

Harmonising Guidelines for Prescribing in South Africa

Gary Reubenson

24 November 2022



**PREVENTING ANTIMICROBIAL
RESISTANCE TOGETHER**



Declaration of Potential Conflicts of Interest

No relevant financial or commercial COIs

Member of MAC on AMR

Member of NEMLC

Vice-chair of Paediatric ERC of NEMLC

Member Gauteng AMS committee

Member of RMMCH PTC

Chair NMCH PTC

Co-author of existing guidelines (URTI, C.diff, meningitis)

AWaRe Classification of Antibiotics

Included in WHO draft EML & to be included in NEMLC guidelines

ACCESS GROUP

- first or second choice antibiotics
- offer the best therapeutic value, while minimizing the potential for resistance

WATCH GROUP

- first or second choice antibiotics
- only indicated for specific, limited number of infective syndromes
- more prone to be a target of antibiotic resistance and thus prioritized as targets of stewardship programs and monitoring

RESERVE GROUP

- “last resort”
- highly selected patients (life-threatening infections due to multi-drug resistant bacteria)
- closely monitored and prioritized as targets of stewardship programs to ensure their continued effectiveness



SCAN ME

PREVENTING ANTIMICROBIAL
RESISTANCE TOGETHER

Existing Guidelines

Department of Health

- NEMLC – PHC, Adult, Paediatric

WHO

- EML Antibiotic Book – final version expected soon

IMCI

CDDEP African Treatment Guidelines

SAASP

Individual Conditions or
Clinical Syndromes

- Pneumonia
- URIs
- Bronchiolitis, etc.

General Principles

All aim to improve care

Some include focus on clinical diagnosis e.g. AOM, ABRS

Potentially include laboratory stewardship aspects, especially specimen collection

Many highlight where antimicrobials are not indicated

- Watchful Waiting & Symptomatic Treatment

Should provide evidence for recommendations, strength of recommendations, disclosures, external comments

General Principles

Recognise local circumstances

- Microbiology and AMR
- Available medicines

May contradict each other (& themselves!)

Provide guidance, but not prescriptive

- Valid reasons exist to deviate from guidelines

May justifiably vary: PHC vs. Paediatric vs. Adult

- But, preferably should align



<u>Access</u>	<u>Watch</u>	<u>Reserve</u>
Amikacin	Azithromycin	Aztreonam
Amoxicillin	Cefaclor	Cefiderocol
Amoxicillin + clavulanic acid	Cefepime	Ceftaroline
Ampicillin	Cefotaxime	Ceftazidime + avibactam
Benzathine	Cefoxitin	Colistin
benzylpenicillin	Ceftazidime	Daptomycin
Benzylpenicillin	Ceftriaxone	Eravacycline
Cefadroxil	Ciprofloxacin	Faropenem
Cefalexin	Clarithromycin	Fosfomicin
Cefazolin	Doripenem	Imipenem + cilastatin + relebactam
Chloramphenicol	Ertapenem	Linezolid
Clindamycin	Erythromycin	Meropenem + vaborbactam
Cloxacillin	Fusidic Acid	Minocycline
Doxycycline	Imipenem/cilastatin	Oritavancin
Flucloxacillin	Kanamycin	Polymixin B
Gentamicin	Levofloxacin	Tedizolid
Metronidazole	Meropenem	Tigecycline
Nitrofurantoin	Moxifloxacin	
Sulfamethoxazole + trimethoprim	Neomycin	
Phenoxymethylpenicillin	Ofloxacin	
	Piperacillin + tazobactam	
	Rifampicin	
	Tobramycin	
	Vancomycin	

AWaRe



SCAN ME

PREVENTING ANTIMICROBIAL RESISTANCE TOGETHER

When are antibiotics not needed?

Acute diarrhoea, unless significant blood

Bronchitis

Pharyngitis & Tonsillitis in young children & most adults (3-21y)

AOM and sinusitis (if mild)

Some Eye & Skin Infections (if mild)

When are antibiotics recommended?

- **AOM & ABRS** – when clinical diagnosis correct!
- **Pharyngitis** – right age group
- **COPD exacerbations** – if not mild
- **Pneumonia**
- **SSTIs**
- **UTIs**
- **Bacterial lymphadenitis**
- **Diarrhoea** – cholera, bloody, immune-suppressed
- **Enteric Fever**
- **Meningitis**
- **Bacterial sepsis**
- **Neonatal Sepsis**

Selected Example: AOM



Acute Otitis Media

Acute Otitis Media

Acute Otitis Media

Page 2 of 2

Definition

Infection of the middle ear that occurs mostly in children under 5 years of age and is rare in adults, often as a complication of a viral upper respiratory tract infection

Diagnosis

Clinical Presentation

Acute onset of ear pain (unilateral or bilateral), fever ($\geq 38.0^{\circ}\text{C}$), +/- ear discharge

Microbiology Tests

- Not needed unless a complication is suspected
- Cultures of pus from perforated ear drums should not be used to guide treatment

Other Laboratory Tests

Not needed unless a complication is suspected

Imaging

Not needed unless a complication (e.g. mastoiditis, brain abscess) is suspected

Otoscopy

Required for definitive diagnosis if available:
Bulging, inflamed/congested tympanic membrane (may be opaque/show decreased mobility)

Most Likely Pathogens

Respiratory viruses (most cases):

- Respiratory syncytial virus
- Rhinovirus
- Coronavirus (including SARS-CoV-2)
- Influenza virus (A and B)

Bacteria (rarely bacterial superinfections can occur):

- Streptococcus pneumoniae*
- Haemophilus influenzae*
- Moraxella catarrhalis*
- Streptococcus pyogenes* (group A *Streptococcus*)

Prevention

Overlaps with prevention of upper respiratory tract infections; hand hygiene, vaccination against *S. pneumoniae*, *H. influenzae* and influenza viruses can be useful

Treatment

Clinical Considerations

Important: Most non-severe cases can be managed symptomatically with **no antibiotic treatment**

- Instruct patients to monitor symptoms and report back in case they worsen/persist after few days

Antibiotics should be considered if:

- Severe symptoms (e.g. systemically very unwell, severe ear pain, fever $\geq 39.0^{\circ}\text{C}$)

Symptomatic Treatment

Ibuprofen 200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen) 500 mg-1 g q4-6h (Max 4 g/day)

- Hepatic impairment/cirrhosis: Max 2 g/day

Antibiotic Treatment

Antibiotic treatment is not required in the great majority of cases (see "Clinical Considerations" when antibiotics may be indicated)

All dosages are for normal renal function

First Choice

Amoxicillin 500 mg q8h ORAL

Second Choice

Amoxicillin-clavulanic acid 500 mg+125 mg q8h ORAL

Antibiotic Treatment Duration

5 days

Page 1 of 2

Definition

Infection of the middle ear that occurs mostly in children under 5 years of age, often as a complication of a viral upper respiratory tract infection

Most Likely Pathogens

Respiratory viruses:

- Respiratory syncytial virus
- Rhinovirus
- Coronavirus (including SARS-CoV-2)
- Influenza virus (A and B)

Bacteria (rarely bacterial superinfections can occur):

- Streptococcus pneumoniae*
- Haemophilus influenzae*
- Moraxella catarrhalis*
- Streptococcus pyogenes* (group A *Streptococcus*)

Prevention

Overlaps with prevention of upper respiratory tract infections; hand hygiene, vaccination against *S. pneumoniae*, *H. influenzae* and influenza viruses can be useful

Diagnosis

Clinical Presentation

Acute onset of ear pain (unilateral or bilateral), fever +/- ear discharge

Microbiology Tests

- Not needed unless a complication is suspected
- Cultures of pus from perforated ear drums should not be used to guide treatment

Other Laboratory Tests

Not needed unless a complication is suspected

Imaging

- Not needed unless a complication (e.g. mastoiditis, brain abscess) is suspected

Otoscopy

Required for definitive diagnosis if available:
Bulging, inflamed/congested tympanic membrane (may be opaque/show decreased mobility)

Treatment

Clinical Considerations

Important: Most non-severe cases can be managed symptomatically with no antibiotic treatment, especially in children >2 years of age

- Instruct caregivers to monitor symptoms and report back in case they worsen/persist after few days

Antibiotics should be considered if:

- Severe symptoms (e.g. systemically very unwell, severe ear pain, fever $\geq 39.0^{\circ}\text{C}$)
- Immunosuppressed children
- Bilateral acute otitis media in children <2 years

Symptomatic Treatment

Ibuprofen (do not use if <3 months of age)

- Pain control/antipyretic: 5-10 mg/kg q6-8h

Oral weight bands:

6-10 kg	50 mg q8h
10-15 kg	100 mg q8h
15-20 kg	150 mg q8h
20-30 kg	200 mg q8h
≥ 30 kg	Use adult dose

OR

Paracetamol (acetaminophen)

- Pain control/antipyretic: 10-15 mg/kg q8h

Oral weight bands:

3-6 kg	60 mg q8h
6-10 kg	100 mg q8h
10-15 kg	150 mg q8h
15-20 kg	200 mg q8h
20-30 kg	300 mg q8h
≥ 30 kg	Use adult dose

Antibiotic Treatment

Antibiotic treatment is not required in the great majority of cases (see "Clinical Considerations" when antibiotics may be indicated)

All dosages are for normal renal function

First Choice

Amoxicillin 40-50 mg/kg/dose q12h ORAL

Oral weight bands:

3-6 kg	125 mg q12h
6-10 kg	250 mg q12h
10-15 kg	500 mg q12h
15-20 kg	750 mg q12h
20-30 kg	1000 mg q12h
≥ 30 kg	Use adult dose

Second Choice

Amoxicillin-clavulanic acid 40-50 mg/kg/dose of amoxicillin component q12h OR 30 mg/kg/dose q8h ORAL

Oral weight bands:

3-6 kg	250 mg of amox/dose q12h
6-10 kg	375 mg of amox/dose q12h
10-15 kg	500 mg of amox/dose q12h
15-20 kg	750 mg of amox/dose q12h
20-30 kg	1000 mg of amox/dose q12h
≥ 30 kg	Use adult dose

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

Antibiotic Treatment Duration

5 days

19.4.2 OTITIS MEDIA, ACUTE

H66.9

DESCRIPTION

Inflammation of the middle ear characterised by:

- » pain
- » loss of hearing
- » red bulging eardrum
- » drum perforation
- » fever in about half of the cases
- » loss of the normal light reflex of the eardrum

Mild redness of the eardrum and rubbing the ear are not reliable signs.

GENERAL MEASURES

- » Do not instil anything into the ear.
- » Avoid getting the inside of the ear wet.
- » Dry mop ear if discharge is present.
- » Do not plug the ear with cotton wool, etc.
- » Exclude HIV infection as a contributing factor for recurrent ear infection.

MEDICINE TREATMENT

Children

- Amoxicillin, oral, 45 mg/kg/dose 12 hourly for 5 days.

Weight kg	Dose mg	Use one of the following:				Age Months/years
		Syrup mg/ 5mL		Capsule mg		
		125	250	250	500	
>3.5–5 kg	175 mg	7 mL	3.5 mL	–	–	>1–3 months
>5–7 kg	250 mg	10 mL	5 mL	–	–	>3–6 months
>7–11 kg	375 mg	15 mL	7.5 mL	–	–	>6–18 months
>11–14 kg	500 mg	–	10 mL	2	1	>18 months–3 years
>14–17.5 kg	750 mg	–	15 mL	3	–	>3–5 years
>17.5–25 kg	1000 mg	–	20 mL*	4	2	>5–7 years
>25–30 kg	1250 mg	–	25 mL*	5	–	>7–10 years
>30 kg	1500 mg	–	–	6	3	>10 years

- Review response after 5 days.
- If pain or discharge persists, consider alternative diagnosis and continue antibiotics for a further 5 days.

LoE:III³⁸⁶

LoE:III³⁸⁷

Adults

- Amoxicillin, oral, 1500 mg 12 hourly for 5 days.

LoE:III³⁸⁸

or poor response to 10-day course of amoxicillin in the previous 30 days;

Children

- Amoxicillin/clavulanic acid, oral, 15–25 mg/kg/dose of amoxicillin component, 8 hourly for 5–10 days.

Weight kg	Dose mg (amoxicillin component)	Use one of the following			Age months/years
		Susp 125/31.5 mg/5 mL	Susp 250/62.5 mg/5 mL	Tablet 500/125 mg/tab	
>3.5–5kg	75 mg	3 mL	1.5 mL	–	>1–3 months
>5–7 kg	100 mg	4 mL	2mL	–	>3–6 months
>7–9 kg	150 mg	6 mL	3 mL	–	>6–12 months
>9–11 kg	200 mg	8 mL	4 mL	–	>12–18 months
>11–14 kg	250 mg	10 mL	5 mL	–	>18 months–3 years
>14–17.5 kg	300 mg	12 mL	6 mL	–	>3–5 years
>17.5–25	375 mg	15 mL	7.5 mL	–	>5–7 years
>25–35 kg	500 mg	20 mL	10 mL	1 tablet	>7–11 years

Children > 35 kg and adults

Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 to 10 days.

LoE:III³⁸⁹

Severe penicillin allergy:

Z88.0

LoE:III³⁹⁰

Children

- Macrolide, e.g.:
- Azithromycin, oral, 10 mg/kg daily for 3 days. See dosing table, pg 23.2.

Children > 35 kg and adults

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

Pain:

Children

- Paracetamol, oral, 10–15 mg/kg/dose 6 hourly when required. See dosing table, pg 23.8.

LoE:II³⁹¹

Adults

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

For patients with upper respiratory tract congestion, secondary to allergy: (T78.4)

- Non-sedating antihistamine, oral, e.g.:
- Cetirizine, oral, 10 mg daily for 10 days.

LoE:II³⁹²

For management of allergic rhinitis, see section 19.1: Allergic rhinitis.

Selected Example: AOM

17.4 OTITIS MEDIA, ACUTE

H66.9

DESCRIPTION

Inflammation of the middle ear of rapid onset.

MEDICINE TREATMENT

In previously untreated patients:

- Amoxicillin, oral, 1000 mg 8 hourly for 5 days.

Patients not responding to amoxicillin:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 h

Severe penicillin allergy: (Z88.0)

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

For patients with upper respiratory tract congestion, secondary to allergy: (T78.4)

- Non-sedating antihistamine, oral, e.g.:
- Cetirizine, oral, 10 mg daily for 10 days.

LoE:II^x

For management of allergic rhinitis, see section 17.2: Rhinitis, allergic, persistent.

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.

If pain is not controlled, see chapter 26: Pain.

LoE:III^{xi}

REFERRAL

- » No response to amoxicillin/clavulanic acid.
- » No pain relief despite treatment.
- » Bulging eardrum, not responding to treatment after 24 hours.
- » Swelling and pain on palpation of the mastoid process.
- » Recurrent otitis media.

Selected Example: AOM

17.7 OTITIS MEDIA, ACUTE (AOM)

H66.9

DESCRIPTION

- » Inflammation of the middle ear that may be complicated by perforation and a purulent ear discharge, which usually resolves spontaneously within 14 days. Acute otitis media (AOM) needs to be distinguished from otitis media with effusion (OME), which is NOT treated with antibiotics.

DIAGNOSTIC CRITERIA

- » Frequently preceded by a viral upper respiratory tract infection.
- » Pain (earache; not due to referred pain), irritability and fever.
- » Acute purulent otorrhoea may develop with associated relief of otalgia.

OR at least one of the following:

- » Distinct fullness or bulging of the tympanic membrane.
- » Marked redness of the tympanic membrane.

Signs and Symptoms	Otitis Media with Effusion	Acute Otitis Media
Impaired hearing	Mild-to-moderate	Mild-to-moderate
Pain (otalgia)	No	Moderate-to-severe
Tenderness	No	No
Purulent drainage (otorrhoea)	No	Only after perforation of tympanic membrane
Bacterial infection	No	Yes
Systemic symptoms (i.e. fever, malaise)	No	Yes

GENERAL AND SUPPORTIVE MEASURES

- » Avoid getting the inside of the ear wet.

MEDICINE TREATMENT

- Amoxicillin, oral, 45 mg/kg/dose 12 hourly for 10 days.
 - Maximum dose: 1.5 g 12 hourly.

LoE I²

Note: For poor response to amoxicillin therapy, or in patients who have received amoxicillin in the last 30 days:

- Amoxicillin/clavulanic acid, oral, 45 mg/kg/dose of amoxicillin component, 12 hourly for 10 days (amoxicillin/clavulanic acid in a ratio of 14:1).
 - Maximum dose of amoxicillin component: 1.5 g 12 hourly.

LoE III^{1, 2, 3}

For pain and fever:

- See Chapter 20: Pain Control, section 20.1.2: Management of pain.

REFERRAL

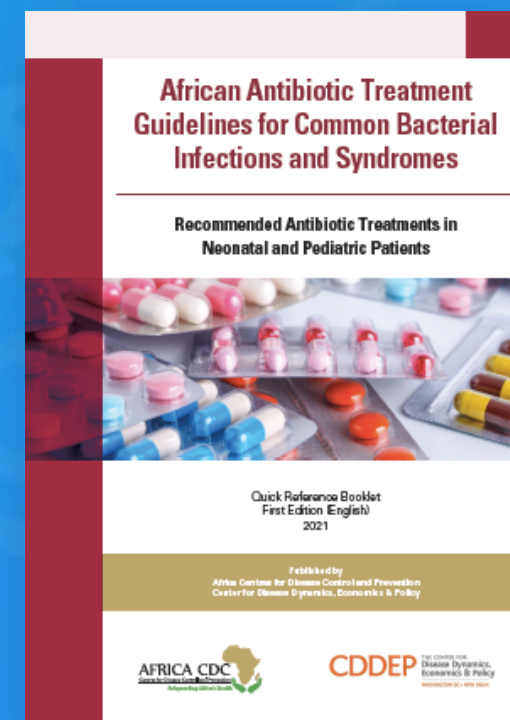
- » If symptoms persist despite appropriate antibiotic therapy, the patient shows severe toxicity or there is progression beyond the middle ear, refer to ENT specialist.

Acute Otitis Media

Clinical definition:

Acute infection and inflammation of the middle ear. Common symptoms include ear pain and difficulty hearing. Common bacterial etiologies include *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, *S. aureus*, *Group A Streptococcus* sp.

Preferred antibiotic choice(s)			
Drug	Formulation	Dosage	Duration
Amoxicillin (PO)	Powder for oral liquid: 125 mg (as trihydrate)/5 mL; 250 mg (as trihydrate)/5 mL; Solid oral dosage form: 250 mg; 500 mg (as trihydrate)	500 mg 8 hourly	5 days
Alternative antibiotic choice(s) ^A			
Amoxicillin + clavulanic acid (PO)	Oral liquid: 125 mg amoxicillin + 31.25 mg clavulanic acid/5 mL AND 250 mg amoxicillin + 62.5 mg clavulanic acid/5 mL; Tablet: 500 mg (as trihydrate) + 125 mg (as potassium salt)	500 mg of amoxicillin component 12 hourly	5 days
In case of confirmed drug allergy or medical contraindication			
Azithromycin (PO)	Capsule: 250 mg; 500 mg (anhydrous); Oral liquid: 200 mg/5 mL	500 mg daily	3 days



PREVENTING ANTIMICROBIAL
RESISTANCE TOGETHER

Acute Otitis Media

Clinical definition:

Acute infection with inflammation of the middle ear. Common symptoms include fever, ear pain, ear discharge and difficulty hearing. Common bacterial pathogens include *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*.

Infant, Child & Adolescent

Preferred antibiotic choice

Drug	Formulation	Dosage	Duration
Amoxicillin (PO) ^A	Powder for oral liquid: 125 mg (as trihydrate) /5 mL; 250 mg (as trihydrate) /5 mL; Solid oral dosage form: 250 mg; 500 mg (as trihydrate)	40-45 mg/kg/dose 12 hourly, maximum dose 1.5 g 12 hourly	5 – 10 days

For patients who received amoxicillin in the previous 30 days or for those who are non-responsive to first-line treatment with amoxicillin after 48 – 72 hours

Amoxicillin + clavulanic acid (PO) ^A	Oral liquid: 125 mg amoxicillin + 31.25 mg clavulanic acid/5 mL; 250 mg amoxicillin + 62.5 mg clavulanic acid/5 mL; Tablet: 500 mg (as trihydrate)	40 – 45 mg/kg of amoxicillin component per dose 12 hourly, maximum dose of amoxicillin component: 875 mg 12 hourly. (Refer to Other Notes ^B below for guidance on	5 – 10 days
---	--	---	-------------

African Antibiotic Treatment Guidelines for Common Bacterial Infections and Syndromes

Recommended Antibiotic Treatments in Neonatal and Pediatric Patients



Quick Reference Booklet
First Edition English
2021

Published by
Africa Centre for Disease Control and Prevention
Center for Disease Dynamics, Economics & Policy



In case of confirmed drug allergy or medical contraindication

Azithromycin ^C	Oral liquid: 200 mg/5 mL; Capsule: 250 mg; 500 mg (anhydrous).	10 mg/kg once daily, maximum daily dose 500 mg	3 – 5 days
---------------------------	--	--	------------

A. If a patient cannot tolerate oral antibiotics (e.g. persistent vomiting), IV or IM antibiotics may be considered:

- Ampicillin (25 mg/kg/dose 6 hourly, Maximum dose: 500 mg 6 hourly), or
- Ceftriaxone (50 mg/kg/dose once daily, Maximum dose: 1 g daily)

B. Current widely available oral liquid formulations contain amoxicillin + clavulanic acid in a 4:1 ratio. To achieve 40-45 mg/kg/dose of amoxicillin component, when using the 4:1 formulation, prescribe amoxicillin + clavulanic acid 10-15 mg/kg/dose of amoxicillin component 12 hourly and separately prescribe amoxicillin 30-35 mg/kg/dose 12 hourly in order not to exceed the maximum recommended dose of clavulanic acid (10 mg/kg/day) thereby reducing the risk of antibiotic-associated diarrhoea. If oral liquid formulations with a higher dose of amoxicillin are available (7:1 ratio – 400 mg amoxicillin + 57.5 mg clavulanic acid/5 mL, or 14:1 ratio – 600 mg amoxicillin + 42.9 mg clavulanic acid/5 mL), these may be dosed at 40-45 mg/kg dose of amoxicillin component 12 hourly without a separate amoxicillin prescription (the clavulanic acid dose will not be exceeded). If the 7:1 ratio tablet formulation is available (875 mg amoxicillin + 125 mg clavulanic acid clavulanic acid) it may be prescribed 12 hourly for children weighing 25 kg or more.

C. If a patient fails macrolide therapy, consider ceftriaxone or refer to a specialist.

Principles of Stewardship:

- Practice watchful waiting and withhold antibiotics except for patients with severe symptoms, those less than 2 years of age, and patients with bilateral disease.
- Repeated courses of antibiotics in children with chronic otitis media and/or otorrhoea are ineffective and should be avoided. Expert advice or referral to an ENT specialist and audiologist if available should be considered.

Now What?

Perfect harmonisation is impossible


At least, principles should be concordant

Initiative underway to compare WHO & NEMLC recommendations and try reconcile discrepancies




PHC, Adult, & Paediatric STGs aim to align as far as possible

- Please inform us if you encounter any areas of concern!



Knowledge Hub Resources



Primary Healthcare Standard Treatment Guidelines and Essential Medicine List 8th edition - and Individual NEMLC-approved chapters for the 9th edition



Primary Healthcare Standard Treatment Guidelines and Essential Medicines List 7th edition - 2020



Paediatric Hospital Level STGS and EML 4th Edition 2017



Hospital Level (Adults) Standard Treatment Guidelines and Essential Medicines List 2nd Edition



PREVENTING ANTIMICROBIAL
RESISTANCE TOGETHER

Resources



World Health Organization AWaRe

WHO Essential Medicines List Antibiotic Book

Infographics

Draft for public comment Version 1.1 (Nov 16, 2021)



African Antibiotic Treatment Guidelines for Common Bacterial Infections and Syndromes

Recommended Antibiotic Treatments in Neonatal and Pediatric Patients

Quick Reference Booklet
First Edition (English)
2021

Published by
Africa Centre for Disease Control and Prevention
Center for Disease Dynamics, Economics & Policy

AFRICA CDC
CDDEP



A POCKET GUIDE TO ANTIBIOTIC THERAPY FOR ADULTS IN SOUTH AFRICA

SEAN WASSERMAN
TOM BOYLES
MARC MENDELSON

ON BEHALF OF THE SOUTH AFRICAN ANTIBIOTIC STEWARDSHIP PROGRAMME (SAASP)

SAASP
SOUTH AFRICAN ANTIBIOTIC STEWARDSHIP PROGRAMME

1 | Page



PREVENTING ANTIMICROBIAL RESISTANCE TOGETHER