

WHO EML Antibiotic Working Group

Increasing **AWaRe-ness!**

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On behalf of the EML Antibiotic Working Group

2017 WHO EML Expert Committee developed the **AWaRe** classification of Essential Antibiotics
Access/ Watch/Reserve (Traffic light)

ACCESS group: narrow spectrum affordable antibiotics widely available.

WATCH group: broader spectrum antibiotics used for specific and limited indications due to higher resistance and toxicity potential.

RESERVE group: last resort antibiotics that should be used only when other antibiotics have failed or for treatment of multi-resistant bacteria.

“EM List - WHAT TO USE”

Access	
• Amikacin	• Cloxacillin
• Amoxicillin	• Doxycycline
• Ampicillin	• Gentamicin
• Amoxicillin–clavulanic acid	• Metronidazole
• Benzathine benzylpenicillin	• Nitrofurantoin
• Benzylpenicillin	• Phenoxymethyl penicillin
• Cefazolin	• Procaine penicillin
• Chloramphenicol	• Spectinomycin
• Clindamycin	• Sulfamethoxazole–trimethoprim

Watch	
• Azithromycin	• Vancomycin (intravenous* and oral)
• Cefixime	• Ciprofloxacin
• Ceftriaxone	• Clarithromycin
• Cefotaxime	• Meropenem*
• Ceftazidime*	• Piperacillin–tazobactam
• Cefuroxime	

Reserve*	
• Fosfomycin (intravenous)	• Ceftazidime–avibactam
• Linezolid	• Meropenem–vaborbactam
• Colistin	• Plazomicin
• Polymyxin B	

- **2019 EML** committee expanded the **AWaRe** classification to around 200 antibiotics
- A new category of Not recommended was added – mainly inappropriate Fixed-Dose Combinations of multiple broad-spectrum antibiotics.
- WHO General Programme of Work (GPW) now includes a Target indicator that the proportion of **Access** antibiotics should be more than **60%** of total antibiotic use at country level
- <https://adoptaware.org/>

Background - EML Antibiotic Working Group

- **WHO Mandate in 2016** to continuously *review and update the evidence for antibiotics listed on the EML* to optimize use of antimicrobials in human health (Objective 4 – AMR Global Action Plan).
 - Infection based (rather than drug based) approach to empiric treatment
 - **Reviews of systematic reviews and meta-analysis of all antibiotic RCTs and clinical guidelines for each infection between 1996-2016 was conducted by** McMaster University (WHO Collaborating Center).
- **Prevention** of the emergence of resistance
 - Focussing on optimising use of narrow spectrum antibiotics where appropriate
- **Parsimony**
 - Harmonising the use of essential antibiotics where appropriate
- **Benefits and harms**
 - Balancing efficacy and toxicity, selection of resistance
- **Practicality – pragmatic dosing schedules, considering formulation and implementation requirements**
- **Align with the WHO** list of Critically Important Antimicrobials for human medicine (where possible)
- **Align with existing WHO** guidelines (when available)
 - STIs, pediatric guidelines (e.g. pneumonia)

General principles of AWaRe

- **Goal of optimising use of narrow spectrum Access antibiotics**
- Provide guidance on **Symptomatic care** and **when to prescribe/not prescribe** using a risk-based approach (mild/severe symptoms; ill/not ill; underlying disease such as HIV/malnutrition/no underlying disease)
- Guidance regarding diagnostics was given where there was a **clear evidence base** for their added utility (choice of tests based on collaboration with the WHO EDL)
- Standardisation of guidance for drug/dose/duration across infections to simplify future implementation (and formulation development e.g. for children in collaboration with **WHO GAP-f**)

- **Guidance varied based on different rates of AMR for common infections assessed using GLASS data.**
- **RESERVE antibiotics – criteria for selection and stewardship, short drug summaries and guidance on when to use specific drugs in relevant infections – clear linkage to WHO AB Pipeline**
- Primary care focussed stewardship goals – closely aligned to WHO ASP Toolkit and WHO Policy Guidance on Integrated Stewardship Activities
- Wide endorsement globally on AWaRe as a policy tool at Global level and individual countries – rapid uptake

2021 - WHO EML Antibiotic Handbook

- To provide simple guidance on “HOW TO USE” the antibiotics on the EML to manage common infections
- Guidance for 36 infections; a strong focus on primary care also facility/hospital setting, children and adults.
 - acute bacterial infections (not TB/viral/fungal/parasitic infections)
 - **Recommendations on empiric antibiotic treatment** (i.e. presumptive diagnosis not requiring any laboratory diagnostic)
 - Includes guidance on making the clinical Diagnosis, the Decision if antibiotic needed, the choice of Drug, Dose, Duration
 - Short summaries of key features of microbiology, epidemiology, clinical presentation, diagnostics (in collaboration with EDL), prevention
 - **Target audience: all health professionals giving antibiotics**
 - Handbook, app, simple infographic formats – to be launched in 2021.

Potential Primary Care Goals for optimising use of Access antibiotics (increasing use of narrow spectrum AB, reducing broad spectrum use)

- At least **80% of Antibiotic Prescribing in Primary Care** should be **Access** antibiotics

Potential Primary Care Goals for safely reducing inappropriate prescribing (reducing total AB use)

- **60 % of 10 most common infections in primary care can be treated symptomatically/no AB for mild cases**
- **In some settings around half of patients attending a Primary Health Care facility receive an antibiotic (WHO goal of 30%).**
- **Critical importance of maintaining/enhancing “Access to Access” antibiotics in most vulnerable populations, but also “Access to Reserve”**

Common Primary Care Infections	Recommended AWaRe antibiotic
Bronchitis	None
Pharyngitis	Access
Otitis Media	Access
Sinusitis	Access
CAP (mild)	Access
COPD exacerbations	Access
UTI Lower	Access
Dental	Access
SSTI	Access
Acute Bacterial Diarrhoea	Watch

DRAFT Recommendations

Potential use of AWaRe in developing policy goals

Variation of antibiotic use by countries/regions

The proportion of countries where 60% of total oral antibiotic use was of Access antibiotics was 59/75 (78.7%), but only 14/75 (18.7%) reached 80% of oral Access antibiotic use (Table 1, Figure 5).

Table 1. Number of countries/regions that reached potential goals of oral Access antibiotic use

Access antibiotics accounted for	60% of total oral antibiotic use	70% of total oral antibiotic use	80% of total oral antibiotic use	90% of total oral antibiotic use
HICs, n/39 (%)	31 (79.5)	21 (53.8)	7 (17.9)	0 (0.0)
LMICs, n/36 (%)	28 (77.8)	23 (63.9)	7 (19.4)	0 (0.0)
Total, n/75 (%)	59 (78.7)	44 (58.7)	14 (18.7)	0 (0.0)

HICs, high-income countries/regions; LMICs, low-middle-income countries/regions

The proportion of oral Watch antibiotics for each country varied between 12.1% to 81.5% of total use (median 34.9% in HICs and 38.2% in LMICs) (Figure 5). The use of Not-Recommended antibiotics was higher in LMICs (6.2% of total) compared to HICs (0.7%). The use of oral Reserve antibiotics was very low with the highest proportions in Japan, Egypt, and India (1.2%, 0.7%, and 0.4%, respectively).

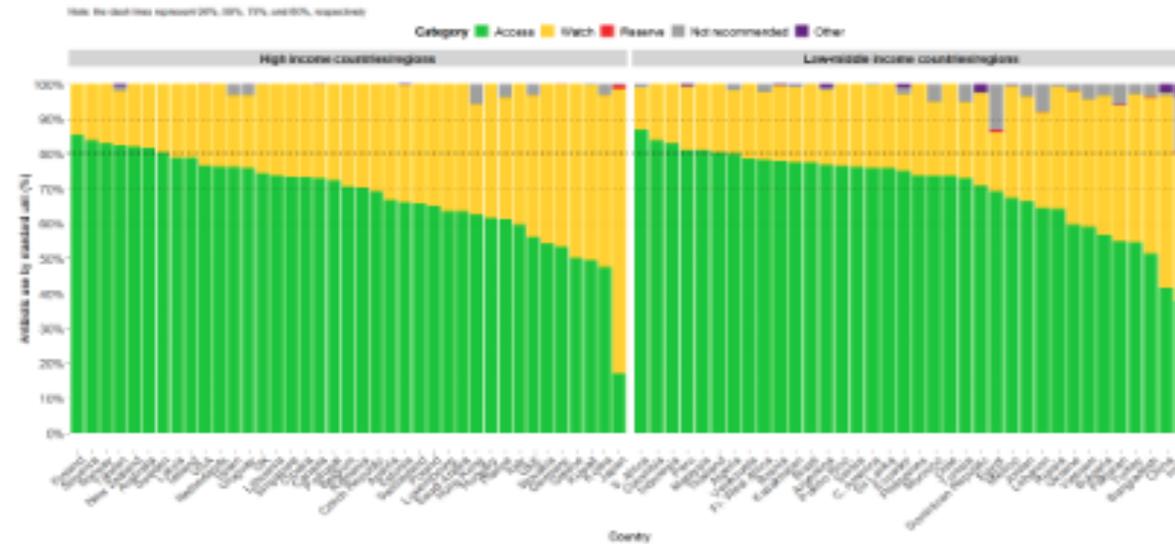


Figure 5. Oral antibiotic use by AWaRe system in 75 countries/regions in 2015

The AWaRe system

- Continuous re-evaluation of *which are the essential* antibiotics on the EML, the drug, indication, dose and formulation – generic and new agents
- Handbook provides a platform to build *future implementation programs on improving the use of antibiotics*
- Working with GARDP, GLASS, CIA, AMR teams to develop a coherent evidence-based quality improvement program around the optimal use of antimicrobials
- Continuous update of the AWaRe categorisation of antibiotics and improving the evidence base for these groups
- More formal evaluation of RESERVE antibiotics and assisting with a program of enhanced access – defining unmet public health needs
- Better RCT evidence for future policy interventions, country level adoption and implementation

MANY THANKS

- **ALL MEMBERS OF EML SECRETARIAT AND ANTIBIOTIC WG (Veronica Zanichelli-!).**
- **GLASS** : participated in meetings and exchanged ideas on how AMR surveillance data could be used (including for future updates)
- **AMR/AMS group:** participated in meetings and exchanged ideas for possible future implementation of the Handbook and linkage with Toolkit.
- **MCA:** harmonising with IMCI and Pocket book
- **EDL:** informed the choice of laboratory tests to include
- **NICE:** assisted meetings based on their summaries of the evidence (particularly on symptomatic care)
- **McMaster University** (WHO Collaborating Center): reviewed the evidence for the EML application, updated the reviews and conducted new reviews.
- **SPECTRUM** (mobile platform for infectious diseases): developed infographics based on the content of the chapters