Worcestershire Acute Hospitals NHS Trust

INTRAVENOUS AMINOPHYLLINE FOR ADULTS GUIDELINE

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

Aminophylline is a smooth muscle relaxant and bronchodilator. It is indicated for the treatment of severe acute asthma not responding to treatment with bronchodilators, steroids and magnesium as per the BTS/SIGN guidelines. Aminophylline may be considered for patients with an acute COPD exacerbation who have had an inadequate response to nebulised therapy. Due to its narrow therapeutic index, monitoring of plasma levels are vital to ensure its safe and effective use.

This guideline is for use by the following staff groups:

All doctors, registered nurses and pharmacists involved with the prescribing, administration and monitoring of IV aminophylline.

Lead Clinician(s)

Millie Harris	Lead Pharmacist for Respiratory
Approved by Respiratory Directorate Committee on:	15th November 2023
Approved by Medicines Safety Committee on: *Where medicines included in guideline*	13th March 2024
Review Date: This is the most current document and should be used until a revised version is in place	13th March 2027

Key amendments to this guideline

Date	Amendment	Approved by:
13th March 24	New document approved	Respiratory Directorate/Medicines Safety Committee

INTRAVENOUS AMINOPHYLLINE FOR ADULTS GUIDELINE

INDICATION

Aminophylline is a smooth muscle relaxant and bronchodilator. It is indicated for the treatment of severe acute asthma not responding to treatment with bronchodilators, steroids and magnesium as per the BTS/SIGN guidelines. Aminophylline may be considered for patients with an acute COPD exacerbation who have had an inadequate response to nebulised therapy.

CONTRAINDICATIONS	CAUTIONS – MONITOR FOR TOXICITY
• Hypersensitivity to ethylenediamine • Allergy to the theophyllines, caffeine or theobromine • Concomitant use with other xanthine drugs • Acute porphyria	• Age over 55 years • Hepatic disease • Heart failure See Summary of Product Characteristics for full list

PRESCRIBING GUIDE

LOADING DOSE

For all patients **NOT** already taking oral theophylline. For patients already taking oral therapy, proceed to maintenance dose.

Dose	Fluid	Rate
5mg/kg, up to a dose of 500mg Use ideal body weight if BMI >30kg/m^2 (see below for calculation)	100mL sodium chloride 0.9%	Over at least 20 minutes Maximum rate 25mg/min
Ideal body weight (kg) Male: 50kg + (0.91 × [height in centimetres − 152.4]) Female: 45.5kg + (0.91 × [height in centimetres − 152.4]		

If acute adverse effects occur, slow the rate or stop the infusion for 5-10 minutes.

MAINTENANCE DOSE

Patient	Dose and rate	Fluid
Elderly or heart failure Non-smoking adult Smoking adult	0.3mg/kg/hour 0.5mg/kg/hour 0.7mg/kg/hour	1000mg in 1 litre sodium chloride 0.9%

Note: recommended dilution gives a 1mg/mL strength, therefore dose in mg/hour equals the rate in mL/hour.

Due to the high pH, it is preferable to give via a central venous access device. However, practically this may be unavailable so administer via a large peripheral vein, monitoring insertion site closely using a recognised phlebitis scoring tool. Resite cannula at first signs of inflammation.

MONITORING

- ECG prior to administration to assess for arrhythmia and QTc interval prolongation
- Serum potassium levels daily
- Heart rate and blood pressure. Ideally patients should be in a high care setting with continuous monitoring. If unavailable, heart rate and blood pressure should be assessed at baseline, then every 30 minutes for 2 hours at a minimum. Subsequent monitoring as per NEWS scoring unless otherwise stated by a doctor
- Plasma-theophylline level as outlined below

Theophylline has a narrow therapeutic index and plasma levels should be kept between **10-20mg/L**. Lower levels may be acceptable if deemed clinically effective.

	Initial level	Repeat level
Loading dose given	6 hours after initiating therapy	Levels should be repeated every **24 hours** thereafter
Increased risk of toxicity	6 hours after initiating therapy	
No loading dose given	24 hours after initiating therapy	

The plasma theophylline level may be increased in heart failure, hepatic impairment and viral infections. The plasma theophylline level may be decreased in those who smoke and by alcohol consumption.

Infusion rates may be adjusted using the following equation:

$$\textbf{New infusion rate} = \frac{\textbf{15 x current infusion rate}}{\textbf{current theophylline level}}$$

Signs of toxicity include arrhythmias, seizures, hypotension, hypokalaemia, vomiting, hyperglycaemia, restlessness and pupillary dilation. The risk increases if serum levels >20mg/L.

INTERACTING MEDICATIONS

Drugs which may increase theophylline levels	Macrolide antibiotics, fluoroquinolone antibiotics, fluconazole, propranolol, oral contraceptives, calcium channel blockers, methotrexate*
Drugs which may decrease theophylline levels	Carbamazepine, phenytoin, rifampicin, barbiturates*
Other interactions	Lithium – aminophylline increases the excretion of lithium, decreasing its therapeutic efficacy Beta$_2$ agonists – increased risk of cardiac arrhythmias Beta blockers – antagonism of bronchodilator effects*

*This list is not exhaustive - see Summary of Product Characteristics for full list

CONVERTING TO ORAL THEOPHYLLINE MR

1. Calculate the total IV aminophylline administered over 24 hours
2. Multiply this amount by 0.8
3. Divide by 2 to create BD dosing regimen

4. Tablets available as Uniphyllin Continus® - 200mg, 300mg and 400mg or Nuelin SA® 175mg and 250mg. Round to the most practical dose

For example, if a patient is receiving 21mg/hour, the total daily dose is 504mg. To convert to an oral theophylline dose, 504mg x 0.8 = 403mg daily. A suitable theophylline dose is Uniphyllin Continus® 200mg twice daily.

Plasma levels should be checked 5 days after initiating oral treatment.

Monitoring

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?**
	Safe and effective prescribing and monitoring of aminophylline infusions in line with treatment guidelines including: • Correct dosing • Appropriate monitoring - both physical observations and bloods (serum potassium and plasma levels) • Converting to oral theophylline if appropriate	Review of prescribing at time of patient presentation.	As patients prescribed aminophylline present.	Ward round reviews by doctors and clinical pharmacists.	Inappropriate prescribing reported on Datix system.	As patients prescribed aminophylline present.

References

British Thoracic Society/SIGN. SIGN 185: British guideline on the management of asthma. Available from: https://www.sign.ac.uk/our-guidelines/british-guideline-on-the-management-of-asthma/

Electronic medicines compendium. Aminophylline hydrate 25mg/ml Solution for injection **-** Summary of Product Characteristics**.** May 2023. Available from: https://www.medicines.org.uk/emc/product/6560 [accessed 19/10/23]

NICE - British National Formulary. Aminophylline. Available from: https://bnf.nice.org.uk/drugs/aminophylline/ [accessed 19/10/23]

MEDUSA injectable medicines guide. Aminophylline. Aug 2019. Available from: https://www.medusaimg.nhs.uk/IVGuideDisplay.asp [accessed 19/10/23]

Contribution List

Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Dr Bethan Barker – Respiratory Consultant
Bijal Gondalia – Respiratory Pharmacist
Dr Clare Hooper – Respiratory Consultant
Dr Jamie Johnstone – Respiratory Consultant
Dr Andrew Crawford – Respiratory Consultant
Dr Kate Cusworth – Respiratory Consultant
Dr Abhimanyu Lal – Respiratory Consultant
Dr See Ling Tan – Respiratory Consultant
Dr Gulfam Mussawar – Respiratory Consultant
Dr Muhammad Niazi – Respiratory Consultant

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Respiratory Directorate Committee (15/11/23)
Specialty medicine DMB (29/1/24)

Supporting Document 1 - Equality Impact Assessment Tool

. To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

Worcestershire Acute Hospitals NHS Trust

Worcestershire Acute Hospitals NHS Trust

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	x	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	**Millie Harris**

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Millie Harris	**Lead Respiratory Pharmacist**	**Millie.harris@nhs.net**
Date assessment completed			

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title: IV aminophylline for adult's guideline**			
What is the aim, purpose and/or intended outcomes of this Activity?	Provide guidance to doctors, nurses and pharmacists on the safe prescribing, administration and monitoring of IV aminophylline.			
Who will be affected by the development & implementation of this activity?	❑ ☑ ❑ ❑	Service User Patient Carers Visitors	☑ ❑ ❑ ❑	Staff Communities Other _____
Is this:	☑ Review of an existing activity – patients already being prescribed IV aminophylline but no trust guideline available ❑ 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.	British National Formulary Summary of Product Characteristics Medusa BTS/SIGN guidelines on the management of asthma
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	Respiratory consultants Respiratory pharmacist Above professionals experienced in the prescribing and monitoring of IV aminophylline.
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	☑			Guideline created for adults
Disability		☑		
Gender Reassignment		☑		
Marriage & Civil Partnerships		☑		
Pregnancy & Maternity		☑		
Race including Traveling Communities		☑		
Religion & Belief		☑		
Sex		☑		
Sexual Orientation		☑		
Other Vulnerable and Disadvantaged		☑		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
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	Millie Harris
Date signed	19/10/23
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.