Continuous Intravenous Vancomycin Infusion in Adult Intensive Care Units at UHL.

Prescription Chart and Guideline

Addressograph S Number Name DOB
Site: LRI / GH
Date

Chart ……..of ……

1. Introduction and Who Guideline applies to

This guideline covers the use of intravenous vancomycin prescribed as a continuous infusion, on the adult intensive care (ICU) areas in the University Hospitals of Leicester (UHL) at the LRI and GH sites.

Continuous infusion intravenous vancomycin administration entails administering a loading of vancomycin followed immediately with a maintenance infusion, i.e. no breaks in infusions.

Continuous infusion of vancomycin is for treatment only and is preferred, when practical, for patients with severe or deep-seated infections (e.g. pneumonia, endocarditis, bone and joint infections or whilst on Extracorporeal Membrane Oxygenation (ECMO) or Continuous Venovenous Haemodiafiltration (CVVHDF).

Information regarding antimicrobials can also be found on the Antimicrobial website/app.

Vancomycin can also be administered as an intermittent (pulsed) infusion – refer to existing UHL guidance in the Antimicrobial website/app.

1.1 Contra-indications

- Contra-indications – hypersensitivity to vancomycin or any of the excipients.

1.2 Cautions

- To avoid the risk of vancomycin infusion reaction (previously referred to as “red-neck/red-man syndrome”), pain or muscle spasm, ensure that the administration rate is not faster than 10 mg per minute. See tables for timings during loading and maintenance.
- If the patient weighs more than the adjusted body weight for their height then the adjusted body weight needs to be used to estimate their renal function when calculating the initial maintenance dose.
- Concurrent administration of neurotoxic and / or nephrotoxic agents increases the risk of adverse effects. Cautious co-administration is advised with the following:
    - Amphotericin
    - potent diuretics
    - Aminoglycosides
    - NSAIDs, and
    - ACE inhibitors
- Patients with previous hearing loss.

The above list is not exhaustive – for further information consult with:

- The BNF
- The ICU ward pharmacy team for your site or the on-call pharmacist via switchboard
- The Summary of Product Characteristics (eSPC) for a full list https://www.medicines.org.uk/emc/search?q=%22Vancomycin%22
- Further information including contact details for the medical microbiology service can be found on the Antimicrobial website/app “UHL key contact information”.

1.3 Exclusion

This guideline doesn’t apply to

- Patients with Creatinine Clearance (CrCl) of less than 20 ml/min unless on CVVHDF.
- Patients on overnight CVVHDF
- Patients on SLED, IHD or any other modalities of dialysis.
- Patients not on ICU
- Please refer to standard intermittent dosing regimens in these particular patient groups and/or contact the pharmacy or renal team for advice as needed.

The prescription on the ICU drug chart must indicate the patient is on continuous intravenous vancomycin infusion.

2.1 Prescribing and documentation

STEP 1: Do you need to load?

If a patient is admitted to ICU on intermittent vancomycin:

- Use **ACTUAL** body weight
- Loading doses are not required if switching to 24 hour vancomycin infusion ICU guideline from intermittent regimens used on baseline ward within UHL.
- Move to step 2 to calculate Creatinine Clearance or step 3 if started on CVVHDF (prescribe initial maintenance dose as per Table 3a or 3b) no earlier than 6 hours after last dose.
- **Do not miss doses** unless there is a suspicion of elevated levels.
- For all other patients newly initiated on vancomycin prescribe a loading dose as indicated in Table 1.

Table 1: Initial LOADING dose in newly started patients

ACTUAL Body Weight	Dose	Volume of fluid* for PERIPHERAL use	Volume of fluid* for CENTRAL use	Infusion Duration
<40 kg	750 mg	250 ml	100 ml	90 minutes
40 – 59 kg	1000 mg	250 ml	100 ml	120 minutes
60 – 90 kg	1500 mg	500 ml	250 ml	180 minutes
>90 kg	2000 mg	500 ml	250 ml	240 minutes

* Can be diluted in either 0.9% Sodium Chloride or 5% Glucose.
There is no need to remove a volume equivalent to the reconstituted vials.

Maintenance dose must be prescribed and started immediately after loading dose has been administered to facilitate continuous intravenous infusion

STEP 2: Calculate Creatinine Clearance if not on CVVHDF

Despite its limitations in estimating renal function, the Cockcroft-Gault equation is used to calculate Creatinine Clearance (CrCl) to provide an estimate to determine the initial maintenance dose in step 3.

The use of estimated glomerular filtration rate (eGFR) is NOT recommended or validated for vancomycin dosing.

CrCl should be calculated on initiation in all patients not on CVVHDF and especially in all patients who have recently trialled off CVVHDF. This, along with urine output, is used to help establish a suitable maintenance dose in worsening renal function and/or renal function recovery post CVVHDF or AKI.

If the patient's urine output has reduced since creatinine was monitored, do not rely on this CrCl as an estimate. If anuric or oliguric (i.e., urine output <0.5 ml/kg/hr), consider if the patient is going to be filtered with CVVHDF. If so dose according to Table 3c in step 3.

Dosing Weight: Use actual body weight or adjusted body weight, whichever is lower:

Table 2: **Adjusted** Body Weight Table

Height		Dosing Weight (kg)	
Metres	Feet. Inches	Men (kg)	Women (kg)
1.52	5' 0"	60	55
1.54	5' 1"	63	57
1.57	5' 2"	66	60
1.60	5' 3"	68	63
1.62	5' 4"	71	66
1.65	5' 5"	74	68.5
1.67	5' 6"	77	71
1.70	5' 7"	79	74
1.72	5' 8"	83	77
1.75	5' 9"	85	80
1.77	5' 10"	88	82
1.80	5' 11"	90	85
1.82	6' 0"	93	88
1.85	6' 1"	96	90
1.87	6' 2"	99	93
1.90	6' 3"	101	96
1.93	6' 4"	104	99
1.95	6' 5"	107	102

- To calculate, use the online calculator on the Trust Antimicrobial website/app. This is located under 'Tools' on the mobile app.
- If unavailable, use the equation below:

Estimation of creatinine clearance (CrCl) using Cockcroft Gault equation

$$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{dosing weight in kg} \times 1.23 \text{ for males OR } 1.04 \text{ for females}}{\text{serum creatinine (micromol/L)}}$$

Dosing Weight: Use the lower of the actual body weight or adjusted body weight

STEP 3: Prescribe the INITIAL MAINTENANCE Continuous Infusion Dose

Due to stability, the total daily dose must be administered as TWO consecutive 12 hour infusions

Table 3a: INITIAL MAINTENANCE (PATIENTS NOT ON CVVHDF)

Dosing Weight: Use the lower of the actual body weight or adjusted body weight

CrCl (mL/min)	Dose to be administered over 12 hours as continuous intravenous infusion.
>110	1500 mg
90-110	1250 mg
75-89	1000 mg
55-74	750 mg
40-54	500 mg
30-39	375 mg
20-29	250 mg
<20	NOT RECOMMENDED $

$ Contact Pharmacy, the microbiologist or refer to the Antimicrobial website/app if further advice is needed.

Table 3b: CVVHDF INITIAL MAINTENANCE

USE ACTUAL BODY WEIGHT

Actual body weight	Dose to be administered over 12 hours as continuous intravenous infusion.
OVER 100 kg	1000 mg
50-100 kg	750 mg
UNDER 50 kg	500 mg

Volumes for peripheral or central infusions can be found in Table 3c overleaf

Notes:

- Patients who have unusual clinical characteristics, such as extremes of body weight, age and chronic metabolic disorders, may require further dose adjustments and require closer monitoring. Contact the pharmacist for advice.
- Patients on CVVHDF may have augmented renal clearance if treatment has been commenced for acidosis, alkalosis, fluid or drug removal only. Discuss with your Pharmacist should this be a possibility.
- Dosing schedule for initial maintenance dose on CVVHDF, is based on local practice and experience by ICU medical and pharmacy teams, using the Prismaflex machines and ST150 or Oxiris filter sets. Caution should be exercised in the event of filter set shortages and substitutions, or if the machine is set up for a different modality of treatment (e.g. CVVH, SLED, HD).

INFUSION RATES AND VOLUMES

- **Infusions can be diluted in either 0.9% Sodium Chloride or 5% Glucose. Initial bag sizes written in [brackets]**
- **There is no need to remove a volume equivalent to the reconstituted dose in the vials**
- **Do not administer more than 5g in a 24 hour period**
- **Giving sets to be changed at 72 hrs for continuous infusions**

Table 3c: Vancomycin infusion volume and rates

12 hourly dose	PERIPHERAL line		CENTRAL line	
	Total volume ** (ml)	Rate of infusion (ml/hour)	Total volume ** (ml)	Rate of infusion (ml/hour)
2500 mg	[500ml] 580	48.3	[250ml] 321	26.8
2250 mg	[500ml] 575	47.9	[250ml] 316	26.3
2000 mg	[500ml] 570	47.5	[250ml] 311	25.9
1750 mg	[500ml] 565	47.1	[250ml] 306	25.5
1500 mg	[250ml] 301	25.1	[250ml] 301	25.1
1250 mg	[250ml] 296	24.7	[100ml] 136	11.3
1000 mg	[250ml] 291	24.3	[100ml] 131	10.9
750 mg	[250ml] 286	23.8	[100ml] 126	10.5
500 mg	[100ml] 121	10.1	[100ml] 121	10.1
375 mg	[100ml] 118.5	9.9	[100ml] 118.5	9.9
250 mg	[100ml] 116	9.7	[100ml] 116	9.7

Initial bag sizes are written in [brackets]

Notes

Bag overages

- The above rates of infusion take account of average industry variances in filling volume of the Baxter fluid bag. In other words each bag has an overage i.e.
  - 100ml bag = 111ml; 250ml bag = 271ml; 500ml bag = 530ml

Reconstitutes vancomycin vials

- Each 500mg vial of reconstituted vancomycin makes 10ml and
- Each 1000mg vial of reconstituted vancomycin makes 20ml

****Total volume** = Volume of fluid in bag including average variance
PLUS
Volume of reconstituted powder

STEP 4: Monitor the Vancomycin Levels and Reassess the Continuous Infusion Dose

General points

- Target concentration levels for continuous intravenous vancomycin infusions are not the same as that used for intermittent infusions. Please refer to the Antimicrobial website/app for appropriate levels in intermittent vancomycin infusions.
- Document any action taken in the medical notes.
- Review the need for vancomycin on a daily basis.

Plasma concentrations are meaningless unless the timing of both DOSE and LEVELS are accurately recorded

- Due to wide variability in the body's handling of vancomycin, early analysis of vancomycin levels is required to ensure that the dosage regimen is appropriate.
- Take a sample **12** hours after starting the continuous infusion (this will usually be during the second 12 hourly bag), then all subsequent levels daily (with morning bloods) unless otherwise directed. (Avoid sampling via the line used for vancomycin infusion.)
- Levels **can** be taken whilst the infusion is still being administered. They **do not** need to be taken when the bags are changed.
- Levels **can** be taken on the routine morning bloods if the continuous infusion has been running for a minimum of 12 hours.
- Samples must be labelled as "**RANDOM**" on Nervecentre to distinguish from other vancomycin protocols.
- **Infusions must be continued whilst awaiting levels, unless specified by the senior doctor on duty.**
- Monitor creatinine and urine output daily.
- Record the time the blood sample was drawn on the request form and the sample tube.

Target vancomycin concentrations

- The target range for all patients including those that are **seriously ill (severe or deep-seated infections including ECMO and endocarditis), is 20.1 – 25 mg/L.**
- Levels of 15.1 - 20 mg/L may be clinically appropriate in some patients. These individual cases will be discussed with the medical microbiologist and the ICU team, with clear documentation of target levels.
- If the patient is failing to respond, seek advice from microbiology or an infection specialist.

Adjustment of vancomycin doses - continuous infusion

- Always check that the dosage history and sampling time are appropriate before interpreting the result.
- Seek advice from pharmacy or microbiology if you need help to interpret the result.

If the measured concentration is unexpectedly HIGH or LOW, consider the following:

- Were the dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Renal function:
  - Has the patient stopped or started renal filtration or has there been an issue with filtration sets (i.e., downtime, filter set changes, clotted etc.)
  - Has it declined or improved?
  - Has the urine output declined?
  - Is the patient in urinary retention?
- Does the patient have oedema or ascites?

If concerned that the level reported is anomalous, take another sample (mark as urgent) before modifying the dosage regimen and / or contact pharmacy for advice

Table 4: Adjustment of Vancomycin Doses – continuous infusion

Vancomycin Concentration	Suggested dose change Do not administer more than 5g in a 24 hour period
0 – 10 mg/L	• STOP the continuous infusion • Reload according to Table 1 • Then restart the continuous infusion at a higher dose by increasing the 12 hourly dose by moving UP two rows in Table 3c
10.1 – 15 mg/L	• Move UP two rows in Table 3c
15.1 – 20 mg/L[#]	• Move UP one row in Table 3c • After discussion with microbiology a target of 15 to 20 mg/L may be clinically appropriate
20.1 – 25 mg/L	• If the patient is responding, maintain the present dosage regimen • If the patient is not responding contact microbiology for advice and consider alternative antibiotics
25.1 – 30 mg/L	• Move DOWN one row in Table 3c
>30.1 mg/L	• Move DOWN two rows in Table 3c

[#] **Levels of 15 to 20 mg/L may be clinically appropriate in some patients. These individual cases will be discussed with the medical microbiologist and the ICU team, with clear documentation of target levels.**

Start time of infusion after maintenance dose changed

Where Vancomycin levels indicate a dose needs amending, prescribe the new required dose and change bags as soon as possible. DO NOT wait for current bag to be completed. This action will prevent ongoing low levels or ongoing exposure to elevated levels

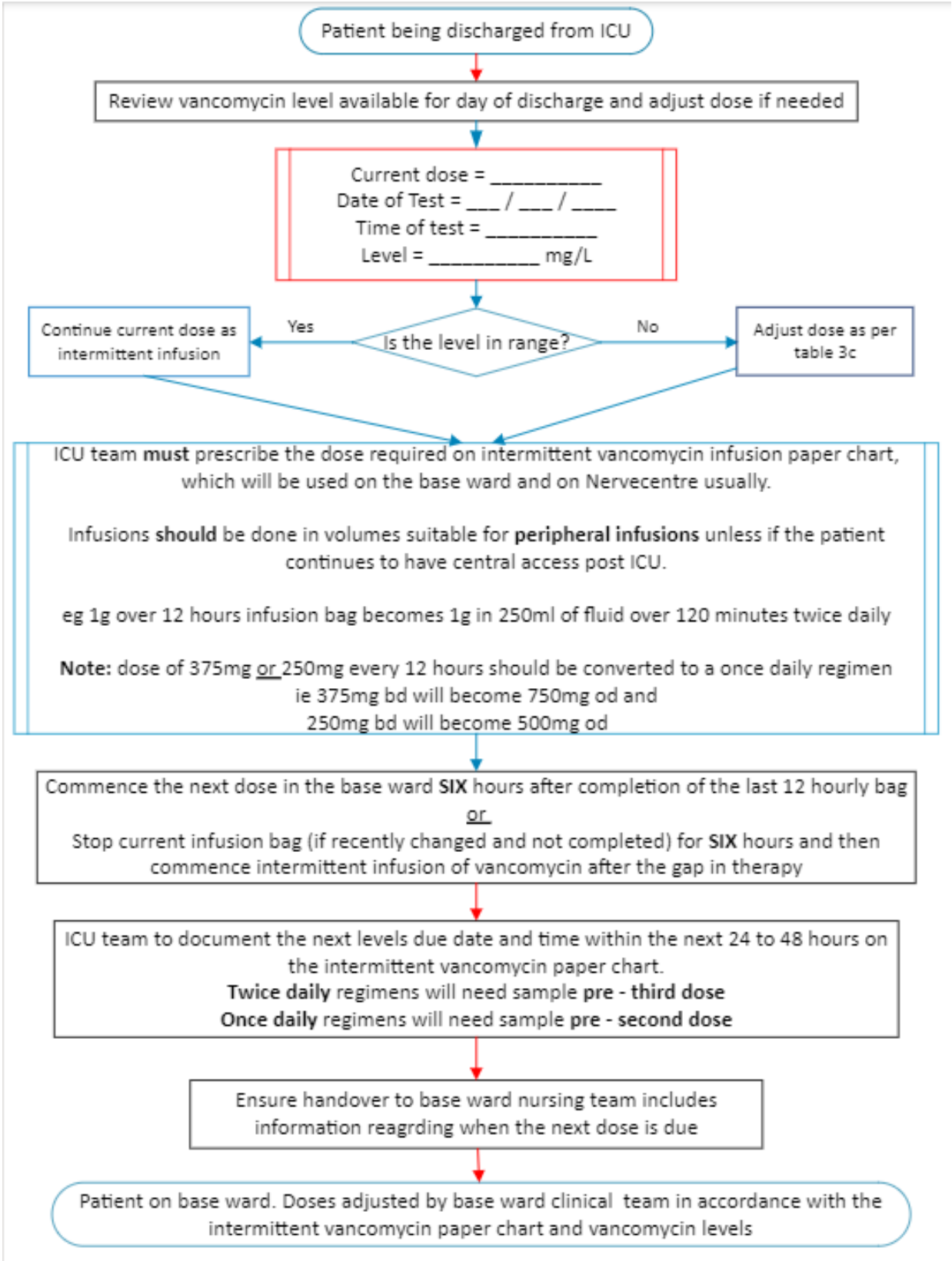
Level timing after dose change

After each dose change a vancomycin level must be taken after 12 hours, whilst the second bag at the new dose is being administered.

For practical purposes this can be timed to coincide with the routine morning bloods as long as at least 12 hours have passed.

STEP 5: Converting Continuous infusion to Intermittent Infusion vancomycin

Patients may be discharged back to base ward with continued need for Vancomycin. In order to convert patients back to intermittent infusions please follow the flowchart 1 below.



Flowchart 1: process to convert continuous vancomycin infusions to intermittent infusions

2.2 Trouble shooting for common scenarios

2.2.1 Level of vancomycin is not available and current bag is finished or due to finish infusing and no new prescription is written

- Ensure that a vancomycin level has been requested and sent to pathology.
- If required nurse or doctor can consider ringing the pathology department to establish the result

- If result **available** via phonecall
    - document level and contact details of laboratory staff
    - prescribe next two doses
- If result still **pending**
    - Inform pathology department of urgent need for result whilst on AICU**.**
    - Prescribe last dose to prevent break in therapy.
    - Re-check nervecentre for levels regularly.
    - Once received adjust dose as needed in Table 4.

2.2.2 Pause or stoppage in vancomycin therapy

If continuous vancomycin therapy has been stopped/paused, the infusions should be restarted at the previous rate as soon as practicable

Less than 4 hours	This may occur where patients have gone to XRAY, CT scans and short procedures. **No alteration to schedule of serum levels is advised**.
More than 4 hours	This may occur where access issues occur or patients have gone for long procedures. A **random level** should be taken at **6 hours** to check the level is in range. The dose may need to be altered as per Tables 4 and 3c, if out of range a subsequent level will be needed after 12 hours.

2.2.3 Interruption to CVVHDF therapy and continuation of vancomycin

- The ICU consultant in charge of the unit must be informed of the interruption to CVVHDF
- Patients who have stopped/paused CVVHDF for short term (e.g. line has clotted and awaiting new vas-cath) or longer term (e.g. trialling of CVVHDF), must continue vancomycin infusions and have levels of vancomycin taken **6 hours after stopping/pausing** CVVHDF even if dialysis is restarted
- Patients should be monitored for continued oliguria/anuria, alterations in diuretic therapy and worsening creatinine/urea levels as these patients may have higher vancomycin levels
- Doses should be adjusted as per Table 3c and previous doses should be immediately stopped when adjustments are made. Repeat vancomycin must be taken 6 hours after each dose alteration until the patient is in therapeutic range of 20.1 to 25 mg/L (See figure 2 below)

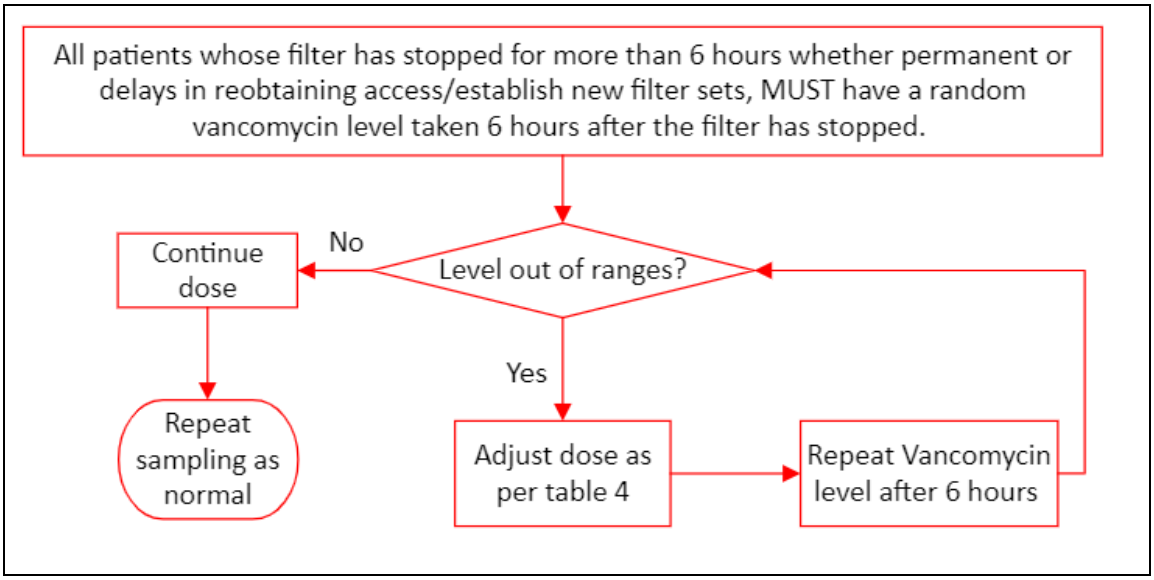


Figure 2: Sampling times of vancomycin with CVVHDF breaks in therapy

2.2.4 Dose has recently been changed and a level has been taken during the first new bag.

- **Vancomycin levels taken during the first bag after a change of dose will not represent the new steady state of vancomycin.**
- Levels should be taken during the second 12 hourly bag or in the morning bloods so long as the second bag has already being initiated.
- If a sample has been taken during the first bag a repeat sample should be sent and the infusions continued until the result is established. Dose adjustments should only happen after this has occurred.

3. Education and Training

Are there any new skills required to implement the guideline? Is a training programme being provided to support implementation or is it more a case of 'awareness raising'

If there are no education or training requirements please state 'None'.

No specific training or skills required.

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Safety incidences with continuous vancomycin infusions	Through Datix submissions	Medicine Safety Lead Pharmacist	Yearly	To ITAPS Q&S and AWP

5. Supporting References

1. Adapted from https://www.sapg.scot/media/4624/intravenous-vancomycin-use-in-adults-continuous-infusion-v01.pdf Accessed 1/02/22
2. A H Thomson et al (2009) Development and evaluation of vancomycin dosage guidelines designed to achieve new target concentrations, *J Antimicrob Chemother* (2009) 63 (5): 1050-1057.
3. M J Rybak et al (2020) Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health-Syst Pharm* (2020) 77 (11): 835 to 863. DOI 10.1093/ajhp/zxaa036.
4. B Philips. (2022) Vancomycin Drug profile in *Critical Illness*. Royal Pharmaceutical Society of Great Britain Online. Access via Medicines Complete. https://www.medicinescomplete.com/#/content/critical/98. Accessed 25th January 2023.

6. Key Words

List of words, phrases that may be used by staff searching for the Guidelines on PAGL. If none – state none.

- Vancomycin
- Critical Care
- Antibiotic

CONTACT AND REVIEW DETAILS	
Guideline Leads (Name and Title) Peeyoosh Pankhania - Advanced Specialist Pharmacist – ITAPS Graziella Isgro – Consultant in ICM and ECMO	**Executive Lead** ITAPS Pharmacy team

Guideline Authors (Name and Title)	Guideline Reviewed and Ratified by:
Peeyoosh Pankhania - Advanced Specialist Pharmacist – ITAPS Graziella Isgro – Consultant in ICM and ECMO Rosalind Saunders – Consultant Microbiologist	ITAPS Quality and Safety Board – May 2023 ITAPS Core Group – May 2023 Antimicrobial Working Party - July 2022

Details of Changes made during review:

V1:

- New guideline

V2:

- Added clarity to Step 1 page 3 and sentence in introduction page 2, to start continuous infusion bag immediately after loading dose
- Amended Step 3 maintenance dose page 14 to include
  - Infusion rates and total infusion volume reflective of and reference to Table 3c (page 6)
  - Instructions to document any issues on page 15 (previously on page 13)
  - Formating changes to include clearer instruction around giving set changes
- Instructions to change bag immediately if dose changes (i.e. not to wait for previous bag to finish) added to
  - Page 8, below dose adjustment Table 4
  - Page 14 maintenance dose prescription page
- Section 2.2 Trouble shooting for common scenarios. Page 10
  - Added extra section plan for vancomycin levels not available when maintenance bag is due to change . section 2.2.1.
  - Re-numbered subsequent trouble shooting plan
- Table 3c removed 50ml bag sizes for central use and switched to minimum 100ml bag size, to help mitigate infusions running out early
- Alterations to page 14 prescribing page to include clearer instructions

Adult ICU Vancomycin Continuous Infusion Prescription Chart

Weight Actual	**(kg)**	**Addressograph** **Name:** **S number:** **DOB:**
Weight Adjusted (See Table 2)	**(kg)**	
Height	**(metres)**	
Allergies	**Reactions**	

STEP 1: Loading or Stat dose

Stat doses (See Tables 1 and 4) & Loading doses (Sign Nervecentre for each bags change)

Prescription							Administration				Pharmacist Check
Date to be given	Time to be given	Vancomycin dose	Fluid	Volume	Infusion time	Prescribers name and signature	Given by	Checked by	Start Time	Finish Time	
Example 01/01/24	***10:00***	***1000mg***	***Sodium Chloride 0.9%***	***250ml***	***120 minutes***	***Dr S.S. Signature***	***AB***	***CD***	***10:00***	***12:00***	***PH***

STEP 2: Calculate Creatinine Clearance if not on CVVHDF

Calculated Creatinine Clearance	**---------- (ml/min)**	**Date Calculated**	**----/----/----**

Vancomycin Levels Record				**Target levels 20.1 to 25 mg/L (unless directed otherwise)**				
Date	Time level due	Requested by: Prescribers name and signature	Time level collected (Nurse to document)	Vancomycin Level (mg/L)	If not on CVVHDF		Dose Change required: Yes/no	Review by: Prescribers name and signature
					Creatinine Clearance (ml/min)	Signs of Anuric/oliguric?		
Example 02/01/24	***22:00***	***Dr S.S. Signature***	***22:00***	***15.3***	***57***	***No***	***Yes***	***Dr S.S. Signature***

Notes

- Levels can be taken on the morning bloods (avoid sampling from the line used to infuse vancomycin). The patient must have had a minimum of 12 hours of the maintenance infusion.
- Levels must be clearly documented with the time the sample was collected
- Samples must be labelled as **RANDOM LEVEL** to distinguish from other vancomycin protocols

STEP 3: Prescribe Maintenance Dose

Vancomycin infusion must be administered over 12 hours.
Prescribe the initial maintenance dose depending on the CrCl in Table 3a (or if they are on CVVHDF as in Table 3b).
All further doses to be adjusted as documented in Table 4
Infusions must be continued whilst awaiting levels, unless specified by the senior doctor on duty. I.e continue the current dose until the level is received and reviewed. Giving sets to be changed at 72 hrs for continuous infusions

Addressograph

Name:

S number:

DOB:

Maintenance doses, infusion volumes and rate of infusions appropriate for IV access can be found in Table 3c.	**All bags run over 12 hours. #**	**Sign Nervecentre chart for all bag changes (i.e. loading and maintenance doses)**	**Document any issues/problems on page 15**

Prescription								**Administration**				
Date	Time to be given	Vancomycin Dose (over 12 hours)	Central or Peripheral	Infusion fluid	Total Volume (ml)	Rate of infusion (ml/hour)	Prescribers signature and Name	Given by:	Checked by:	Start time	Finish time	Pharmacist Check
Example 1/1/2024	*14:00*	*1000mg*	*Central*	*Glucose 5%*	*131ml*	*10.9*	*Dr S.S. Signature*	*AB*	*CD*	*14:30*	*02:30*	*PH*

 # Where vancomycin levels indicate a dose needs amending, prescribe the new required dose and change bags as soon as possible.

DO NOT wait for current bag to be completed. This action will prevent ongoing low levels or ongoing exposure to elevated levels

The following page can be used to document issues encountered

Any entries must be dated, timed and include the staff members name.

Potential issues include

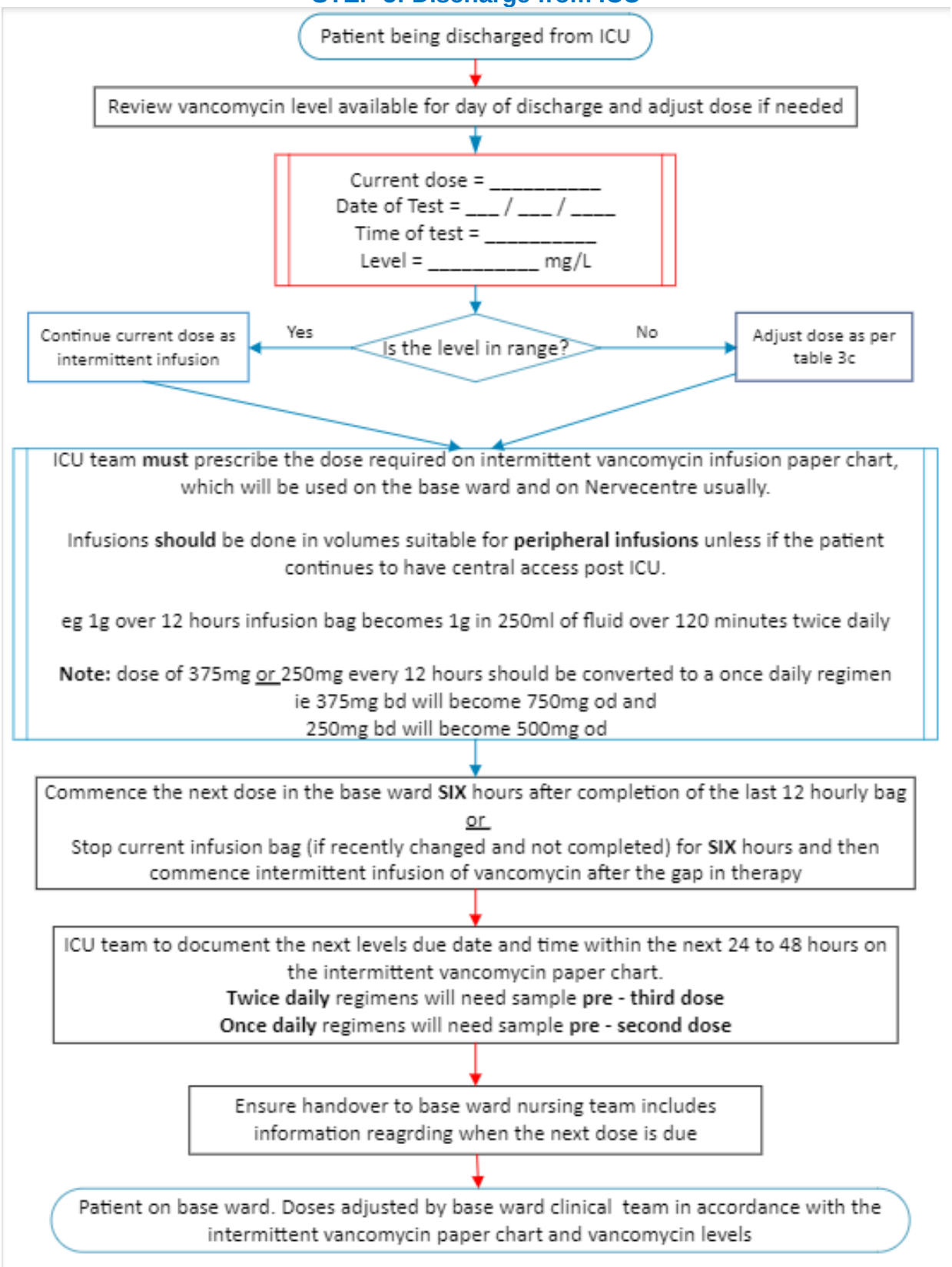
- Why vancomycin infusions are held (include dates, times, durations and reasons (ie in theatre/scans/procedures/line problems etc).
- For all infusions which finish more than 30 minutes before anticipation
- Other issues

Entry notes	Date/time/staff name

STEP 4: Monitor the Vancomycin Levels and Reassess the Continuous Infusion Dose

Adjust dose according to Table 4 above in the guideline and prescribe in the chart under Step 3

STEP 5: Discharge from ICU



Note: Discharged patients do not usually receive CVVHDF. Any adjustments made for use in CVVHDF must be reviewed in the context of ongoing need for and modality of renal preplacement required, if any.