# SESLHD PROCEDURE COVER SHEET



NAME OF DOCUMENT	Intra-Pleural Fibrinolysis - Medical Management of Empyema
TYPE OF DOCUMENT	Procedure
DOCUMENT NUMBER	SESLHDPR/631
DATE OF PUBLICATION	April 2024
RISK RATING	Medium
LEVEL OF EVIDENCE	National Safety and Quality Health Service Standards: Standard 1 – Clinical Governance Standard 4 – Medication Safety
REVIEW DATE	April 2027
FORMER REFERENCE(S)	N/A
EXECUTIVE SPONSOR	SESLHD Clinical Stream Director, Medicine
AUTHOR	A/Prof Ben Kwan Sutherland Hospital Respiratory Medicine
POSITION RESPONSIBLE FOR THE DOCUMENT	SESLHD Clinical Stream Manager, Medicine carolyn.smith1@health.nsw.gov.au
FUNCTIONAL GROUP(S)	Cardiac and Respiratory Care
KEY TERMS	Empyema, Intra-pleural Fibrinolysis, Alteplase / Dornase Alfa, intra-pleural fibrinolytic therapy, Respiratory
SUMMARY	Intra-pleural Fibrinolysis, in appropriately selected patients, is an option for the treatment of empyema or fibrin bands that develop within complex pleural fluid collections. Intra-pleural fibrinolysis is aimed at dissolving the fibrin bands that develop within a complex pleural fluid collection or empyema and will aid the drainage of that effusion / collection. This is performed via an intercostal catheter or pigtail pleural catheter, inserted into the pleural space to remove fluid from the pleural cavity and attached to an underwater seal drain (UWSD). Current evidence recommends, instillation of a solution of 5mg dornase alfa in 50mL of sodium chloride 0.9% and 2.5-10mg alteplase in 50mL of sodium chloride 0.9% into the pleural cavity every 12 hours up to three consecutive days.

COMPLIANCE WITH THIS DOCUMENT IS MANDATORY

This Procedure is intellectual property of South Eastern Sydney Local Health District.

Procedure content cannot be duplicated.



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

#### 1. POLICY STATEMENT

This procedure should be used in conjunction with:

- NSW Ministry of Health Information Bulletin IB2023 052 Consent to gender affirming medical treatment – update to Consent to Medical and Healthcare Manual
- NSW Ministry of Health Policy Directive PD2017 032 Clinical Procedure Safety
- NSW Ministry of Health Policy Directive PD2022 032 Medication Handling
- SESLHDPR/528 Sedation: Procedural Sedation (Adults, Ward, Clinic and Imaging areas)
- SGSHHS Underwater Seal Drain (UWSD)
- SGSHHS Intravenous (IV) medication, therapy and additives
- NSW ACI ACI/D14/2115 Minimum Standards Safe Procedural Sedation
- NSW ACI ACI/D14/1571 Pleural Drains in Adults A Consensus Guideline.

#### 2. BACKGROUND

#### **Treatment Aim:**

- Intra-pleural Fibrinolysis, in appropriately selected patients, is an option for the treatment
  of empyema or fibrin bands that develop within complex pleural fluid collections. Other
  therapeutic alternatives include surgical decortication or video-assisted thoracoscopic
  (VATS) procedure (i.e., performed by a cardiothoracic surgeon in an operating theatre).
  Intra-pleural fibrinolysis can be used where other therapeutic alternatives are
  inappropriate or contra-indicated.
- Intra-pleural fibrinolysis is aimed at dissolving the fibrin bands that develop within a complex pleural fluid collection or empyema and will aid the drainage of the effusion / collection. Treatment includes instillation of a solution of 5mg dornase alfa in 50mL of sodium chloride 0.9% and clinician-determined variable dosage (multiples of 2.5mg) between 2.5mg 10mg alteplase in 50mL of sodium chloride 0.9% into the pleural cavity via an intercostal catheter or pigtail pleural catheter connected to an UWSD.\*
- Suction to aid pleural drainage before and after Intra-pleural fibrinolysis is usually unnecessary. When suction is applied it should not exceed -20cm of H2O or equivalent.
- This procedure may be performed twice daily up to three consecutive days (total 6 doses, with at least 6 hours in between doses).

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 1 of 9



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

#### **Definitions and Abbreviations:**

Етруета	A collection of purulent material in the pleural space. Usually secondary	
	to pneumonia.	
Intercostal catheter	costal catheter  A catheter enabling drainage of air or fluid from the pleural space,	
(ICC)	allowing negative intra-thoracic pressures to be re-established leading	
	to lung re-expansion.	
Loculations/septations	A group of chambers / cavities usually isolated from surrounding	
_	structures (as by a fibrous tissue septum).	
Pigtail pleural catheters A small bore catheter specifically used in draining loculated pleural		
(PPC)	effusion. PPC are efficacious and comfortable with minimal risk of	
	complications.	
Tunnelled indwelling	Soft silicone small bore catheter surgically inserted, that allows	
pleural catheter (TPC)	intermittent ambulatory drainage of pleural fluid into underwater seal	
	drainage system or plastic vacuum bottles.	
Pleural effusion	A collection of fluid in the pleural space. The fluid restricts expansion of	
	the lung reducing vital capacity and the volume of air available for	
	gas exchange.	
Video-assisted	Video-assisted thoracoscopic surgery is a type of thoracic surgery	
thoracoscopic surgery	performed using a small video camera that is introduced into the	
(VATS)	patient's chest via small incisions.	

### Indications for intra-pleural fibrinolysis

- Community or hospital acquired pneumonia complicated by thoracic empyema or
  pleural sepsis as defined by pleural fluid with the physical characteristics of pus, a
  positive gram stain for bacteria, pH<7.10, lactate dehydrogenase (LDH) >1000IU/L,
  pleural fluid / blood glucose ratio <0.25 and differential cell count confirming a
  predominance of neutrophils (>10000/mm³ or 10x109/L)
- Loculations / septations may be confirmed on ultrasound (preferable) or CT scan imaging.

#### **Contraindications for Fibrinolytic**

- Treatment with streptokinase (not available in Australia), dornase alfa or urokinase in the past two years for empyema (excluded in MIST-2). Repeated systemic administration of streptokinase has been linked with a higher incidence of allergic reaction and formation of anti-streptokinase antibody which may reduce its therapeutic efficacy.
- Past medical history of coagulopathy, excessive bleeding states or anticoagulation / antiplatelet medications (recommend INR < 1.5 and partial thromboplastin time (PT) < 50s, and platelet count >100)
- 3. Presence of a bronchopleural fistula
- 4. Haemorrhagic stroke, cranial neoplasms, cranial surgery, head trauma within the preceding 14 days or recent major surgery within 10 days. **Discussion with the Neurologist involved or Surgeon (if patient has had recent surgery) is advised.**
- 5. Previous hypersensitivity reaction to dornase alfa or urokinase / streptokinase
- 6. Overwhelming sepsis.

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 2 of 9



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

### Patients on antiplatelet agents or anticoagulants

- In patients on antiplatelet agents (other than aspirin) or therapeutic anticoagulation, the medication should be withheld before administration of intrapleural fibrinolytics if it is clinically feasible and appropriate. Discussion with relevant AMO or Haematology regarding clinical need of antiplatelet/anticoagulants is advised.
- In patients with clinically significant systemic coagulopathy, fibrinolytics should be avoided unless the coagulopathy is corrected.

### **Prerequisites for Fibrinolytic**

- Patients selected for fibrinolytic therapy should have clear clinical and laboratory evidence of a complex pleural effusion or empyema.
- There should be evidence of lung re-expansion without evidence of bronchial obstruction or fibrotic-trapped lung after the pleural effusion has been drained.

## Lower dosing

- There is clinical report to suggest that starting with dosage less than 5mg alteplase might be as effective as 5mg alteplase, and emerging evidence 5mg alteplase is as effective as 10mg alteplase. If lesser dosage of alteplase is administered, dose escalation up to 10mg may be considered if clinical and radiological improvement is not seen.
- There is weak evidence to suggest that once or twice daily instillation of intrapleural alteplase and dornase alfa have similar efficacy and safety. If a once daily regimen is selected, changing to twice daily dosing should be considered if clinical and radiological improvement is not seen.

#### 3. RESPONSIBILITIES

- **3.1 Line Managers will:** ensure staff have the necessary training to perform their clinical roles in relation to this procedure and have access to necessary equipment. That a dedicated airway monitor is present throughout the procedure if sedation is given.
- **3.2 Medical staff will:** undergo any necessary training in relation to performing the procedure. The proceduralist will ensure there is a dedicated airway monitor present throughout the procedure if sedation is given.

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 3 of 9



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

#### 4.1 PROCEDURE

## 4.1 Necessary Equipment / Consumables and Medication / Solutions

Equipment / Consumables	Medications / Solutions	
<ul> <li>Large dressing pack and extra wool swabs</li> <li>1 x sterile pot / container</li> <li>4 x 50ml catheter tip or luer lock syringe</li> <li>10 ml syringe</li> <li>18g needles</li> <li>2 x Howard Kelly (atraumatic/smooth) tubing clamps</li> <li>Disposable draw sheet</li> <li>Personal protective equipment including eye protection and sterile gloves.</li> <li>Underwater Seal Drainage system (UWSD)</li> <li>Sterile labels and pen.</li> </ul>	<ul> <li>5mg of dornase alfa (obtained from pharmacy) diluted in 50mL sodium chloride 0.9%</li> <li>2.5mg - 10mg of alteplase (obtained from pharmacy) diluted in 50mL of sodium chloride 0.9%</li> <li>Sterile bottle 0.9% sodium chloride</li> <li>Chlorhexidine or iodine antiseptic (ensure no allergy to these agents).</li> </ul>	

## 4.2 Pre-procedure preparation

- 1. An ultrasound of the pleural space must be obtained prior to the procedure to estimate the quantity of fluid, degree of loculation / adhesion within the fluid and incomplete lung re-expansion ("trapped lung").
- 2. Informed and written consent MUST be obtained as per NSW Ministry of Health Information Bulletin IB2023 052 Consent to gender affirming medical treatment update to Consent to Medical and Healthcare Manual
- Clinical procedure safety checklist Level 2 (or 3 if procedural sedation administered)
   MUST be conducted to determine correct patient, procedure and site as per <u>NSW</u>
   Ministry of Health Policy Directive PD2017 032 Clinical Procedure Safety
- All patients should be commenced on pulse oximetry prior to and monitored throughout the procedure. A full set of observations including pulse and blood pressure should be undertaken just prior to the procedure according to <u>SESLHDPR/528 – Sedation: Procedural Sedation (Adults, Ward, Clinic and Imaging Areas)</u>

**NB** Intrapleural fibrinolysis via TPC is restricted to Sutherland Hospital and St George Hospital within SESLHD

#### 4.3 Premedication

 Premedication administered as per written order (for IV medication administration refer to relevant site documents) – if IV midazolam or fentanyl is administered it must be administered by a MO (not the proceduralist) according to NSW ACI ACI/D14/2115

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 4 of 9
COMPLIANCE WITH THIS DOCUMENT IS MANDATORY



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

Minimum Standards - Safe Procedural Sedation. Flumazenil and naloxone (reversal agent for midazolam and fentanyl respectively) should be readily accessible in the procedural room at the time of the procedure. **NB:** An extra RN for airway management must also be present in compliance with NSW ACI policy.

- All medications i.e., alteplase, dornase alfa and sodium chloride 0.9% flushes, premedications must be prescribed on the inpatient electronic medication chart.
- Ensure that the patient receives adequate analgesia by using a suitable pain scale to assess the efficacy of analgesia pre and post administration.
- If the patient is very anxious, an anti-anxiolytic agent may be considered (coadministration of anxiolytic agent increases the risk of central nervous system depression with midazolam / fentanyl).

### 4.4 Procedure for Alteplase / Dornase Alfa instillation

### **Policy Points:**

Preparation and instillation of alteplase into the pleural space must be carried out by a MO using aseptic technique.

This procedure may be performed twice daily up to three consecutive days (6 doses). Ensure there is at least 6 hours in between doses.

Number of doses should be individualised on the basis of condition (e.g., trends in serum inflammatory markers, fever curve, and white cell count) and radiographic (e.g., effusion improvement on chest radiography and bedside ultrasonography) response to treatment

This is a two person procedure. Assistance from a RN is required.

Chest tube should be clamped for at least 1 h after administration of intrapleural fibrinolytic and dornase alfa therapy.

A dedicated airway monitor must be present throughout the procedure if procedural sedation is given.

A chest xray post procedure can be considered to assess response.

Suction to aid pleural drainage before and after intra-pleural fibrinolysis is usually unnecessary. When suction is applied it should not exceed -20cmH2O or equivalent.

# intrapleural fibrinolysis via TPC is only restricted to Sutherland Hospital and St George Hospital within SESLHD

#### 4.4.1 Alteplase / Dornase Alfa Preparation

Step 1. Draw up 10mL of water for injection and inject into alteplase vial to reconstitute it. The solution must be clear and colourless.

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 5 of 9



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

- Step 2. Add the alteplase solution (medically prescribed dose only, discard excess dose if required) to the sterile pot container from the large sterile dressing pack.
- Step 3. Then add 40mL of sodium chloride 0.9% to the alteplase in the pot. Stir with end of syringe to combine.
- Step 4. Draw up the alteplase solution into one 50mL syringe (LABEL it alteplase).
- Step 5. Draw up two 2.5mL dornase alfa ampoules and add these to a new sterile pot container.
- Step 6. Then add 45mL of sodium chloride 0.9% to the dornase alfa in the pot. Stir with end of syringe to combine.
- Step 7. Draw up the dornase alfa solution into one 50mL syringe (LABEL it dornase alfa).
- Step 8. Stability of dornase alfa diluted in NS or sterile water has not been formally evaluated; use immediately after preparation.

### 4.4.2 Ensuring Tube Patency

- Step 1. Turn off the three way tap or clamp the catheter to the patient.
- Step 2. Take a 50mL syringe with 30mL of sodium chloride 0.9% in it.
- Step 3. Connect the syringe to either the three-way tap or catheter.
- Step 4. Either turn the three way tap off towards the underwater sealed drain or release the clamp.
- Step 5. Using the 50mL syringe filled with 30mL of sodium chloride 0.9% draw back and insert the sodium chloride 0.9% and then draw back to check patency of the catheter.
- Step 6. Unless the catheter fluid is oscillating with respiration then the procedure cannot proceed.

#### 4.4.3 Alteplase / Dornase Instillation

- Step 1. Turn the three way tap off or clamp the drain to the patient.
- Step 2. Connect the syringe containing alteplase solution to the catheter and turn the three way tap off towards the underwater sealed drain or release the clamp.
- Step 3. Slowly inject the solution.
- Step 4. Attach syringe containing 10mL of sodium chloride 0.9% to catheter instil saline towards the patient.
- Step 5. Turn the three way tap off to the patient or clamp the drain.
- Step 6. Connect the syringe containing dornase alfa solution to the catheter and turn the three way tap off towards the underwater sealed drain or release the clamp
- Step 7. Slowly inject the solution.
- Step 8. Turn the three way tap off to the patient or clamp the drain
- Step 9. Attach syringe containing 10mL of sodium chloride 0.9% to catheter instil saline towards the patient.
- Step 10. Turn three way tap on and flush the drain.
- Step 11. Turn the three way tap off to the patient or clamp the drain for at least 60 minutes.

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 6 of 9



## Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

### 4.4.4 Management Post Intra-Pleural Fibrinolysis

- Following instillation of the alteplase / dornase alfa, chest tube should be clamped for at least 1 hour
- The PPC, TPC# or ICC is then allowed to be on free drainage
- Output via the drain may be blood stained. Periodic monitoring of Hb levels is recommended according to the clinical situation
- Post procedure chest X Ray to be performed within 24 hours
- After the alteplase / dornase alfa has been instilled, flush the drain with 10-20mL of sodium chloride 0.9% every six (6) hours until drain is removed. Sodium chloride 0.9% flushes should be documented in the clinical notes and electronic medication chart
- The number of doses should be individualised on the basis of clinical response (e.g., trends in serum inflammatory markers, fever curve, and white cell count) and radiographic (e.g., effusion improvement on chest radiography and bedside ultrasonography) response to treatment
- Maximal treatment dosage is 2 instillations daily up to total of 3 days (i.e. 6 instillations in total).
- Provided the pleural fluid has been drained to the satisfaction of the MO, then the ICC or PPC will be requested for removal as per written medical orders found within the electronic medical record
- During the administration of this therapy, vital signs observations are to be attended every 15 minutes, then hourly for 4 hours and 4 hourly for 24 hours post therapy
- Required observations as per facility UWSD management CBR (refer to facility UWSD clinical business rule).
  - POWH:
    - POWH CLIN003 Chest Drains: Insertion Management and Removal
  - SGH:
    - SGH CLIN 654 Indwelling Pleural Catheter (IPC) Insertion and Management
  - TSH:
    - TSH CLIN 620 Insertion Of Intercostal (ICC), Pleural Catheters (PPC), Management Of Underwater Seal Drain (UWSD) And Removal
- The patient should be assessed for pain and receive regular analgesia post procedure as clinically indicated and as prescribed by the MO.

#### 5. DOCUMENTATION

- UWSD chart
- Premedication must be prescribed on the medication chart
- Alteplase / dornase alfa / sodium chloride 0.9% flushes must be prescribed on the inpatient medication chart
- MO to document the procedure, outcome and further instructions in the clinical notes.

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 7 of 9



# Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

- MO to order CXR post procedure
- Nursing staff to document UWSD observations and any unexpected post procedures observations and patient reports of pain post procedure.

#### 6. AUDIT

Via incidents and IMS+.

#### 7. REFERENCES

1.	Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema (Cochrane Review). Cameron RJ, Davies HRHR.2009. Cochrane Collaboration.		
2.	Intra-pleural fibrinolytic therapy versus placebo, or a different fibrinolytic agent, in the treatment of adult parapneumonic effusions and empyema (Cochrane Review). Altmann ES et al. HRHR.2019. Cochrane Collaboration.		
3.	Standard Operating Procedure for alteplase/dornase alfa. Y C Gary Lee MBChB PhD FCCP FRACP. Respiratory Dept, Sir Charles Gairdner Hospital, WA March 2011		
4.	Intrapleural Fibrinolytic Therapy for Empyema and Pleural Loculation: Knowns and Unknowns. Idell S and Rahman NM. Annals of the American Thoracic Society 2018		
5.	Use of fibrinolytics and deoxyribonuclease in adult patients with pleural empyema: a consensus statement. Chaddha U, et al. Lancet Resp Med 2021		
6.	Popowicz N et al. Dose De-escalation of Intrapleural Tissue Plasminogen Activator Therapy for Pleural Infection. Ann Am Thorac Soc. 2017 Jun;14(6):929-936.		
7.	Akulian, J et al, Bleeding Risk With Combination Intrapleural Fibrinolytic and Enzyme Therapy in Pleural Infection, Chest 2022 162(6), 1384-1392		
8.	Popowicz N et al. Alteplase Dose Assessment for Pleural infection Therapy (ADAPT) Study-2: Use of 2.5mg alteplase as a starting intrapleural dose. Respirology. 2022;27(7):510-516.		
9.	NSW Ministry of Health Information Bulletin IB2023 052 - Consent to gender affirming medical treatment – update to Consent to Medical and Healthcare Manual		
10.	NSW Ministry of Health Policy Directive PD2017_032 - Clinical Procedure Safety		
11.	NSW Ministry of Health Policy Directive PD2022_032 - Medication Handling		
12.	SESLHDPR/528 – Sedation: Procedural Sedation (Adults, Ward, Clinic and Imaging Areas)		
13.	POWH Clinical Business Rule CLIN003 Chest Drains: Insertion		

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 8 of 9

# Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

	Management and Removal	
14.	SGH Clinical Business Rule CLIN 654 Indwelling Pleural Catheter (IPC) Insertion and Managing	
4.5		
15.	TSH Clinical Business Rule CLIN 620 Insertion Of Intercostal (ICC), Pleural	
	Catheters (PPC), Management Of Underwater Seal Drain (UWSD) And	
	Removal	

#### 8. VERSION AND APPROVAL HISTORY

Date	Version No.	Author and approval notes	
August 2018	DRAFT	Draft approved by Dr Ben Kwan (Author) and Dr Mark Sader (Executive Sponsor)	
September 2018	DRAFT	Processed by Executive Services prior to submission to SESLHD Quality Use of Medicine Committee and SESLHD Clinical and Quality Council	
October 2018	1	Approved by SESLHD Quality Use of Medicines Committee and SESLHD Clinical and Quality Council for publishing.	
October 2021	2	Minor review by A/Prof Ben Kwan (Author). Approved by Executive Sponsor. To be tabled at Quality Use of Medicines Committee.	
December 2021	2	Endorsed by Quality Use of Medicines Committee with minor amendments.	
January 2022	2	Processed and published by SESLHD Policy	
24 April 2024	2.1	Minor review to update alteplase dosage and administration process (Dr Arnab Chatterjee and Mary Dunford CNC in consultation with A/Prof Ben Kwan, Dr Eric Wong, Dr Fedil Metti). Added step 8 to 4.4.1. Approved by SESLHD Drug and Therapeutics Committee.	

Version: 2.1 Ref: T18/49386 Date: 24 April 2024 Page 9 of 9