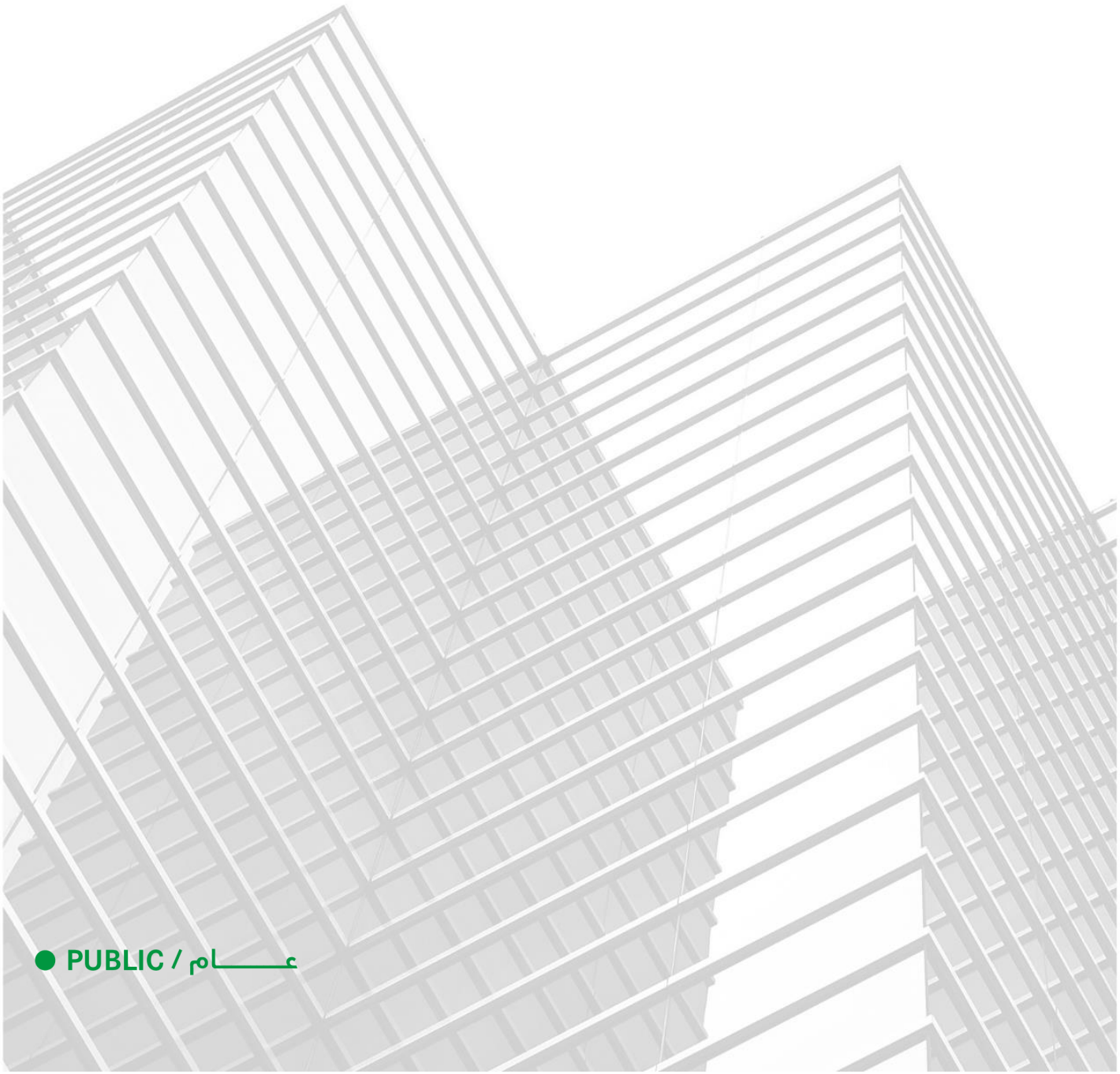
دائـــرة الـصـحـة
DEPARTMENT OF HEALTH

GUIDELINES FOR THE MANAGEMENT OF PARACETAMOL TOXICITY



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1. Guideline Purpose and Brief

These guidelines seek to optimize and standardize the diagnosis and management of paracetamol (APAP) toxicity among children and adults in Abu Dhabi. By empowering all healthcare providers with the latest evidence, these guidelines aim to:

- Reduce morbidity and mortality
- Improve the quality of care
- Identify high-risk patients
- Avoid unnecessary interventions
- Reduce healthcare expenditures
- Raise awareness

These guidelines apply to all cases of confirmed or suspected APAP overdose or toxicity across all age groups in the Emirate of Abu Dhabi. However, final clinical judgment remains with the treating physicians, who may need to adapt management based on individual patient factors.

2. Definitions and Abbreviations

No.	Term / Abbreviation	Definition
2.1	AC	Activated charcoal
2.2	AIDS	Acquired Immunodeficiency Syndrome
2.3	ALT	Alanine transaminase
2.4	AST	Aspartate transaminase
2.5	APAP	N-acetyl-para-aminophenol
2.6	DoH	Department of Health
2.7	EXTRIP	Extracorporeal Treatments in Poisoning workgroup
2.8	INR	International Normalized Ratio
2.9	INH	Isoniazid
2.10	IV	Intravenous
2.11	NAAR	Non allergic anaphylactoid reaction
2.12	NAC	N-acetylcysteine
2.13	NAPQI	N-acetyl-p-benzoquinone imine
2.14	PDIS	Poison & Drug Information Service
2.15	TAT	Turnaround time

3. Recommendations for the diagnosis and management of APAP toxicity

3.1. Criteria to consult Poison & Drug Information Service (PDIS)

3.1.1. PDIS should be contacted for all patients presenting with a suspected or confirmed paracetamol overdose. Call 800-424, 24/7**.**

3.1.2. A particular emphasis should be placed on patients presenting with the features below to help develop optimal management plans:[1]

3.1.2.1. Large overdoses of immediate or modified-release paracetamol ≥ 30 g or ≥ 500 mg/kg

3.1.2.2. Triple the nomogram line paracetamol concentration

3.1.2.3. Hepatotoxicity (ALT > 1000 IU/L)

3.1.2.4. Overdoses in neonates and pregnant women

3.1.2.5. Intravenous paracetamol overdoses

3.2. Risk assessment of potential toxic paracetamol dose that may be associated with acute liver injury

3.2.1. **Acute single ingestion:** Defined as any intentional overdose of paracetamol, including multiple or staggered ingestions over more than 2 hours: Ingestion of ≥ 10 g or ≥ 200 mg/kg (whichever is less).

3.2.2. **Repeated supratherapeutic ingestion:**[1] Defined as an ingestion of excessive amounts taken for therapeutic intent. The following doses serve as guidelines for asymptomatic patients at risk for acute liver injury: ≥ 10 g or ≥ 200 mg/kg (whichever is less) over 24 hours or ≥ 12 g or ≥ 300 mg/kg (whichever is less) over 48 hours or ≥ daily therapeutic dose per day for more than 48 hours in patients with symptoms such as abdominal pain, nausea, or vomiting*. All other symptomatic patients should be assessed with alanine aminotransferase (ALT) and paracetamol levels.

Period of Ingestion	Dose
24 hours	≥ 10g or ≥ 200mg/kg
48 hours	≥ 12g or ≥ 300mg/kg
> 48 hours	≥ Therapeutic dose & symptomatic*

* The therapeutic daily dose of paracetamol is 60 mg/kg over 24 hours and up to a maximum of 4 g/day in an adult patient, and 60mg/kg/day in pediatric patient.

3.3. Two-bag N-acetylcysteine regimen[2]

3.3.1. N-acetylcysteine (NAC) is the treatment of choice for paracetamol overdose. Intravenous NAC has replaced oral NAC in the DOH Standard for Antidote Stocking in Healthcare Facilities as the preferred formulation due to better tolerability,

shorter treatment duration, guaranteed delivery, easier administration in compromised patients, and more predictable pharmacokinetics. Although the three-bag intravenous regimen remained the standard of care for years, it has been associated with dosing errors and delays in therapy. Nonallergic anaphylactoid reactions (NAAR) have also been reported due to large amounts of NAC being infused during the first hour.

3.3.2. Recent evidence suggests that a two-bag regimen is safe and effective in the treatment of paracetamol poisoning, and it has been used as the first-line recommendation in Australia, New Zealand, Denmark, and Sweden.[2] As a simpler regimen, it is associated with fewer adverse reactions, decreased resource utilization, and fewer dosing errors. The two-bag regimen is also associated with a lower rate of NAAR.

3.3.3. Two-bag regimen intravenous administration recommendations:

3.3.3.1. **Initial infusion:** 200 mg/kg (max. 22 g) in dextrose 5% or sodium chloride 0.9% 500 mL given over 4 hours (peds: 7 mL/kg up to 500 mL of either solution).

3.3.3.2. **Second infusion:** 100 mg/kg (max. 11 g) in dextrose 5% or sodium chloride 0.9% 1000 mL to be given over 16 hours (peds: 14 mL/kg up to 1000 mL of either solution).

3.3.4. If ongoing NAC infusion is required, it should be continued at the same rate as the second infusion (100 mg/kg over 16 hours).

3.3.5. Patients with massive ingestions or placed on hemodialysis may require higher doses of NAC (200 mg/kg over 16 hours). This should only be started after consultation with the PDIS.

3.4. Guidelines for immediate-release paracetamol ingestion

3.4.1. The Rumack-Matthew Nomogram can only be used for therapy decision-making in acute ingestions of immediate-release paracetamol with a **known** time of ingestion [Appendix I, II].

3.4.2. **For patients presenting less than 2 hours from the time of ingestion:**[1]

3.4.2.1. 0.5-1 g/kg activated charcoal (AC) can be given to stable and alert patients presenting within 2 hours of the toxic solid ingestion (may extend to 4 hours following a massive immediate-release ingestion of > 30 g or ≥ 500 mg/kg).

3.4.2.2. AC contraindications include altered mental status, unresponsiveness, vomiting, seizures, suspected ileus (absent bowel sounds).

3.4.2.3. Pediatric: Flavoring such as chocolate syrup may be added to make AC more palatable for children.

3.4.2.4. Induction of emesis and gastric lavage are contraindicated.

3.4.2.5. Paracetamol level should **only be taken 4 hours post-ingestion**; the level should then be plotted on the Rumack-Matthew Nomogram to determine the need for NAC therapy.

3.4.2.6. For pediatric patients < 6 years old with liquid paracetamol ingestion refer to recommendation 3.9.

3.4.3. **For patients presenting 2-8 hours from the time of ingestion and levels of paracetamol will return within 8 hours of ingestion:**

3.4.3.1. Serum paracetamol concentration and ALT should be collected within 4-8 hours of ingestion in cases where the time of ingestion is accurately established, and the level should be plotted on the Rumack-Matthew Nomogram.

3.4.3.2. For levels below the nomogram line of toxicity, no further medical interventions are required. For levels on or above the line, NAC therapy, as detailed in recommendation 3.1, must be initiated as soon as possible (CAVEAT: For levels double or more the toxic nomogram line, consider high-dose NAC).

3.4.4. **For patients presenting 8-24 hours from the time of ingestion, or levels of paracetamol will not return within 8 hours of ingestion:** [1,3]

3.4.4.1. Start NAC infusion immediately (per recommendation 3.3) and collect serum paracetamol and ALT levels.

3.4.4.2. If paracetamol levels are below the nomogram line and ALT ≤ 50 U/L, no further treatment is required, and NAC infusion should be discontinued.

3.4.4.3. If paracetamol levels are above the nomogram line or ALT > 50 U/L, continue NAC infusion (refer to recommendation 3.3), unless the paracetamol level is double the nomogram line.

3.4.5. **For patients presenting > 24 hours from the time of ingestion:** [1,3]

3.4.5.1. Start NAC infusion immediately (per recommendation 3.3) and collect serum paracetamol and ALT levels.

3.4.5.2. If paracetamol concentration is < 10 mg/L and ALT ≤ 50 U/L, no further treatment is required, and NAC infusion should be discontinued.

3.4.5.3. If paracetamol concentration is > 10 mg/L or ALT > 50 U/L, complete the standard infusion regimen as per recommendation 3.3.

3.4.6. **For patients with unknown time of ingestion:** [1,3]

3.4.6.1. Start NAC immediately if the time of ingestion is unknown and the dose is ≥ 10 g or ≥ 200 mg/kg (whichever is less) or unknown.

3.4.6.2. Investigate serum paracetamol concentration and ALT levels.

3.4.6.2.1. If paracetamol concentration is < 10 mg/L and ALT < 50 U/L, no further treatment is required, and NAC infusion should be discontinued.

3.4.6.2.2. If paracetamol concetration is > 10 mg/L or ALT > 50 U/L, complete the full course of NAC.

3.4.7. Regardless of ingestion time, all patients with an initial paracetamol concentration more than double the nomogram line should receive high-dose acetylcysteine. The second bag dose should be doubled to 200 mg/kg IV over 16 hours.

3.4.8. Paracetamol and ALT levels should be repeated 2 hours before finishing the treatment regimen, and the infusion should be continued or discontinued based on criteria for cessation as per recommendation 3.11 (NOTE: Gaps in therapy must be avoided).

3.4.9. Paracetamol serum concentration is a Tier 1 STAT assay that must be available in all hospitals admitting cases with acute poisoning, with a required **turnaround time (TAT) of 2 hours or less** according to DOH Standard for Clinical Toxicology Testing in Clinical Laboratories.

3.4.10. Suicidal patients require a full work-up, including serum paracetamol, ALT, salicylate levels, and ethanol levels in cases of altered mental status. Psychiatric consultation should be conducted prior to medical clearance.

3.5. Guidelines for multiple or staggered immediate-release paracetamol ingestion

3.5.1. Definition: Multiple or staggered paracetamol ingestions over more than 2 hours for deliberate self-harm.

3.5.2. Staggered ingestion treatment should follow the guidelines for acute immediate-release paracetamol ingestion using the earliest time of ingestion for the Rumack-Matthew Nomogram (i.e., where time of ingestion is uncertain, use a time-anchoring strategy). If the paracetamol level is above the nomogram line, initiate NAC therapy.

3.5.3. Commence NAC therapy (per recommendation 3.3) if it is more than 8 hours since the first dose of paracetamol or concentration cannot be obtained within 8 hours.

3.5.4. If the paracetamol concentration was measured within 2 hours of the last ingested paracetamol dose, it should be repeated after 2 hours to account for any ongoing absorption. NAC therapy should be started (or continued) if either concentration is above the treatment line.

3.6. Repeated supratherapeutic ingestion[1,3]

3.6.1. Refer to recommendation 3.2 for details on supratherapeutic ingestion.

3.6.2. High-risk factors for paracetamol toxicity following supratherapeutic ingestions include chronic heavy ethanol use, chronic ingestion of INH, febrile illnesses in

infants and young children, malnutrition, catabolic states (e.g., post-surgical), AIDS, and anorexia. Regardless, the mainstay of management is to identify the two conditions that warrant NAC therapy: Detectable paracetamol yet to be metabolized and potentially serious hepatic injury as indicated by ALT and/or other clinical features.

3.6.3. Patients meeting the criteria for supratherapeutic ingestions must have paracetamol and ALT levels done [Appendix III].

3.6.4. If the paracetamol level is > 20 mg/L (132 µmol/L) or ALT > 50 U/L, patients should get treatment with NAC. Repeat paracetamol and ALT levels 8 hours after the first levels.

3.6.5. If ALT is < 50 U/L or static and paracetamol < 10 mg/L (66 µmol/L), no further treatment is required.

3.6.6. If the paracetamol level is > 10 mg/ L and ALT > 50 U/L at 8 hours after the first level, NAC should be continued, and ALT must be rechecked every 12 hours.

3.6.7. NAC can be stopped when all the criteria for cessation are met (per recommendation 3.11).

3.6.8. Small fluctuations in ALT (± 20 U/l or ± 10 %) are common and do not indicate the need for ongoing NAC therapy.

3.6.9. ALT > 1000 U/L should get a full 20-hour course of NAC and the PDIS should be notified.

3.7. Modified-release paracetamol ingestions

3.7.1. Modified-release paracetamol constitutes 69% modified release and 31% immediate release in a 665 mg tablet form.

3.7.2. All modified-release paracetamol overdose ≥ 10 g or ≥ 200 mg/kg (whichever is less) should be given activated charcoal up to 4 hours after ingestion [Appendix IV].

3.7.3. For massive overdose ≥ 30 g or ≥ 500 mg/kg, activated charcoal may be beneficial beyond 4 hours due to delayed absorption which can occur up to 24 hours.

3.7.4. Paracetamol concentrations are used to guide the dose of NAC which may be increased in case of massive ingestions (refer to 3.7.7), and to determine the need for further decontamination if the levels remain unchanged or high (indicating ongoing gastrointestinal absorption).

3.7.5. Patients ingesting toxic doses of modified-release paracetamol and presenting ≥ 4 hours post-ingestion require immediate initiation of NAC therapy. Two sets of paracetamol levels should be taken 4 hours apart to guide further decontamination and therapy.

3.7.5.1. If either paracetamol concentration is above the nomogram line, the standard NAC infusion should be completed per recommendation 3.3.

3.7.5.2. If the levels are double the nomogram line, the second bag infusion should be doubled to 200 mg/kg over 16 hours.

3.7.6. ALT and paracetamol concentrations should be taken before stopping the NAC. Therapy should be discontinued if the patient meets all the criteria per recommendation 3.11.

3.7.7. For massive ingestions, the second bag infusion can be doubled to 200 mg/kg over 16 hours. Two sets of paracetamol concentrations should be taken 4 hours apart to assess for further decontamination and therapy. ALT and paracetamol concentrations should be taken before stopping NAC. Therapy should be stopped if the patient meets all the criteria per recommendation 3.11.

3.7.8. Patients ingesting < 10 g and < 200 mg/kg should have two serum paracetamol concentrations taken, one 4 hours after ingestion and another 2-4 hours after the first. If either is above the nomogram line, NAC should be started.

3.7.9. Commence higher doses of NAC if paracetamol levels remain at 100 mg/L or more (> 660 µmol/L).

3.8. Co-ingestion of paracetamol and anticholinergic or opioid medications

3.8.1. Various combination drugs containing paracetamol, and anticholinergic or opioid medications are available on the market. When such combinations are ingested, delayed or prolonged absorption of paracetamol is a concern.

3.8.2. If the paracetamol level at 4-24 hours is ≤ 10 mg/L, an additional paracetamol level or NAC therapy is unnecessary. For any concentration above the toxic nomogram line, NAC should be started.

3.8.3. If the patient presents with anticholinergic or opioid effects and paracetamol levels are > 10 mg/L but lower than the toxic nomogram line, another level should be repeated 2-4 hours after the first level and NAC should be started as per the same recommendation as immediate release ingestions, if paracetamol level is plotted at/above the nomogram line.

3.9. Pediatric liquid paracetamol ingestion[1]

3.9.1. For children under the age of 6 years with suspected liquid paracetamol overdose of more than 200 mg/kg, a paracetamol level should be checked at least 2 hours post-ingestion.

3.9.1.1. For levels at 2-4 hours that are below 150 mg/L (1000 µmol/L), NAC is not required.

3.9.1.2. If the concentration at 2 hours is greater than 150 mg/L (1000 µmol/L), the level should be repeated at 4 hours post-ingestion and NAC should be administered if that level is ≥ 150 mg/L (1000 µmol/L).

3.9.2. A 2-hour paracetamol level should only be drawn in healthy pediatric patients < 6 years of age with isolated liquid paracetamol overdose. All other cases should have a 4-hour level.

3.9.3. For pediatric patients presenting after 4 hours of ingestion or aged > 6 years, the adult protocol must be followed.

3.10. Criteria for continuation of NAC infusion

3.10.1. Acetylcysteine should be continued at a rate of at least 100 mg/kg over 16 hours until criteria for discontinuing NAC have been achieved.

3.10.2. Higher infusion rates might be necessary for massive ingestions, particularly if the paracetamol concentration at the end of the first bag of acetylcysteine is 100 mg/L or higher (660 µmol/L). This should be decided in consultation with the PDIS.

3.11. Criteria for cessation of NAC infusion

3.11.1. NAC can be stopped in patients who have received the infusion for more than 20 hours if ALL the following criteria have been met:

3.11.1.1. Normal or down-trending ALT or AST from peak levels (25-50%)

3.11.1.2. INR < 2

3.11.1.3. Patient clinically stable

3.11.1.4. Paracetamol concentration < 10 mg/L

3.12. Indication for hemodialysis[4]

3.12.1. Enhanced elimination with hemodialysis can be done in certain cases that fit the criteria listed by the EXTRIP workgroup. It is encouraged to consult the PDIS before initiating hemodialysis.

3.12.2. Recommendations of the EXTRIP workgroup can be summarized as follows:

3.12.2.1. Hemodialysis is not indicated in most paracetamol overdose cases unless certain conditions are established. It is only suggested in cases of severe paracetamol poisoning.

3.12.2.2. Hemodialysis should be considered when NAC is unavailable or serious concerns regarding allergy to NAC exist.

3.12.2.3. Hemodialysis is suggested in any of the following circumstances:

3.12.2.3.1. If NAC is NOT administered and the paracetamol level is more than 1000 mg/L

3.12.2.3.2. If NAC is NOT administered and the patient presents with altered mental status, metabolic acidosis, elevated lactate, and the paracetamol level is more than 700 mg/L

3.12.2.3.3. If NAC is administered and the patient presents with altered mental status, metabolic acidosis, elevated lactate, and the paracetamol level is more than 900 mg/L

3.12.2.4. The decision to cease hemodialysis should be based on the patient's clinical improvement (e.g., resolution of acidosis and improvement in mental status).

3.12.2.5. Intermittent hemodialysis is preferred in cases requiring extracorporeal treatment, while intermittent hemoperfusion or continuous renal replacement therapy are valid alternatives if intermittent hemodialysis is unavailable. In neonates, exchange transfusion should be considered as an alternative.

3.12.2.6. NAC therapy should be continued during hemodialysis at a rate of 200 mg/kg for the second bag.

3.13. Use of fomepizole in paracetamol poisoning[5]

3.13.1. Recent scientific evidence has emerged on fomepizole (4-methylpyrazole) in the treatment of massive paracetamol poisoning.

3.13.2. Fomepizole, an alcohol dehydrogenase inhibitor, is traditionally used as the preferred antidote for toxic alcohol poisonings (e.g., methanol, ethylene glycol). However, it is also a potent inhibitor of CYP2E1, the enzyme responsible for converting paracetamol into its hepatotoxic metabolite N-acetyl-p-benzoquinone imine (NAPQI). By inhibiting the formation of NAPQI, fomepizole prevents necrosis in paracetamol-poisoned hepatocytes. There is also evidence that contrary to NAC, fomepizole can also support hepatocyte regeneration in the recovery phase and prevent acute kidney injury.

3.13.3. Clinicians are encouraged to consult the PDIS and medical toxicologist on-call for cases of massive ingestion to discuss the use of fomepizole, especially when hemodialysis is inaccessible.

3.14. Criteria for ICU admission

3.14.1. Patients with fulminant liver failure should be managed in an intensive care unit (ICU) and may require referral to liver transplant unit (as per recommendation 3.15).

3.14.2. Other criteria for ICU admission include massive ingestions (> 30 g or ≥ 500 mg/kg), metabolic acidosis, coagulopathy, hepatic encephalopathy, hypoglycemia and the need for intensive supportive care.

3.15. Criteria for referral to liver transplant unit[6]

3.15.1. Patients presenting with paracetamol poisoning are at greatest risk for severe liver failure when there is a delay in NAC administration, in patients with staggered

overdoses, preceding alcohol and anticonvulsant usage, with a background of chronic liver disease, or with severe cachexia or malnutrition. These clinical features should be considered when anticipating and planning for transferring patients to a liver transplant center.

3.15.2. Risk assessment and referral to a liver transplant unit following paracetamol toxicity should be made with the ICU or inpatient teams.

3.15.3. The decision for liver transplant should be made by the liver transplant facility while considering the modified King's College criteria as detailed below:

3.15.3.1. Arterial pH < 7.3

3.15.3.2. INR > 6.5 (PT > 100 sec)

3.15.3.3. Creatinine > 300 µmol/L

3.15.3.4. Grade III or IV hepatic encephalopathy

3.15.4. Other predictors of poor prognosis without a transplant:

3.15.4.1. Lactate > 3.5 mmol/L after fluid resuscitation (< 4 hours) OR lactate > 3 mmol/L after full fluid resuscitation (12 hours)

3.15.4.2. Phosphate level > 3.75 mg/dL (1-2 mmol/L) at 48-96 hours

3.16. Criteria for management of acute immediate-release paracetamol ingestion in remote facilities with no access to 24-hour pathology services[1]

3.16.1. Patients can be managed in remote facilities without access to 24-hour pathology services, provided NAC is available and the patient is not at high risk for liver failure.

3.16.2. For patients presenting with ingestion of < 10 g and < 200 mg/kg:

3.16.2.1. Asymptomatic patients can be discharged with advice to return in case any GI symptoms develop.

3.16.2.2. All symptomatic patients should be commenced on NAC and transferred to a facility with available laboratory services.

3.16.3. For patients presenting with ≥ 10 g or ≥ 200 mg/kg (whichever is less) but < 30 g ingested:

3.16.3.1. Administer activated charcoal if the ingestion occurred < 2 hours earlier.

3.16.3.2. Commence NAC:

3.16.3.2.1. If acetylcysteine started > 8 hours after ingestion, transfer the patient to a facility with laboratory services.

3.16.3.2.2. If acetylcysteine started < 8 hours after ingestion, complete 20 hours of infusion, and assess for nausea, vomiting, and abdominal pain. If the patient is asymptomatic following 20 hours of infusion, proceed to

discharge home and advise to return in case of recurring symptoms. If the patient is symptomatic, continue acetylcysteine and transfer to a hospital with pathology service.

3.16.4. For patients presenting with ≥ 30 g or ≥ 500 mg/kg (whichever is less) ingested:

3.16.4.1. Offer activated charcoal if ingestion occurred < 4 hours earlier.

3.16.4.2. Commence NAC and transfer to a hospital with pathology service.

3.17. Criteria for treatment of intravenous paracetamol overdose[3,7,8]

3.17.1. Diagnosis of intravenous paracetamol overdose should be based on the dose administered rather than the paracetamol level, and clinicians should not wait for paracetamol concentration levels before starting treatment in case it is needed.

3.17.2. The use of the Rumack-Matthew nomogram has not been validated and is not recommended in cases of intravenous overdose. If the IV dose administered is not known, the clinician should contact PDIS and order a paracetamol level as soon as possible.

3.17.3. Patients who were exposed to IV paracetamol overdose should be treated with NAC if they received a single dose ≥ 150 mg/kg, except children younger than 6 years, who should be treated with NAC if they received a single dose ≥ 90 mg/kg or a cumulative dose ≥ 150 mg/kg over 24 hours.[3]

3.17.4. In patients who weigh > 110 kg, the toxic dose should be calculated from a maximum weight of 110 kg.[3]

3.18. Criteria for management of nonallergic anaphylactoid reactions to NAC[9]

3.18.1. Nonallergic anaphylactoid reactions (NAAR) to NAC are well recognized in paracetamol overdose treatment. They are not thought to be true immunologic (allergic) responses but rather direct dose-dependent effects on histamine release, typically occurring within the first two hours of infusion. The two-bag NAC regimen is associated with a lower rate of NAAR.

3.18.2. These reactions are rarely life-threatening and can be successfully and easily treated with antihistamine. They should not preclude NAC administration when clinically indicated as benefits of NAC in treating paracetamol overdose usually outweigh the risks of these reactions.

3.18.3. Nevertheless, patients receiving IV NAC warrant close monitoring, and all essential medications and equipment necessary to manage anaphylaxis should be readily available when NAC is initially administered.

3.18.4. Effects range from mild flushing to urticaria, angioedema, or bronchospasm. Hypotension may occasionally occur. Asthmatic patients may be at higher risk of NAAR.

3.18.5. A history of previous anaphylactoid reactions to NAC is not a contraindication to its use. If there is concern of recurrence of the reaction the patient may be pre-treated with an antihistamine 15 minutes before commencement of the infusion.

3.18.6. Dermal Flushing

3.18.6.1. Halve the NAC infusion rate and, if there is no improvement, administer an antihistamine such as loratadine or cetirizine.

3.18.6.2. Once the reaction settles the NAC infusion can be raised to its former rate.

3.18.7. Urticaria

3.18.7.1. Halve the NAC infusion rate and administer an antihistamine such as loratadine or cetirizine.

3.18.7.2. Stop NAC infusion if there is no rapid relief. Once the reaction settles NAC infusion can be recommenced at one quarter its previous rate and titrated to its former level.

3.18.8. Severe Anaphylactoid Reaction

3.18.8.1. Stop NAC infusion and administer an antihistamine.

3.18.8.2. Treat other symptoms (e.g., bronchospasm, hypotension) according to the standard protocols.

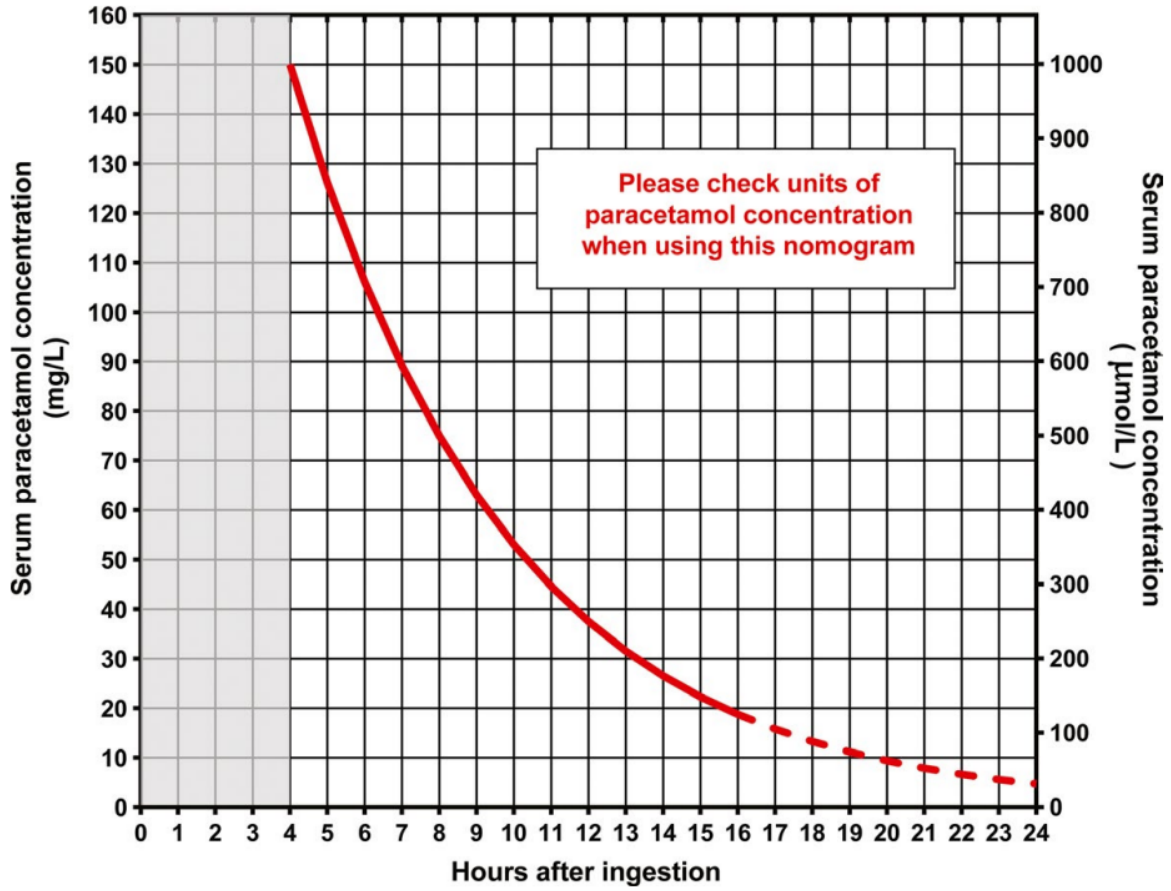
3.18.8.3. After the patient is asymptomatic for one hour, recommence NAC infusion at one quarter the previous rate and titrate slowly to its former level. Repeat reactions, after adequate treatment, are unlikely on recommencement of NAC infusion.

4. Relevant References Documents

No.	Reference Date	Reference Name	Relation Explanation / Coding / Publication Links
1	March 2020	Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand	Chiew, A. L., Reith, D., Pomerleau, A., et al. (2020). Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand. Medical Journal of Australia, 212(4), 175-183.
2	2023	Is Two Better Than Three? A Systematic Review of Two-bag Intravenous N-acetylcysteine Regimens for Acetaminophen Poisoning.	Cole, J. B., Oakland, C. L., Lee, S. C., et al. (2023). Is two better than three? A systematic review of two-bag intravenous N-acetylcysteine regimens for acetaminophen poisoning. Western Journal of Emergency Medicine, 24(6), 1131–1145.
3	2023	Management of Acetaminophen Poisoning in the US and Canada: A Consensus Statement.	Dart, R. C., Mullins, M. E., Matoushek, T., et al. (2023). Management of acetaminophen poisoning in the US and Canada: A consensus statement. JAMA Network Open, 6(8), e2327739.
4	2014	Extracorporeal treatment for acetaminophen poisoning: recommendations from the EXTRIP workgroup	Gosselin S, Juurlink DN, Kielstein JT, et al (2014). Extracorporeal treatment for acetaminophen poisoning: recommendations from the EXTRIP workgroup. Clin Tox. 2014;52(8):856–867.
5	2023	Fomepizole should be used more liberally in paracetamol overdose.	Filip, A. B., & Mullins, M. E. (2023). Fomepizole should be used more liberally in paracetamol overdose. British Journal of Clinical Pharmacology, 89(2), 594–598.
6	1999	Indications for referral and assessment in adult liver transplantation: a clinical guideline	Devlin J, O'Grady J. (1999). Indications for referral and assessment in adult liver transplantation: a clinical guideline. Gut. 1999; 45(6):VI1–VI22.
7	2019	Goldfrank's Toxicologic Emergencies	Nelson, L. S., Howland, M., et al. (2019). Goldfrank's toxicologic emergencies (11th ed.). McGraw-Hill Education.
8	2022	Poisoning & Drug Overdose	Olson, K. R., Smollin, C. G., et al. (2022). Poisoning & drug overdose (8th ed.). McGraw-Hill Education.
9	1998	Management of anaphylactoid reactions to intravenous N-acetylcysteine	Bailey, B., & McGuigan, M. A. (1998). Management of anaphylactoid reactions to intravenous N-acetylcysteine. Annals of Emergency Medicine, 31(6), 710-715.
10	1989	King’s College criteria (KCC) for liver transplantation	O'Grady, J. G., Alexander, G. J., Hayllar, K. M., et al. (1989). Early indicators of prognosis in fulminant hepatic failure. Gastroenterology, 97, 439-445.
11	2023	DOH Standard for Antidote Stocking in Healthcare Facilities	https://www.doh.gov.ae/-/media/28AED73AD38A4D7A97282F5DCB690D0F.ashx
12	2024	DOH Standard for Clinical Toxicology Testing In Clinical Laboratories.	https://www.doh.gov.ae/-/media/75BD15D65E1F4D86A07709D7CBC86DFF.ashx

5. Appendices

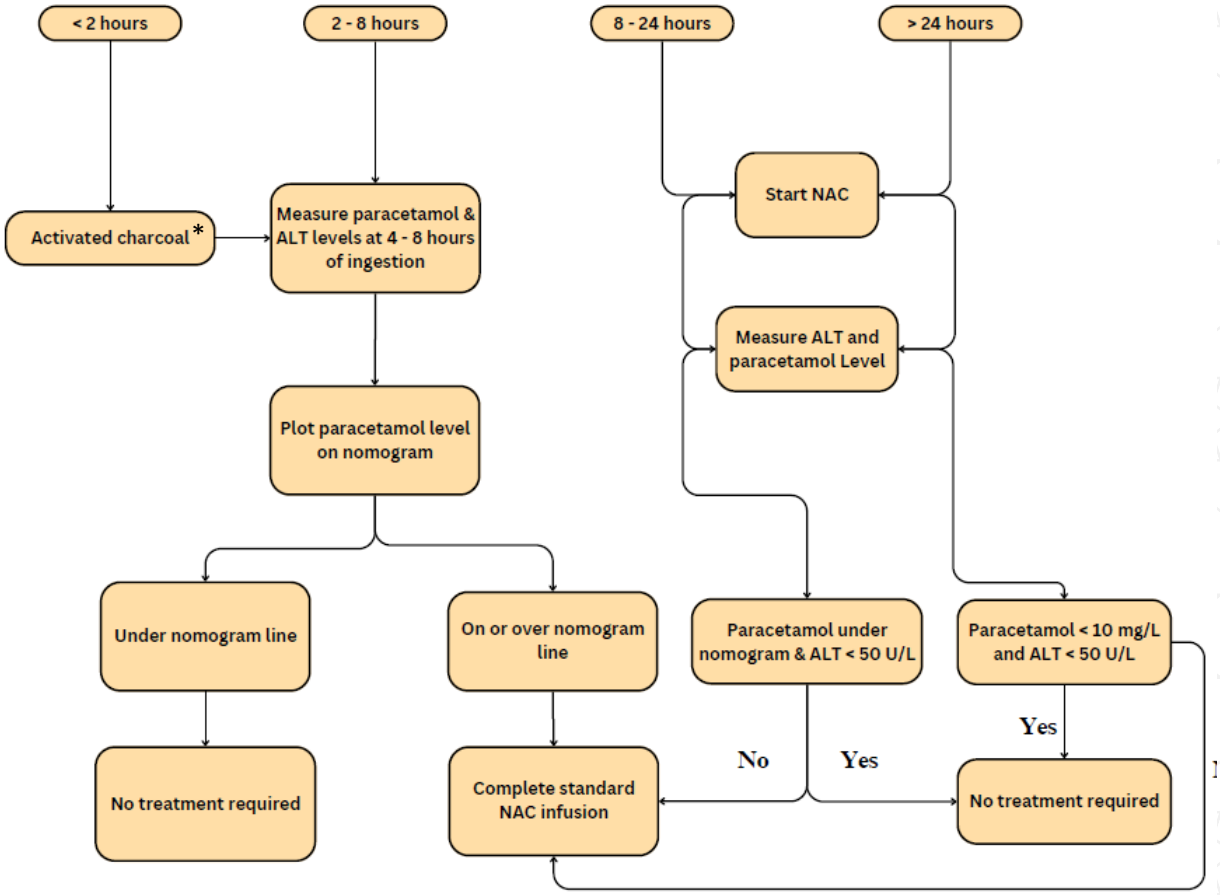
Appendix I – Revised Rumack-Matthew Nomogram[3]



The nomogram can only be used for acute ingestions of immediate-release paracetamol with a known time of ingestion within the 4-24 hour period following the overdose. In acute staggered ingestions use the earliest time of ingestion for the paracetamol nomogram.

Conversion unit formula of paracetamol: mg/L x 6.62 = µmol/L

Appendix II – Pathway for treatment of acute immediate release paracetamol ingestion

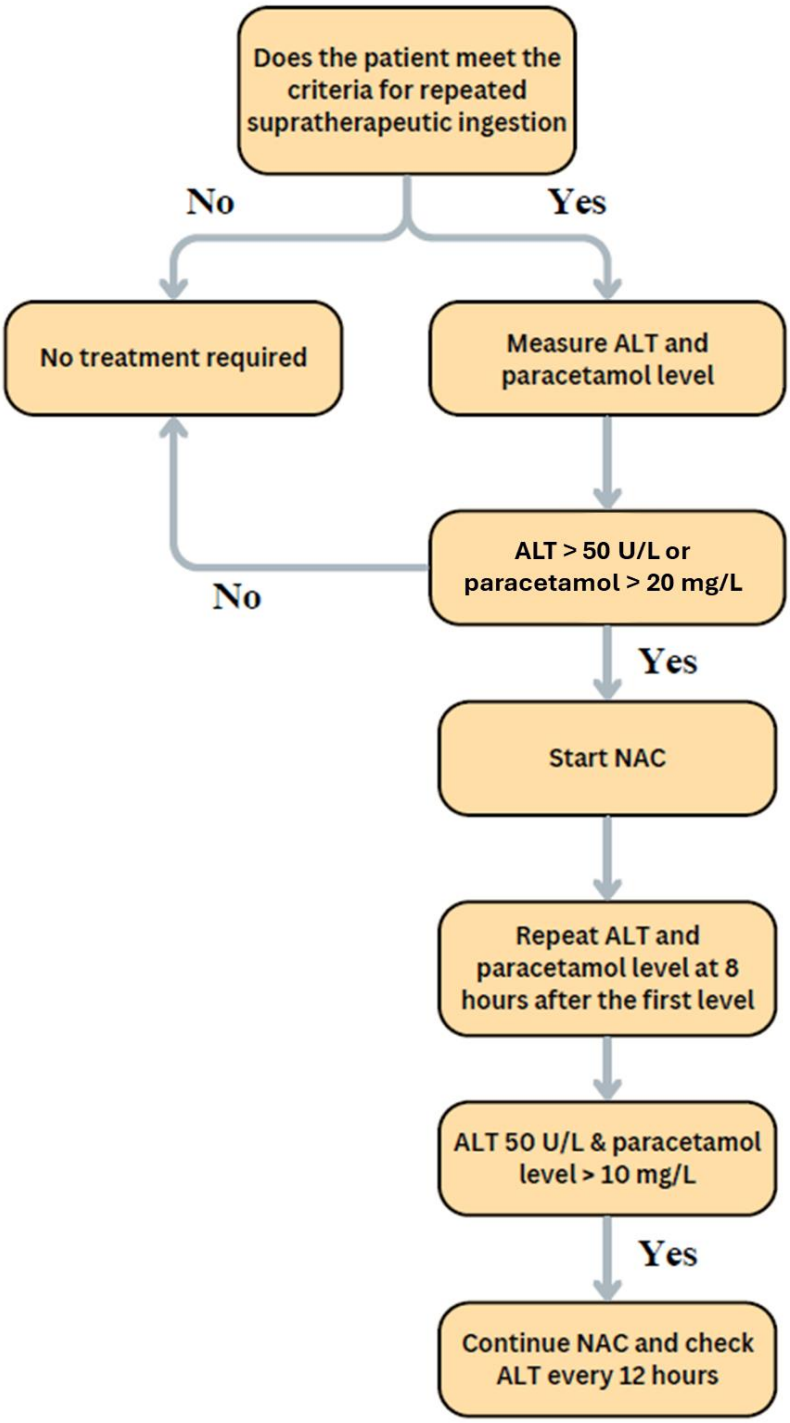


Paracetamol concentration double the nomogram line should complete NAC infusion with double dose of second bag (200 mg/kg).

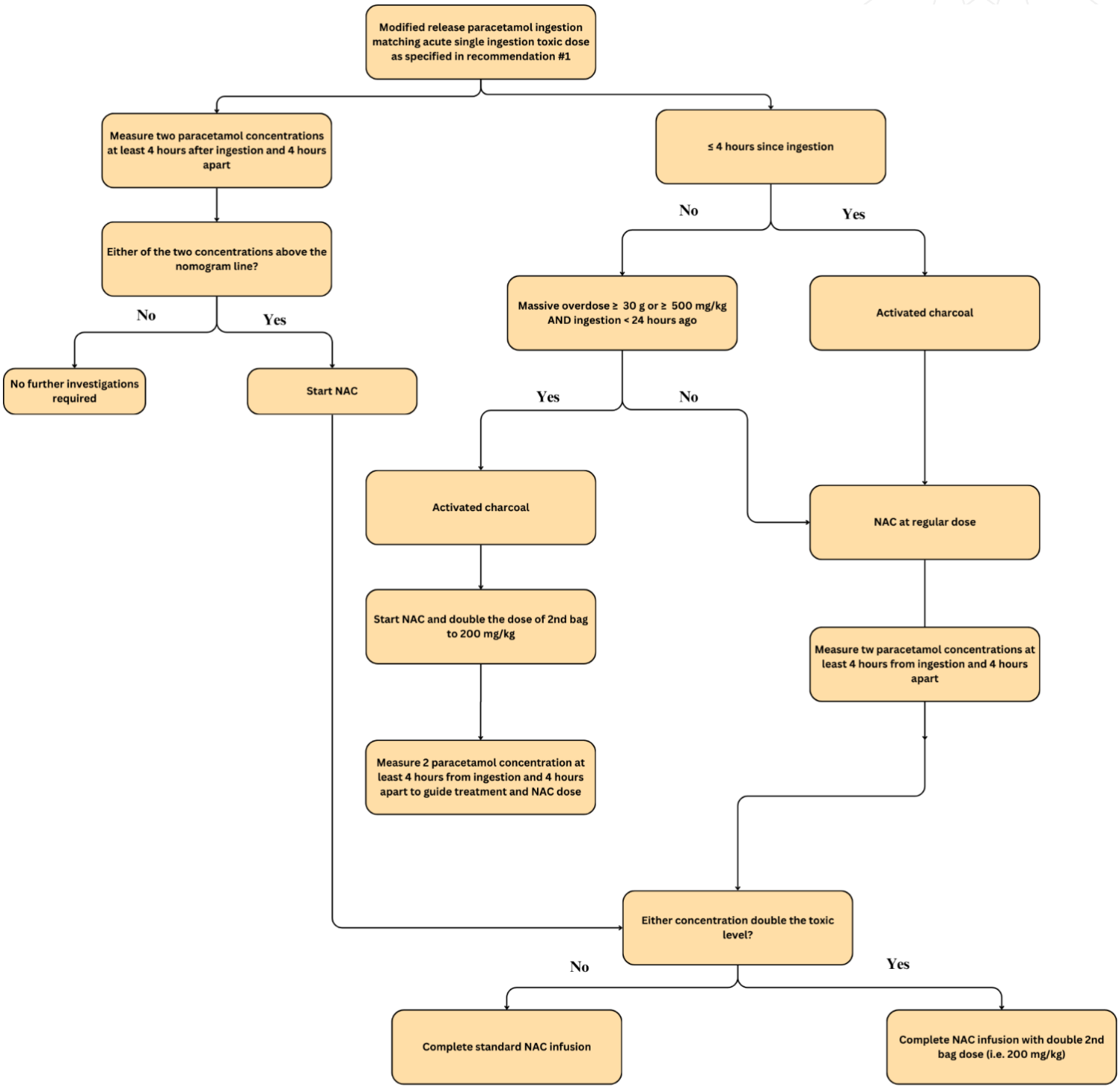
*Activated charcoal is given to cooperative adult with no contraindications if:

The formulation is a solid (e.g. tablets, capsules),
If at least 10 g or 200 mg/kg (whichever is less) is ingested within 2 hours of the overdose
If at least 30 g is ingested within 4 hours of the overdose

Appendix III – Pathway for treatment of supratherapeutic paracetamol ingestion



Appendix IV – Pathway for treatment of acute modified release paracetamol ingestion



Measure ALT and paracetamol levels in all patients 2 hours before the end of the regimen.
See recommendation # 10 for NAC discontinuation.