1. Introduction and Who Guideline applies to

The following recommendations should be regarded as a guide only. They are based on information provided by manufacturers where available, otherwise on clinical experience, and may therefore be outside a product's license.

This guideline applies to adult patients undergoing renal replacement therapy via continuous venous-venous haemodiafiltration mode only.

The advice is based on information available at the time of writing or review, and is subject to change. For up to date information refer to:

- Your Ward Pharmacist
- The Antimicrobial Pharmacist Team (x 7493 or 07950 882 930)
- The on-call pharmacist(s) (out of hours, via switchboard)
- Summary of Product Characteristics (https://www.medicines.org.uk/emc/)
- Or Medicines Information (6491 or medicines.info@uhl-tr.nhs.uk)

2. Guideline Standards and Procedures

The guideline is presented as a reference table on the following pages. Please ensure you read all the information available as multiple products may be included and advice on monitoring and administration may also be given.

Where a range of doses or intervals are recommended, care must be taken when choosing the correct dose, taking into consideration clinical circumstances e.g. Where higher doses within a range are required for certain infections in normal renal function, the higher end of the CVVHDF (adjusted dose range is likely to be required also).
Advice from medical microbiologists, antimicrobial pharmacists, or ICU pharmacists may differ from this document, depending on the individual patient's clinical presentation and scenario. For example:

- No dose modification may be needed if CVVHDF is used solely to correct fluid, electrolyte or acid base imbalances if patients' urine output is adequate, and appropriately concentrated.
- In acutely critically ill patients, most antimicrobials should be given at the full dose for the first 24-48h. Dose reduction should be considered when there is objective evidence that the patient is responding to therapy, or there are concerns relating to potential toxicity.

- Drug clearance in patients on CVVHDF may vary depending on the type of filter set being used and the effluent dose (which can be established by looking at the screen of the machine itself).
- Dose adjustments should be made according to a patient's response to treatment. Dose recommendations for patients on CVVHDF do not apply to patients on other forms of renal replacement therapy. **This document does not include data on drug**

dosing in adults receiving Hi-Flux Intermittent Haemodialysis (IHD) or Slow Low Efficiency Dialysis (SLED)- Refer to guideline C29/2020

- Actual body weight should be used to calculate doses unless specified. Consider using adjusted body weight if BMI>30kg/m^2.

- For obese patients (actual body weight>20% over IBW) (see table below), the adjusted body weight should be used to calculate dose.

Ideal Body Weight and Overweight Chart					
Height		MEN		WOMEN	
ft. inches	cm	IBW (kg)	Overweight If >kg	IBW (kg)	Overweight If >kg
5.0	152.40	50	60	45.5	54.5
5.1	154.94	52.3	62.5	47.8	57
5.2	157.48	54.6	65.5	50.1	60
5.3	160.02	56.9	68	52.4	63
5.4	162.56	59.2	71	54.7	65.5
5.5	165.10	61.5	74	57.0	68.5
5.6	167.64	63.8	76.5	59.3	71
5.7	170.18	66.1	79	61.6	74
5.8	172.72	68.4	82	63.9	76.5
5.9	175.26	70.7	85	66.2	79.5
5.10	177.80	73.0	87.5	68.5	82.2
5.11	180.34	75.3	90	70.8	85
6.0	182.88	77.6	93	73.1	87.5
6.1	185.42	79.9	96	75.4	90
6.2	187.96	82.2	98.5	77.7	93
6.3	190.50	84.5	101.5	80.0	96
6.4	193.04	86.8	104	82.3	98.5
6.5	195.58	89.1	107	84.6	101.5

- **Adjusted Body Weight (AdjBW) = IBW + 0.4 [actual body weight (kg) – ideal body weight (kg)]**

Please contact your ward pharmacist, an antimicrobial pharmacist, or Medicines Information if you require further advice.

▲ = Unlicensed dose, common practice ● = Unlicensed dose, local practice at UHL
LD = Loading dose MD = Maintenance dose

DRUG	DOSE IN CVVHDF
ABACAVIR	AS NORMAL▲
ACICLOVIR IV	5-10MG/KG TDS FOR24-48HR THEN BD ▲ Dose by Adjusted Body Weight in obese patients **Use higher end of dosing range for confirmed HSV encephalitis or pneumonitis** Discuss with ICU pharmacist or antimicrobial pharmacist if therapeutic drug monitoring (levels) need to be taken.
ACICLOVIR oral *HERPES SIMPLEX – mild to moderate severity*	200MG 3-4 X DAILY▲
ACICLOVIR oral *VARICELLA ZOSTER – mild to moderate severity*	400 - 800MG BD-TDS▲
AMIKACIN	15-20MG/KG Loading dose then adjust dose and frequency according to levels. (Max. single dose 1500MG) Maintenance dose: 7.5MG/KG OD to 25MG/KG 48hourly Daily trough levels: aim for <5mg/L For severe infections/refractory shock/MDR organism use higher end of dosage.
AMOXICILLIN IV/ORAL	AS NORMAL
AMBISOME (LIPOSOMAL AMPHOTERICIN B)	AS NORMAL
ATRIPLA® *efavirenz 600mg* *emtricitabine 200mg* *tenofovir disoproxil 245mg*	**DO NOT USE** SEE INDIVIDUAL DRUGS AND GIVE SEPARATELY

DRUG	DOSE IN CVVHDF
AZITHROMYCIN oral	AS NORMAL
AZTREONAM IV	Initial full dose for 24-48hr then 50% of normal dose
BENZYLPENICILLIN	2.4–14.4G DAILY IN 4-6 DIVIDED DOSES FOR 24-48HR THEN 2.4G EVERY 6 HOURS ●
CASPOFUNGIN	AS NORMAL
CEFALEXIN	250-500MG BD-TDS▲
CEFOTAXIME	AS NORMAL
CEFTAZIDIME	2G TDS FOR 48HR THEN 2G BD▲
CEFTAZIDIME-AVIBACTAM (Zavicefta)	2.5G TDS for 48hr then 1.25-2.5G TDS
CEFTOLOZANE-TAZOBACTAM (Zerbaxa)	AS NORMAL Discuss with ICU pharmacist or antimicrobial pharmacist for advice
CEFTRIAXONE	AS NORMAL
CEFUROXIME IV	750MG-1.5G BD
CIPROFLOXACIN/ENTERAL	500MG BD ▲ Enteral feeding tubes 750MG BD▲ **Enteral feed dose higher than oral dose to compensate for anticipated enteral feed interaction (if a reliable feed break can be established, the dose should revert to 500mg BD)** **Crush and disperse. Ciprofloxacin tablets for feeding tube use**

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DRUG	DOSE IN CVVHDF
CIPROFLOXACIN IV	400MG BD▲ **Consider 400mg TDS for high dose CRRT or MDR or >90kg**
CLARITHROMYCIN oral/IV	AS NORMAL ●
CLINDAMYCIN oral	AS NORMAL▲
CLINDAMYCN IV	AS NORMAL▲
CO-AMOXICLAV oral	AS NORMAL▲
CO-AMOXICLAV IV	AS NORMAL▲
COMBIVIR® *lamivudine 150mg* *zidovudine 300mg*	DO NOT USE See individual drugs and give separately
CO-TRIMOXAZOLE oral or IV TREATMENT *(TRIMETHOPRIM + SULFAMETHOXAZOLE)* *Consider taking plasma samples (no sooner than 2 days from initiation) to monitor for accumulation and efficacy – Discuss with ICU or antimicrobial pharmacist.*	STENOTROPHOMONAS TREATMENT (in critically unwell patients) 90 MG/KG/DAY IN 2-4 DIVIDED DOSES FOR 3 DAYS THEN 60MG/KG ●
	PCP TREATMENT 120MG/KG/DAY IN 2-4 DIVIDED DOSES FOR 3 DAYS THEN 60MG/KG ▲
	OTHER INDICATIONS 50% OF NORMAL DOSE AT NORMAL FREQUENCY ▲
CO-TRIMOXAZOLE oral PROPHYLAXIS *(TRIMETHOPRIM + SULFAMETHOXAZOLE)*	AS NORMAL▲
DAPTOMYCIN IV	6-8MG/KG EVERY 24HOURS ▲ Monitor more frequently. Baseline and regular CK monitoring required. Increase monitoring frequency for those at risk of muscle damage.

DRUG	DOSE IN CVVHDF
	Discuss with ward or antimicrobial pharmacists before taking daptomycin assays/levels
DARUNAVIR	AS NORMAL▲
DIDANOSINE	150MG/DAY (≥60KG) OR 100MG/DAY (<60KG) AS A SINGLE DAILY DOSE▲
DOXYCYCLINE	AS NORMAL
EFAVIRENZ	AS NORMAL
EMTRICITABINE	Tablets: 200 mg every 72 hours. Oral solution: 80 mg daily.
ERTAPENEM	500 MG – 1G OD▲
ERYTHROMYCIN oral and IV	AS NORMAL▲
ETHAMBUTOL	15 MG/KG EVERY 24–36 HOURS OR 7.5–15 MG/KG/DAY. ▲ Consider monitoring plasma levels, particularly if there is poor clinical progress.
ETRAVIRINE	AS NORMAL
FIDAXOMICIN	AS NORMAL▲
FLUCLOXACILLIN IV and oral	AS NORMAL▲

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DRUG	DOSE IN CVVHDF
FLUCONAZOLE ORAL AND IV	Treatment dose: 400MG BD● Prophylaxis dose: 200mg BD ●
FLUCYTOSINE	50MG/KG OD ▲ Monitor serum levels
FOSAMPRENAVIR	AS NORMAL
FOSFOMYCIN (ORAL)	DO NOT USE – NOT EFFECTIVE
FOSFOMYCIN (IV)	AS NORMAL
GANCICLOVIR IV (see valganciclovir for oral dosing)	2.5MG/KG OD ●
GENTAMICIN ONCE DAILY (Hartford Nomogram) (FOLLOW GENTAMICIN PRESCRIBING CHART – discuss with pharmacist regarding monitoring)	USE CONVENTIONAL DOSING – see below
GENTAMICIN CONVENTIONAL(FOLLOW AVAILABLE PRESCRIBING CHARTS – If no suitable chart available discuss with pharmacist regarding prescribing and monitoring)	2–3 MG/KG DAY IN DIVIDED DOSES AND MONITOR LEVELS
GENTAMICIN – FOR ENDOCARDITIS (USED AS AN ADJUNCT – No chart available, discuss with pharmacist regarding prescribing and monitoring)	1MG/KG EVERY 24 HOURS
ISONIAZID oral	AS NORMAL▲
ITRACONAZOLE oral	AS NORMAL ▲ NOT REMOVED BY CVVHDF, **AVOID IN CONCOMITANT HEPATIC FAILURE**

DRUG	DOSE IN CVVHDF
ITRACONAZOLE IV	AVOID
KALETRA® *LOPINAVIR 200MG* *RITONAVIR 50MG*	AS NORMAL
KIVEXA® *ABACAVIR 600MG* *LAMIVUDINE 300MG*	**DO NOT USE** SEE INDIVIDUAL DRUGS AND GIVE SEPARATELY
LAMIVUDINE	HIV: 150MG STAT, THEN 50MG OD▲ HEPATITIS: 35MG STAT THEN 15MG OD
LEVOFLOXACIN oral and IV	500MG STAT THEN 250MG-500MG OD▲
LINEZOLID IV/oral	AS NORMAL
LOPINAVIR	SEE KALETRA®
MARAVIROC	150MG OD IF GIVEN WITH POTENT CYP3A4 INHIBITOR AS NORMAL IF GIVEN WITHOUT POTENT CYP3A4 INHIBITOR
MEROPENEM	1G TDS ● 2G TDS IN ECMO/CNS INFECTION
METRONIDAZOLE oral	AS NORMAL
METRONIDAZOLE IV	AS NORMAL

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DRUG	DOSE IN CVVHDF
MICAFUNGIN	AS NORMAL
MOXIFLOXACIN	AS NORMAL
NEVIRAPINE	AS NORMAL
NITROFURANTOIN	DO NOT USE – NOT EFFECTIVE
PHENOXYMETHYL-PENICILLIN (PENICILLIN V)	AS NORMAL▲
PIPERACILLIN / TAZOBACTAM	4.5G TDS▲ (increase to QDS in severe infections/ neutropenic sepsis/ECMO)
PIVMECILLINAM	AS NORMAL
POSACONAZOLE	ORAL: AS NORMAL IV: Discuss with ICU pharmacist or antimicrobial pharmacist for advice
PYRAZINAMIDE	AS NORMAL
RALTEGRAVIR	AS NORMAL
RIFAMPICIN oral / IV	AS NORMAL
RITONAVIR	AS NORMAL ▲
SAQUINAVIR	AS NORMAL
STAVUDINE	15MG BD (< 60KG) OR 20MG BD (> 60KG) ▲
TEICOPLANIN Monitor levels regularly	LOADING DOSE : AS NORMAL DAY 1-4 MAINTENANCE DOSE : NORMAL DOSE EVERY 72 HOURS ***OR*** 33% OF THE FULL DOSE EVERY 24 HOURS ▲

DRUG	DOSE IN CVVHDF
TEMOCILLIN	Discuss with ICU pharmacist or antimicrobial pharmacist for advice
TENOFOVIR DISOPROXIL	245 MG EVERY 72–96 HOURS OR 66 MG (2 SCOOPS) ONCE DAILY.
TIGECYCLINE	AS NORMAL
TIPRANAVIR	AS NORMAL
TRIMETHOPRIM	AS NORMAL▲
TRIZIVIR® *ABACAVIR 300MG* *LAMIVIDINE 150MG* *ZIDOVUDINE 300MG*	**DO NOT USE** SEE INDIVIDUAL DRUGS AND GIVE SEPARATELY
TRUVADA® *EMTRICITABINE 200MG* *TENOFOVIR DISOXOPRIL 245MG*	**DO NOT USE** SEE INDIVIDUAL DRUGS AND GIVE SEPARATELY
VALGANCICLOVIR oral INDUCTION TREATMENT FOR 21 DAYS	450MG EVERY 48 HOURS▲
VALGANCICLOVIR oral MAINTENANCE/PREVENTION	450MG TWICE WEEKLY
VANCOMYCIN IV ONLY (oral is not absorbed so dose as normal in all degrees of renal impairment) Monitor levels DO NOT USE VANCOMYCIN CHART TO DOSE ON CVVHDF< USE CHART ONLY TO RECORD DOSES ADMINISTERED AND LEVELS TAKEN	LD: AS PER VANCOMYCIN CHART● MD: AS PER ICU PHARMACIST OR AS PER BODY WEIGHT- SEE BELOW • UNDER 50KG: 500MG BD • 50-100KG: 750MG BD • OVER 100KG; 1000MG BD Daily levels until therapeutic level achieved. titrate dose/frequency as per vanc chart

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DRUG	DOSE IN CVVHDF
VORICONAZOLE oral	AS NORMAL MONITOR LEVEL
VORICONAZOLE IV	AS NORMAL Use adjusted body weight where actual BMI > 35 kg/m2 MONITOR LEVELS First level day 5 after starting treatment
ZIDOVUDINE oral/IV	AS NORMAL

3. Education and Training

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
Appropriateness of dosing for patients on CVVH/CVVHDF	Annual Antimicrobial Prescribing Audits and ad-hoc prescribing audits	Antimicrobial Pharmacists ITAPS Pharmacy team	Annually	TIPAC AWP CMG Boards

5. Supporting References

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- *Cotterill S. Antimicrobial Prescribing in Patients on Haemofiltration. J Antimicrob Chemother 1995;36:773-80*
- *The Renal Drug Database. Available via https://www.renaldrugdatabase.com/ [accessed on-line 24/03/2021*
- *Clinical Practice Guidelines: Renal Replacement Therapy for Critically Unwell Adult Patients: Guidelines for best practice and service resilience during COVID-19*

6. Key Words

- RRT
- Filtration
- CVVH
- CVVHDF
- Dosing
- Antimicrobial
- Antibiotic

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Details of Changes made during review:

New guideline:

- Reference to the drug dosing in adults receiving Hi-Flux Intermittent Haemodialysis (IHD) or Slow Low Efficiency Dialysis (SLED).

- Dosing update to reflect national consensus based on the clinical practice guidelines