Worcestershire Acute Hospitals NHS Trust

GUIDELINE/PROTOCOL FOR INTRAPLEURAL USE OF TISSUE PLASMINOGEN ACTIVATOR AND DORNASE ALPHA IN PLEURAL INFECTION

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

Pleural infection carries a high mortality rate. Surgical drainage is required in those where drainage through a chest tube and antibiotics fail. However not all patients are deemed fit for surgical management of pleural infection. Instillation of Tissue Plasminogen Activator (t-PA, Alteplase®) and Dornase Alpha (DNase, Pulmozyne®) are reserved for selected cases to drain infected fluid/treat pleural infection when thoracic surgery is not an appropriate treatment option

This guideline is for use by the following staff groups :

The instillation of intrapleural t-PA and DNase should be limited to suitably trained members of the respiratory team.

Lead Clinician(s)

Dr Clare Hooper	Respiratory Consultant (pleural lead)
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Approved by Medicines Safety Committee: 9th July 2025

Review Date: 9th July 2028
This is the most current document and should be used until a revised version is in place

Key amendments to this guideline

Date	Amendment	Approved by:
13/07/2025	Lower dose of alteplase added to prescription section for clarity	Medicines Safety Committee

GUIDELINE/PROTOCOL FOR INTRAPLEURAL USE OF TISSUE PLASMINOGEN ACTIVATOR AND DORNASE ALPHA IN ADULTS WITH PLEURAL INFECTION

Introduction

Pleural infection hospitalises over 65,000 people in the UK and USA each year and its incidence is increasing worldwide (Farjah F et al 2007). The mortality rate is between 10 and 20% and approximately a third of patients fail conventional therapy (drainage of infected fluid via chest tube and antibiotics) and then require invasive surgical drainage or succumb to their illness (Maskell et al 2005). The median duration of hospital stay for these patients is 12 to 15 days with 25% hospitalised for more than a month (Farjah 2007, Maskell 2005).

Treatment failure is often due to inadequate drainage of the infected fluid due to loculations, septations, and increased fluid viscosity (Maskell 2005, Rahman 2011). Treatment with tissue plasminogen activator (t-PA) or human recombinant DNase (DNase) alone have proven ineffective (Rahman 2011, Maskell 2015). It is unclear why fibrinolytic agents alone do not appear to be helpful in patients with extensive deposition of fibrin in the pleural space (Florova 2010), but is suggested that free DNA cleavage is necessary to reduce fluid viscosity and permit pleural clearance by the fibrinolytic drug (Rahman 2011).

The intrapleural therapy of combined tissue plasminogen activator (t-PA) and human recombinant DNase (DNase) in the management of pleural infection has been shown to improve drainage of infected fluid, reduce the need for surgical intervention (Rahman et al 2011), and decrease the length of hospital stay (Rahman 2011, Piccolo 2014). Similar success rates have been replicated in two other open-label series and using the same combination doses (Majid et al 2016, Mehta et al 2016). ADAPT also found similar success rates using a lower starting dose of t-PA (5mg) (Popowicz et al 2017).

Details of Guideline

Eligibility criteria

- Radiological imaging suggesting residual fluid and a non-draining but adequately-placed and patent chest tube (or indwelling pleural catheter).
- Clinical evidence of infection with pleural fluid macroscopically purulent, positive on bacterial culture or positive for bacteria on Gram's staining, or pleural fluid pH less than 7.2.
- Patients fit for thoracic surgery but transfer delayed, and interim measures needed. In this event use should be agreed with the surgeon before proceeding.
- Patients unfit for thoracic surgery and medical management agreed.
- Diagnosis of pleural infection.

Contraindications to tPA+DNase

Absolute contraindications

- Allergy to alteplase or dornase alpha.
- Recent stroke, major haemorrhage or major trauma.
- Major surgery in the past week.
- Irreversible bleeding diathesis or platelet count <50.
- Active bleeding or risk of bleeding e.g. aortic dissection, aneurysm, oesophageal varices, gastric ulceration.
- Recent haemothorax or intercostal artery injury.
- Previous pneumonectomy on the affected side.
- Pregnancy or breastfeeding.
- Patients under 18 years of age.

Relative contraindications

- Previous treatment with fibrinolytics (streptokinase, alteplase, urokinase) prior to this episode.
- History of intrapleural bleeding prior to this episode.
- Anticoagulation (e.g. warfarin/DOAC), an uncorrected coagulopathy or severe renal or hepatic impairment.
- Use of antiplatelet therapy e.g. clopidogrel or platelet count <100.

Respiratory Consultant to consider pause of anticoagulation/antiplatelet medication required as per WAHT-RES-027

The Respiratory consultant treating the patient may consider a reduction in dose to less than half dose in the context of a significant bleeding risk.

Patient information and consent

- Patients who are to undergo tPA+DNase treatment should have the treatment intent and possible complications explained to them.
- Potential complications of tPA+DNase include:
  - Pain whilst chest drain is clamped to leave treatment in situ.
  - Increased fluid output volume.
  - Change in fluid colour, often becoming blood stained.
  - Intrapleural haemorrhage requiring blood transfusion.
- Anticoagulation, an uncorrected coagulopathy or severe renal or hepatic impairment may increase the risks of pleural bleeding and the risks and benefits of intrapleural fibrinolytics should be considered carefully alongside alternative management.
- If available, patients should be provided with a treatment information leaflet.
- Written consent should be obtained prior to the procedure and verbal consent prior to each administration as per other prescribed medications.

Prescription

This medication can only be prescribed by a respiratory specialist on the recommendation of a consultant chest physician. This is an unlicensed use of alteplase and dornase alpha. Contact pharmacy to arrange supply.

The standard prescription is:

- **Intrapleural alteplase 10mg BD** (at least 6 hours apart) for 3 days.

Reconstitute 10mg alteplase with 10ml water for injection then further dilute in 20ml sodium chloride 0.9% and administer via chest drain. Clamp for 1 hour then allow drainage for 1 hour (reduce dose to 5mg or less may be considered if significant bleeding risk) (Popowicz et al 2017, Roberts et al 2022).

- **Dornase alpha 5mg BD** (at least 6 hours apart) for 3 days. Dilute 5mg in 30ml water for injection and administer via chest drain. Clamp for 1 hour then allow free drainage for 1 hour.

Administration

This medication should be administered by a respiratory specialist with experience in its use using aseptic technique throughout.

- **Equipment**
  - Alteplase (tPA)
  - Dornase Alpha (DNase) – nebuliser solution.
  - Sterile field
  - Sterile gloves
  - Disposable apron
  - Chlorhexidine swab x 2
  - 50ml luer lock syringes x 3
  - Blunt fill needles x 3
  - 100mls sodium chloride 0.9%
  - 30mls water for injection
  - 3 way tap if not already in situ

Method

1. Inform patient about procedure, gain consent and check allergy status.
2. Check baseline NEWS.
3. Ensure drain patent.
4. Ensure tPA and DNase prescribed and dispensed from pharmacy.
5. Prepare a sterile field with all equipment necessary for procedure.
6. Wash hands, apply apron and sterile gloves.
7. In 50ml luer lock syringe reconstitute 10mg alteplase with 30ml sodium chloride 0.9% and label.
8. Draw up 20ml sodium chloride 0.9% in 50ml luer lock syringe
9. Ensure 3 way tap in closed position, remove cap from side port and clean with chlorhexidine swab.

10. Attach the syringe containing sodium chloride 0.9% to the side port, open 3 way tap to the patient (closed to drain bottle) and administer 10mls intrapleurally to ensure drain patent.
11. Close 3 way tap to patient and remove syringe.
12. Attach syringe containing alteplase, open 3 way tap to patient and administer intrapleurally.
13. Close 3 way tap to patient and remove syringe.
14. Attach the syringe containing sodium chloride 0.9% to the side port, open 3 way tap to the patient (closed to drain bottle) and administer 10mls intrapleurally.
15. Close 3 way tap to patient, remove syringe, clean port and replace cap.
16. Leave clamped for 1 hour.
17. After 1 hour, open 3 way tap to chest drain bottle and allow free drainage for 1 hour. Apply thoracic suction if required and prescribed.
18. Prepare a sterile field and all equipment necessary for remaining procedure.
19. Wash hands, apply apron and sterile gloves.
20. In 50ml luer lock syringe reconstitute 5mg Dornase Alpha in 30ml water for injection and label.
21. Draw up 20ml sodium chloride 0.9% in 50ml luer lock syringe
22. Ensure 3 way tap in closed position, remove cap from side port and clean with chlorhexidine swab.
23. Attach the syringe containing sodium chloride 0.9% to the side port, open 3 way tap to the patient (closed to drain bottle) and administer 10mls intrapleurally to ensure drain patent.
24. Close 3 way tap to patient and remove syringe.
25. Attach syringe containing dornase alpha, open 3 way tap to patient and administer intrapleurally.
26. Close 3 way tap to patient and remove syringe.
27. Attach the syringe containing sodium chloride 0.9% to the side port, open 3 way tap to the patient (closed to drain bottle) and administer 10mls intrapleurally.
28. Close 3 way tap to patient, remove syringe, clean port and replace cap.
29. Leave clamped for 1 hour.
30. After 1 hour, open 3 way tap to chest drain bottle and allow free drainage for 1 hour. Apply thoracic suction if required and prescribed.

Monitoring

- 30 minute NEWS and chest drain observations during and for 4 hours following administration of tPA+DNase then as per NEWS recommendation.
- All patients should be monitored for adverse events/signs of bleeding e.g. intrapleural haemorrhage, haemoptysis, gastrointestinal bleeding. All adverse events should be recorded via Datix system and reported to MHRA.
- Treatment should cease if the patient clinically deteriorates.
- Patient should be reviewed daily by a respiratory Physician or Registrar. This review will generally include assessment of infection, bleeding and any potential drug reaction. This will ensure that on-going drug delivery is safe and necessary.

Troubleshooting

Spot ch

Patient complains of pain during flush or tPA+DNase instillation

- Stop instillation.
- Do not proceed with rest of procedure.
- Inform medical or senior nursing staff and document as necessary.
- Return circuit to free drainage.

- Administer analgesia if needed and as prescribed.

Patient complains of pain whilst tPA+DNase in-situ

- Return circuit to free drainage.
- Inform medical or senior nursing staff and document as necessary.
- **Do not give following dose of tPA+DNase unless recommended by respiratory Consultant following review.**
- Administer analgesia if needed and as prescribed.

Fluid appears more bloodstained

- Inform medical or senior nursing staff and document as necessary.

Evidence or strong suspicion of intrapleural bleeding

- Inform medical and senior nursing staff urgently.
- Transfer patient to high care for continuous monitoring.
- Ensure patient has IV access, urgently.
- Take bloods for FBC, clotting, Group and save and U&E's urgently.
- Review drug chart and stop all antiplatelet and/or anticoagulant medications.
- Take sample of pleural fluid in ABG syringe directly from drain, measure haematocrit on ward blood gas analyser (>50% of serum haematocrit is diagnostic for haemothorax).
- Consider further management which may include CT thorax with angiography; intercostal artery embolization/ligation (thoracic surgery) and/or blood transfusion/fluid resuscitation.

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?**
	Procedure should be performed by Respiratory Registrars, Consultant or ANP/ACP deemed competent in the procedure	Spot check Documentation	Yearly	ANP/ACP/Consultant	Respiratory lead Consultant	Yearly
	Correct procedure followed	Spot check Documentation	Yearly	ANP/ACP/Consultant	Respiratory lead Consultant	Yearly

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- Roberts ME, Rahman NM, Maskell NA etal (2022) British Thorax Society guideline for pleural disease *Thorax* accessed online https://doi.org/10.1136/thorax-2022-219784
- Piccolo F, Pitman N, Bhatngar R et al (2014) *Intrapleural tissue plasminogen activator and deoxyribonuclease for pleural infection:an effective and safe alternative to surgery.* Ann Am Thoracic society 11: 1419-1425
- Popowicz N, Bintcliffe O, De Fonseka D et al (2017) *Dose de-escalation of intrapleural tissue plasminogen activator therapy for pleural infection: the ADAPT project* Annals of the American Thoracic Society 14(6) 929-936
- WAHT-RES-027 Policy and procedure for non medical practitioners to perform chest drain insertion and pleural aspiration

Contribution List

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

Designation	
Clare Hooper	Respiratory Consultant
Bilal Niazi	Respiratory Consultant
Gulfram Mussawar	Respiratory Consultant
Kate Cusworth	Respiratory Consultant
Jamie Johnstone	Respiratory Consultant
Andy Crawford	Respiratory Consultant
Abhi Lal	Respiratory Consultant
Bethan Barker	Respiratory Consultant
Raj Anandavelu	Respiratory Consultant
Millie Harris	ARU Pharmacist

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

Committee
Respiratory Consultant team/directorate meeting

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 Patient Carers Visitors	❑ ❑ ❑ ❑	Staff Communities Other _____

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		x		
Disability		x		
Gender Reassignment		x		
Marriage & Civil Partnerships		x		
Pregnancy & Maternity		x		
Race including Traveling Communities		x		
Religion & Belief		x		
Sex		x		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Sexual Orientation		x		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)		x		
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)		x		

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	Heather Lloyd
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