N-Acetylcysteine Dosing Guidelines for Paracetamol Overdose in Adults

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

INTRODUCTION

Managing patients with paracetamol overdose is common in A&E and AMU departments. N-Acetylcysteine is the treatment of choice but the calculations are complicated both for the prescriber and for the administrator. Evidence suggests that errors are common. As suboptimal treatment can adversely affect patient outcome it is important that these errors are minimised[1]. Dosing charts have been suggested by the Department of Health as a risk reduction strategy and have improved accuracy of calculations in a recent trial[1].

This guideline covers all adult patients needing N-acetycysteine treatment after paracetamol overdose

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS:

All qualified healthcare professionals involved in prescribing, administering or monitoring N-acetylcysteine in paracetamol overdose

Lead Clinician(s)

James France	Emergency Medicine Consultant (A&E), WRH
Approved by Medicines Safety Committee	1st July 2019
Approved by Divisional Governance Committee::	20th August 2019
Review Date:	20th August 2022

This is the most current document and is to be used until a revised version is available

Key amendments to this guideline

Date	Amendment	By:
25/09/2007	Guideline approved by Medicines Safety Committee	
17/08/2011	No amendments made to guideline	I Levett
04/09/2013	Dose 1 should now be over 1 hour not 15 minutes	I Levett
20.01.2015	Removal of hypersensitivity as a contraindication to treatment with N'acetylcysteine. Managing infusion related events. Appendices: paracetamol overdose treatment normogram, patient advice leaflets	J.France
06.04.2016	Advice on how to printout Patient Advice Leaflets	J France
04.12.2017	Sentence added in at the request of the Coroner	
06.04.2018	Document extended with no changes	J France
18.06.2019	Document reviewed and extended without changes	I Levett

N-Acetylcysteine Dosing Guidelines for Paracetamol Overdose in Adults

INTRODUCTION

Managing patients with paracetamol overdose is common in A&E and MAU departments. N-Acetylcysteine is the treatment of choice but the calculations are complicated both for the prescriber and for the administrator. Evidence suggests that errors are common. As suboptimal treatment can adversely affect patient outcome it is important that these errors are minimised[1]. Dosing charts have been suggested by the Department of Health as a risk reduction strategy and have improved accuracy of calculations in a recent trial[1].

GUIDELINE

The infusion volumes quoted in this guideline are for adults only. Please refer to the National Poisons Centre and toxbase[1] for children's dose regimens.

Once the need for N-acetylcysteine has been confirmed using the paracetamol overdose guidelines / toxbase[1] and paracetamol overdose treatment normogram (where applicable – see appendix 1) then weigh the patient, rounding up to the nearest 10kg.

Use the Additional Documents section of Patient First to print out a prescription chart with all the doses already calculated by selecting the correct weight range for the patient. When using the Patient First pre-printed prescription chart ensure the patient's weight is entered into the appropriate box, by hand, on the pre-printed prescription sheet as well as ensuring that each dose of N'Acetylcysteine prescribed (signed).
Alternatively the three infusions can then be prescribed as separate doses either on a casualty card or on an infusion chart using the Adult Dosage Table below.

Patients should be given a patient advice leaflet when they receive either a full or a partial treatment course with N'Acetylcysteine (appendices 2,3)[1] which can be printed out directly from the 'Advice Sheet' section of Patient First.

Adult Dosage Table

Adult acetylcysteine prescription (each ampoule = 200mg/mL acetylcysteine)					Please circle appropriate weight and volume.	
Regimen	First Infusion		Second Infusion		Third Infusion	
Infusion fluid	200 mLs 5% glucose or sodium chloride 0.9%		500 mLs 5% glucose or sodium chloride 0.9%		1000 mLs 5% glucose or sodium chloride 0.9%	
Duration of infusion	1 hour		4 hours		16 hours	
Drug dose	150 mg/kg acetylcysteine		50 mg/kg acetylcysteine		100 mg/kg acetylcysteine	
Patient Weight[1]	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate
kg	mL	mL/h	mL	mL/h	mL	mL/h
40-49	34	234	12	128	23	64
50-59	42	242	14	129	28	64
60-69	49	249	17	129	33	65
70-79	57	257	19	130	38	65
80-89	64	264	22	131	43	65
90-99	72	272	24	131	48	66
100-109	79	279	27	132	53	66
≥110	83	283	28	132	55	66

[1] Dose calculations are based on the weight in the middle of each band. If the patient weighs less than 40kg use the paediatric dosage table.
[2] Ampoule volume has been rounded up to the nearest whole number

MANAGING INFUSION RELATED EVENTS

Intravenous N'Acetylcysteine (NAC) can cause anaphylactoid reaction or local effects. Adverse effects are more likely if paracetamol levels are low or absent, in women, in patients with a family history of allergies or asthma. Reactions can occur in up to 20% of patients, usually soon or after the first infusion.

Features:

- Nausea, vomiting, urticarial rash, angioedema, tachycardia, bronchospasm are relatively common.
- Hypotension and collapse are rare.
- Very rarely, in severe cases, respiratory depression, renal failure and disseminated intravascular coagulation.

Action:
● **Stop the infusion** is usually all that is required.
● Give H1 antihistamine if necessary (eg. Chlorphenamine 10mg IV).
● Give nebulised salbutamol if bronchospasm is significant.
● For adverse reactions developing during the first or second bag of the infusion regime, it is essential that the NAC infusion should be started again once the reaction is settling. This should be at an infusion rate of 50mg/kg over 4 hours (ie. the second bag), followed by the final (third bag) 16hour infusion (100mg/kg over 16h). Further reactions are almost unknown.
● Other measures as dictated by the patient's condition.
● Report reaction using the yellow card scheme.

MANAGING PATIENTS WHO HAVE PREVIOUSLY HAD A REACTION TO N'ACETYLCYSTEINE

● A previous anaphylactoid reaction to N'Acetylcysteine (NAC) is **NOT a contra-indication** to further a treatment course. NAC is more likely to cause adverse effects if paracetamol concentrations are low or absent. Adverse reactions are more likely women, in asthmatics, and in patients with a family history of allergy.

Action:
● In patients with a history of repeated reactions to N'Acetylcysteine, prophylactic treatment with a H1 and H2 antihistamine (eg. Chlorphenamine 10mg IV and Ranitidine 50mg in 20ml over 2 mins IV) should be considered.
● Pretreatment with nebulised salbutamol may be considered in those patients with a history of bronchospasm following N'Acetylcysteine.
● Consider giving the first bag more slowly than normal eg. over 2 hours instead of one hour, if the patient has had a previous severe reaction to NAC

Monitoring Tool

This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
P2	Weight written on pre-printed chart	Note audit	yearly	Discretion audit lead	Emergency department	yearly
P2	Prescription signed	as above	as above	as above	as above	as above

REFERENCES

1. Toxbase: http://www.spib.axl.co.uk Accessed July 1014

CONTRIBUTION LIST

Key individuals involved in developing the document

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Circulated to the chair of the following committee's / groups for comments

Name	Committee / group
Vicky Morris	Medicines Safety Committee

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

		Yes/No	Comments
1.	**Does the policy/guidance affect one group less or more favourably than another on the basis of:**	NO	
	• Age	NO	
	• Disability	NO	
	• Gender reassignment	NO	
	• Marriage and civil partnership	NO	
	• Pregnancy and maternity	NO	
	• Race	NO	
	• Religion or belief	NO	
	• Sex	NO	
	• Sexual Orientation	NO	
2.	**Is there any evidence that some groups are affected differently?**	NO	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	NO	
4.	**Is the impact of the policy/guidance likely to be negative?**	NO	
5.	**If so can the impact be avoided?**		
6.	**What alternatives are there to achieving the policy/guidance without the impact?**		
7.	**Can we reduce the impact by taking different action?**		

If you have identified a potential discriminatory impact of this key document, please refer it to Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact Human Resources.

Supporting Document 2 – Financial Impact Assessment

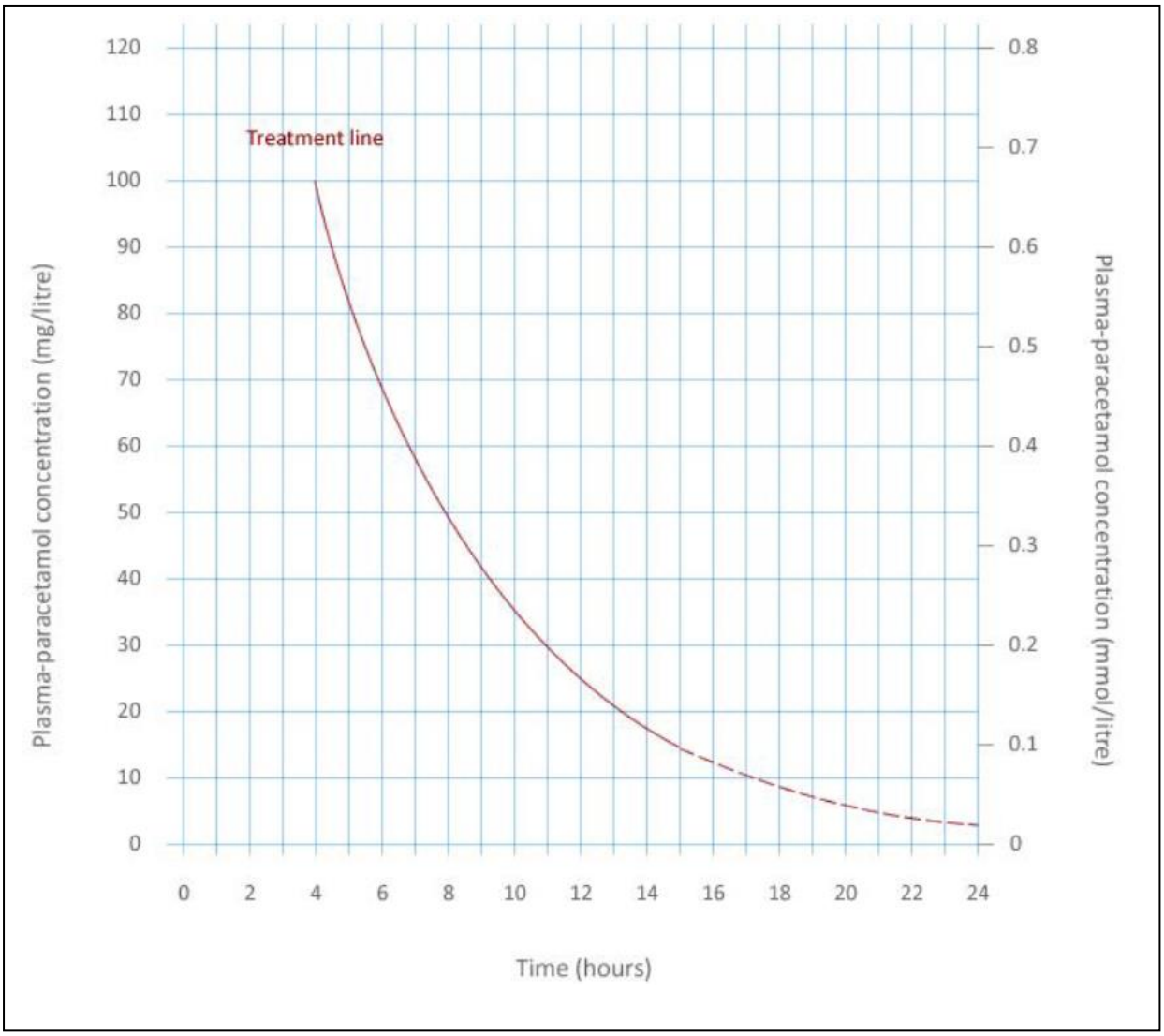
To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	NO
2.	Does the implementation of this document require additional revenue	NO
3.	Does the implementation of this document require additional manpower	NO
4.	Does the implementation of this document release any manpower costs through a change in practice	NO
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	NO
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval

Appendix One

Paracetamol Overdose Treatment Normogram



Appendix Two

Patient Information Sheet on Paracetamol Poisoning - Patient receiving full course of antidote

You have been given this sheet as you have received treatment in hospital following a paracetamol overdose.

What are the risks of paracetamol?

Paracetamol is a common painkiller that is normally safe but can be harmful to the liver, and rarely the kidneys, when taken in excess.

What are the risks to me?

You have been assessed by the medical team and based on the information you have provided and the result of blood tests, you have received treatment with acetylcysteine (NAC) to minimise any damage to your liver.

What should I do now?

Blood tests taken at the end of treatment indicated that no further treatment was required and you have been discharged home.

However, if you develop any of the following symptoms you must seek medical advice **immediately**:

- Abdominal pain, nausea, vomiting
- Discolouration of the skin or whites of the eyes (turn yellow)
- Confusion or drowsiness
- Difficulty in passing urine

Are there any long-term health effects?

Your blood tests indicated that no further treatment was required.

There should not be any long-term health effects.

If you have any further questions or require further medical help call the number below or use the NHS 111 service (dial 111)

Accident & Emergency Department
Worcestershire Royal Hospital
Charles Hastings Way, Newtown Road Worcester WR5 1DD
Telephone: 01905 763333

Appendix Three

Patient Information Sheet on Paracetamol Poisoning - Patient part-treated or not treated with Antidote

You have been given this sheet as you have been assessed / treated in hospital following a paracetamol overdose.

What are the risks of paracetamol?

Paracetamol is a common painkiller that is normally safe but can be harmful to the liver, and rarely the kidneys, when taken in excess.

What are the risks to me?

You have been assessed by the medical team in hospital and based on the information that you have provided and the result of blood tests, it is very unlikely that you will develop liver damage and it is safe to allow you home.

It is **very** important that the information you provide is as accurate as possible:

- Are you certain when you took the tablets?
- How many did you take?
- Did you take the tablets all at once or over more than an hour?

If you feel any of the information you have told us may not be correct, **you should inform the doctor or nurse immediately as you may be at risk of developing liver damage**.

What should I do now?

You have been assessed by a medical team and discharged home.
However, if you develop any of the following symptoms you must seek medical advice **immediately**:

- Abdominal pain, nausea, vomiting
- Discolouration of the skin or whites of the eyes (turn yellow)
- Confusion or drowsiness
- Difficulty in passing urine

Are there any long-term health effects?

Based on the information you provided and the blood test results, the risk of developing liver damage is very low and you are not predicted to have any long-term health effects.

If you have any further questions or require further medical help call the number below or use the NHS 111 service (dial 111)

Accident & Emergency Department
Worcestershire Royal Hospital
Charles Hastings Way, Newtown Road Worcester WR5 1DD
Telephone: 01905 763333