Worcestershire Acute Hospitals NHS Trust

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. 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 (18 years or over) needing 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 acetylcysteine in paracetamol overdose

Lead Clinician(s)

James France	Emergency Medicine Consultant (A&E), WRH
Approved by Divisional Governance Committee:	7th February 2024
Approved by Medicines Safety Committee	14th February, 2024
Review Date:	7th February 2027

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 nomogram, 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
10.09.2020	Introduction of SNAP regime	J France
12.01.2024	Review and update in accordance NPIS guidance	J France
14.02.2024	Approved by MSC	

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 separate guideline regarding acetylcysteine dosing in children or Toxbase [1].

Once the need for acetylcysteine has been confirmed (see Toxbase for the most up to date guidance) 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 acetylcysteine is prescribed (signed).
Alternatively, if not using the pre-printed ED drug charts the two infusions can be prescribed as separate doses either on the ED drug chart or on an infusion chart using the Adult Dosage Table in appendix1.

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

The acetylcysteine (AC) treatment regime on the pre-printed prescription charts and in the adult dosage table in appendix 1 is the **Scottish and Newcastle Acetylcysteine Protocol (SNAP regime)**. The SNAP regime is a 12hr infusion (2 separate bags) compared to the traditional 21hr infusion regime (3 separate bags), see appendix 4. The total dose of intravenous acetylcysteine is the **same** as the standard 21-hour regimen (i.e. 300 mg/kg) but the rate and duration of treatment is different which results in a lower peak plasma acetylcysteine concentration and a significantly lower risk of anaphylactoid reactions, as described on Toxbase. [2] More than two years of using the SNAP regime in routine clinical practice in large centres has confirmed that it produces fewer adverse drug reactions and has similar efficacy with regards preventing liver injury when compared to the 21hr NAC regime. The SNAP regime also reduces treatment interruptions and shortens the length of treatment without compromising antidote effectiveness. [3]. As a result, although it differs from the licensed regime and is therefore `off-label`, the adoption of the SNAP regime has become much more widespread, including it being listed alongside the 21hr regime on the Toxbase website [3]. A joint position statement from the National Poisons Information Service (NPIS) and the British Association for the Study of the Liver (BASL) and the Royal College of Emergency Medicine (RCEM) supports the use of the SNAP regime in both adults and children [4].

The SNAP regime from the patient's perspective:
This is a 'new' way of giving acetylcysteine that is not yet licensed by the Medicines and Healthcare Regulatory Authority (MHRA), however specialist units with experience of treating patients with paracetamol overdoses, believe that SNAP is better because

- it uses the same dose of acetylcysteine but involves fewer infusions through a drip than the old method (two infusions instead of three)
- it requires a shorter time on the drip for most patients (12 hours instead of 21)
- side effects such as itching and vomiting (being sick) are less common
- it is likely to be as effective at preventing liver damage as the old method of giving acetylcysteine.

Appendix 4 contains the 21hr dosage table for those clinicians not wanting to use the ED pre-printed SNAP regimes.

Appendix 5 contains an example of the ED pre-printed SNAP regime for a patient weighing between 70 and 79 kg.

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 12.01.2024
2. Toxbase: https://www.toxbase.org/General-Info/Antidotes---doses-and-sources/Acetylcysteine-antidote/ Accessed 12.01.24
3. Pettie JM, Caparrotta TM, Hunter RW et al. Safety and Efficacy of the SNAP 12-hour Acetylcysteine Regime for the Treatment of Paracetamol Overdose. EclinicalMedicine 11 (2019) 11-17. https://doi.org/10.1016/j.eclinm.2019.04.005
4. Use of SNAP Regimen for the Treatment of Paracetamol Toxicity in adults and chldren. Joint Statement NPIS, BASL, RCEM. May 2023 https://res.cloudinary.com/studio-republic/images/v1685112241/Use-of-the-SNAP-Regimen-for-the-Treatment-of-Paracetamol-Toxicity-in-adults-and-children/Use-of-the-SNAP-Regimen-for-the-Treatment-of-Paracetamol-Toxicity-in-adults-and-children.pdf?_i=AA Accessed 12.01.24

CONTRIBUTION LIST

Key individuals involved in developing the document

Name	Designation
James France	Consultant Emergency Medicine (A&E), WRH

Circulated to the following individuals for comments

Name	Designation
Nick Turley	Clinical Lead Emergency Medicine (A&E), WRH
Abdul Jalil	Clinical Lead Emergency Medicine (A&E), AH
Jules Walton	Divisional Medical Director Urgent Care
David Hornsby	Matron, Emergency Medicine(A&E), WRH
Marc Tarrant	Matron, Emergency Medicine(A&E), AH
Tina Evans	Lead Pharmacist – Urgent Care
Miguel Marimon	Consultant Acute Physician, WRH
Aruna Maharaja	Clinical Lead Acute Medicine, WRH
David Brocklebank	Clinical Lead Acute Medicine, AH
James Risley	Clinical Director Gastroenterology
Andrew Burtenshaw	Clinical Director Intensive Care

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

Name	Committee / group
	Medicines Safety Committee

Supporting Document 1 - Equality Impact Assessment Tool

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust		Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
Date assessment completed			

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title:**			
What is the aim, purpose and/or intended outcomes of this Activity?				
Who will be affected by the development & implementation of this activity?	❑	Service User	❑	Staff
	❑	Patient	❑	Communities
	❑	Carers	❑	Other _____
	❑	Visitors	❑	
Is this:	❑ Review of an existing activity			

	❑ New activity ❑ Planning to withdraw or reduce a service, activity or presence?
What information and evidence have you reviewed to help inform this assessment? (Please name sources, eg demographic information for patients / services / staff groups affected, complaints etc.	
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	
Summary of relevant findings	

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age				
Disability				
Gender Reassignment				
Marriage & Civil Partnerships				
Pregnancy & Maternity				
Race including Traveling Communities				
Religion & Belief				
Sex				
Sexual Orientation				

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)				
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)				

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
		.		
How will you monitor these actions?				
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)				

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	
Date signed	
Comments:	
Signature of person the Leader Person for this activity	
Date signed	
Comments:	

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

Acetylcysteine SNAP Doses - Adults and children weighing 40 kg or more (the modified 12-hour IV regimen) [1]

Preparation and Administration of Infusions

NB: For patients on renal replacement therapy the dose of acetylcysteine should be doubled.

First Infusion

- Add the appropriate volume of acetylcysteine (100 mg/kg body weight, maximum 11 g) to 200 mL 5% glucose or 0.9% sodium chloride, infused over 2 hours.

Add the appropriate volume of acetylcysteine (200 mg/kg body weight, maximum 22 g) to 1000 mL 5% glucose or 0.9% sodium chloride and infuse over the next 10 hours.

Acetylcysteine prescription for adults and children weighing 40 kg or more (each ampoule = 200 mg/mL acetylcysteine)				
12-hour Regimen	First Infusion		Second Infusion	
Infusion fluid	200 mL 5% glucose or 0.9% sodium chloride		1000 mL 5% glucose or 0.9% sodium chloride	
Duration of infusion	2 hours		10 hours	
Drug dose	100 mg/kg acetylcysteine		200 mg/kg acetylcysteine	
Patient Weight[1]	Ampoule volume[2]	Infusion Rate	Ampoule volume[2]	Infusion Rate
kg	mL	mL/h	mL	mL/h
40-49	23	112	45	105
50-59	28	114	55	106
60-69	33	117	65	107
70-79	38	119	75	108
80-89	43	122	85	109
90-99	48	124	95	110
100-109	53	127	105	111
≥110	55	128	110	111

[1] Dose calculations are based on the weight in the middle of each band. If the patient weighs less than 40 kg use the paediatric dose table.

[2] Ampoule volume (volume of concentrated NAC [200 mg/mL] extracted from ampoules) has been rounded up to the nearest whole number.

Appendix Two - Patient information leaflet

Worcestershire Royal Hospital
Emergency Department
Patient Advice Sheet

Worcestershire Acute Hospitals NHS Trust

Paracetamol Excess

Patient treated with Antidote

You have been given this sheet as you have been discharged after assessment and/or 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 (AC) 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. The treatment is highly effective. However, If you develop any of the following symptoms, you must seek medical advice immediately:

- Abdominal pain, nausea, vomiting
- Discolouration (yellow) 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 NHS111 (see below)

Emergency Department,
Worcestershire Royal Hospital,
Tel: 01905 733065

NHS 111: Telephone 111
NHS 111 Website: https://111.nhs.uk/, www.nhs.uk

Appendix Three - Patient information leaflet

Worcestershire Royal Hospital
Emergency Department
Patient Advice Sheet

NHS Worcestershire Acute Hospitals NHS Trust

Paracetamol Excess

Patient part-treated or not treated with Antidote

You have been given this sheet as you have been discharged after assessment and/or 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 are currently deemed to be suitable for discharge. If blood tests relating to paracetamol overdose are currently completely normal, there are no additional risks to you from this overdose. If your tests are abnormal, you may be at a small risk of developing or worsening damage to the liver if you take paracetamol too soon after discharge.

What should I do now?

Check immediately with a member of your healthcare team if you are not sure whether blood tests relating to paracetamol overdose are normal at this time. If the blood tests are normal, you don't need to do anything else unless you develop new symptoms, in which case you should seek medical advice as soon as possible.

You should ask your doctor or nurse how long to avoid paracetamol.

If you develop any of the following symptoms, there may be a possibility that your overdose has resulted in an unexpected deterioration in your health, and you must seek medical advice immediately:

- Abdominal pain, nausea, vomiting
- Discolouration (yellow) 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 NHS111 (see below)

Emergency Department,
Worcestershire Royal Hospital,
Tel: 01905 733065

NHS 111:
NHS 111 Website:

Telephone 111
https://111.nhs.uk/, www.nhs.uk

Appendix 4 21hour (3 bag) N'Acetylcysteine Infusion Regime

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

Appendix 5 Example of ED Pre-printed N'Acetylcysteine Prescription Chart - front

Emergency Department **ADULT INTRAVENOUS ACETYLCYSTEINE INFUSION CHART**

Worcestershire Acute Hospitals NHS Trust

ADDRESSOGRAPH	ALLERGIES/ADVERSE DRUG REACTIONS
Name.....	NONE KNOWN ☐ Signature:
Hosp No:	DATE / DRUG/FOOD/OTHER / REACTION DETAILS
NHS No:	
D.O.B..... Male Female	

CONSULTANT:	WARD:	Enter patient weight here:

ONLY Use this chart if your patient requires an AC (Parvolex ®) infusion following an overdose of paracetamol and weighs between: 70-79kg

For Obese patients weighing more than 110 kg: Calculate AC dose using 110kg rather than actual body weight
For pregnant patients: Calculate AC dose using the patient's actual pregnant weight

DATE	ADDITIVE DRUG / FLUID (USE BLOCK CAPITALS)	DOSE (Units) / Vol (ml)	Route	Duration/ Rate of Admin	Signature	Date Began	Time Began	Prepared By / Checked By	Pharm Use
	ACETYLCYSTEINE (200mg/ml) / **GLUCOSE 5%**	7600mg (38ml) / **200mls**	IV	2 hour / 119ml/h					
	ACETYLCYSTEINE (200mg/ml) / **GLUCOSE 5%**	15000mg (75ml) / **1000mls**	IV	10 hours / 108ml/h					
			IV						

As Required Medication – see overleaf for guidance

DRUG (APPROVED NAME) Chlorphenamine					DATE	TIME	DOSE	ROUTE	SIG
DIRECTIONS/MAX FREQ	DOSE	ROUTE IV	DOSE	ROUTE PO					
4-6 hours	10-20mg		4mg						
START DATE	SIGNATURE		MAX DOSE / 24 HRS 40mg						

DRUG (APPROVED NAME) Salbutamol				DATE	TIME	DOSE	ROUTE	SIG
DOSE	ROUTE	DOSE	ROUTE					
2.5-5mg	Neb							
DATE	SIGNATURE	FREQUENCY PRN						

Appendix 5 continued – Reverse of ED Prescription Chart

MANAGING INFUSION RELATED EVENTS

Intravenous Acetylcysteine (AC) can cause an 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 AC infusion should be started again once the reaction is settling. Restart AC at half rate for 30 minutes and then recommenced as per normal protocol. Further reactions are rare.
- 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 ACETYLCYSTEINE

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

Action:

- In patients with a history of repeated reactions to Acetylcysteine, prophylactic treatment with a H1 antihistamine (eg. Chlorphenamine 10mg IV) should be considered.
- Pre-treatment with nebulised salbutamol may be considered in those patients with a history of bronchospasm following Acetylcysteine.

WHEN TO REPEAT THE SECOND ACETYLCYSTEINE INFUSION

Following blood sampling (U&Es, LFTs, Paracetamol & INR), just before the end of the second bag, if any of the criteria below apply then the second 10hr infusion should be prescribed and administered for a second time.

- ALT > upper limit normal or
- ALT doubles or more from admission (even if in normal range) or
- Paracetamol concentration >10mg/L

The decision regarding whether more AC is required at the end of 12-hours is dependent on the ALT and paracetamol level. The INR does not influence this decision at this specific time point. However, in cases of ALT rise then the INR is a necessary marker of severity. Consult TOXBASE if in any doubt and after extended (third bag) treatment.

12/01/24