CHAPTER 9
SYSTEMIC AND HEALTHCARE-ASSOCIATED INFECTIONS

ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship refers to a systematic approach to optimising the appropriate use of an antibiotic to improve patient outcome(s) and limit emergence of resistant pathogens, whilst ensuring patient safety. It is one arm of the national and international response to the increasing public health crisis of antibiotic resistance. A critical component is adequate infection control. Antibiotics should only be used for the treatment and prevention of bacterial infections. The following checklist will help optimise prescribing:

Checklist for optimal antibiotic prescribing
1. **Medicine** – which is the narrowest-spectrum antibiotic that I can use to treat this bacterial infection?
2. **Dose** – many antibiotics require weight-based dosing and their dosing depends on renal and/or hepatic function.
3. **Dose frequency** – dependent on the half-life of the drug and whether the activity of the antibiotic depends on the time above the MIC, the peak concentration relative to MIC, or the area under the concentration/time curve. Guidance for dosing frequency may require therapeutic drug monitoring, e.g. vancomycin and aminoglycosides.
4. **Duration** – should be dictated by evidence from randomised controlled trials whenever possible. Expert opinion from national and international guidelines should be consulted where evidence is weak.
5. **Route** – most antibiotics have good oral bioavailability, but some infections will require intravenous therapy either for the whole or part of the course. Patients who are critically ill, or who would be expected to have impaired gastrointestinal absorption of medicines (e.g. excessive vomiting) may also require intravenous antibiotics initially.
6. **De-escalation** – applies to the spectrum of antibiotic use and route of administration. All attempts to convert early from parenteral to oral use should be made.
MIC = minimum inhibitory concentration. Further guidance on local antimicrobial stewardship can be found online: https://knowledgehub.health.gov.za/content/antimicrobial-resistance

9.1 HEALTHCARE-ASSOCIATED AND HOSPITAL ACQUIRED INFECTIONS

DEFINITION AND PRINCIPLES

Patients with healthcare associated and hospital acquired infections are at

increased risk of being infected with drug resistant organisms. A hospital acquired infection is a new infection that develops after at least 48 hours of hospitalisation without evidence that the infection was present or incubating at the time of admission. Healthcare-associated infections should also be considered in persons with extensive healthcare contact such as: residence in a nursing home or other long-term care facility, hospitalisation in an acute care hospital for >2 days during the prior 90 days, or attendance at a hospital or haemodialysis clinic during the prior 30 days.

It is essential to obtain specimens for culture and sensitivity testing in all cases before starting antibiotics.

Empiric therapy suggestions below are only rough guidelines due to heterogeneity of resistance patterns between facilities and over time. Close liaison with regional microbiologists and regular review of hospital antibiotic policy based on local resistance patterns are essential.

9.1.1 INTRAVASCULAR CATHETER INFECTIONS

L53.9/T80.2 + (B95.8/Y84.8/B37.8)

PERIPHERAL LINE INFECTION:

Common organisms:

» coagulase negative staphylococci, particularly *S. epidermis*
» *S. aureus*

GENERAL MEASURES

» **NB: Always remove the intravascular line at the site of infection.**
» Small, localised areas of erythema at the catheter insertion site will usually resolve without antibiotic therapy after catheter removal.

MEDICINE TREATMENT

Patients with larger areas of erythema and tenderness extending beyond the insertion site who are systemically well:

- Clindamycin, oral, 450 mg 8 hourly for 5 days. *LoE:IIIb*[i]

If patients are systemically unwell, they should be treated as for a central venous catheter related systemic blood infection.

SHORT-TERM CENTRAL VENOUS CATHETER INFECTION: GENERAL MEASURES

Obtain microbiologic specimens: peripheral blood culture, blood culture from central catheter prior to removal, and culture of the catheter tip.

If peripheral blood culture is negative but central catheter culture is positive:

» Monitor closely for signs of infection and repeat peripheral blood cultures accordingly.

» If central line has grown S. aureus, 5-7 days of treatment is recommended (provided that peripheral blood cultures remain negative).

If peripheral blood culture is positive:

» Remove catheter, and treat with systemic antibiotics, guided by the culture results.

» Duration of antibiotic therapy should generally be for 48–72 hours after resolution of fever except for:
- confirmed *S. aureus* infection and *LoE:IIIb[ii]*
- candidaemia,

where treatment should be continued for 2 weeks after the 1st negative blood culture. *LoE:IIIb[iii]*

» For candidaemia and *S. aureus* infection, perform blood cultures every 2-3 days after therapy has been initiated until 2 consecutive cultures are negative, and 2 weeks after the 1st negative blood culture.

Empiric antibiotic therapy (prior to obtaining susceptibility results):
***S. aureus* infection** (B95.8/Y84.8)

- 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).
  - Tailor therapy to drug-susceptibility results. *LoE:IIIa[iv]*

Candidaemia (B37.8/Y84.8)

» Candida isolated from blood culture should **always** be treated, even if the fever has settled after line removal because of a high risk of late complications.

» Candidaemia with species other than Candida albicans is becoming increasingly common – these species are often resistant to azoles.

» Treatment duration should extend for a minimum of two weeks following the first negative blood culture.

Empiric antifungal therapy:

- Amphotericin B, IV, 0.7 mg/kg daily. *LoE:IIa[v]*
  - Ensure adequate hydration to minimise nephrotoxicity (See Appendix II for preventing, monitoring and management of toxicity). *LoE:Ia[vi]*

Follow up susceptibility:

Once improved, if sensitive, complete course with:

- Fluconazole, oral, 400 mg daily. *LoE:IIa[vii]*

If invasive candidiasis (resistant to fluconazole/amphotericin B or renal impairment is present and amphotericin B cannot be used):

- Echinocandins. (Specialist motivation). *LoE:IIIb[viii]*

REFERRAL/CONSULTATION

» *S. aureus* endocarditis.

9.1.2 SURGICAL WOUND INFECTIONS

T81.4 + (Y83.0-6/Y83.8-9/B95.6/U82.1)

DESCRIPTION

Gram positive bacteria, especially *S. aureus*, are the commonest cause.
Gram negative and anaerobic bacteria are important causes following gynaecological and intestinal surgery.

GENERAL MEASURES

» Microbiologic specimen (in patients with a larger area of erythema or systemic evidence of infection): deep wound swab (NOT a superficial swab), aspirate of pus, or tissue biopsy, and blood culture.
» Suture removal plus incision and drainage is essential.
» Antibiotics are not usually necessary unless there is marked surrounding cellulitis or features of systemic infection.

MEDICINE TREATMENT

Empiric antibiotic therapy:
Total duration of therapy should not exceed 7 days.

If surrounding cellulitis or systemic sepsis does not involve the gastro-intestinal (GI) or female genital tract:

- Cefazolin, IV, 1 g 8 hourly. *LoE:IIa*[ix]

Check Gram stain of exudate. If organism is gram negative:
STOP cefazolin and give:

- Piperacillin/tazobactam, IV, 4.5 g 8 hourly. *LoE:IVb*

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours:

- Flucloxacillin, oral, 500 mg 6 hourly. *LoE:IVb*[x]

Severe penicillin allergy: (Z88.0)

- Clindamycin, IV, 600 mg 8 hourly.

Check Gram stain of exudate. If organism is gram negative:
ADD:

- Ertapenem, IV, 1 g daily. *LoE:Ia*[xi]

Follow with oral therapy as soon as patient can swallow and the temperature has been <37.8°C for 24 hours, based on culture results:

- Clindamycin, oral, 450 mg 8 hourly. *LoE:IIIb*[xii]

If surgery involved female uro-genital tract open GIT:
T81.4 + (Y83.6/Y83.8)

- Ceftriaxone, IV, 2 g daily.

AND

- Metronidazole, IV, 500 mg 8 hourly. *LoE:IIIb*[xiii]

Methicillin (cloxacillin) resistant *S. aureus* (MRSA):
T81.4 + (B95.6+U82.1+Y83.9)

- Vancomycin, IV, 25–30 mg/kg as a loading dose.
  - Follow with 15–20 mg/kg/dose 12 hourly. See Appendix II for guidance on prescribing and monitoring.

LoE:IIIb[xiv]

9.1.3 HOSPITAL-ACQUIRED PNEUMONIA (HAP) AND VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

J12.0-3/J12.8-9/J13/J14/J15.0-9/J16.0/J16.8/J18.0-2/J18.8-9 + (Y95)

DESCRIPTION

HAP is defined as a new lung infiltrate (not present on admission) plus clinical evidence that the infiltrate is an infection (e.g. new onset of fever, purulent sputum, leukocytosis) occurring >48 hours after admission to hospital. HAP has a high morbidity and mortality; early appropriate antibiotic therapy is essential.

Infection may be due to multi-drug resistant organisms, particularly in patients with prior intravenous antibiotic use within 90 days. *LoE:Iia*[xv]

Ventilator-associated pneumonia (VAP) occurs >48 hours after intubation. VAP is more often due to multi-drug resistant organisms than HAP.

GENERAL MEASURES

» Microbiologic specimens: blood culture and sputum/tracheal aspirate bacterial culture. Therapy should be adjusted according to culture result. A good quality Gram stain may be useful in guiding the choice of initial therapy.
» If patient is neutropenic – See section 2.2: Febrile neutropenia.

MEDICINE TREATMENT

Empiric antibiotic therapy

» Treatment duration: 7 days. *LoE:Iia*[xvi]
» 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). *LoE:IIIb*[xvii]

OR ALTERNATIVELY:

- Cefepime, IV, 2 g 12 hourly as monotherapy. (See Appendix II for guidance on dosing in renal impairment). *LoE:IIIb*[xviii]

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. *LoE:IIIb*[xix]

OR

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

LoE:IVb[xx]

Note:

» De-escalate as soon as the culture is available.
» For severe pencillin allergy, consult an infectious diseases specialist or microbiologist.

9.1.4 URINARY TRACT INFECTIONS, CATHETER ASSOCIATED

T83.5 + (Y84.6+N39.0)

DESCRIPTION

» Common organisms: resistant aerobic gram-negative bacteria.
» Microbiologic specimen: blood culture and Mid-stream/Catheter specimens of urine (MSU/CSU) for microscopy and bacterial culture.
» In most patients with long-term catheters, bacteria cultured on CSU represent colonisation rather than infection – only treat with antibiotics if features of sepsis or pyelonephritis are present.

GENERAL MEASURES

» Remove catheter.

MEDICINE TREATMENT

Empiric antibiotic therapy:

- Amikacin, IV, 15 mg/kg daily for 7 days.

OR

If local resistance patterns show low level resistance to ciprofloxacin or culture shows sensitivity:

- Ciprofloxacin, oral, 500 mg 12 hourly for 7 days. *LoE:IIIb*[xxi]

9.2 ADULT VACCINATION

Note: As COVID vaccination recommendations are being updated regularly as new evidence emerges, please consult the latest National Department of Health vaccine policy recommendations.

Vaccine	Indications	Comments
• Influenza vaccine Z25.1	» Pregnant women » Elderly patients >65 years. » HIV-infected patients. » Patients with chronic pulmonary or cardiac conditions, or malignancy » Healthcare workers with direct patient contact.*	○ Contraindication: <6 months of age. ○ Dose: IM, 0.5 mL ○ Repeat annually. ○ Severe egg allergy is not an absolute contraindication to the inactivated influenza vaccine. However, it is recommended that individuals reporting a history of severe egg allergy are vaccinated in a setting equipped to manage allergic reactions.
• Pneumococcal vaccine (23 valent polysaccharide) Z23.8	» Asplenic patients. » Chronic cerebrospinal fluid (CSF) leak.	○ Contraindication: pregnancy. ○ Dose: IM, 0.5 mL Booster: after 5 years and at 65 years of age. *LoE:IIIb*[xxii]
• Hepatitis B vaccine** Z24.6	» High risk groups, e.g. hospital personnel or sexual contacts of infected patients. » Sexual assault.	○ Dose: IM, 1 mL immediately then 1 mL after 1 month and 1 mL 6 months after 1st dose. ○ Administer deep IM in deltoid muscle.
• Tetanus toxoid vaccine Z23.5	» Booster when there is a high risk for tetanus.(unless given in previous 5 years) e.g. contaminated wound or pregnant women to prevent neonatal tetanus	○ Dose: IM, 40 IU (0.5 mL).

Table 9.1: Adult vaccination

*Healthcare workers are not routinely offered immunisation during the annual campaign. Although it is recommended that healthcare workers are vaccinated against influenza, they will not be provided with publicly funded vaccines unless they fall within any of the designated high-risk groups.

** Not to be given to patients who have already been immunised.

Note: Prioritisation strategies may vary in a pandemic.

9.2.1 RABIES VACCINATION

Z24.2

*Rabies is a notifiable medical condition.

See the Primary Health Care STGs and EML - Section 21.3.1.1: Animal bites.

9.3 BRUCELLOSIS

A23.0-3/A23.8-9
*Notifiable medical condition.

DESCRIPTION

Zoonotic infection, usually due to *B. abortus* in South Africa. Infection is usually acquired from unpasteurised milk products or handling raw meat.

MEDICINE TREATMENT

- Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

AND

- Gentamicin, IV, 6 mg/kg daily for 3 weeks (see Appendix II for guidance on prescribing). *LoE:IVb*[xxiii]
  - Preferred regimen for osteo-articular or cardiac involvement.

Alternatively, REPLACE gentamicin with rifampicin:

- Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.

Exclude TB before starting rifampicin-based therapy.

9.4 EMERGING RESPIRATORY PATHOGENS

9.4.1 MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS INFECTION: MERS COV

B34.2/J16.8 + (B97.2)
*Notifiable medical condition.

Note: Consult most recent guidelines from the National Department of Health/ NICD.

DESCRIPTION

Middle East Respiratory Syndrome (MERS) is a viral respiratory illness caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Individuals with MERS-CoV present with a wide spectrum of clinical presentation, ranging from asymptomatic infection to acute upper respiratory illness and rapidly progressing lower respiratory illness, respiratory failure, septic shock, and multi-organ failure resulting in death.

A typical presentation of MERS includes:

- » Fever (>38°C)
- » Cough
- » Chills or rigors
- » Shortness of breath

Presentation may also include haemoptysis, sore throat, myalgias, diarrhoea, vomiting, and abdominal pain.

Complications:

- » Severe pneumonia
- » ARDS
- » Acute renal failure
- » Refractory hypoxaemia

GENERAL MEASURES

- » **Ensure that patients suspected to have MERS Coronavirus are isolated at all times to limit further exposure.**
- » Discuss and manage all suspected, probable cases and contacts in consultation with the regional virologist or infectious diseases specialist at the referral centre/NICD.
- » Transfer of patients should only occur once all relevant arrangements have been made to limit further exposure to a potential contagious and life threatening agent.
- » Record and follow-up all patient contacts.

Prevention

- » Practise handwashing and careful disposal of materials that are infected with nasal secretions.
- » Use antiseptic/disinfectant solutions containing choroxylenol, benzalkonium chloride, and/or cetrimide. Chlorhexidine has been shown to be ineffective.
- » Add droplet precautions to the standard precautions. Airborne precautions should be applied when performing aerosol-generating procedures.

MEDICINE TREATMENT

- » Treatment is supportive.
- » No antiviral agents or vaccines are currently available.

REFERRAL

- » All cases after consultation with infectious diseases specialist and NICD.

9.4.2 CORONAVIRUS DISEASE-19 (COVID-19)

U07.1/U07.2

*Notifiable medical condition.

Note: Consult the most recent NICD guidelines on the clinical management of suspected or confirmed Covid-19 disease, available at: https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/covid-19-guidelines/clinical-management-of-suspected-or-confirmed-covid-19-disease/

DESCRIPTION

Coronavirus Disease of 2019 (COVID-19) is a viral, respiratory illness caused by SARS-CoV-2. Infection may be asymptomatic, and the majority of symptomatic infections (>80%) are characteristed by mild upper- and/or lower

respiratory tract symptoms. However, a minority of patients may develop severe disease requiring supplementary oxygen or, in severe cases, mechanical ventilation.

A typical presentation of COVID-19 includes some or all of the following:
» fever, chills or rigors, cough, dyspnoea, anosmia, dysgeusia, myalgias, sore throat, nausea, vomiting and/or diarrhoea.
» Atypical presentations are increasingly being recongised, including large vessel strokes (see section 14.1.1: Stroke) and diabetic ketoacidosis (see section 8.6.2: Diabetic ketoacidosis [DKA] and hyperosmolar hyperglycaemic state [HHS]).

Complications:
» Refractory hypoxaemia
» Long-COVID
» ARDS
» MIS-C and MIS-A

Diagnosis
Samples should be sent for SARS-CoV-2 PCR testing. Upper respiratory tract samples from all suspected patients should be sent – a nasopharyngeal swab is preferred, but in patients where this is not possible (e.g. recent nasal surgery, or severe coagulopathy), an oropharyngeal, nasal mid-turbinate, or anterior nares swab can be collected instead. Lower respiratory tract samples (e.g. sputum, tracheal aspirates) may be sent in addition if available.

GENERAL MEASURES
» If COVID-19 is suspected, isolate patient to limit further exposure.
» Adhere to standard contact and droplet precautions.
» Apply precautions against airborne transmission when performing aerosol-generating procedures such as intubation or nasogastric suctioning.

Management
» Give supplemental oxygen if required, targeting an SpO_2 of ≥90% for non-pregnant adults (≥94% for pregant women). Titrate oxygen therapy to reach targets by means of a nasal cannula, simple face mask or face mask with a reservoir bag, as appropriate.

	Nasal cannula	Simple face mask	Face mask with reservoir bag
Flow rate	1-5 L/min	6-10 L/min	10-15 L/min
FiO_2 estimate	0.25-0.4	0.4-0.6	0.6-0.95

» Patients who have respiratory failure despite maximal face mask oxygen should be promptly identified and considered for possible escalation of respiratory support with high flow nasal cannula oxygen, continuous positive airway presure, or intubation and mechanical ventilation as

appropriate.

» The use of the prone position in non-intubated, conscious patients who are hypoxaemic may be beneficial. *LoE:IIIb*[xxiv]

MEDICINE TREATMENT

Note: Antibiotics are of no value for the treatment of confirmed COVID-19 unless there is clear evidence of a co-existing infection.

Thromboprophylaxis: (Z29.2)

All hospitalised patients with COVID-19 require prophylaxis against venous thromboembolic disease, in the absence of any contraindications (see section 2.8: Venous thrombo-embolism).

- Low molecular weight heparin, e.g.: *LoE:IIIb*[xxv]
- Enoxaparin, SC, 40 mg daily.
  - Reduce dose to 20 mg daily in patients with renal failure (eGFR <30 mL/minute).

OR

- Unfractionated heparin, SC, 5 000 units 12 hourly.

Note: Patients with D-dimer >1.5 mg/L or requiring a non-rebreather mask or more should be considered for therapeutic doses of LMWH or unfractionated heparin (see section 2.8: Venous thrombo-embolism).

- Low molecular weight heparin, e.g.: *LoE:IIIb*[xxvi]
- Enoxaparin, SC, 1.5 mg/kg daily,

OR

- Enoxaparin, SC, 1 mg/kg 12 hourly.

In morbid obesity, dosing of LMWH should be individualised in discussion with a specialist.

In renal failure (eGFR <30 mL/minute), the recommended therapeutic dose of LMWH is 1 mg/kg daily.

Evidence indicates that PTT monitoring is not necessary with weight-based dosing of unfractionated heparin. However, in patients with morbid obesity and renal failure (eGFR <30 mL/minute), unfractionated heparin should be used with PTT monitoring to maintain the PTT at 1.5 to 2.5 times the control. PTT should be taken 4 hours after SC dose.

In non-pregnant patients who require supplemental oxygen:

- Corticosteroids, e.g.: *LoE:Ia*[xxvii]
- Dexamethasone, IV, 6 mg daily for up to 10 days, or until discharge.

In pregnant patients who require supplemental oxygen:
If corticosteroids are also needed to accelerate fetal lung maturity:
See section 6.11.1: Preterm labour (PTL) and preterm prelabour rupture of membranes (PPROM).
If corticosteroids are not needed for fetal lung maturity:
- Corticosteroids, e.g.:
- Dexamethasone, IV, 6 mg daily for up to 10 days, or until discharge.

If there is a concern of in-utero steroid exposure, use corticosteroid therapy with less placental transfer:
- Prednisone, oral 40 mg daily, for up to 10 days, or until discharge.

OR
- Hydrocortisone, IV, 80 mg 12 hourly for up to 10 days, or until discharge.

Note:
» See section 6.5: COVID-19 in pregnancy. *LoE:IIIb*[xxviii]

Corticosteroids cross the placenta and may have long-term, deleterious effects on the child.

9.5 HAEMORRHAGIC FEVER SYNDROME

A98.0-5/A98.8/A99
*Notifiable medical condition.

DESCRIPTION

Characterised by high fever, together with disseminated intravascular coagulation (DIC) and bleeding tendency. Other symptoms and organ involvement vary according to the causative virus.

Some important causes other than viral haemorrhagic fevers (VHF) are:
» severe bacterial infections, particularly N. meningitidis,
» severe tick bite fever,
» severe falciparum malaria,
» fulminant hepatitis,
» leptospirosis, and
» other causes of DIC or bleeding tendency.

Endemic causes of VHF in South Africa are Crimean-Congo fever and Rift Valley fever, both of which may be transmitted between humans by means of blood and body fluids.

GENERAL MEASURES

» A detailed travel and clinical history is crucial.
» If VHF is suspected, isolate patient in a single room and take proper precautions to limit further exposure.
» Precautions should include:

- long sleeved disposable gown,
- vinyl or rubber apron if the patient is bleeding,
- two pairs of latex gloves, one below the gown and one over the gown,
- disposable face mask, preferably with a visor,
- goggles if a mask is used without a visor, and
- waterproof boots or 2 pairs of overshoes, one over the other.

» Exclude alternate diseases by means of appropriate laboratory testing.
» Testing for VHF may be required, both to confirm or, to exclude the possibility of VHF - this must be arranged with the NICD (see above), before sending the specimens, as specific precautions apply.
» Support patients with packed red cells and fresh frozen plasma, as required - See section 23.5.2: Anaemia in critical care.
» Record and follow up all patient contacts.

Severe bacterial infections can mimic the features of haemorrhagic fever syndrome. Broad-spectrum antibiotics, e.g. ceftriaxone, IV, 2 g daily, are indicated in every case until the diagnosis is confirmed.

REFERRAL

» Discuss and manage all suspected VHF cases in consultation with the Regional Virologist or Infectious Diseases Consultant at the referral centre.
» Cases may also be discussed with the Special Pathogens Unit of the National Institute for Communicable Diseases (NICD):
Tel: 011 386 6000, Outbreak hotline: 082 883 9920.
» Transfer of patients should only occur once all relevant arrangements have been made to limit further exposure to a potentially contagious and life-threatening virus.

9.6 HYDATID DISEASE

B67.0-9

DESCRIPTION

Cysts of *E. granulosus*, acquired from ingestion of helminth ova passed out in dog faeces, particularly in sheep-farming areas. Cysts may occur in any organ but are most commonly found in the liver and lungs.

GENERAL MEASURES

Definitive treatment with surgery or PAIR (**P**ercutaneous **A**spiration **I**njection of helminthicidal agent and **R**e-aspiration) is preferred for all accessible lesions.

MEDICINE TREATMENT

With medical therapy, cure is achieved in about half, improvement in about a quarter and no response in about a quarter of cases:

- Albendazole, oral, 15 mg/kg/day up to maximum of 400 mg 12 hourly with meals. *LoE:IIIb*[xxix]
  - Duration is 3–6 months according to response on imaging for inoperable cysts **or** 14–28 days before and 28 days after PAIR/surgery. *LoE:Ia*[xxx]
  - Monitor liver function tests and FBCs monthly.

REFERRAL

All cases to a centre with experience in surgery and PAIR.

9.7 MALARIA

See the Primary Health Care STGs and EML - Section 10.7: Malaria.

9.7.1 MALARIA, UNCOMPLICATED

B50.0/B50.8-9/B51.0/B51.8-9/B52.9/B53.0/B53.8/B54
*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 10.7.1: Malaria, non-severe/uncomplicated.

9.7.2 MALARIA, SEVERE

B50.0/B50.8
*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 10.7.2: Malaria, severe/complicated.

DESCRIPTION

P. falciparum malaria with one or more of the following features:

- » severe general body weakness (prostration)
- » impaired consciousness
- » renal dysfunction
- » repeated vomiting
- » severe diarrhoea
- » severe anaemia (Hb <6 g/dL)
- » haemoglobinuria
- » acidosis (plasma bicarb <15 mmol/L)
- » abnormal bleeding (e.g. epistaxis)
- » convulsions
- » heavy parasitaemia (≥5%)
- » ARDS
- » shock
- » hypoglycaemia
- » clinical jaundice

GENERAL MEASURES

» Maintain hydration but avoid excessive fluid administration as this could contribute to the development of ARDS (especially in pregnancy).
» Transfuse if haemoglobin <6 g/dL.
» There is no convincing evidence of benefit for the use of exchange transfusion.

MEDICINE TREATMENT

Intravenous therapy:

- Artesunate, IV, 2.4 mg/kg at 0, 12 and 24 hours; then daily until patient is able to tolerate oral therapy.
  - Administer at least 3 IV doses before switching to oral artemether/lumefantrine.

LoE:Ia[xxxi]

Follow intravenous therapy with oral therapy:

- Artemether/lumefantrine 20/120 mg, oral, 4 tablets per dose, taken with fat-containing food or full cream milk to ensure adequate absorption.
  - Give the first dose immediately.
  - Give the second dose 8 hours later.
  - Then 12 hourly for another 2 days. (6 doses given over 3 days, i.e. 24 tablets in total).

» Monitor treatment response with regular blood smears.

» An increase in parasitaemia may occur within 24 hours due to release of sequestrated parasites, but a reduction should be seen after 48 hours.

» Gametocytes may appear after this stage – this does NOT mean failure of therapy as gametocytes may persist for up to 2 weeks after successful therapy. Only the reappearance of trophozoites or failure to clear them means failure.

Consider concomitant bacteraemia in patients with severe malaria, especially if they have neutrophilia.

REFERRAL

» Patient in need of ventilation or dialysis if these are unavailable on site.

9.8 SCHISTOMIASIS

B65.0-3/B65.8-9

*Notifiable medical condition.

DESCRIPTION

A parasitic infestation with:

» *Schistosoma haematobium*: primarily involves the bladder and renal tract, or

» *Schistosoma mansoni*: primarily involves the intestinal tract.

Acute schistosomiasis syndrome

» Typically occurs in travellers to endemic areas with freshwater exposure 3-7 weeks before onset.

» Clinical features include fever, rigors/chills, urticaria, angioedema, myalgias, arthralgias, dry cough, diarrhoea, abdominal pain, and headache. Symptoms are usually relatively mild and resolve spontaneously over a period of a few

days to a few weeks.
» The eosinophil count is almost invariably markedly elevated.
» Diagnosis is confirmed serologically – eggs are seldom seen in stool or urine.
» Differential diagnosis includes urinary tract infection; glomerulonephritis; HIV; gastroenteritis (Salmonella); hepatitis A, B and C; and malaria.

Chronic schistosomiasis
» Most individuals with schistosomiasis infection are asymptomatic.
» *S. haematobium* may present with macroscopic haematuria and urinary symptoms. Chronic bladder involvement and urinary tract involvement may cause urinary incontinence and obstructive uropathy.
» *S. mansoni* may present with chronic or intermittent dysentery. Periportal fibrosis and portal hypertension may occur.
» Pulmonary hypertension and central nervous system involvement (particularly myelopathy) are uncommon complications.
» Definitive diagnosis is by finding eggs in urine (*S. haematobium*), stool (*S. mansoni*), or on biopsy. Serology is usually positive.

MEDICINE TREATMENT

Acute schistosomiasis syndrome
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

Note: Praziquantel may cause life-threatening deterioration if given in acute schistosomiasis. *LoE:IIIb*[xxxii]

4-6 weeks later, after symptoms have resolved:
- Praziquantel, oral, 40 mg/kg as a single dose.

AND *LoE:IIIb*[xxxiii]
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

Note: Optimum time for administration of praziquantel is uncertain but sufficient time is required for the worms to mature.

If eosinophilia and high antibody titres are still present after 4-6 weeks, repeat praziquantel treatment:
- Praziquantel, oral, 40 mg/kg as a single dose. *LoE:IIIb*[xxxiv]

Chronic schistosomiasis
Manage as recommended in PHC STGs and EML, section 10.12: Schistosomiasis (bilharzia).

9.9 TETANUS

A35
*Notifiable medical condition.

DESCRIPTION

Painful muscle spasms and rigidity following inoculation by trauma of

Clostridium tetani spores, which germinate and produce toxins. The wound may be trivial and healing may have occurred before presentation. Incubation period is 3-21 days. Tetanus may be localised, with muscle spasms near the site of inoculation, or generalised, with spasm of the jaw muscles being a common presenting sign.

GENERAL MEASURES

» These patients need to be managed in a high care setting where ventilation is available.
» Maintain and protect airway.
» Monitor ECG and blood pressure.
» Maintain and replace IV fluids.
» Wound management is essential with debridement and removal of any foreign bodies.

MEDICINE TREATMENT

For rigidity, spasms: (R25.2)

- Diazepam, IV, 10 mg 4 hourly for 24 hours.
  - Consider switch to oral therapy after 24 hours as prolonged parenteral diazepam administration can cause acidosis.
  - Titrate to effect: doses as high as 50–100 mg two hourly may be required. *LoE:IIIb*[xxxv]
  - Higher doses require monitoring for respiratory depression.
  - Use muscle relaxants sparingly as these may exacerbate autonomic instability.

Antibiotic treatment:

- Metronidazole, IV, 500 mg 8 hourly for 10 days. *LoE:IIIb*[xxxvi]

For passive immunisation: (Z23.5)

- Tetanus immunoglobulin, IM, 3 000 units as a single dose.

For active immunisation of all patients (as clinical tetanus does not always confer immunity): (Z23.5)

- Tetanus toxoid vaccine, IM, 0.5 mL, total of 3 doses:
  - on admission,
  - at 4 weeks, and
  - at 6 months.
  - Administer at a different site to that used for administering tetanus immunoglobulin.

For pain:

- Paracetamol, oral, 500 mg -1 g 4–6 hourly when required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.
- Morphine, IV, to a total maximum dose of 10 mg (See *LoE:IIa*[xxxvii]

Appendix II, for individual dosing and monitoring for response and toxicity).

For shock, dehydration, maintenance of hydration: R57.9 + (A35)
- IV fluids.

For prophylaxis for deep vein thrombosis: (Z29.2)
See section 2.8.1: Venous thrombo-embolism - Prophylaxis.

REFERRAL
» All cases to a facility with resources for artificial mechanical ventilation.

9.10 TICK BITE FEVER
A77.0-3/A77.8-9/A93.8

DESCRIPTION
Tick-borne infection due to *R. conorii*, acquired from dogs, or *R. africae*, acquired from cattle and game. The hallmark of tick bite fever is the eschar, a round black lesion ± 5 mm in diameter with an inflammatory halo that occurs in about two thirds of patients with *R. conorii* and in most cases of *R. africae* infection, where multiple eschars are common. A rash develops on about the third day of illness in about two thirds of patients with *R. conorii* (less common with *R. africae* infection). In *R. conorii* infection the rash is maculopapular and involves the palms and soles. In *R. africae* infection the rash is sparse and may be vesicular. Headache is a prominent symptom.

MEDICINE TREATMENT
Non-pregnant:
Treatment duration: Treat for 7 days (if afebrile), or until at least 3 days after the fever has subsided.
- Doxycycline, oral, 100 mg 12 hourly. *LoE:IIIb*[xxxviii]

If pregnant: O98.5 + (A77.0-3/A77.8-9/A93.8) *LoE:IVb*[xxxix]
- Doxycycline, oral, 100 mg 12 hourly for 2 days. *LoE:IIIb*[xl]

Then switch to:
- Azithromycin, oral, 500 mg 12 hourly for 3 days. *LoE:IIIb*[xli]

If patient is unable to tolerate oral therapy:
- Ciprofloxacin, IV, 400 mg 8 hourly.
  Note: Ciprofloxacin has inferior efficacy compared to doxycycline. Oral doxycycline should be commenced as soon as possible.

Note:
» Tick bite fever responds rapidly to treatment. Fever persisting for >48 hours after initiation of treatment should prompt consideration of an alternative or additional diagnosis. *LoE:Ivb*[xlii]

9.11 TYPHOID FEVER (ENTERIC FEVER)

A01.0-4

*Notifiable medical condition (Typhoid fever).

DESCRIPTION

Systemic infection due to *S. enteritica* serotype Typhi or related organisms (e.g. *S. paratyphi*, *S. choleraesuis*). Initial symptoms are abdominal pain, headache, cough and fever, with diarrhoea developing after a few days. Bacteraemia is common in the first week of illness, subsequently stool culture has the highest yield.

GENERAL MEASURES

» Transfusion is indicated for severe haemorrhage.
» Replace fluid and electrolytes.
» Contact isolation during acute phase of illness.

MEDICINE TREATMENT

Antibiotic therapy:

Note: There is increasing resistance to ciprofloxacin in South Africa. Ensure that specimens are sent for culture and sensitivity prior to commencing antibiotic therapy.

Total duration of antibiotic therapy: 10 days.

- Ceftriaxone, IV, 2 g 12 hourly. *LoE:IIIb*[xliii]

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours, based on culture sensitivity results:

- Ciprofloxacin, oral, 500 mg 12 hourly. *LoE:Ivb*

Note:

» Stool cultures must be repeated at weekly intervals after clinical recovery to ensure that a carrier state has not developed.
» Two consecutive negative stool cultures are required to exclude carrier state. This is of vital importance in patients whose occupation includes handling of food, whereby negative stool culture results are required before they can be medically permitted to resume their occupational duties.

Chronic carriers: (Z22.0)

- Ciprofloxacin, oral, 500 mg 12 hourly for 6 weeks (if sensitive to ciprofloxacin).
  - Advise strict hand washing.
  - Avoid food preparation for others during severe illness.

REFERRAL

» Surgical consultation for complications such as intestinal haemorrhage, threatening bowel perforation or localisation with metastatic infection with or without abscess formation, and peritonitis.
» Drug resistant organism: consult microbiology/infectious diseases services.

9.12 VARICELLA (CHICKENPOX), COMPLICATED

B01.1-2† + (G02.0*/G05.1*+J17.1*)/B01.8

GENERAL MEASURES

» Cool, wet compresses or tepid water baths.
» Body hygiene to prevent secondary infection.
» Advise against scratching.

MEDICINE TREATMENT

Antiviral therapy is required in complicated cases, e.g.:
» chickenpox pneumonia,
» pregnancy,
» neurological involvement, and
» chickenpox in immunocompromised patients.

Antiviral therapy:

Aciclovir, IV, 10 mg/kg 8 hourly for 7 days.
- Infuse aciclovir over one hour.

For varicella without neurological involvement, when the patient's clinical condition improves, the 7-day course can be completed with:

- Antiviral (active against varicella zoster), e.g: *LoE:IVb*[xliv]
- Aciclovir, oral, 800 mg five times daily.
  - Doses are given 4 hourly, except for dose scheduled for the middle of the night.

Secondary infection

B02.8

Treat secondary bacterial infection if suspected.

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

OR

- Cefalexin, oral, 500 mg 6 hourly for 5 days.

Passive immunization following significant exposure: (Z29.1)

Criteria for eligibility [Both a) and b) below are required]:

a) Significant exposure - Household contacts exposed to/ patients lying adjacent to (same ward) those diagnosed with varicella.
b) Severe immunological compromise and lack of varicella-directed immunity (i.e. no history of chickenpox/shingles, or negative VZV IgG).

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 600 units.
  - Administer within 96 hours of significant exposure. *LoE:IVb*[xlv]

9.13 ZOSTER (SHINGLES)

B02.9

DESCRIPTION

Dermatomal eruption of vesicles on an erythematous base due to varicella-zoster virus (lies dormant in nerve ganglia following chickenpox).

GENERAL MEASURES

» Isolate from immunocompromised or pregnant non-immune individuals (who may develop severe chickenpox).
» Offer HIV test, especially in patients <50 years of age.

MEDICINE TREATMENT

Antiviral therapy should be provided for:
» Immunocompromised patients, provided that active lesions are still being formed, and
» Immunocompetent individuals provided they present within 72 hours of onset of clinical symptoms.

▪ Antiviral (active against herpes zoster) e.g.:
- Aciclovir, oral, 800 mg five times daily for 7 days (given 4 hourly except for the dose scheduled for the middle of the night). *LoE:IVb*[xlvi]

For zoster with secondary dissemination or neurological/ complicated eye involvement (i.e. complicated herpes zoster ophthalmicus e.g. acute retinal necrosis (ARN), optic neuropathy or orbitopathy):
B02.0-3[†]+(H03.1*/H13.1*/H19.2*/H19.0*/H22.0*)/ B02.7+(G02.0*/G05.1*/G53.0*/ G63.0*)/B02.8

- Aciclovir, IV, 10 mg/kg 8 hourly for 7 days.
  - Infuse aciclovir over one hour.
  - The course can be completed with aciclovir, oral, 800 mg five times daily.
  - Dose adjustment based on renal clearance (See Appendix II for guidance on prescribing and monitoring).

LoE:IVb[xlvii]

Secondary infection

B02.8

This is seldom present and is over-diagnosed. The vesicles in shingles often contain purulent material, and erythema is a cardinal feature of shingles.
If there is suspected associated bacterial cellulitis:

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

For pain:

Pain is often very severe and requires active control. Combination of different classes of analgesics is often necessary.
Recommended therapy for acute phase of infection, e.g.:

- Paracetamol, oral, 500 mg -1 g 4–6 hourly when required (to a

maximum of 4 g in 24 hours).
- Maximum dose: 15 mg/kg/dose.

AND/OR

If pain is not adequately controlled:

- Tramadol, oral, 50–100 mg 6 hourly.

See chapter 26: Pain.

Post-herpetic neuralgia: B02.2+(G53.0*)

Initiate adjuvant therapy early if indicated.

- Amitriptyline, oral, 10 mg at night.
  - Titrate as necessary to a maximum dose of 150 mg.

See section 26.1.4: Neuropathic pain.

REFERRAL

» Refer to an ophthalmologist if there is ocular involvement with ophthalmic zoster (if the tip of the nose is involved then ocular involvement is much more likely). See section 18.4: Herpes zoster ophthalmicus.
» Patients who develop complications e.g. myelitis.

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SOUTH AFRICAN ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 9: SYSTEMIC AND HEALTHCARE-ASSOCIATED INFECTIONS
NEMLC RECOMMEDATIONS FOR MEDICINE AMENDMENTS (2020-4 REVIEW CYCLE)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guidelines (STGs).

A: NEW ADDITIONS:

CONDITION	MEDICINE MANAGEMENT	MEDICINE ADDED
9.4.2 Coronavirus disease-19 (COVID-19)		
- *supplemental oxygen*	Yes	Oxygen
- *thromboprophylaxis*	Yes	LMWH therapeutic class
		Enoxaparin, parenteral as an example of LMWH therapeutic class
		Unfractionated heparin
-*therapeutic treatment with heparin*	Yes	LMWH therapeutic class
		Enoxaparin, parenteral as an example of LMWH therapeutic class
		Unfractionated heparin
-*non-pregnant, requiring supplemental oxygen*	Yes	Corticosteroid therapeutic class
		Dexamethasone, parenteral as an example of corticosteroid class
-*pregnant, requiring supplemental oxygen*		
○ *fetal lung maturity **also** required*	Yes	Cross referred to section 6.11.1: Preterm labour (PTL) and preterm pre-labour rupture of membranes (PPROM) (Betamethasone, parenteral)
		Cross referred to section 6.11.1: Preterm labour (PTL) and preterm pre-labour rupture of membranes (PPROM) (Dexamethasone, parenteral)
○ *fetal lung maturity **not** required*	Yes	Corticosteroid therapeutic class
		Dexamethasone, parenteral as an example of corticosteroid class
○ *concern of in-utero steroid exposure*	Yes	Prednisone, oral
		Hydrocortisone, parenteral
- *management of covid-19 in uncontrolled diabetics*	No	No, but hyperglycaemia in COVID-19 to be treated as in other critically ill patients (target blood glucose of ≤10 mmol/L)

B: MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/AMENDED
Antimicrobial Stewardship	-	Cross reference to the local AMR website added
9.1.1 Intravascular catheter infections – empiric antibiotic therapy		
- *S aureus*	Vancomycin, IV	Dosing amended
- *Candidaemia – intolerant to amphotericin B (renal impairment)*	Fluconazole, oral	Dose amended
- *Candidaemia – intolerant to amphotericin B (renal impairment)*	Fluconazole, oral	Deleted
	Echinocandins	Retained as specialist motivation
9.1.2 Surgical Wound infections		
- *Empiric antibiotic therapy –surgical site infections*	Cefazolin	Retained –cefazolin retained as an alternative to cloxacillin due to ongoing supply constraints
- *Surgical site infections - Gram stain of exudate, gram negative organism*	Cefazolin	Amended – empiric cefazolin therapy to be discontinued and Piperacillin/tazobactam monotherapy recommended
- *Gram stain of exudate, Gram negative organism* *Severe penicillin allergy*	Ertapenem	Retained
	Vancomycin, IV	Dosing amended

-Methicillin (cloxacillin) resistant S. aureus (MRSA)	Linezolid	Not added
-Female uro-genital tract surgery or open GIT surgery	Co-amoxiclav	Not added
9.1.3 Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP)		
- *Empiric antibiotic therapy*	Empiric antibiotic therapy	Duration amended
	Ceftriaxone, IV	Deleted
	Severe penicillin allergy	Guidance added
	Antibiotic treatment protocol for HAP/VAP	Amended
	Carbapenems (imipenem/cilastin AND meropenem)	Note added (avoid imipenem/cilastan in patients with CNS disorders or history of seizures – use meropenem)
9.1.4 Urinary tract infections, catheter associated		
- *Empiric antibiotic therapy*	Empiric therapy - duration of treatment	Duration amended to 7 days
	Amikacin	Retained as monotherapy
9.2 Adult vaccination		
- *COVID-19*	COVID-19 vaccination	Guidance added
-Influenza	*Influenza vaccine*	Indications aligned
-Tetanus	Tetanus toxoid vaccine	Indications aligned
9.3 Brucellosis	Medicine treatment - rifampicin	Guidance clarified
9.4 Emerging Respiratory pathogens		
- Middle east respiratory syndrome infection	MERS COV	STG separated from COVID-19
9.6 Hydatid disease	Albendazole	Guidance amended
9.9 Tetanus	General measures	Amended
	Paracetamol	Dose amended
9.10 Tick bite fever		
- Pregnancy	Doxycycline	Added as initial therapy
	Azithromycin	Retained
	Ciprofloxacin, IV	Retained
9.12 Varicella (chickenpox), complicated		
-Antiviral therapy	Aciclovir	Guidance clarified
-Secondary infection	Flucloxacillin, oral	Added
	Cefalexin, oral	Added
- VZIG	Varicella-zoster immunoglobulin (VZIG), IM	Indication amended
	Varicella-zoster immunoglobulin (VZIG), IM	Maximum dose amended
9.13 Zoster (shingles)		
-Eye involvement	Aciclovir, IV	Guidance clarified
-Pain management	Paracetamol	Dose amended
	Tramadol	Dose amended
-Post-herpetic neuralgia	Amitriptyline	Dose amended

C. SUBSEQUENT UPDATES TO THE 2020-4 EDITION

Version no.	Section	Amendments
1.1	1.1.3 Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP)	**Seizure risk with carbapenems** Recommendation for the preferential use of meropenem over imipenem/cilastatin for patients with CNS disorders or a history of seizure disorders, deleted.

ANTIMICROBIAL STEWARDSHIP

A cross-reference to the national antimicrobial resistance guidance as published on the Knowledge Hub has been added: https://knowledgehub.health.gov.za/content/antimicrobial-resistance

9.1.1 INTRAVASCULAR CATHETER INFECTIONS

Guidance for peripheral and central catheter infections were separated out for clarity.
For peripheral blood line infections, microbiological specimens are not usually indicated unless patient systemically unwell, and the following additional STG text was added:

- » If peripheral blood culture negative but central catheter culture positive, monitor closely for signs of infection, and repeat peripheral blood cultures accordingly. If central line has grown *S. aureus*, 5-7 days of treatment is recommended (assuming peripheral blood cultures remain negative).
- » If peripheral blood culture is positive, remove catheter, and treat with systemic antibiotics, guided by the culture results.

Empiric antibiotic therapy

- ***S. aureus* infection**

Vancomycin, IV: *dosing amended*
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).

Level of Evidence: Very low certainty evidence, conditional recommendation
Note: Dosing of vancomycin in Appendix II: Prescribing information for specific medicines has likewise be updated.

- **Candidaemia – follow up susceptibility**

Fluconazole, oral dose: *amended*
Following empiric initiation of amphotericin B, IV for the management of candideamia in central venous catheter-associated infections, patients can be switched to oral fluconazole once there is clinical improvement and if the organism is susceptible to fluconazole. The dose of fluconazole has been corrected to 400 mg daily in line with the SAMF 14th Edition.

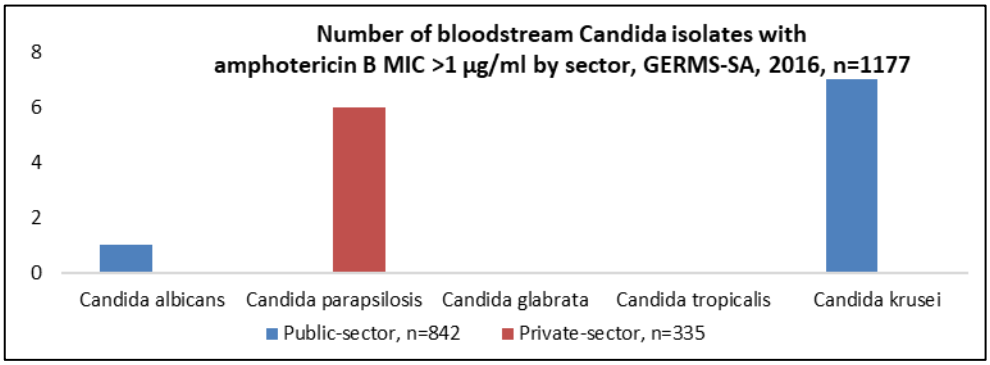
AMENDED FROM:
Follow up susceptibility:
- Once improved, if sensitive complete course with:
- Fluconazole, oral, 800 mg daily.

AMENDED TO:
Follow up susceptibility:
Once improved, if sensitive, complete course with:
- Fluconazole, oral, 400 mg daily.

- **Candidaemia – intolerant to amphotericin B (renal impairment)**

Fluconazole, oral: *deleted*
Echinocandins: *retained as specialist motivation*
As echinocandins are included on the Tertiary & Quaternary EML (June 2022), it was considered more rational to consider echinocandins on specialist motivation, than dose-adjusted oral fluconazole in the renally impaired patient who cannot use amphotericin B. Furthermore, in the previous review cycle, the Adult Hospital Level Committee collaborated with NICD and the following was discussed:

ADULT HOSPITAL LEVEL COMMITTEE MINUTES OF THE MEETING OF 23 NOVEMBER 2017:
Echinocandins: *Surveillance data suggests that this is the most ideal first-line agent, but it is very expensive.*



Amphotericin B: *Still a reliable first-line antifungal agent, but has serious adverse effects.*

Candida auris: *Cases of drug-resistant candida auris bloodstream infections recorded by NICD. However, based on CDC cut-off values; despite 85% resistance to fluconazole; only 13% of isolates reported to be resistant to amphotericin B and <1% resistant to echinocandin.*
Thus, the text of the STG was amended to recommend treatment with fluconazole, oral, only once susceptibility has been confirmed.

Level of Evidence: Low certainty evidence, conditional recommendation

9.1.2 SURGICAL WOUND INFECTIONS

Cefazolin, IV: retained
Cefazolin IV has been retained for empiric therapy of surgical wound infections due to ongoing supply constraints with cloxacillin.

Cefazolin, IV: amended
For surgical wound infections with a Gram-negative culture on the gram exudate, piperacillin/tazobactam monotherapy is recommended, and empiric cefazolin should be discontinued

Ertapenem, IV: retained
For surgical wound infections in patients with a severe penicillin allergy with a Gram-negative organism on the exudate, ertapenem is recommended for patients with a history of penicillin allergy. From a stewardship perspective, ertapenem has a narrower spectrum of activity compared to imipenem and meropenem and would be considered as the preferred option for patients with a severe penicillin allergy.

Vancomycin, IV: dosing amended
Aligned with section 9.1.1: Intravascular catheter infections (see above). Furthermore, the statement recommending verification of MRSA has been deleted as the recommendation applies to the management of confirmed MRSA. Amendments as tabulated below:

AMENDED FROM:
Methicillin (cloxacillin) reistant *S. aureus* (MRSA)
T81.4+ (B95.6+U82.1+Y83.9)
- Vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly. (See Appendix II for guidance on prescribing and monitoring).
  - Drain wound and obtain cultures to verify MRSA.

AMENDED TO:
Methicillin (cloxacillin) resistant *S. aureus* (MRSA):
T81.4 + (B95.6+U82.1+Y83.9)
- Vancomycin, IV, 25–30 mg/kg as a loading dose. Follow with 15–20 mg/kg/dose 12 hourly.
  - See Appendix II for guidance on prescribing and monitoring.

Linezolid, IV: not added
Vancomycin has been retained for the management of surgical wounds associated caused by methicillin (cloxacillin) resistant S. aureus (MRSA) as it is less costly than linezolid.

Co-amoxiclav, IV: not added
Combination therapy with ceftriaxone and metronidazole, IV has been retained for the management of female uro-genital tract surgery or open GIT surgery as the combination is less costly than co-amoxiclav IV and there is no evidence to suggest that the risk of the development of resistance favours co-amoxiclav.

9.1.3 HOSPITAL-ACQUIRED PNEUMONIA (HAP) AND VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

Title of this STG was amended from "*Hospital-acquired pneumonia (HAP)"* to align with international best practice.

Empiric antibiotic therapy: *duration amended*
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[1] that cite the following systematic reviews:

Ventilator-associated pneumonia:

[1] Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, et al. Management of Adults With Hospital-acquired and Ventilator-associated 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.

- *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.
  - 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 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.

- *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 difference3.40 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.

- 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.

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).

Level of Evidence: Moderate certainty evidence, strong recommendation

Hospital-acquired pneumonia *(non-VAP):*

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 – see above. 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.

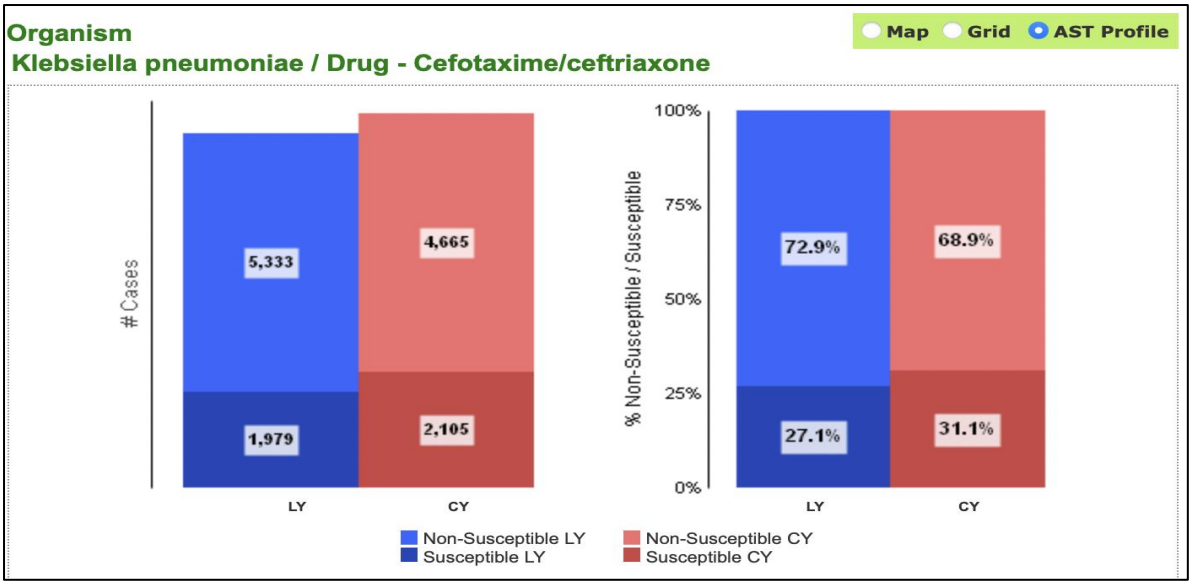
Level of Evidence: Low certainty evidence, strong recommendation

Ceftriaxone, IV: *deleted*

Common hospital-acquired pneumonia pathogens include *Klebsiella* and *Pseudomonas*. As per latest GERMS-SA surveillance, data, in public sector, 71% of invasive isolates are resistant to ceftriaxone (note, this figure includes community-acquired infections too; the resistance rate for hospital-acquired pneumonia is likely even higher than this figure). Pseudomonas is intrinsically resistant to ceftriaxone (i.e., 100% resistance).

[2] Pugh R, Grant C, Cooke RP, Dempsey G. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev. 2015 Aug 24;2015(8):CD007577.

[3] Dimopoulos G, Poulakou G, Pneumatikos IA, Armaganidis A, Kollef MH, Matthaiou DK. Short- vs long-duration antibiotic regimens for ventilator-associated pneumonia: a systematic review and meta-analysis. Chest. 2013 Dec;144(6):1759-1767.



Source: NICD antimicrobial surveillance reporting dashboard.
Level of Evidence: Low certainty evidence, conditional recommendation

NEMLC MEETING OF 25 AUGUST 2022:
Recommendations:

- More granular data should be sourced from NICD to allow for a detailed interrogation of the resistance to cephalosporins.
- Inclusion of the link to the NICD dashboard, to encourage end-users to engage with the dashboard to prompt clinicians to seek local facility level data as an aid to improved prescribing and antibiotic stewardship

Following NEMLC's request at the meeting of 25 August 2022, the following was accessed from NICD AMR surveillance dashboard.

AST results stratified by province for 2021, for the public sector shows very high levels of ceftriaxone resistance across provinces.

Klebsiella pneumoniae / Drug - Cefotaxime/ceftriaxone

	Total Cases		Susceptible				Intermediate				Resistant				Not Reported			
Province	**# CY**	**# LY**	**# CY**	**% CY**	**# LY**	**% LY**	**# CY**	**% CY**	**# LY**	**% LY**	**# CY**	**% CY**	**# LY**	**% LY**	**# CY**	**% CY**	**#LY**	**% LY**
Eastern Cape	**666**	641	123	**18.5%**	145	22.6%	1	**0.2%**		0.0%	542	**81.4%**	496	77.4%	0	**0.0%**	(1)	-0.2%
Free State	**374**	310	112	**29.9%**	93	30.0%		**0.0%**	1	0.3%	262	**70.1%**	216	69.7%	2	**-0.5%**	0	0.0%
Gauteng	**3,048**	3,474	1,073	**35.2%**	947	27.3%	2	**0.1%**	1	0.0%	1,973	**64.7%**	2,526	72.7%	13	**-0.4%**	(20)	-0.6%
KwaZulu-Natal	**1,021**	1,116	295	**28.9%**	269	24.1%	1	**0.1%**	2	0.2%	725	**71.0%**	845	75.7%	4	**-0.4%**	(6)	-0.5%
Limpopo	**315**	346	59	**18.7%**	80	23.1%	3	**1.0%**	5	1.4%	253	**80.3%**	261	75.4%	0	**0.0%**	0	0.0%
Mpumalanga	**356**	286	64	**18.0%**	34	11.9%	3	**0.8%**		0.0%	289	**81.2%**	252	88.1%	1	**-0.3%**	0	0.0%
North West	**275**	348	80	**29.1%**	94	27.0%	1	**0.4%**		0.0%	194	**70.5%**	254	73.0%	0	**0.0%**	(1)	-0.3%
Northern Cape	**39**	58	19	**48.7%**	20	34.5%		**0.0%**		0.0%	20	**51.3%**	38	65.5%	0	**0.0%**	0	0.0%
Western Cape	**676**	734	283	**41.9%**	294	40.1%		**0.0%**		0.0%	393	**58.1%**	440	59.9%	7	**-1.0%**	(4)	-0.5%
Total	**6,770**	**7,313**	**2,108**	**31.1%**	**1,976**	**27.0%**	**11**	**0.2%**	**9**	**0.1%**	**4,651**	**68.7%**	**5,328**	**72.9%**	**27**	**-0.4%**	**(32)**	**-0.4%**

Across districts (excluding districts with < 20 Klebsiella pneumoniae blood cultures in the year (2021), the median resistance percentage across 39 districts was 69%, with an IQR of 66-81%.

The reported cases are likely an underestimate of ceftriaxone resistance in HAP as:
1. They include a minority of community-acquired infections, which generally have less resistance than hospital-acquired infections.
2. For other, less common, microbiological causes of HAP, the ceftriaxone resistance profile will be much worse - e.g. Pseudomonas (intrinsically resistant) or Acinetobacter spp. (near universal resistance).

Severe penicillin allergy: *guidance added*
For severe penicillin allergy, guidance was added to consult an infectious diseases specialist or microbiologist.
Level of Evidence: Very low certainty evidence, conditional recommendation

Antibiotic treatment protocol for HAP/VAP: *amended*
Carbapenems (imipenem/cilastin AND meropenem): *note added (to avoid imipenem/cilastin in patients with CNS disorders or history of seizures – use meropenem)*

The STG was editorially amended so that the antibiotic treatment protocol for HAP/VAP provided guidance towards a carbapenem-sparing approach, and the note for use of carbapenems (imipenem/cilastin and meropenem) was added (aligned with SAMF, 2022), from:

AMENDED FROM:

MEDICINE TREATMENT

Empiric antibiotic therapy

Duration: 10 days.

HAP with no prior intravenous antibiotic use within 90 days:

- Ceftriaxone, IV, 2 g daily.

and

- Amikacin, IV, 15 mg/kg daily.

Severe Penicillin allergy: (Z88.0)

- Moxifloxacin, oral/IV, 400 mg daily.

and

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

HAP with prior intravenous antibiotic use within 90 days *and VAP.*

Antibiotic choice will depend on local susceptibility patterns. One or more of the following antibiotics/classes must be available, dependant on local susceptibility patterns:

- 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

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

OR

Instead of piperacillin/tazobactam + amikacin **OR** cefepime:

Carbapenem with activity against Pseudomonas:

- Imipenem/cilastan, IV, 1000/1000 mg 8 hourly (except CNS infections or known epileptics).

OR

Instead of piperacillin/tazobactam + amikacin **OR** cefepime **OR** imipenem:

- Meropenem, IV, 2 g 8 hourly (CNS infections or known epileptics).

Note: De-escalate as soon as the culture is available.

AMENDED TO:

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.

Level of Evidence: Guidelines[4]

And the following STG text was added, providing a cross-reference to section 2.2 for the management of febrile neutropenia:

Note: If patient is neutropaenic - See section 2.2: Febrile neutropenia.

[4] SAMF, 2022

Seizure risk with carbapenems

Preferential use of meropenem over imipenem in patients with a history of seizure disorders: Deleted

The recommendation to preferentially consider meropenem over imipenem/cilastatin has subsequently been removed in version 1.1 of the chapter, as there are reports of seizures occurring with both carbapanem options.

A meta-analysis of RCTs undertaken by Cannon et al (2014)[5] was the most recently identified SR review following a quick Pubmed search. A brief summary of this SR is included below:

- The objective of the SR was to estimate the risk of seizures with carbapenem versus non-carbapenem antibiotics and where possible, directly compare the seizure risk of various carbapenem antibiotics (imipenem, meropenem, ertapenem and doripenem). For the purposes of this document, reporting is limited to comparative risks of meropenem versus imipenem.
- Pubmed and EMBASE searches were conducted from Jan 1966 to Nov 2013. Manufacturers were contacted for unpublished data.
- The risk difference analysis (an estimate of the absolute risk of events between the two arms and allowed for inclusion of all studies meeting inclusion criteria regardless of whether or not an event occurred, included 169 studies. This analysis demonstrated an increased risk of seizures with carbapenems - among patients exposed to carbapenems there were an additional 2 patients with seizures per 1000 persons (95% CI 0.001, 0.004) compared with patients in the non-carbapenem group. The authors concluded that imipenem exposure was responsible for this difference as the risk difference for imipenem was 0.004 (95% CI 0.002, 0.007), whereas meropenem, ertapenem and doripenem were not associated with increased seizure risk. Furthermore, the estimated risk of seizure was numerically higher in those receiving higher doses of imipenem, as the pooled risk differences for ≤2g/day and 2g/day were 0.003 (95% CI 0.0005, 0.006) and 0.008 (95% CI 0.004, 0.013), respectively.
- However on analysis of head to head studies of imipenem versus meropenem (n=21), no differences were noted in the risk differences for seizure risk with imipenem compared with meropenem (0.001, 95%CI20.003,0.006; Figure 1). Seven of these 21 studies reported at least one seizure which were pooled to calculate the summary odds ratio for seizure risk as a head to head comparison. The point estimate demonstrated a higher frequency of seizures in the imipenem-treated patients (OR 1.48, 95%CI 0.54, 4.04; Figure 2), however, the difference was not statistically significant.
- The authors concluded that, although the overall frequency of seizures in patients receiving carbapenems is low, when compared with non-carbapenems there is a significantly increased risk of seizures associated with carbapenem usage, and that the increased risk was predominantly attributable to imipenem-related studies i.e. seizure risk for meropenem was comparable to non-carbapenem antibiotics. Additionally, the authors reported that the risk of seizure with imipenem was not increased when comparing studies that included patients with a history of seizure (n=21) with those that excluded patients with a seizure history (n=7), although the latter group may have been too small to detect a significant difference. In contrast however, in the head to head comparisons between imipenem and meropenem, no difference in seizure risk was identified in the risk difference analysis and in the 7 studies where at last one seizure was reported, no significant difference was identified, although the pooled 'OR numerically implicated imipenem over meropenem'.
- Some of the limitations of this review include:
  - » heterogeneity in the study populations (i.e. the population included in the imipenem versus non-carbapenem comparator analysis is not the same as the meropenem versus non-carbapenem comparator or the imipenem versus meropenem head-to-head analyses,
  - » seizure history as an exclusion criterion (significantly more meropenem studies and imipenem versus meropenem head-to-head studies excluded patients with a seizure history than did imipenem studies),
  - » Most studies included in the review did not provide sufficient detail on risk factors for seizures e.g. CNS injury or disease, history of seizure and/or receipt of concomitant medications known to decrease the seizure threshold, and as meningitis itself may cause seizures, it was not always possible to attribute the cause of seizures as drug or non-drug related.

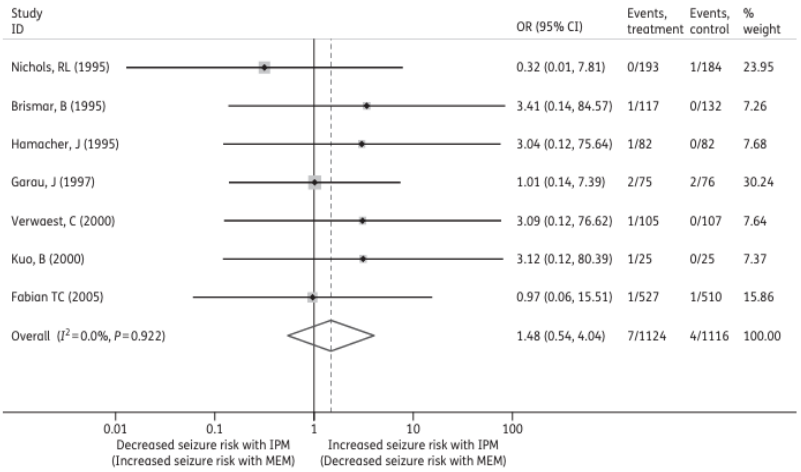
[5] Cannon JP, Lee TA, Clark NM, Setlak P, Grim SA. The risk of seizures among the carbapenems: a meta-analysis. J Antimicrob Chemother. 2014 Aug;69(8):2043-55. doi: 10.1093/jac/dku111. Epub 2014 Apr 16. PMID: 24744302.

Figure 1: Risk difference of seizure for carbapenems, versus non-carbapenem comparators

Carbapenem/study population	Number of studies	RD	95% CI
All carbapenems			
overall	169	0.002	0.001, 0.004
β-lactams only	129	0.002	−0.0003, 0.004
non-meningitis studies	166	0.003	0.001, 0.004
Imipenem			
overall	107	0.004	0.002, 0.007
adults	95	0.005	0.003, 0.008
adults, TDD ≤2 g	63	0.003	0.0005, 0.006
adults, TDD >2 g	32	0.008	0.004, 0.013
β-lactams only	76	0.004	0.001, 0.007
non-meningitis studies	107	0.004	0.002, 0.007
Meropenem			
overall	41	0.0002	−0.004, 0.005
β-lactams only	35	0.0003	−0.005, 0.005
non-meningitis studies	38	0.001	−0.002, 0.005
Ertapenem			
overall	19	0.0002	−0.002, 0.003
Doripenem			
overall	2	−0.007	−0.018, 0.004
Imipenem vs meropenem			
overall	21	0.001	−0.003, 0.006

TDD, total daily dose.

Figure 2: Comparison of the OR for seizures with imipenem (IPM) vs meropenem (MEM)



Updates to version 1.1 of the STG are as tabulated below. Due to historic reports of supply constraints with these medicines, both imipenem/cilastatin and meropenem have been retained on the EML.

AMENDED FROM (Ed 2020-4 v1.0):	AMENDED TO (Ed 2020-4 v1.1)
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.	**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. **OR** • 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

9.1.4 URINARY TRACT INFECTIONS, CATHETER ASSOCIATED

Empiric antibiotic therapy: duration amended

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[6].

Amikacin, IV: retained

Aminoglycosides reach high concentrations in the urine which makes monotherapy treatment suitable for the management of UTIs[7].

9.2 ADULT VACCINATION

COVID-19 vaccination: *guidance added*

As COVID vaccination recommendations are being updated regularly as new evidence emerges, guidance was provided to consult the latest National Department of Health vaccine policy recommendations.

Influenza vaccination: *indications aligned*

Indications aligned with PHC Chp 13 Immunisations STG – refer to table below.

Tetanus toxoid vaccine: *indications aligned*

Indications aligned with PHC Chp 13 Immunisations STG – refer to table below.

AMENDED FROM:

Vaccine	Indications	Comments
• Influenza vaccine Z25.1	Pregnant women Elderly patients >65 years. HIV-infected patients. Patients with chronic pulmonary, cardiac, and renal conditions. Healthcare workers with direct patient contact.**	○ Contraindication: severe egg allergy, <6 months of age. ○ Dose: IM, 0.5 mL. ○ Repeat annually.
• Tetanus toxoid vaccine Z23.5	Booster when there is a high risk for tetanus e.g. contaminated wound or pregnant women to prevent neonatal tetanus.	○ Dose: IM, 40 iu (0.5 mL).

AMENDED TO:

Vaccine	Indications	Comments
• Influenza vaccine Z25.1	» Pregnant women » Elderly patients >65 years. » HIV-infected patients. » Patients with chronic pulmonary or cardiac conditions, or malignancy Healthcare workers with direct patient contact.*	○ Contraindication: <6 months of age. ○ Dose: IM, 0.5 mL ○ Repeat annually. Severe egg allergy is not an absolute contraindication to the inactivated influenza vaccine. However, it is recommended that individuals reporting a history of severe egg allergy are vaccinated in a setting equipped to manage allergic reactions.
• Tetanus toxoid vaccine Z23.5	Booster when there is a high risk for tetanus.(unless given in previous 5 years) e.g. contaminated wound or pregnant women to prevent neonatal tetanus	Dose: IM, 40 IU (0.5 mL).

9.3 BRUCELLOSIS

Medicine treatment – rifampicin: *guidance clarified*

[6] Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, Saint S, Schaeffer AJ, Tambayh PA, Tenke P, Nicolle LE; Infectious Diseases Society of America. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010 Mar 1;50(5):625-63. doi: 10.1086/650482. PMID: 20175247.

[7] https://www.knowledgehub.org.za/system/files/elibdownloads/2022-03/Gentamicin%20for%20UTI-Adult%20review_November2019.pdf

The caution to exclude TB has been clarified as applicable to rifampicin-based therapy rather than being applicable to treatment with doxycycline and/or gentamicin. Amendments are as tabulated below:

AMENDED FROM:

MEDICINE TREATMENT

Exclude TB before starting therapy.

- Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

AND

- Gentamicin, IV, 6 mg/kg daily for 3 weeks (see Appendix II for guidance on prescribing).
  - Preferred regimen for osteo-articular or cardiac involvement.

OR

- Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

AND

- Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.

AMENDED TO:

MEDICINE TREATMENT

- Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

AND

- Gentamicin, IV, 6 mg/kg daily for 3 weeks (see Appendix II for guidance on prescribing).
  Preferred regimen for osteo-articular or cardiac involvement.

Alternatively, REPLACE gentamicin with rifampicin:

- Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.

Exclude TB before starting rifampicin-based therapy.

9.4 EMERGING RESPIRATORY PATHOGENS

This section has been separated out into two STGs:
9.4.1 Middle East Respiratory Syndrome Infection: MERS COV and
9.4.2 Coronavirus Disease-10 (COVID-19)
Details provided below.

9.4.1 MIDDLE EAST RESPIRATORY SYNDROME INFECTION: MERS COV

STG amended as detailed below:

.4.1 MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS INFECTION: MERS COV

B34.2/U07.1

*Notifiable medical condition.

Note: Consult most recent guidelines from National Department of Health/ NICD.

DESCRIPTION

Middle East Respiratory Syndrome (MERS) is a viral respiratory illness caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Individuals with MERS-CoV present with a wide spectrum of clinical presentation, ranging from asymptomatic infection to acute upper respiratory illness, and rapidly progressing lower respiratory illness; respiratory failure, septic shock and multi-organ failure resulting in death.

A typical presentation of MERS includes:

» fever (>38°C), chills or rigors, cough, shortness of breath

Presentation may include:

» hemoptysis, sore throat, myalgias, diarrhoea, vomiting, abdominal pain

Complications:

» severe pneumonia
» ARDS
» acute renal failure
» refractory hypoxaemia

GENERAL MEASURES

All suspected, probable cases and contacts must be discussed and managed in consultation with the regional virologist or infectious diseases specialist at the referral centre.

Transfer of patients will only occur once all relevant arrangements have been made to limit further exposure to a potential contagious and life threatening agent.

Droplet precautions should be added to the standard precautions. Airborne precautions should be applied when performing aerosol-generating procedures.

ISOLATE SUSPECTED SYMPTOMATIC CASES AT ALL TIMES.

If MERS coronavirus is suspected, isolate patient to limit further exposure.

MANAGEMENT

Treatment

Treatment is supportive.
No antiviral agents or vaccines are currently available.
Management of contact: consult with NICD and isolate contact.
Record and follow-up all patient contacts.

Prevention

Handwashing and the careful disposal of materials infected with nasal secretions. Antiseptic/disinfectant solutions:choroxylenol, benzalkonium chloride, and cetrimide. Chlorhexidine has been shown to be ineffective.

REFERRAL

All cases after consultation with infectious diseases and NICD

9.4.2 CORONAVIRUS DISEASE -19 (COVID-19)

COVID-19: new STG added: A new STG was added to the chapter as follows:

9.4.2 CORONAVIRUS DISEASE -19 (COVID-19)

Note: Consult most recent NICD guidelines on the clinical management of suspected or confirmed Covid-19 disease available at: https://www.nicd.ac.za/diseases-a-z-index/covid-19/covid-19-guidelines/

Description

Coronavirus Disease of 2019 (COVID-19) is a viral respiratory illness caused by SARS-CoV-2. Infection may be asymptomatic, and the majority of symptomatic infections (>80%) are characteristed by mild upper- and/or lower respiratory tract symptoms. However, a minority of patients may develop severe disease requiring supplementary oxygen or, in severe cases, mechanical ventilation.

A typical presentation of COVID-19 includes some or all of:

- fever, chills or rigors, cough, dyspnoea, anosmia, dysgeusia, myalgias, sore throat, nausea, vomiting and/or diarrhoea.
- Atypical presentations are increasingly being recongised, including large vessel strokes (see section 14.1.1: Stroke), and diabetic ketoacidosis (see section 8.6.2: Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS)).

Complications:

» refractory hypoxaemia
» long-COVID
» ARDS
» MIS-C and MIS-A

Diagnosis

Samples should be sent for SARS-CoV-2 PCR testing. An upper respiratory tract sample should be sent from all suspected patients – a nasopharyngeal is preferred, but in patients where this is not possible (e.g. recent nasal surgery, or severe coagulopathy), an oropharyngeal, nasal mid-turbinate, or anterior nares swab can be collected instead. Lower respiratory tract samples (e.g. sputum, tracheal aspirates) may be sent in addition if available.

General measures

If COVID-19 is suspected, isolate patient to limit further exposure.
Standard, contact and droplet precautions should be adhered to. Airborne precautions should be applied when performing aerosol-generating procedures, such as intubation or nasogastric suctioning.

Management

Give supplemental oxygen if required, targetting an SpO_2 of ≥90% for non-pregnant adults (≥94% for pregant women). Titrate oxygen therapy to reach targets by means of a nasal cannula, simple face mask or face mask with a reservoir bag, as appropriate.

	Nasal cannula	Simple face mask	Face mask with reservoir bag
Flow rate	1-5 L/min	6-10 L/min	10-15 L/min
FiO_2 estimate	0.25-0.4%	0.4-0.6%	0.6-0.95%

Patients who have respiratory failure despite maximal face mask oxygen should be promptly identified and considered for possible escalation of respiratory support with high flow nasal cannula oxygen, continuous positive airway presure, or intubation and mechanical ventilation as appropriate.
The use of the prone position in non-intubated, conscious patients who are hypoxaemic may be beneficial.

Medicine treatment

Note: antibiotics are of no value for the treatment of confirmed covid-19, unless there is clear evidence of a coexisting infection.

Thromboprophylaxis:

All hospitalised patients with COVID-19 require prophylaxis against venous thromboembolic disease, in the absence of any contraindications (see section 2.8: Venous thrombo-embolism).

- Low molecular weight heparin, e.g.:
- Enoxaparin, SC, 40 mg daily.
  - Reduce dose to 20 mg daily in patients with renal failure (eGFR <30 ml/minute).

OR

- Unfractionated heparin, SC, 5 000 units 12 hourly.

Note: If patients with D-dimer >1.5 mg/L or requiring a non-rebreather mask or more should be considered for therapeutic doses of LMWH or unfractionated heparin (see section 2.8: Venous thrombo-embolism).

- Low molecular weight heparin, e.g.:
- Enoxaparin, SC, 1.5 mg/kg daily,

OR

- Enoxaparin, SC, 1 mg/kg 12 hourly.

In morbid obesity dosing of LMWH should be individualised, in discussion with a specialist.
In renal failure (eGFR <30 mL/minute), the recommended therapeutic dose of LMWH is 1 mg/kg daily.

Evidence indicates that PTT monitoring is not necessary with weight- based dosing of unfractionated heparin. However, in patients with morbid obesity and renal failure (eGFR <30 mL/minute) unfractionated heparin should be used with PTT monitoring to maintain the PTT at 1.5 to 2.5 times the control. PTT should be taken 4 hours after SC dose.

In non-pregnant patients who require supplemental oxygen

- Corticosteroids, e.g.:
- Dexamethasone, IV, 6 mg daily for up to 10 days, or until discharge.

In pregnant patients who require supplemental oxygen

Corticosteroids crosses the placenta and may have long-term deleterious effects on the child.

If corticosteroids are also needed to accelerate fetal lung maturity: (See section 6.12: Preterm labour (PTL) and preterm prelabour rupture of membranes (PPROM).

If corticosteroids are not needed for fetal lung maturity:

- Corticosteroids, e.g.:
- Dexamethasone, IV, 6 mg daily for up to 10 days, or until discharge.

If there is a concern over in-utero steroid exposure, use alternative therapy (with less placental transfer):

- Prednisone, oral 40 mg daily, for up to 10 days, or until discharge.

OR

- Hydrocortisone, IV, 80 mg 12 hourly for up to 10 days, or until discharge.

See section 6.7: COVID-19 in pregnancy

9.6 HYDATID DISEASE

Medicine treatment - albendazole: *Guidance amended*

Guidance on the administration of albendazole has been amended to align with the package insert[8], which recommends that albendazole be taken with meals rather than with a fatty meal. Amendment as tabulated below:

AMENDED FROM:

MEDICINE TREATMENT

- Albendazole, oral, 15 mg/kg/day up to maximum of 400 mg 12 hourly with a fatty meal (e.g. a glass of full cream milk).

AMENDED TO:

MEDICINE TREATMENT

With medical therapy, cure is achieved in about half, improvement in about a quarter and no response in about a quarter of cases:

- Albendazole, oral, 15 mg/kg/day up to maximum of 400 mg 12 hourly with meals.

9.9 TETANUS

General measures: *Amended*

The recommendation to 'alleviate fever with mechanical cooling methods' was deleted from the list of general measures. While the observational study by Lee et al[9] suggests an increased risk of mortality in patients with fever and sepsis who were given paracetamol, the study did have some significant methodological shortcomings. The lack of adjustment for baseline differences between septic and non-septic groups could have driven the association of paracetamol with increased mortality. It was furthermore noted that the use of paracetamol for alleviating fever associated with sepsis, is not a routine exclusion in local or international clinical guidelines i.e. the findings by Lee et al has not been universally adopted.

Medicine treatment – paracetamol for pain: *Dose amended*

Dosing guidance of paracetamol for the management of pain has been amended to align with the Pain chapters.

AMENDED FROM:

8 Package Insert. Wormadole 400mg chewable tablets. Shanur Healthcare (Pty) Ltd. Date of revision of text 22 January 2024.

9 Lee BH, Inui D, Suh GY, Kim JY, Kwon JY, Park J, et al: Fever and Antipyretic in Critically ill patients Evaluation (FACE) Study Group. Association of body temperature and antipyretic treatments with mortality of critically ill patients with and without sepsis: multi-centered prospective observational study. Crit Care. 2012 Feb 28;16(1):R33. https://www.ncbi.nlm.nih.gov/pubmed/22373120

For pain:
- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AMENDED TO:
For pain:
- Paracetamol, oral, 500 mg -1 g 4–6 hourly when required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

9.10 TICK BITE FEVER

In pregnancy
Doxycycline: *Added as initial therapy*
Azithromycin: *Retained*

Aligned with NEMLC-approved PHC STG (Section 10.14: Tick bite fever)[10]:

NEMLC MEETING OF 23 JUNE 2022 - NEMLC REPORT OF THE PHC INFECTIONS CHAPTER
In pregnancy
Doxycycline: Added as initial therapy
Azithromycin: Retained

Doxycycline is antibiotic of choice for the treatment of tick bite fever.[11] However, doxycycline is generally avoided for use in pregnancy, as other tetracyclines have been associated with adverse effects on fetal teeth and bones.[12] A systematic review[13] demonstrated that doxycycline use by these patient groups had a safety profile that differed from that of tetracycline, with no correlation between doxycycline and teratogenic effects during pregnancy or dental staining in children. In addition, a retrospective cohort study suggests that doxycycline (and other antibiotics – azithromycin, ciprofloxacin and amoxicllin) used by pregnant women should not result in a greater incidence of overall major congenital malformations in their infants.[14]
As there is a high fetal risk associated with rickettsial illnesses in pregnancy (higher than in malaria),[15] treatment with doxycycline outweighs the risks and consequences of the side effects associated with doxycycline. Early initiation of empirical doxycycline, to bypass any diagnostic challenges associated with rickettsial infections may likely save lives and prevent severe disease.

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

STG text was updated as follows:

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

Then switch to:

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

Level of Evidence: Very low certainty, conditional recommendation

Unable to tolerate oral therapy

Ciprofloxacin, IV: *Retained*

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.

[10] Minutes of the NEMLC meeting of 23 June 2022
[11] Frean J, Grayson W. South African Tick Bite Fever: An Overview. Dermatopathology (Basel). 2019 Jun 26;6(2):70-76. https://pubmed.ncbi.nlm.nih.gov/31700846/
[12] SAMF, 2022
[13] 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/
[14] Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer SM, Gideon PS, et al. Antibiotics potentially used in response to bioterrorism and the risk of major congenital malformations. Paediatr Perinat Epidemiol. 2009 Jan;23(1):18-28. https://pubmed.ncbi.nlm.nih.gov/19228311/
[15] McGready R, Prakash JA, Benjamin SJ, Watthanaworawit W, Anantatat T, Tanganuchitcharnchai A, et al. Pregnancy outcome in relation to treatment of murine typhus and scrub typhus infection: a fever cohort and a case series analysis. PLoS Negl Trop Dis. 2014 Nov 20;8(11):e3327. https://pubmed.ncbi.nlm.nih.gov/25412503/

9.12 VARICELLA (CHICKENPOX), COMPLICATED

Antiviral therapy – acyclovir: *Guidance clarified*

Guidance on the switch from IV to oral aciclovir has been clarified as tabulated below. Patients with neurological involvement should be retained on aciclovir IV for the full duration of treatment as adequate therapeutic levels cannot be achieved with oral aciclovir.

Secondary Infection – flucloxacillin, oral : A*dded*

Secondary Infection – cefalexin, oral : A*dded*

Guidance on the treatment of secondary bacterial infection has been added to the EML as tabulated below:

AMENDED FROM:

MEDICINE TREATMENT

Antiviral therapy is required in complicated cases, e.g.:

- » chickenpox pneumonia,
- » pregnancy,
- » neurological involvement, and
- » chickenpox in immunocompromised patients.

- Aciclovir, IV, 10 mg/kg administrerd over one hour 8 hourly for 7 days.

The course can be completed with:

- Antiviral, (active against varicella zoster), e.g:
- Aciclovir, oral, 800 mg five times daily.

Treat secondary bacterial infection if suspected.

For close contacts (household contacts or patients in adjacent beds in the same ward) who are severely immunologically compromised and are not immune (i.e. no history of chickenpox/shingles or negative VZV IgG), following a significant exposure (household contacts): (Z29.1)

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 625 units.

Administer within 96 hours after significant exposure

AMENDED TO:

MEDICINE TREATMENT

Antiviral therapy is required in complicated cases, e.g.:

- » chickenpox pneumonia,
- » pregnancy,
- » neurological involvement, and
- » chickenpox in immunocompromised patients.

Antiviral therapy:

- Aciclovir, IV, 10 mg/kg 8 hourly for 7 days.
  - Infuse aciclovir over one hour.

For varicella without neurological involvement, when the patient's clinical condition improves, the 7-day course can be completed with:

- Antiviral (active against varicella zoster), e.g:
- Aciclovir, oral, 800 mg five times daily.
  - Doses are given 4 hourly, except for dose scheduled for the middle of the night.

Secondary infection

B02.8

Treat secondary bacterial infection if suspected.

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

OR

- Cefalexin, oral, 500 mg 6 hourly for 5 days.

Passive immunization following significant exposure: (Z29.1)

Criteria for eligibility [Both a) and b) below are required]:

a. Significant exposure - Household contacts exposed to/ patients lying adjacent to (same ward) those diagnosed with varicella.
b. Severe immunological compromise and lack of varicella-directed immunity (i.e. no history of chickenpox/shingles, or negative VZV IgG).

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 600 units.
  - Administer within 96 hours of significant exposure.

Varicella-zoster immunoglobulin (VZIG), IM: *indication amended*

Varicella-zoster immunoglobulin (VZIG), IM: *maximum dose amended*

The indication for VZIG was amended to align with the Centers for Disease Control and Prevention (CDC) guidelines[16] and corrected as tabulated below. The maximum dose has been capped at 600 units (3 ampoules) for ease of administration as the product available locally is a 200IU/2mL formulation[17].

AMENDED FROM:

For patients who are severely immunologically compromised and are not immune: (Z29.1)

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 625 units.
  - Administer within 96 hours after significant exposure.

AMENDED TO:

Passive immunization following significant exposure: (Z29.1)

Criteria for eligibility (Both are required):

c. Significant exposure - Household contacts exposed to/ patients lying adjacent to (same ward) those diagnosed with varicella

d. Severe immunological compromise and lack of varicella-directed immunity (i.e. no history of chickenpox/shingles, or negative VZV IgG)

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 600 units.
  - Administer within 96 hours of significant exposure

Level of Evidence: Low certainty evidence, conditional recommendation

9.13 ZOSTER (SHINGLES)

Zoster with eye involvement – aciclovir, IV: *Guidance clarified*

Guidance on the use of aciclovir IV for herpes zoster ophthalmicus (HZO) has been clarified in alignment with revised guidance in the AH Eye chapter section 18.4: Herpes zoster ophthalmicus.

AMENDED FROM:

For zoster with secondary dissemination or neurological/ eye involvement:

B02.0-3†+(H03.1*/H13.1*/H19.2*/H19.0*/H22.0*)/ B02.7+(G02.0*/G05.1*/G53.0*/ G63.0*)/B02.8

- Aciclovir, IV, 10 mg/kg administred over one hour 8 hourly for 7 days.
  - The course can be completed with aciclovir, oral, 800 mg five times daily.
  - Dose adjustment based on renal clearance (See Appendix IIfor guidance on prescribing and monitoring).

AMENDED TO:

For zoster with secondary dissemination or neurological/ complicated eye involvement (i.e. complicated herpes zoster ophthalmicus e.g. acute retinal necrosis (ARN), optic neuropathy or orbitopathy):

B02.0-3†+(H03.1*/H13.1*/H19.2*/H19.0*/H22.0*)/ B02.7+(G02.0*/G05.1*/G53.0*/ G63.0*)/B02.8

- Aciclovir, IV, 10 mg/kg 8 hourly for 7 days.
  - Infuse aciclovir over one hour.
  - The course can be completed with aciclovir, oral, 800 mg five times daily.
  - Dose adjustment based on renal clearance (See Appendix II for guidance on prescribing and monitoring).

Pain management - paracetamol: *Dose amended*

Dosing guidance of paracetamol for the management of pain has been amended to align with the Pain chapters.

AMENDED FROM:

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AMENDED TO:

For pain:

- Paracetamol, oral, 500 mg -1 g 4–6 hourly when required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

[16] Centers for Disease Control and Prevention (CDC). Updated recommendations for use of VariZIG--United States, 2013. MMWR Morb Mortal Wkly Rep. 2013 Jul 19;62(28):574-6.

[17] SAMF 14th edition, Varicella-zoster immunoglobulin monograph, pg 373

Pain management - tramadol: *Dose amended*

Dosing guidance of tramadol for the management of pain has been amended to align with the Pain chapters as tabulated below:

AMENDED FROM:

If pain is not adequately controlled:

- Tramadol, oral, 50–100 mg 4–6 hourly.

See chapter 26: Pain

AMENDED TO:

If pain is not adequately controlled:

- Tramadol, oral, 50–100 mg 6 hourly.

See chapter 26: Pain.

Post-herpetic neuralgia – amitriptyline: *Dose amended:*

Dosing guidance of amitriptyline for the management of post-herpetic neuralgia has been amended to align with the Pain chapters Section 26.1.4: Neuropathic pain, as tabulated below:

AMENDED FROM:

Post-herpetic neuralgia: B02.2+(G53.0*)

Initiate treatment with adjuvant therapy early.

- Amitriptyline, oral, 25 mg at night.
  - Titrate as necessary to a maximum of 75 mg.

See section 26.1.4: Neuropathic pain.

AMENDED TO:

Post-herpetic neuralgia: B02.2+(G53.0*)

Initiate adjuvant therapy early if indicated.

- Amitriptyline, oral, 10 mg at night.
  - Titrate as necessary to a maximum dose of 150 mg.

See section 26.1.4: Neuropathic pain.

C. EDITORAL CHANGES

The associated EML chapter has been subject to clinical editorial review following NEMLC ratification of the chapter. These amendments are detailed below.

9.1.1 INTRAVASCULAR CATHETER INFECTIONS

AMENDED FROM:

PERIPHERAL LINE INFECTION:

Common organisms:

coagulase negative staphylococci, particularly *S. epidermis*

S. aureus

The intravascular line should always be removed.

Small, localised area of erythema at the catheter insertion site will usually resolve without antibiotic therapy.

In patients with larger areas of erythema and tenderness extending beyond the insertion site who are systemically well:

- Clindamycin, oral, 450 mg 8 hourly for 5 days.

If patients are systemically unwell they should be treated as for a central venous catheter related systemic blood infection.

AMENDED TO:

PERIPHERAL LINE INFECTION:

Common organisms:

- coagulase negative staphylococci, particularly *S. epidermis*
- *S. aureus*

GENERAL MEASURES

NB: Always remove the intravascular line at the site of infection.

Small, localised areas of erythema at the catheter insertion site will usually resolve without antibiotic therapy after catheter removal.

MEDICINE TREATMENT

Patients with larger areas of erythema and tenderness extending beyond the insertion site who are systemically well:

- Clindamycin, oral, 450 mg 8 hourly for 5 days.

If patients are systemically unwell they should be treated as for a central venous catheter related systemic blood infection.

9.8 SCHISTOMIASIS

AMENDED FROM:
MEDICINE TREATMENT
Acute schistosomiasis syndrome
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

4-6 weeks later, after symptoms have resolved:
- Praziquantel, oral, 40 mg/kg as a single dose.

AND
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

Optimum time for administration of praziquantel is uncertain but sufficient time is required for the worms to mature.

If in 4-6 weeks, eosinoplilia present and high antibody titres, repeat praziquantel treatment:
Praziquantel, oral, 40 mg/kg as a single dose

AMENDED TO:
MEDICINE TREATMENT

Acute schistosomiasis syndrome
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

Note: Praziquantel may cause life-threatening deterioration if given in acute schistosomiasis.

4-6 weeks later, after symptoms have resolved:
- Praziquantel, oral, 40 mg/kg as a single dose.

AND
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

Note: Optimum time for administration of praziquantel is uncertain but sufficient time is required for the worms to mature.

If eosinophilia and high antibody titres are still present after 4-6 weeks, repeat praziquantel treatment:
- Praziquantel, oral, 40 mg/kg as a single dose.

9.11 TYPHOID FEVER (ENTERIC FEVER)

AMENDED FROM:
MEDICINE TREATMENT
Antibiotic therapy
Note: There is increasing resistance to ciprofloxacin in South Africa and it is important to send specimens for culture and sensitivity prior to commencing antibiotic therapy.

Total duration of antibiotic therapy: 10 days.
- Ceftriaxone, IV, 2 g 12 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8^{o}C for 24 hours, based on culture sensitivity results:
- Ciprofloxacin, oral, 500 mg 12 hourly.

Stool cultures must be repeated at weekly intervals after convalescence to ensure that a carrier state has not developed. Two consecutive negative stool cultures are required to exclude carrier state. This is of vital importance in food handlers, who must not be permitted to return to work until stools are negative.

AMENDED TO:

MEDICINE TREATMENT

Antibiotic therapy:

Note: There is increasing resistance to ciprofloxacin in South Africa. Ensure that specimens are sent for culture and sensitivity prior to commencing antibiotic therapy.

Total duration of antibiotic therapy: 10 days.

- Ceftriaxone, IV, 2 g 12 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8 °C for 24 hours, based on culture sensitivity results:

- Ciprofloxacin, oral, 500 mg 12 hourly.

Note:

Stool cultures must be repeated at weekly intervals after clinical recovery to ensure that a carrier state has not developed.

Two consecutive negative stool cultures are required to exclude carrier state. This is of vital importance in patients whose occupation includes handling of food, whereby negative stool culture results are required before they can be medically permitted to resume their occupational duties.