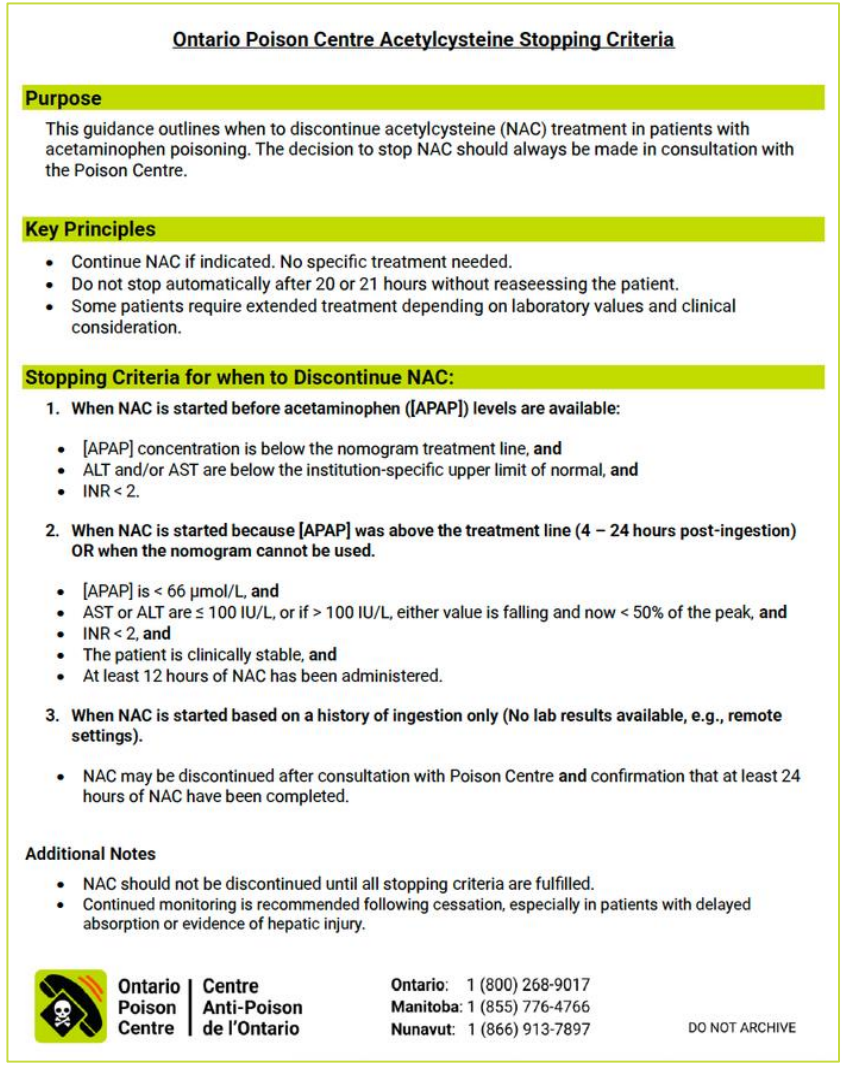
Patient Care Resources

IV Acetylcysteine (NAC)

- Monitoring & Discontinuation
  - Recommended Bloodwork
  - NAC Stopping Criteria



Ontario Poison Centre Acetylcysteine Stopping Criteria

Purpose

This guidance outlines when to discontinue acetylcysteine (NAC) treatment in patients with acetaminophen poisoning. The decision to stop NAC should always be made in consultation with the Poison Centre.

Key Principles

- Continue NAC if indicated. No specific treatment needed.
- Do not stop automatically after 20 or 21 hours without reaseessing the patient.
- Some patients require extended treatment depending on laboratory values and clinical consideration.

Stopping Criteria for when to Discontinue NAC:

1. **When NAC is started before acetaminophen ([APAP]) levels are available:**
   - [APAP] concentration is below the nomogram treatment line, **and**
   - ALT and/or AST are below the institution-specific upper limit of normal, **and**
   - INR < 2.
2. **When NAC is started because [APAP] was above the treatment line (4 – 24 hours post-ingestion) OR when the nomogram cannot be used.**
   - [APAP] is < 66 µmol/L, **and**
   - AST or ALT are ≤ 100 IU/L, or if > 100 IU/L, either value is falling and now < 50% of the peak, **and**
   - INR < 2, **and**
   - The patient is clinically stable, **and**
   - At least 12 hours of NAC has been administered.
3. **When NAC is started based on a history of ingestion only (No lab results available, e.g., remote settings).**
   - NAC may be discontinued after consultation with Poison Centre **and** confirmation that at least 24 hours of NAC have been completed.

Additional Notes

- NAC should not be discontinued until all stopping criteria are fulfilled.
- Continued monitoring is recommended following cessation, especially in patients with delayed absorption or evidence of hepatic injury.

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DO NOT ARCHIVE

NAC Labs & Stopping Criteria

Treat with NAC until:

- ✓ APAP **< 66 µmol/L** (< 10 mg/L)
- ✓ **AND** AST or ALT **≤ 100 U/L** (or falling, and < 50% of peak)
- ✓ **AND** INR **< 2**
- ✓ **AND** the patient is **clinically stable**
- ✓ **AND at least 12 hours of NAC has been given**

Including loading dose

Case: Acute Ingestion

80 kg

09:30 labs:

APAP **74** µmol/L (**11** mg/L)

AST **106**, ALT 92

VBG, lactate, electrolytes, creatinine, PT, INR

→ *within normal reference range*

Stopping Criteria **NOT** met

Continue **IV NAC** 1200 mg/hour

Repeat bloodwork in 12 hours

Case: Acute Ingestion

80 kg

21:30 labs:

APAP < 66 µmol/L (< 10 mg/L)

AST 86, ALT 88

VBG, lactate, electrolytes, creatinine, PT, INR

→ *within normal reference range*

✓ Stopping Criteria **MET**

IV NAC discontinued

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Patient Care Resources

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  - Fomepizole

Ontario & Nunavut

Manitoba

Every case has nuance.

Clinical judgment matters.

The Ontario Poison Centre is here 24/7 to support you.

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Looking for More Detail?

Access webinar recording

for a more in-depth overview of acetaminophen toxicity and management.

ontariopoisoncentre.ca
manitobapoison.ca

SLIDE DECK

Q & A

Contact for follow-up questions.

katie.orr@sickkids.ca

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