

Most cases of malaria in India are reported from villages in rural and tribal regions, but awareness about malaria is inadequate among tribal communities. Villagers first approach traditional healers and informal health service providers for fever examination, which delays the correct diagnosis and treatment of malaria.⁹ Around 40% of malaria cases are managed by the community health worker, known as the Accredited Social Health Activist (ASHA). However, the ASHAs are overburdened by other health-care tasks, and malaria is low on their list of priorities. Periodical training and assessment of ASHAs in every district could play a pivotal role in malaria elimination programmes. Moreover, to effectively contain the spread of malaria by increasing the penetration of diagnostic and treatment facilities in tribal communities, mobile malaria clinics should be established at weekly markets in India, where people with symptoms of malaria could undergo on-the-spot diagnosis and treatment.

The implementation of the test, treat, and track strategy has resulted in the capture of most cases of malaria by active and passive surveillance, but poor drug compliance has emerged as a new implementation problem. Poor drug quality and compliance could lead to the development of drug resistance, and awareness programmes about dose compliance might prove effective in delaying antimalarial drug resistance.¹⁰ The medical community should not forget that India managed to come close to malaria eradication in the early 1960s, but malaria re-emerged as a major public health problem because of negligence and inadequate management. Therefore, malaria should be countered with full force to achieve the desired success this time. To identify, articulate, prioritise, and respond to the research needs of the country's goal to eliminate malaria, the Indian Council of Medical Research has formed Malaria Elimination Research Alliance India,¹¹

which uses unique cooperation between the public, private, and non-profit sectors to bring simple solutions to complex diagnostic challenges.

The attainment of malaria elimination will certainly depend on a strong political commitment and the integrated use of a combination of diagnostic tools to test and treat malaria patients; strengthening malaria diagnosis is key to the success of the malaria elimination programme.

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We declare no competing interests.

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Encouraging AWaRe-ness and discouraging inappropriate antibiotic use—the new 2019 Essential Medicines List becomes a global antibiotic stewardship tool

WHO's Essential Medicines List (EML) in 2017 provided guidance on antibiotic use for common clinical infections and classified the included antibiotics into Access, Watch,

and Reserve (AWaRe) groups. Antibiotics in the Access and Watch groups were selected on the basis of their indication as first-choice or second-choice treatments, spectrum

of activity, and potential for inducing antimicrobial resistance, whereas Reserve antibiotics were selected as last-resource treatments for multidrug-resistant infections.¹ The AWaRe categorisation was designed as a simple policy tool to classify the most used antibiotics globally for stewardship and surveillance purposes. However, 2017 AWaRe groups did not include some widely prescribed antibiotics, creating a large “Others or unclassified” group. This classification limits studies of antibiotic consumption as shown in a 2018 WHO report² and a 2019 study³ that investigated the use of paediatric antibiotics per AWaRe group in 70 countries. In 2019, the EML Committee clearly distinguished between the need to continue to include essential antibiotics in the EML and the need to classify most antibiotics used globally into AWaRe groups.⁴

The 2019 EML contains 37 antibiotics that are considered essential in treating 26 of the most common and severe clinical infections, focusing on low-income and middle-income settings.⁴ For example, first-generation cephalosporins such as cefazolin, listed in EML for surgical prophylaxis, are classified into the Access group because of their narrow spectrum. By contrast, second-generation cephalosporins are classified into the Watch group because of the increased risk of extended-spectrum β-lactamase (ESBL) selection⁵ and *Clostridioides difficile* infection.⁶ Seven new antibiotics were reviewed for inclusion in the 2019 EML: ceftazidime–avibactam, ceftolozane–tazobactam, delafloxacin, eravacycline, meropenem–vaborbactam, omadacycline, and plazomicin. Of these, only ceftazidime–avibactam, meropenem–vaborbactam, and plazomicin were recommended for the EML, as these antibiotics have a favourable safety profile with in-vitro evidence of activity against carbapenem-resistant organisms. All antibiotics in the 2019 EML are classified into AWaRe groups because different levels of stewardship are required through targeted actions to encourage their optimal use (figure). In addition to the 37 essential antibiotics, the Committee expanded the AWaRe grouping to a total of 180 antibiotics (appendix). Further work is planned to define the optimal choice of drug, dose, duration, and delivery or formulation for each infection and develop simple clinical guidance tools.

The AWaRe groups are now explicitly linked to the WHO Priority Pathogens List.⁷ New antibiotics eligible for the Reserve category must be active, at least in vitro, against organisms of critical or high priority on the Priority

Pathogens list.⁷ Fourth-generation cephalosporins in the AWaRe list were reclassified from the Reserve group to the Watch group, but were removed from the EML as they were not recommended by the Expert Committee as first-choice or second-choice therapies in any of 26 infectious syndromes reviewed.^{4,8} Similarly, other antibiotics such as aztreonam, ceftaroline, daptomycin, and tigecycline were removed because they were not deemed to be of sufficiently high priority for multidrug-resistant infections (aztreonam and tigecycline), because of safety concerns (eg, tigecycline has a black-box warning from the US Food and Drug Administration), or because EML-listed alternatives were available, such as linezolid for meticillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci (ceftaroline and daptomycin).

Recognising the need to stop the inappropriate use of antibiotics, the EML Committee recommended that WHO add a group to the AWaRe classification tool for antibiotics that are not used on the basis of sound evidence or recommended in high-quality international guidelines, particularly for fixed-dose combinations of multiple broad-spectrum antibiotics. Antibiotics in this group are not included in the EML and their use should be actively and strongly discouraged. The Committee also recommended reclassifying faropenem from the Watch to the Reserve group because it is likely to be used inappropriately

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	

See Online for appendix

Figure: Antibiotics included in 2019 WHO Essential Medicines List by AWaRe group

*Antibiotics listed in the complementary list of the 2019 WHO Essential Medicines List, indicating the need for specialist supervision.

and could promote the spread of carbapenemase-producing Enterobacteriaceae.⁹

Listing new antibiotics with activity against carbapenem-resistant organisms is challenging. The EML Committee noted that there was “very limited clinical trial evidence” comparing the efficacy of the newly added antibiotics against infections caused by carbapenem-resistant bacteria and their approval was based on small individual clinical studies.⁴ The Committee was very concerned that the current regulatory approval process for new drugs targeting the Critical group of the Priority Pathogens does not adequately meet the major public health need for clear evidence-based guidance on the optimal management of carbapenem-resistant infections. The Committee calls for urgent collaboration between relevant stakeholders to design and implement comparative trials including new and old antibiotics. Such trials would aim to establish the optimal management of carbapenem-resistant infections in adults and children.

The new AWaRe groups can be used in studies of consumption and use (eg, point prevalence surveys at the hospital level), focusing on both absolute and relative ratios of use of Access, Watch, and Reserve antibiotics.¹⁰ Further studies of antibiotic use in the community setting can be developed to monitor patterns of consumption and prescription. The AWaRe groups are presented using a traffic light approach to show the proportional use of broad-spectrum and narrow-spectrum antibiotics to a variety of stakeholders.

WHO has now recommended that antibiotics in the Access group should account for 60% of total antibiotic consumption at country level. Most respiratory tract infections can be treated with Access antibiotics, but for other infections increased use of Watch and Reserve antibiotics might be appropriate in high-resistance settings. The rapid adoption of AWaRe has shown the need for simple metrics of antibiotic use that can be easily understood by prescribers and policy makers. This extension of the AWaRe classification and targets is aimed at encouraging AWaRe’s implementation as a global tool to improve the quality of antibiotic prescribing and use.

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For WHO’s AWaRe recommendations see <https://adoptaware.org/>