6.2 Antibacterials

To assist in the development of tools for antibiotic stewardship at local, national and global levels and to reduce antimicrobial resistance, three different categories were developed – ACCESS, WATCH and RESERVE groups.

Group 1 - KEY ACCESS ANTIBIOTICS

To improve both access and clinical outcomes antibiotics that were first or second choice antibiotics in at least one of the reviewed syndromes are designated as key ACCESS antibiotics, emphasizing their role as the antibiotics that should be widely available, affordable and quality-assured. ACCESS antibiotics are listed below. Selected ACCESS antibiotics may also be included in the WATCH group.

6.2.1 Beta-lactam medicines		6.2.2 Other antibacterials	
amoxicillin	cefotaxime*	amikacin	gentamicin
amoxicillin + clavulanic acid	ceftriaxone*	azithromycin*	metronidazole
ampicillin	cloxacillin	chloramphenicol	nitrofurantoin
benzathine benzylpenicillin	phenoxymethylpenicillin	ciprofloxacin*	spectinomycin (EML only)
benzylpenicillin	piperacillin + tazobactam*	clarithromycin*	sulfamethoxazole + trimethoprim
cefalexin	procaine benzyl penicillin	clindamycin	vancomycin (oral)*
cefazolin	*meropenem**	doxycycline	*vancomycin (parenteral)**
cefixime*			

Italics = complementary list

*Watch group antibiotics included in the EML/EMLc only for specific, limited indications

The 2017 Expert Committee identified the following antibiotics or antibiotic classes that should be the subject of a specific stewardship focus. Antibiotics or antibiotic classes in these groups are designated accordingly in the EML/EMLc. The "WATCH" and "RESERVE" stewardship groups could assist in activities such as local, national and global monitoring of use; development of guidelines and educational activities.

Group 2 - WATCH GROUP ANTIBIOTICS

This group includes antibiotic classes that have higher resistance potential and so are recommended as first or second choice treatments only for a specific, limited number of indications. These medicines should be prioritized as key targets of stewardship programs and monitoring.

This group includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine[1] and/or antibiotics that are at relatively high risk of selection of bacterial resistance.

Watch group antibiotics
Quinolones and fluoroquinolones e.g. ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin
3rd-generation cephalosporins (with or without beta-lactamase inhibitor) e.g. cefixime, ceftriaxone, cefotaxime, ceftazidime
Macrolides e.g. azithromycin, clarithromycin, erythromycin
Glycopeptides e.g. teicoplanin, vancomycin
Antipseudomonal penicillins + beta-lactamase inhibitor e.g. piperacillin-tazobactam
Carbapenems e.g. meropenem, imipenem + cilastatin
Penems e.g. faropenem

[1] http://apps.who.int/iris/bitstream/10665/251715/1/9789241511469-eng.pdf?ua=1

Group 3 - RESERVE GROUP ANTIBIOTICS

This group includes antibiotics that should be treated as "last resort" options that should be accessible, but whose use should be tailored to highly specific patients and settings, when all alternatives have failed (e.g., serious, life-threatening infections due to multi-drug resistant bacteria). These medicines could be protected and prioritized as key targets of national and international stewardship programs involving monitoring and utilization reporting, to preserve their effectiveness.

Reserve group antibiotics	
Aztreonam	Fosfomycin (IV)
4th generation cephalosporins e.g. cefepime	Oxazolidinones e.g. linezolid
5th generation cephalosporins e.g. ceftaroline	Tigecycline
Polymyxins e.g. polymyxin B, colistin	Daptomycin

6.2.1 Beta-lactam medicines

<table>
<tr><td rowspan="2">amoxicillin</td><td colspan="2">Powder for oral liquid: 125 mg (as trihydrate)/5 mL; 250 mg (as trihydrate)/5 mL [c].

Solid oral dosage form: 250 mg; 500 mg (as trihydrate).

Powder for injection: 250 mg; 500 mg; 1 g (as sodium) in vial.</td></tr>
<tr><td>FIRST CHOICE

- community acquired pneumonia (mild to moderate)
- community acquired pneumonia (severe) [c]
- complicated severe acute malnutrition [c]
- exacerbations of COPD
- lower urinary tract infections
- otitis media
- pharyngitis
- sepsis in neonates and children [c]
- sinusitis
- uncomplicated severe acute malnutrition [c]</td><td>SECOND CHOICE

- acute bacterial meningitis</td></tr>
<tr><td>amoxicillin + clavulanic acid</td><td colspan="2">Oral liquid: 125 mg amoxicillin + 31.25 mg clavulanic acid/5 mL AND 250 mg amoxicillin + 62.5 mg clavulanic acid/5 mL [c].

Tablet: 500 mg (as trihydrate) + 125 mg (as potassium salt).

Powder for injection: 500 mg (as sodium) + 100 mg (as potassium salt); 1000 mg (as sodium) + 200 mg (as potassium salt) in vial.</td></tr>
</table>

<table>
<tr><td></td><td>FIRST CHOICE

- community acquired pneumonia (severe) [c]
- complicated intraabdominal infections (mild to moderate)
- exacerbations of COPD
- hospital acquired pneumonia
- low-risk febrile neutropenia
- lower urinary tract infections
- sinusitis
- skin and soft tissue infections</td><td>SECOND CHOICE

- bone and joint infections
- community-acquired pneumonia (mild to moderate)
- community acquired pneumonia (severe)
- otitis media</td></tr>
<tr><td rowspan="2">ampicillin</td><td colspan="2">Powder for injection: 500 mg; 1 g (as sodium salt) in vial.</td></tr>
<tr><td>FIRST CHOICE

- community acquired pneumonia (severe) [c]
- complicated severe acute malnutrition [c]
- sepsis in neonates and children [c]</td><td>SECOND CHOICE

- acute bacterial meningitis</td></tr>
<tr><td rowspan="2">benzathine benzylpenicillin</td><td colspan="2">Powder for injection: 900 mg benzylpenicillin (= 1.2 million IU) in 5- mL vial [c]; 1.44 g benzylpenicillin (= 2.4 million IU) in 5- mL vial.</td></tr>
<tr><td>FIRST CHOICE

- syphilis</td><td>SECOND CHOICE</td></tr>
<tr><td rowspan="2">benzylpenicillin</td><td colspan="2">Powder for injection: 600 mg (= 1 million IU); 3 g (= 5 million IU) (sodium or potassium salt) in vial.</td></tr>
<tr><td>FIRST CHOICE

-community acquired pneumonia (severe) [c]
- complicated severe acute malnutrition [c]
- sepsis in neonates and children [c]
- syphilis</td><td>SECOND CHOICE
- acute bacterial meningitis[c]</td></tr>
<tr><td rowspan="2">cefalexin</td><td colspan="2">Powder for reconstitution with water: 125 mg/5 mL; 250 mg/5 mL (anhydrous).

Solid oral dosage form: 250 mg (as monohydrate).</td></tr>
<tr><td>FIRST CHOICE</td><td>SECOND CHOICE

- exacerbations of COPD
- pharyngitis
- skin and soft tissue infections</td></tr>
<tr><td rowspan="2">cefazolin* a</td><td colspan="2">Powder for injection: 1 g (as sodium salt) in vial.

* also indicated for surgical prophylaxis.

a >1 month.</td></tr>
<tr><td>FIRST CHOICE</td><td>SECOND CHOICE

- bone and joint infections</td></tr>
</table>

<table>
<tr><td rowspan="2">cefixime
WATCH GROUP</td><td colspan="2">Capsule or tablet: 200 mg; 400 mg (as trihydrate).
Powder for oral liquid: 100 mg /5 mL [c]</td></tr>
<tr><td>FIRST CHOICE</td><td>SECOND CHOICE
- acute invasive bacterial diarrhoea / dysentery
- Neisseria gonorrhoeae</td></tr>
<tr><td rowspan="2">cefotaxime*
WATCH GROUP</td><td colspan="2">Powder for injection: 250 mg per vial (as sodium salt)
* 3rd generation cephalosporin of choice for use in hospitalized neonates.</td></tr>
<tr><td>FIRST CHOICE
- acute bacterial meningitis
-community acquired pneumonia (severe)
- complicated intraabdominal infections (mild to moderate)
- complicated intrabdominal infections (severe)
- hospital acquired pneumonia
-pyelonephritis or prostatitis (severe)</td><td>SECOND CHOICE
- bone and joint infections
-pyelonephritis or prostatitis (mild to moderate)
- sepsis in neonates and children [c]</td></tr>
<tr><td rowspan="2">ceftriaxone* a
WATCH GROUP</td><td colspan="2">Powder for injection: 250 mg; 1 g (as sodium salt) in vial.
* Do not administer with calcium and avoid in infants with hyperbilirubinaemia.
a >41 weeks corrected gestational age.</td></tr>
<tr><td>FIRST CHOICE
- acute bacterial meningitis
-community acquired pneumonia (severe)
- complicated intraabdominal infections (mild to moderate)
- complicated intrabdominal infections (severe)
- hospital acquired pneumonia
- Neisseria gonorrhoeae
-pyelonephritis or prostatitis (severe)</td><td>SECOND CHOICE
- acute invasive bacterial diarrhoea / dysentery
- bone and joint infections
- pyelonephritis or prostatitis (mild to moderate)
- sepsis in neonates and children [c]</td></tr>
<tr><td rowspan="2">☐ cloxacillin*</td><td colspan="2">Capsule: 500 mg; 1 g (as sodium salt).
Powder for injection: 500 mg (as sodium salt) in vial.
Powder for oral liquid: 125 mg (as sodium salt)/5 mL.
*cloxacillin, dicloxacillin and flucloxacillin are preferred for oral administration due to better bioavailability.</td></tr>
<tr><td>FIRST CHOICE
- bone and joint infections
- skin and soft tissue infections</td><td>SECOND CHOICE
- sepsis in neonates and children [c]</td></tr>
</table>

<table>
<tr><td rowspan="3">phenoxymethylpenicillin</td><td colspan="2">Powder for oral liquid: 250 mg (as potassium salt)/5 mL.
Tablet: 250 mg (as potassium salt).</td></tr>
<tr><td>FIRST CHOICE
- community acquired pneumonia (mild to moderate)
- pharyngitis</td><td>SECOND CHOICE</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td rowspan="3">piperacillin + tazobactam
WATCH GROUP</td><td colspan="2">Powder for injection: 2 g (as sodium salt) + 250 mg (as sodium salt); 4 g (as sodium salt) + 500 mg (as sodium salt) in vial</td></tr>
<tr><td>FIRST CHOICE
- complicated intraabdominal infections (severe)
- high-risk febrile neutropenia
- hospital acquired pneumonia</td><td>SECOND CHOICE</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td rowspan="3">procaine benzylpenicillin*</td><td colspan="2">Powder for injection: 1 g (=1 million IU); 3 g (=3 million IU) in vial.
* Procaine benzylpenicillin is not recommended as first-line treatment for neonatal sepsis except in settings with high neonatal mortality, when given by trained health workers in cases where hospital care is not achievable.</td></tr>
<tr><td>FIRST CHOICE
- syphilis [c]</td><td>SECOND CHOICE
- syphilis</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td colspan="3">Complementary List</td></tr>
<tr><td>ceftazidime
WATCH GROUP</td><td colspan="2">Powder for injection: 250 mg or 1 g (as pentahydrate) in vial.</td></tr>
<tr><td rowspan="3">meropenem* a
WATCH GROUP</td><td colspan="2">Powder for injection: 500 mg (as trihydrate); 1 g (as trihydrate) in vial
a >3 months.
*imipenem + cilastatin is an alternative except for acute bacterial meningitis where meropenem is preferred.</td></tr>
<tr><td>FIRST CHOICE</td><td>SECOND CHOICE
- acute bacterial meningitis in neonates [c]
- complicated intraabdominal infections (severe)
- high-risk febrile neutropenia</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td colspan="3">Complementary List – RESERVE GROUP</td></tr>
<tr><td>aztreonam</td><td colspan="2">Powder for injection: 1 g; 2 g in vial</td></tr>
<tr><td>fifth generation cephalosporins
(with or without beta-lactamase inhibitor)
e.g, ceftaroline</td><td colspan="2">Powder for injection: 400 mg; 600 mg (as fosamil) in vial</td></tr>
</table>

fourth generation cephalosporins *(with or without beta-lactamase inhibitor)* *e.g., cefepime*	***Powder for injection:*** *500 mg; 1g; 2g (as hydrochloride) in vial*	
6.2.2 Other antibacterials		
amikacin	**Injection:** 250 mg (as sulfate)/mL in 2- mL vial	
	FIRST CHOICE *-pyelonephritis or prostatitis (severe)*	**SECOND CHOICE** *- high-risk febrile neutropenia* *- sepsis in neonates and children* **[c]**
azithromycin* WATCH GROUP	**Capsule:** 250 mg; 500 mg (anhydrous). **Oral liquid:** 200 mg/5 mL. * also listed for single-dose treatment of trachoma and yaws.	
	FIRST CHOICE *- Chlamydia trachomatis* *- cholera* **[c]** *- Neisseria gonorrhoeae*	**SECOND CHOICE** *- acute invasive bacterial diarrhoea / dysentery* *- Neisseria gonorrhoeae*
chloramphenicol	**Capsule:** 250 mg. **Oily suspension for injection*:** 0.5 g (as sodium succinate)/ mL in 2- mL ampoule. * Only for the presumptive treatment of epidemic meningitis in children older than 2 years and in adults. **Oral liquid:** 150 mg (as palmitate)/5 mL. **Powder for injection:** 1 g (sodium succinate) in vial.	
	FIRST CHOICE	**SECOND CHOICE** *- acute bacterial meningitis*
ciprofloxacin WATCH GROUP	**Oral liquid:** 250 mg/5 mL (anhydrous) **[c]**. **Solution for IV infusion:** 2 mg/ mL (as hyclate) **[c]**. **Tablet:** 250 mg (as hydrochloride).	
	FIRST CHOICE *- acute invasive bacterial diarrhoea / dysentery* *- low-risk febrile neutropenia* *- pyelonephritis or prostatitis (mild to moderate)*	**SECOND CHOICE** *-cholera* *- complicated intraabdominal infections (mild to moderate)*

<table>
<tr><td rowspan="3">clarithromycin*†
WATCH GROUP</td><td colspan="2">Solid oral dosage form: 500 mg.
Powder for oral liquid: 125 mg/5 mL; 250 mg/5 mL
Powder for injection: 500 mg in vial
*erythromycin may be an alternative.
†clarithromycin is also listed for use in combination regimens for eradication of H. pylori in adults.</td></tr>
<tr><td>FIRST CHOICE
-community acquired pneumonia (severe)</td><td>SECOND CHOICE
- pharyngitis</td></tr>
<tr><td></td><td></td></tr>
<tr><td rowspan="3">clindamycin</td><td colspan="2">Capsule: 150 mg (as hydrochloride).
Injection: 150 mg (as phosphate)/ mL.
Oral liquid: 75 mg/5 mL (as palmitate) [c].</td></tr>
<tr><td>FIRST CHOICE</td><td>SECOND CHOICE
- bone and joint infections</td></tr>
<tr><td></td><td></td></tr>
<tr><td rowspan="3">doxycycline a</td><td colspan="2">Oral liquid: 25 mg/5 mL [c]; 50 mg/5 mL (anhydrous) [c].
Solid oral dosage form: 50 mg [c]; 100 mg (as hyclate).
Powder for injection: 100 mg in vial
a Use in children <8 years only for life-threatening infections when no alternative exists.</td></tr>
<tr><td>FIRST CHOICE
- Chlamydia trachomatis
- cholera</td><td>SECOND CHOICE
- cholera [c]
-community acquired pneumonia (mild to moderate)
- exacerbations of COPD</td></tr>
<tr><td></td><td></td></tr>
<tr><td rowspan="3">gentamicin</td><td colspan="2">Injection: 10 mg; 40 mg (as sulfate)/ mL in 2- mL vial.</td></tr>
<tr><td>FIRST CHOICE
- community acquired pneumonia (severe) [c]
- complicated severe acute malnutrition [c]
- sepsis in neonates and children [c]</td><td>SECOND CHOICE
- Neisseria gonorrhoeae</td></tr>
<tr><td></td><td></td></tr>
<tr><td rowspan="3">metronidazole</td><td colspan="2">Injection: 500 mg in 100- mL vial.
Oral liquid: 200 mg (as benzoate)/5 mL.
Suppository: 500 mg; 1 g.
Tablet: 200 mg to 500 mg.</td></tr>
<tr><td></td><td></td></tr>
<tr><td></td><td></td></tr>
</table>

	FIRST CHOICE *- C. difficile infection* *- complicated intraabdominal infections (mild to moderate)* *- complicated intrabdominal infections (severe)* *- Trichomonas vaginalis*	**SECOND CHOICE** *- complicated intraabdominal infections (mild to moderate)*
nitrofurantoin	**Oral liquid:** 25 mg/5 mL **[c]**. **Tablet:** 100 mg.	
	FIRST CHOICE *- lower urinary tract infections*	**SECOND CHOICE**
spectinomycin	**Powder for injection:** 2 g (as hydrochloride) in vial.	
	FIRST CHOICE	**SECOND CHOICE** *- Neisseria gonorrhoeae*
sulfamethoxazole + trimethoprim*	**Injection:** 80 mg + 16 mg/ mL in 5- mL ampoule; 80 mg + 16 mg/ mL in 10- mL ampoule. **Oral liquid:** 200 mg + 40 mg/5 mL. **Tablet:** 100 mg + 20 mg; 400 mg + 80 mg; 800 mg + 160 mg. *single agent trimethoprim may be an alternative for lower urinary tract infection.	
	FIRST CHOICE *- lower urinary tract infections*	**SECOND CHOICE** *- acute invasive diarrhoea / bacterial dysentery*
vancomycin WATCH GROUP	**Capsule:** 125 mg; 250 mg (as hydrochloride).	
		SECOND CHOICE *- C. difficile infection*
Complementary List		
vancomycin *WATCH GROUP*	***Powder for injection:*** *250 mg (as hydrochloride) in vial.*	
	FIRST CHOICE	**SECOND CHOICE** *-high-risk febrile neutropenia*
Complementary List – RESERVE GROUP		
daptomycin	***Powder for injection:*** *350 mg; 500 mg in vial*	
fosfomycin	***Powder for injection:*** *2 g; 4 g (as sodium) in vial*	

oxazolindinones *e.g., linezolid*	***Injection for intravenous administration:*** *2 mg/ mL in 300 mL bag.* ***Powder for oral liquid****: 100 mg/5 mL.* ***Tablet:*** *400 mg; 600 mg.*
polymyxins *e.g., colistin*	***Powder for injection: 1 million I.U. (as colistemethate sodium) in vial***
tigecycline	***Powder for injection:*** *50 mg in vial*

6.2.3 Antileprosy medicines

Medicines used in the treatment of leprosy should never be used except in combination. Combination therapy is essential to prevent the emergence of drug resistance. Colour-coded blister packs (MDT blister packs) containing standard two-medicine (paucibacillary leprosy) or three-medicine (multibacillary leprosy) combinations for adult and childhood leprosy should be used. MDT blister packs can be supplied free of charge through WHO.

clofazimine	**Capsule:** 50 mg; 100 mg.
dapsone	**Tablet:** 25 mg; 50 mg; 100 mg.
rifampicin	**Solid oral dosage form:** 150 mg; 300 mg.

6.2.4 Antituberculosis medicines

WHO recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations, including modified dosage forms, non-refrigerated products and paediatric dosage forms of assured pharmaceutical quality.

ethambutol	**Oral liquid:** 25 mg/ mL **[c]**. **Tablet:** 100 mg to 400 mg (hydrochloride).
ethambutol + isoniazid	**Tablet:** 400 mg + 150 mg.
ethambutol + isoniazid + pyrazinamide + rifampicin	**Tablet:** 275 mg + 75 mg + 400 mg + 150 mg.
ethambutol + isoniazid + rifampicin	**Tablet:** 275 mg + 75 mg + 150 mg.
isoniazid	**Oral liquid:** 50 mg/5 mL **[c]**. **Tablet:** 100 mg to 300 mg. **Tablet (scored):** 50 mg.
isoniazid + pyrazinamide + rifampicin	**Tablet:** 75 mg + 400 mg + 150 mg. 150 mg + 500 mg + 150 mg **(For intermittent use three times weekly).** **Tablet (dispersible):** 50 mg + 150 mg + 75 mg **[c]**.
isoniazid + rifampicin	**Tablet:** 75 mg + 150 mg; 150 mg + 300 mg. 60 mg + 60 mg **(For intermittent use three times weekly).** 150 mg + 150 mg **(For intermittent use three times weekly).** **Tablet (dispersible):** 50 mg + 75 mg **[c].**

pyrazinamide	**Oral liquid:** 30 mg/ mL **[c]**. **Tablet:** 400 mg. **Tablet (dispersible):** 150 mg. **Tablet (scored):** 150 mg.
rifabutin	**Capsule:** 150 mg.* * For use only in patients with HIV receiving protease inhibitors.
rifampicin	**Oral liquid:** 20 mg/ mL **[c]**. **Solid oral dosage form:** 150 mg; 300 mg.
rifapentine*	**Tablet:** 150 mg *For treatment of latent TB infection (LTBI) only
Complementary List	
Reserve second-line drugs for the treatment of multidrug-resistant tuberculosis (MDR-TB) should be used in specialized centres adhering to WHO standards for TB control.	
amikacin	***Powder for injection:*** *100 mg; 500 mg; 1 g (as sulfate) in vial.*
bedaquiline	***Tablet:*** *100 mg.*
capreomycin	***Powder for injection:*** *1 g (as sulfate) in vial.*
clofazimine	***Capsule:*** *50 mg; 100 mg.*
*cycloserine**	***Solid oral dosage form:*** *250 mg.* **Terizidone may be an alternative*
delamanid **a**	***Tablet:*** *50 mg.* **a** >6 years
*ethionamide**	***Tablet:*** *125 mg; 250 mg.* **Protionamide may be an alternative.*
kanamycin	***Powder for injection:*** *1 g (as sulfate) in vial.*
levofloxacin	***Tablet:*** *250mg; 500 mg; 750 mg.*
linezolid	***Injection for intravenous administration:*** *2 mg/ mL in 300 mL bag.* ***Powder for oral liquid****: 100 mg/5 mL.* ***Tablet:*** *400 mg; 600 mg.*
moxifloxacin	***Tablet:*** *400 mg.*
p-aminosalicylic acid	***Granules:*** *4 g in sachet.* ***Tablet:*** *500 mg.*
streptomycin ***[c]***	***Powder for injection:*** *1 g (as sulfate) in vial.*
6.3 Antifungal medicines	

amphotericin B	**Powder for injection:** 50 mg in vial (as sodium deoxycholate **or** liposomal complex).
clotrimazole	**Vaginal cream:** 1%; 10%. **Vaginal tablet:** 100 mg; 500 mg.
fluconazole	**Capsule:** 50 mg. **Injection:** 2 mg/ mL in vial. **Oral liquid:** 50 mg/5 mL.
flucytosine	**Capsule:** 250 mg. **Infusion:** 2.5 g in 250 mL.
griseofulvin	**Oral liquid:** 125 mg/5 mL **[c]**. **Solid oral dosage form:** 125 mg; 250 mg.
itraconazole*	**Capsule**: 100 mg. **Oral liquid:** 10 mg/mL. * For treatment of chronic pulmonary aspergillosis, histoplasmosis, sporotrichosis, paracoccidiodomycosis, mycoses caused by *T. marneffei* and chromoblastomycosis; and prophylaxis of histoplasmosis and infections caused by *T. marneffei* in AIDS patients.
nystatin	**Lozenge:** 100 000 IU. **Oral liquid:** 50 mg/5 mL **[c]**; 100 000 IU/ mL **[c]**. **Pessary:** 100 000 IU. **Tablet:** 100 000 IU; 500 000 IU.
voriconazole*	**Tablet:** 50 mg; 200 mg **Powder for injection:** 200 mg in vial **Powder for oral liquid:** 40 mg/mL *For treatment of chronic pulmonary aspergillosis and acute invasive aspergillosis.
Complementary List	
potassium iodide	***Saturated solution.***