PHC Chapter 10: Infections
AH Chapter 9: Systemic and Healthcare Associated Infections

National Department of Health

Affordable Medicines Directorate
Essential Drugs Program

Primary Healthcare Level Standard Treatment Guidelines – 2020-4 Review cycle
Adult Hospital Level Standard Treatment Guidelines – 2020-4 Review cycle

Evidence

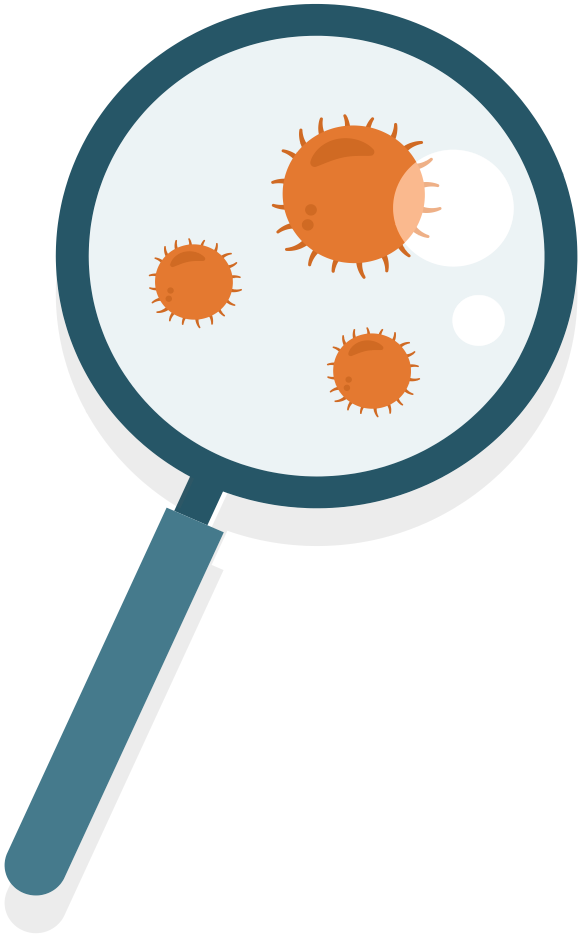
Please access the National Essential Medicines List Committee (NEMLC) report for detailed evidence (including rationale, references and costings) informing decision-making on medicine addition, amendments and deletions:

NHI Website: https://www.health.gov.za/nhi-edp-stgs-eml
Knowledge Hub: www.knowledgehub.health.gov.za/e-library

Disclaimer

This presentation is an implementation tool and should be used alongside the most recently published STGs available on the Knowledge Hub. This information does not supersede or replace the STGs.

Presentation Outline



01	Malaria Prophylaxis
02	Tick Bite Fever in Pregnancy
03	Empiric Antibiotic Therapy for Hospital Acquired Pneumonia (HAP)/ Ventiliator Associated Pneumonia (VAP)
04	Coverage of Organisms with Antibiotics
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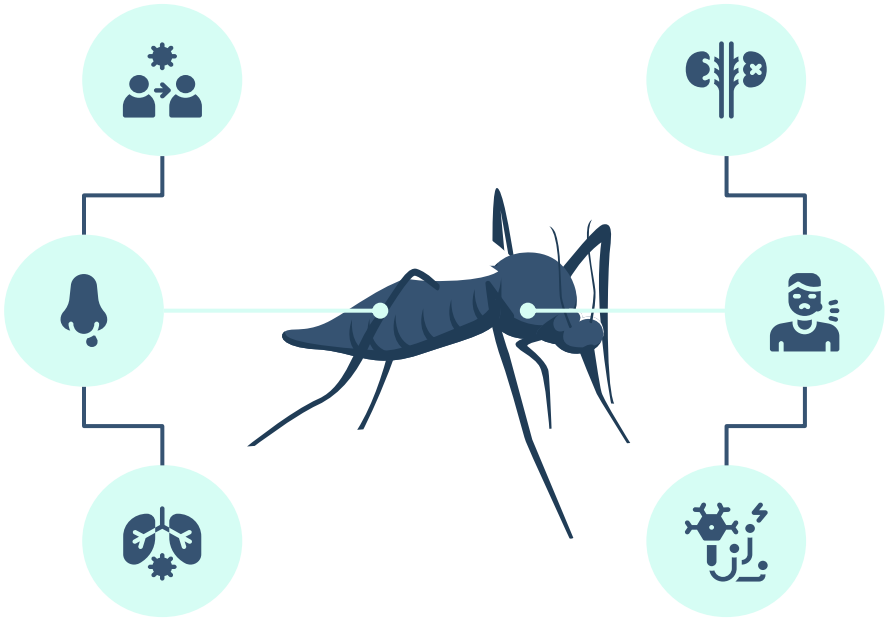
Malaria Prophylaxis

Background

1. Historically, malaria chemoprophylaxis was not considered for inclusion on the national EML

2. This is because the NDoH Malaria Programme was not able to provide estimated numbers of travellers requiring prophylaxis to determine an estimated budget impact



3. A request had been made previously to the Programme to advise of the delivery platform model for malaria chemoprophylaxis.

4. In response to the South African Malaria Elimination Committee case load reports, NEMLC has been able to estimate the budget impact for including malaria prophylaxis at PHC level of care. NEMLC has now included guidance for malaria prophylaxis

Malaria Prophylaxis

Medicine Review: Malaria Prophylaxis

Introduction

- The South African Malaria Elimination Committee reported an increase in malaria cases amongst migrant workers traveling home (mostly across borders in malaria-endemic areas), and motivated that malaria chemoprophylaxis be considered for inclusion on the EML.
- Local resistance to chloroquine and sulfadoxine-pyrimethamine precluded inclusion of these agents from the analysis.
- Currently, registered malaria chemoprophylaxis includes atovaquone-proguanil, doxycycline and mefloquine.
- Mefloquine has recently been discontinued from the South African market and atovaquone-proguanil is non-EML.

Pregnancy and Children

- Pregnant women should avoid travel to malaria-endemic areas. When chemoprophylaxis is required, doxycycline should be avoided due to effects on skeletal development found in animal studies
- There is very limited RCT data in children.

Evidence Review

- An evidence review for malaria chemoprophylaxis (mefloquine, atovaquone-proguanil or doxycycline) was conducted, and one systematic review and 4 RCTs were identified.

Adverse Effects

- Doxycycline users were more likely to have dyspepsia, photosensitivity, vomiting, and vaginal thrush ***(very low-certainty evidence).***

Doxycycline

- Doxycycline (n=34) was shown to be **84% effective at preventing parasitaemia** (95% CI 66 to 92%); NNT 4 (95% CI 3 to 10), ***low certainty evidence***
- **91% effective at preventing clinical malaria** (95% CI 61 to 98%) NNT 16 (95% CI 7 to 47), **low certainty evidence.**
- In a small RCT, mefloquine was also shown to be comparable to doxycycline in preventing asymptomatic (77%; 95% CI 55 to 88%) and symptomatic malaria (81%; 95% CI 44 to 93%), low certainty evidence

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National Department of Health: Affordable Medicines, EDP-Primary Healthcare level. Medicine Review: Malaria Chemoprophylaxis, June2021. http://www.health.gov.za/. https://knowledgehub.health.gov.za/system/files/elibdownloads/2023-09/Medicine%20Reviews%202020_0.zip

Malaria Prophylaxis

NEMLC Recommendation

NEMLC recommended **doxycycline as malaria chemoprophylaxis,** including children ≥8 years of age.

Recommended dosing:

- *Non-pregnant adults:* Doxycycline oral, 100 mg daily, taken from 2 days prior to entering endemic area until 4 weeks after exiting the endemic area
- *Children ≥ 8 years of age:* Doxycycline oral, 2 mg/kg/dose daily, taken from 2 days prior to entering endemic area until 4 weeks after exiting the endemic area.

Malaria Prophylaxis

STG Amendments: PHC Chapter 10

MEDICINE TREATMENT

Prophylaxis

CAUTION

Immunocompromised patients, pregnant women and children <8 years of age should avoid visiting malaria-endemic areas, as they are more prone to the serious complications of malaria.

However, if this cannot be avoided, malaria chemoprophylaxis should be considered (as recommended by the National Guidelines for the Prevention of Malaria (2018) found at: https://www.nicd.ac.za/wp-content/uploads/2019/03/National-Guidelines-for-prevention-of-Malaria_updated-08012019-1.pdf

However, as only doxycycline is provided in the public sector, alternative options for pregnant women and children <8 years of age need to be purchased in the private sector.)

Non-pregnant adults:

- Doxycycline oral, 100 mg daily.
  - Take from 2 days prior to entering endemic area until 4 weeks after exiting the endemic area.

Children ≥8 years of age:

- Doxycycline oral, 2 mg/kg/dose daily.
  - Take from 2 days prior to entering endemic area until 4 weeks after exiting the endemic area.

Note: Doxycycline is contra-indicated in pregnant women, and in children <8 years of age.

Tick Bite Fever in Pregnancy

Doxycycline is the antibiotic of choice for tick bite fever.

However, it usually avoided for use in pregnancy, as other tetracyclines have been associated with adverse effects on foetal teeth and bones.

A systematic review[1] showed that doxycycline in pregnant women had a safety profile that differed from tetracycline, with no correlation to the teratogenic effects.

A retrospective cohort study suggests that doxycycline used by pregnant women should not result in a greater incidence of overall major congenital malformation in their infants.

Due to high maternal and fetal risk associated with rickettsial illness in pregnancy, treatment with doxycycline outweighs the risks.

Early initiation of empirical doxycycline may save lives and prevent severe disease

[1] Cross R, Ling C, Day NP, McGready R, Paris DH. Revisiting doxycycline in pregnancy and early childhood--time to rebuild its reputation? Expert Opin Drug Saf. 2016;15(3):367-82. https://pubmed.ncbi.nlm.nih.gov/26680308)

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National Department of Health: National Department of Health: Essential Drugs Programme. Primary Healthcare level STGs and EML. NEMLC Report - Chapter 10: Infections.
Primary-Healthcare-Chapter-10-Infections_2020-3_with-supporting-NEMLC-report_updatedNovember2023.pdf

2030 NDP

30 YEARS OF FREEDOM
South Africa 1994 - 2024

Tick Bite Fever in Pregnancy

STG Amendments: PHC Chapter 10 and AH Chapter 9

IMPORTANT

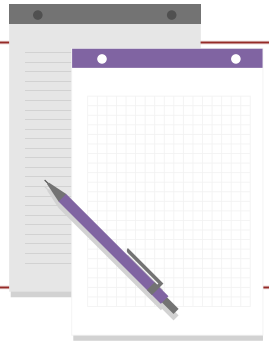
The PHC STGs and EML recommends initial treatment with doxycycline *for 2 days ONLY*, followed by azithromycin, for tick bite fever in pregnancy

In pregnancy:

- *Doxycycline, oral, 100 mg 12 hourly for 2 days.*

Then switch to:

- *Azithromycin, oral, 500 mg 12 hourly for 3 days.*

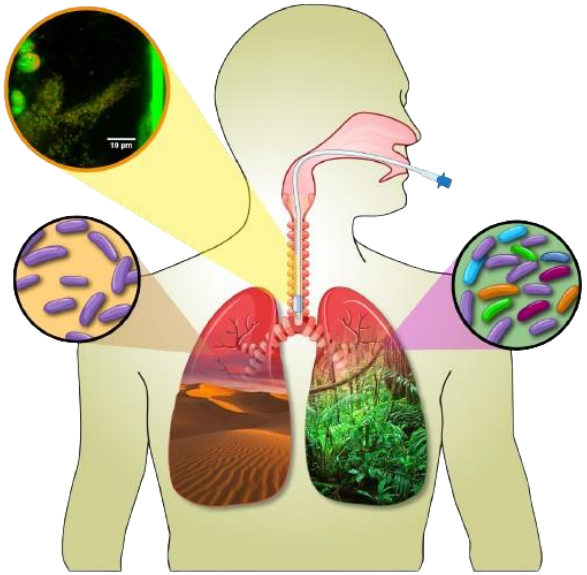


STG Amendments: AH Chapter 9

For patients unable to tolerate oral therapy, including pregnant patients, ***ciprofloxacin 400mg 8 hourly*** has been ***retained***. Although pregnancy is listed as a contraindication to ciprofloxacin, tick bite fever is a life-threatening condition and risk:benefit considerations support treatment with ciprofloxacin IV under these circumstances. It has also been noted that oral doxycycline has superior efficacy compared to ciprofloxacin in the management of tick bite fever, and should be commenced as soon as the patient is able to tolerate oral therapy.

Empiric Antibiotic Therapy for Hospital Acquired Pneumonia (HAP)/ Ventilator Associated Pneumonia (VAP)

Empiric Antibiotic Therapy: Duration of empiric antibiotic therapy amended from “10” to “7” days, aligned with the 2016 Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) Guidelines:



VAP Recommendation:

The IDSA/ATS panel concluded that the evidence indicates that short courses of antibiotics reduce antibiotic exposure and recurrent pneumonia due to MDR organisms and IDSA recommends a 7-day antibiotic course for VAP *(strong recommendation)*

Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, et al. Management of Adults With Hospital-acquired and Ventilatorassociated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. doi: 10.1093/cid/ciw353. Epub 2016 Jul 14. Erratum in: Clin Infect Dis. 2017 May 1;64(9):1298. Erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435. Erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161.

Empiric Antibiotic Therapy for Hospital Acquired Pneumonia (HAP)/ Ventilator Associated Pneumonia (VAP)

Systematic Reviews for VAP:

- 28-day antibiotic-free days: Increased with short courses of antibiotics - mean difference, 4.02 days; 95% CI 2.26 to 5.78 days.
- Recurrent VAP due to MDR pathogens:42.1% vs 62.3%; OR, 0.44; 95% CI 0.21 to 0.95
- Mortality, recurrent pneumonia, treatment failure, hospital length of stay, or duration of mechanical ventilation: no difference
- In the sub-group of patients with VAP due to a non-glucose-fermenting gram-negative bacillus including Pseudomonas and Acinetobacter (33% of patients), short courses of antibiotics were infection (OR 2.18; 95% CI, 1.14 to 4.16), but no other differences were observed for pneumonia recurrence or mortality associated with recurrent infection (OR 2.18; 95% CI, 1.14 to 4.16), but no other differences were observed for pneumonia recurrence or mortality.

2 **Pugh et al (2015)2 : Systematic review of 6 RCTs (n=508) compared short courses of antibiotics (7-8 days) to long courses (10-15 days). Majority of patients had VAP.**

3 **Dimopoulos et al (2013)3 : Systematic review of 4 RCTs (n=883) comparing short courses of antibiotics (7-8 days) to long courses (10-15 days) amongst patients with VAP.**

- 28-day antibiotic-free days: Increased with short courses of antibiotics - mean difference 3.40 days: 95% CI 1.43 to 5.37 days.
- Mortality, recurrent pneumonia, ventilator-free days, duration of mechanical ventilation, or length of ICU stay: no difference

1 **IDSA/ATS Guideline panel's confidence in the results was moderate as many of the RCTs in the systematic reviews had moderate risk of bias**

- Most RCTs were not blinded, recurrence was measured at 30 days (recurrence more likely to occur in short-course antibiotics RCTs) and there was indirectness as the largest trial excluded patients with early VAP.

Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, et al. Management of Adults With Hospital-acquired and Ventilatorassociated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. doi: 10.1093/cid/ciw353. Epub 2016 Jul 14. Erratum in: Clin Infect Dis. 2017 May 1;64(9):1298. Erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435. Erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161.

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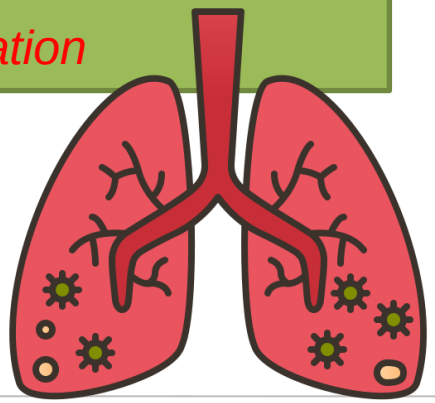
Empiric Antibiotic Therapy for Hospital Acquired Pneumonia (HAP)/ Ventilator Associated Pneumonia (VAP)

Hospital-acquired pneumonia (non-VAP) Recommendation:

- The IDSA/ATS guideline panel found no studies that provided useful data for comparing short-term to long-term antibiotic therapy in HAP; however, the duration of therapy has been studied in VAP.
- Thus, guidance was extrapolated from evidence from VAP; noting that shorter antibiotic course results in reduced antibiotic-related side effects, C. difficile colitis, the potential for antibiotic resistance, and costs *(strong recommendation).*
- The importance of avoiding therapies that are potentially harmful and costly if there is no evidence of benefit was highlighted.
- Level of Evidence: *Low certainty evidence, strong recommendation*



Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, et al. Management of Adults With Hospital-acquired and Ventilatorassociated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. doi: 10.1093/cid/ciw353. Epub 2016 Jul 14. Erratum in: Clin Infect Dis. 2017 May 1;64(9):1298. Erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435. Erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161.

Empiric Antibiotic Therapy for Hospital Acquired Pneumonia (HAP)/ Ventilator Associated Pneumonia (VAP)

STG Amendments: AH Chapter 9

MEDICINE TREATMENT

Empiric antibiotic therapy

Treatment duration: 7 days.

Antibiotic choice should be based on local susceptibility patterns (See National Institute for Communicable Diseases (NICD) AMR Dashboard: www.nicd.ac.za).

- Piperacillin/tazobactam, IV, 4.5 g 8 hourly.

AND

- Amikacin, IV, 15 mg/kg daily (See Appendix II, for individual dosing and monitoring for response and toxicity).

OR ALTERNATIVELY:

- Cefepime, IV, 2 g 12 hourly as monotherapy. (See Appendix II for guidance on dosing in renal impairment).

If high local resistance rates to the above regimens, then consider carbapenem with activity against Pseudomonas:

- Imipenem/cilastatin, IV, 1000/1000 mg 8 hourly as monotherapy.
  - **Note:** Do not use imipenem/cilastatin in patients with central nervous system disorders or history of seizures.

OR ALTERNATIVELY

For patients with CNS disorders incl. epileptics/ those with seizures:

- Meropenem, IV, 2 g 8 hourly as monotherapy.

Note:

» De-escalate as soon as the culture is available.

» For severe pencillin allergy, consult an infectious diseases specialist or microbiologist.

Coverage of Organisms with Antibiotics

Antibiotic	Coverage	Indication	Dosage	Additions/amendments to the AH CH 9 Infections STG
Vancomycin IV	S. *aureus*	Intravascular Catheter Infection	25-30mg/kg empirically as a loading dose; Follow with 15-20mg/kg, 12 hourly	**Dose Amended** – aligned to 2022 SAMF edition
	MRSA	Surgical Wound Infections	25-30mg/kg empirically as a loading dose; Follow with 15-20mg/kg, 12 hourly	**Dose Amended** - Aligned with Above
Cefazolin IV	N/A	Surgical Wound Infections	1g, 8 hourly	**Retained** - For empiric therapy due to Cloxacillin supply issues
Piperacillin/ Tazobactam	*Gram negative organism*	Surgical Wound Infections	4.5g, 8 hourly	**Amended:** Empiric cefazolin therapy to be discontinued and Piperacillin/tazobactam monotherapy recommended
Ertapenem IV	*Gram negative*	Surgical Wound Infections	1g daily	**Retained** - For severe penicillin allergy

National Department of Health: National Department of Health: Essential Drugs Programme. Adult hospital level STGs and EML. NEMLC Report - Chapter 9: Systemic and Healthcare Associated Infections. Adult-Hospital-Ch9_Infections-and-supporting-NEMLC-report_2020-4_Version-1.0_7-June-2024.pdf (health.gov.za)

Other Notable Amendments

Urinary Tract Infections

The duration of therapy for empiric therapy with either amikacin, IV or ciprofloxacin, oral has been amended from 7-14 days to 7 days.

There is growing evidence in support of shorter courses of treatment for UTI, particularly for treatment with aminoglycosides

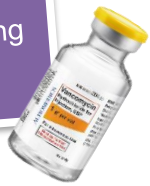
Vancomycin Dosing

Amended as follows to align with the SAMF, 2022 edition:

Vancomycin, IV, 25–30 mg/kg, empirically as a loading dose.

Follow with 15–20 mg/kg/dose 12 hourly.

(See Appendix II for guidance on prescribing and therapeutic drug monitoring).

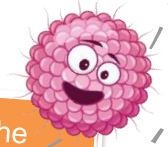


Varicella Zoster Immunoglobulin (VZIG)

The indication for VZIG was amended to align with the Centers for Disease Control and Prevention (CDC) guidelines.

Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.

- o Maximum dose: 600 units.
- o Administer within 96 hours of significant exposure



Covid-19

New STG on the management of Covid-19 was added to the chapter

THANK YOU!!

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South Africa 1994 - 2024