

REMAP-CAP ANTIBIOTIC DOMAIN

This domain aims to determine the effectiveness of different empiric antibiotic strategies for patients with severe community-acquired pneumonia. In this domain, patients are randomised to receive:

- Ceftriaxone + macrolide
- Moxifloxacin or levofloxacin
- Piperacillin-tazobactam + macrolide
- Amoxicillin-clavulanate + macrolide

COMMENCEMENT OF REMAP-CAP ANTIBIOTIC

REMAP-CAP allocates antibiotic agent(s), however, the dose and frequency of the allocated antibiotic therapy are up to the treating clinician.

The antibiotic(s) the patient has been allocated to receive should start immediately after reveal of allocation. If the patient already received dose(s) of the REMAP-CAP allocated antibiotic PRIOR to randomisation, wait until the next dose is due.

DOSING GUIDE

The doses specified below are recommended minimum doses and may be modified according to local guidelines or practice.

- Ceftriaxone ≥ 1 gram administered IV once daily
- Moxifloxacin 400mg administered IV once daily, or levofloxacin 750mg administered IV once daily
- Piperacillin-tazobactam ≥ 4.5 grams administered IV every 8 hours
- Amoxicillin-clavulanate ≥ 1.2 grams administered IV every 8 hours

If no local guidelines exist, it is recommended that subsequent doses will be adjusted for estimated renal function (based on eGFR) as follows:

Agent	eGFR >50 ml/min	eGFR 10-50 ml/min	eGFR <10	Receiving CVVHF
Ceftriaxone	1g-2g IV daily	1g-2g IV daily	1g IV daily	1g IV daily
Piperacillin-tazobactam	4.5g IV q6h	(eGFR 20-40) 4.5g IV q8h	(eGFR <20) 4.5g IV q12h	4.5g IV q8h
Amoxicillin-clavulanate	1200mg IV q8h	1200mg IV q8h	1200mg IV q12h	1200mg IV q8h
Moxifloxacin	400mg IV q24h	400mg IV q24h	400mg IV q24h	400mg IV q24h
Levofloxacin	750mg IV q24h	(eGFR 20-50) 750mg IV load, 750mg IV q48h	(eGFR <20) 750mg IV load, 500mg IV q48hr	750mg IV load, 500mg IV q48hr

MACROLIDE ADMINISTRATION

For patients allocated to receive an intervention including a macrolide in the Antibiotic Domain, the choice of macrolide, as well as the dose, route and frequency of the macrolide therapy are at the discretion of the treating clinician. The REMAP-CAP preferred macrolide is Intravenous Azithromycin.

OTHER ANTIMICROBIAL ADMINISTRATION

Permitted additional antibacterial agents (at the discretion of the treating clinician):

- Vancomycin
- Clindamycin
- Cotrimoxazole
- Gentamicin

Prohibited empiric antibacterial agents - a change to any of these antimicrobials is permitted if it occurs in response to microbiology results (see below):

- Any REMAP-CAP antibiotic(s) the patient was NOT allocated
- Other Beta-Lactams
- Carbapenems (Meropenem, Imipenem, Doripenem, Ertapenem)
- Monobactams (Aztreonam)
- Other Quinolones



SUBSEQUENT ANTIBIOTIC ADMINISTRATION

IMPORTANT: Treating clinicians must document (in the patient's medical record) the reason for **ANY** change to the REMAP-CAP allocated antibiotic therapy during the intervention period.

Duration of empiric therapy

Determined by the following criteria:

- Change to oral antibiotics (as selected by treating clinician) once patient is clinically stable
- Change to a targeted antibiotic therapy if a microbiological diagnosis has been made
- Cease antibiotics if an alternative diagnosis is made
- Cease antibiotics when there is evidence of sufficient clinical improvement, no microbiological diagnosis has been made and no clinical evidence of deep infection (e.g. empyema or lung abscess)
- The duration of antibiotic therapy will be decided by the treating clinician and local guidelines (not determined by REMAP-CAP Antibiotic Domain Protocol).

Changing antibiotic therapy

Changes to the REMAP-CAP allocated antibiotic dose, route and frequency are permitted.

Before changing REMAP-CAP empiric antibiotic (discontinuing REMAP-CAP antibiotic or adding additional antibiotic agents) refer to flow-chart below.

Escalation of antibiotic therapy in the absence of microbiological information is discouraged, however clinicians should always act in the best interests of the patient.

