WHO EML Antibiotic Working Group.
Building AWaRe-ness

Professor Mike Sharland
Chair of the AB WG
St George’s University London
1977

First Model EML

- 16 antibiotics (of 240 medicines ≈ 7%)

First EML children 2007

In a report \(^1\) to the Twenty-eighth World Health Assembly in 1975, the Director-General reviewed the main drug problems facing the developing countries and outlined possible new drug policies. The Director-General also referred to the experience gained in some countries where schemes of basic or essential drugs had been implemented. Such schemes were intended to extend the accessibility of the most necessary drugs to those populations whose basic health needs could not be met by the existing supply system. The Director-General pointed out that the selection of these essential drugs would depend on the health needs and on the structure and development of health services of each country, and that lists of essential drugs should be drawn up locally, and periodically updated, with the advice of experts in public health, medicine, pharmacology, pharmacy and drug management. He also considered that adequate information on the properties, indications and use of the drugs listed should be provided. By resolution WHA28.66, the Health Assembly requested the Director-General to implement the proposals contained in his report and, in particular, to advise Member States on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs.

**Antibacterial drugs**
- ampicillin (1) *
- benzathine benzylpenicillin (5) *
- benzylpenicillin *
- chloramphenicol (7) *
- cloxacillin (penicillinase-resistant, 1)
- erythromycin *
- gentamicin (4) *
- phenoxyethylpenicillin *
- salazosulfapyridine *
- sulfadimidine (1)
- sulfamethoxazole + trimethoprim *
- tetracycline (1, 4) *

**Complementary**
- amikacin (1, 4, 10) *
- doxycycline (6, 5) *
- procaine benzylpenicillin *
- sulfadiazine (7, 8) *

* On 2021 EML/c
Following the AMR Global Action Plan, in 2017 WHO EML AB WG set up to review AB listing on the EML (geographically representative and gender balanced).

The AB WG developed the AWaRe classification of Essential Antibiotics on the EML/c as a simple method to improve stewardship and monitoring.

**A-CESS group**: narrow spectrum, safe, affordable antibiotics widely available.

**Wa-TCH group**: broader spectrum antibiotics used for specific and limited indications due to higher resistance and toxicity potential.

**Re-SERVE group**: last resort antibiotics that should be used only for treatment of multi-resistant bacteria.

---

**“EML - WHAT ANTIBIOTICS TO USE”**

- **2019 EC** expanded the AWaRe classification to over **200 antibiotics not on the EML**
- A new category of **Not Recommended** was added – mainly inappropriate Fixed-Dose Combinations of multiple broad-spectrum antibiotics.
- **WHO 13th General Programme of Work (GPW)** included a Target indicator that at least 60% of total antibiotic use at a country level should be **Access** antibiotics.
22nd EML
• 39 antibiotics
• (8th EMLc - 36)
(of 479 medicines ≈ 8%)
WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2021

To assist in the development of tools for antibiotic stewardship at local, national and global levels and to reduce antimicrobial resistance, the Access, Watch, Reserve (AWaRe) classification of antibiotics was developed — where antibiotics are classified into different groups to emphasize the importance of their appropriate use.

This classification is intended to be used as a tool for countries to better support antibiotic monitoring and stewardship activities. It is not intended as model for the inclusion of antibiotics on national essential medicine lists. Antibiotics classified under AWaRe and also included on the WHO Model Lists of Essential Medicines are indicated in the worksheets.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Class</th>
<th>ATC code</th>
<th>Category</th>
<th>Listed on EML/EMLc 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Aminoglycosides</td>
<td>J01GB06</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Penicillins</td>
<td>J01CA04</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Amoxicillin/clavulanic-acid</td>
<td>Beta-lactam/beta-lactamase-inhibitor</td>
<td>J01CR02</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Penicillins</td>
<td>J01CA01</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Ampicillin/sulbactam</td>
<td>Beta-lactam/beta-lactamase-inhibitor</td>
<td>J01CR01</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Arbekacin</td>
<td>Aminoglycosides</td>
<td>J01GB12</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Aspergillacin</td>
<td>Penicillins</td>
<td>J01CA19</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Azidocillin</td>
<td>Penicillins</td>
<td>J01CE04</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Macrolides</td>
<td>J01FA10</td>
<td>Watch</td>
<td>Yes</td>
</tr>
<tr>
<td>Azlocillin</td>
<td>Penicillins</td>
<td>J01CA09</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Monobactams</td>
<td>J01DF01</td>
<td>Reserve</td>
<td>No</td>
</tr>
<tr>
<td>Bacampicillin</td>
<td>Penicillins</td>
<td>J01CA06</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Bekamycin</td>
<td>Aminoglycosides</td>
<td>J01GB13</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Benzathine-benzylpenicillin</td>
<td>Penicillins</td>
<td>J01CE08</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Benzylpenicillin</td>
<td>Penicillins</td>
<td>J01CE01</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Biapenem</td>
<td>Carbapenems</td>
<td>J01DH05</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Brotidomprin</td>
<td>Trimethoprim-derivatives</td>
<td>J01EA02</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Carbenicillin</td>
<td>Penicillins</td>
<td>J01CA03</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Carindacillin</td>
<td>Penicillins</td>
<td>J01CA05</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Carumonam</td>
<td>Monobactams</td>
<td>J01DF02</td>
<td>Reserve</td>
<td>No</td>
</tr>
<tr>
<td>Cefacetirile</td>
<td>First-generation-cephalosporins</td>
<td>J01DB10</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>Second-generation-cephalosporins</td>
<td>J01DC04</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Cefadroxil</td>
<td>First-generation-cephalosporins</td>
<td>J01DB05</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Cefalexin</td>
<td>First-generation-cephalosporins</td>
<td>J01DB01</td>
<td>Access</td>
<td>Yes</td>
</tr>
<tr>
<td>Cefaloridine</td>
<td>First-generation-cephalosporins</td>
<td>J01DB02</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Cefalotin</td>
<td>First-generation-cephalosporins</td>
<td>J01DB03</td>
<td>Access</td>
<td>No</td>
</tr>
<tr>
<td>Cefamandole</td>
<td>Second-generation-cephalosporins</td>
<td>J01DC03</td>
<td>Watch</td>
<td>No</td>
</tr>
<tr>
<td>Cefapirin</td>
<td>First-generation-cephalosporins</td>
<td>J01DB08</td>
<td>Access</td>
<td>No</td>
</tr>
</tbody>
</table>

257 Antibiotics have an AWaRe group 39 on EML
Around 100 Not Recommended
WHO EML Antibiotic AWaRe Book (2022)

• Now provides simple *guidance* on “HOW TO USE the antibiotics on the EML to manage most common infections
• Guidance for 34 infections; **primary care** and **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**
  – Developed in close collaboration with the WHO Division of AMR (GLASS/ASP) and many other departments
  – Short educational summaries of key features of microbiology, epidemiology, clinical presentation, diagnostics, prevention
  – **Target audience: all health professionals giving antibiotics**
General principles of AWaRe Book

- Goals of improving clinical care and optimise the use of narrow spectrum Access antibiotics (especially in Primary Care)
- 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 essential drug/dose/duration/formulation across infections to simplify future implementation and allow monitoring of the availability in pharmacies of quality and affordable medicines.
- 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 – linked to WHO AB Pipeline and Priority Pathogen List
- Primary and secondary care focussed stewardship goals – closely aligned to WHO ASP Toolkit and WHO Policy Guidance on Integrated Stewardship Activities
- Book designed to support the use of the AWaRe system as a quality improvement tool (and assist with developing policy goals)
Implementation focussed design
The WHO AWaRe (Access, Watch, Reserve) antibiotic book and prevention of antimicrobial resistance

Veronica Zanichelli, Michael Sharland, Bernadette Cappello, Lorenzo Moja, Haileyesus Getahun, Carmem Pessoa-Silva, Hatim Sati, Catharina van Weezenbeek, Hanan Balkhy, Mariângela Simão, Sumanth Gandra & Benedikt Huttner

Abstract Guidance on the appropriate use of antibiotics for common infections is lacking in many settings. The World Health Organization (WHO) has recently released The WHO AWaRe (Access, Watch, Reserve) antibiotic book which complements the WHO Model list of essential medicines and WHO Model list of essential medicines for children. The book gives specific guidance on the empiric use of antibiotics in the model lists with a strong emphasis on the AWaRe framework, which is centred around the risk of antimicrobial resistance development associated with the use of different antibiotics. Recommendations in the book cover 34 common infections in primary and hospital care both for children and adults. The book also includes a section on the use of the last-resort Reserve antibiotics, whose use should be restricted to very selected cases when an infection is confirmed or suspected to be caused by multidrug-resistant pathogens. The book highlights the use of first-line Access antibiotics or no antibiotic care if this is the safest approach for the patient. Here we present the background behind the development of the AWaRe book and the evidence behind its recommendations. We also outline how the book could be used in different settings to help reach the WHO target of increasing the proportion of global consumption of Access antibiotics to at least 60% of total consumption. The guidance in the book will also more broadly contribute to improving universal health coverage.
WHO AWaRe

- Book is a new step for the EML, it has taken nearly 50 years for the “List” of antibiotics to evolve into guidance on optimal “Use”.
- The AWaRe system has been developed to improve the quality of global AB use (over 90% are oral generic antibiotics taken in primary care – Book recommends nearly all should be Access antibiotics; high over-use globally of oral broad-spectrum Watch antibiotics)
- Helping to build the evidence for the **sustainable** use and access to essential Access antibiotics (SDG 3.8 - safe, effective, quality and affordable medicines) and assist with defining measurable impacts of UHC and Triple Billion Target.
- Now significant work on refining and implementing AWaRe

- Thank all members of the WHO EML Secretariat, AB WG, AMR Division, responders to public consultation and all other internal and external collaborators