
Combating Antimicrobial Resistance (AMR) with Rational Use of Antibiotics



A Cipla initiative to fight Anti-Microbial Resistance



Selection and Rational Use of Medicines¹

Key Points and Implications of the WHO AWaRe Classification of Antibiotics



WHO's Global Action Plan on AMR

- **Global Threat:** Antimicrobial resistance (AMR) is a significant threat to global public health and development, contributing to over five million deaths annually.
- **Drivers of AMR:** The inappropriate use and overuse of antibiotics are primary drivers of the global increase in AMR, undermining the effectiveness of these critical medicines.
- **Objectives:** The World Health Organization (WHO) aims to support effective antimicrobial stewardship programs, enhance AMR surveillance, and reduce inappropriate antibiotic consumption through its Global Action Plan on AMR.
- **Stewardship Tools:** To aid in the development of antibiotic stewardship tools at local, national, and global levels, WHO introduced the AWaRe classification of antibiotics.



AWaRe Classification Overview

- **Categories:** The AWaRe classification divides antibiotics into three groups based on their clinical importance and the risk of promoting resistance:¹
 - **Access:** Antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups.
 - **Watch:** Antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance.
 - **Reserve:** Antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics should be treated as “last resort” options.



Implementation and Expansion¹

- **Initial Introduction:** The AWaRe classification was first introduced in 2017, classifying antibiotics in the WHO Model Lists of Essential Medicines into Access, Watch, or Reserve categories by the WHO Expert Committee on Selection and Use of Essential Medicines.
- **Global Application:** In 2019, the Expert Committee recommended extending the AWaRe classification to all commonly used antibiotics globally. This recommendation was based on advice from the **Essential Medicines List** Antimicrobials Working Group and the Expert Committee on Selection and Use of Essential Medicines.
- **Technical Reports:** Detailed methodology and evidence underpinning these recommendations are available in the technical reports of the WHO Expert Committee on Selection and Use of Essential Medicines.



Utility of the AWaRe Classification

- **Policy Makers and Researchers:** The AWaRe classification serves as a critical tool for policymakers and researchers to support antibiotic prescribing, monitoring, and stewardship activities.

- **Healthcare Providers:** It aids healthcare providers in making informed decisions about antibiotic use, thereby promoting rational use and reducing the risk of resistance.

Key Findings from Recent Literature

- **ICMR Annual Report on Antimicrobial Resistance²:** The recent Indian Council of Medical Research (ICMR) report presents data from January 1st, 2023 to December 31st, 2023

Key Highlights of the reports:

The report revealed an alarming trend of increasing antibiotic resistance and declining susceptibility of common pathogenic bacteria. The report is based on the analysis of 99,492 culture-positive isolates from various specimens, including blood, urine, superficial infections, the lower respiratory tract (LRT), deep infections, sterile sites and faeces. Susceptibility to most antibiotics has decreased over time, with piperacillin-tazobactam dropping from 56.8 per cent in 2017 to 42.4 per cent in 2023 and amikacin from 79.2 per cent to 68.2 per cent over the same period, the paper showed. The susceptibility of E coli to carbapenems has also notably declined, with imipenem falling from 81.4 per cent in 2017 to 62.7 per cent in 2023 and meropenem from 73.2 per cent to 66 per cent. Similarly, Klebsiella pneumoniae exhibited reduced susceptibility, with piperacillin-tazobactam falling from 42.6 per cent to 26.5 per cent, imipenem from 58.5 per cent to 35.6 per cent and meropenem from 48 per cent to 37.6 per cent. Fluoroquinolone resistance also increased, with ciprofloxacin susceptibility dropping from 32 per cent to 17.1 per cent over seven years. Pseudomonas aeruginosa also showed a gradual increase in resistance to carbapenems, with imipenem resistance rising from 26 per cent in 2017 to 38.5 per cent in 2023 and meropenem from 31.3 per cent to 34.5 per cent. Resistance to fluoroquinolones has similarly increased, with ciprofloxacin resistance rising from 26 per cent to 38.5 per cent and levofloxacin from 31.3 per cent to 34.5 per cent over the same period. In addition, Salmonella typhi, which causes gastroenteritis (diarrhoea, vomiting, fever and abdominal cramps), showed over 95 per cent resistance to fluoroquinolones. The data indicated a concerning rise in resistance to Critically Important Antibiotics (CIAs) and Highest-Priority Critically Important Antibiotics (HPCIs), which are essential for treating serious human infections. Resistance rates among key bacterial pathogens, such as Escherichia coli, Klebsiella pneumoniae and Staphylococcus aureus, have increased significantly.

- **Ground level utility of Access, Watch, Reserve classification (North India Study):** A study conducted in a tertiary care center in North India found that 57.61% of antibiotics prescribed were in the Access category, 38.27% in Watch, and 4.11% in Reserve. The study involved a total of 123 patients, each of whom received at least one antimicrobial prescription. Metronidazole and ceftriaxone were the most prescribed antibiotics highlighted the need for better antimicrobial prescribing practices and increased awareness of the AWaRe classification among healthcare professionals.³
- **Study to Evaluate the Impact of Increasing the Awareness of AWaRe Antibiotics Classification:** An educational intervention study showed that increasing awareness of the AWaRe classification among hospital clinical staff significantly improved their knowledge and attitudes towards antibiotic prescribing. Post-intervention, the use of Access antibiotics increased by 6.6%, while the use of Watch and Reserve antibiotics decreased by 1.7% and 43.1%, respectively.⁴
- **Study Assessing Consistency and Appropriateness of Antibiotic Prescribing Across Europe:** The PERFORM study revealed that a significant proportion of febrile children with viral infections received systemic antibiotics, predominantly from the Watch category, underscoring the challenge of differentiating bacterial from viral infections in emergency settings.⁵
- **Meta analysis on associations between prior exposure to antibiotics and isolation of critical and high-priority MDROs:** A systematic review and meta-analysis found that prior exposure to Watch and Reserve antibiotics was associated with higher odds of colonization/ infection with multidrug-resistant organisms (MDROs) compared to Access antibiotics. This supports the rationale for optimizing the use of Access antibiotics to reduce global antibiotic resistance.⁶

Summary

The WHO AWaRe classification of antibiotics is a pivotal tool designed to combat antimicrobial resistance by categorizing antibiotics into Access, Watch, and Reserve groups based on their clinical importance and resistance potential.

Studies have shown that increasing awareness and proper implementation of the AWaRe classification can significantly improve antibiotic prescribing practices, thereby reducing the risk of AMR. The classification serves as a valuable resource for policy-makers, researchers, and healthcare providers to promote rational antibiotic use and enhance antimicrobial stewardship efforts globally.

WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2023

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 by WHO as well as Essential Medicines List (EML)-2022 issued by ICMR are indicated in the tables below.

Access Category

Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Amikacin	Aminoglycosides	IV	Yes
Amoxicillin	Penicillins	Oral/IV	Yes
Amoxicillin/clavulanic- acid	Beta-lactam/beta-lactamase-inhibitor	Oral/IV	Yes
Ampicillin	Penicillins	IV	Yes
Ampicillin/sulbactam	Beta-lactam/beta-lactamase-inhibitor	IV	No
Azidocillin	Penicillins	Oral/IV	No
Bacampicillin	Penicillins	Oral	No
Benzathine-benzylpenicillin	Penicillins	IV	Yes
Benzylpenicillin	Penicillins	IV	Yes
Brodinoprim	Trimethoprim- derivatives	Oral	No
Cefadroxil	First-generation-cephalosporins	Oral	Yes
Cefalexin	First-generation-cephalosporins	Oral	No
Cefaloridine	First-generation-cephalosporins	Oral	No
Cefalotin	First-generation-cephalosporins	IV	No
Cefapirin	First-generation-cephalosporins	IV	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Cefatrizine	First-generation-cephalosporins	Oral	No
Cefazedone	First-generation-cephalosporins	IV	No
Cefazolin	First-generation-cephalosporins	IV	Yes
Cefradine	First-generation-cephalosporins	Oral	No
Cefroxadine	First-generation-cephalosporins	Oral	No
Ceftazole	First-generation-cephalosporins	IV	No
Chloramphenicol	Amphenicols	Oral	No
Clindamycin	Lincosamides	Oral/IV	Yes
Clometocillin	Penicillins	Oral	No
Cloxacillin	Penicillins	Oral/IV	Yes
Dicloxacillin	Penicillins	Oral	No
Doxycycline	Tetracyclines	Oral/IV	Yes
Epicillin	Penicillins	Oral/IV	No
Flucloxacillin	Penicillins	Oral	No
Furazidin	Nitrofurans derivatives	Oral	No
Gentamicin	Aminoglycosides	IV	Yes
Hetacillin	Penicillins	Oral	No
Mecillinam	Penicillins	Oral	No
Metampicillin	Penicillins	Oral	No
Meticillin	Penicillins	Oral	No
Metronidazole	Imidazoles	Oral/IV	Yes
Nafcillin	Penicillins	Oral	No
Nifurtinol	Nitrofurans derivatives	Oral	No
Nitrofurantoin	Nitrofurans- derivatives	Oral	Yes
Ornidazole	Imidazoles	Oral/IV	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Oxacillin	Penicillins	Oral	No
Penamecillin	Penicillins	Oral	No
Phenoxymethylpenicillin	Penicillins	Oral	Yes
Pivampicillin	Penicillins	Oral	No
Pivmecillinam	Penicillins	Oral	No
Procaine-benzylpenicillin	Penicillins	IV	Yes
Propicillin	Penicillins	Oral	No
Secnidazole	Imidazoles	Oral	No
Spectinomycin	Aminocyclitols	Oral	No
Sulbactam	Beta-lactamase- inhibitors	IV	No
Sulfadiazine	Sulfonamides	Oral	No
Sulfadiazine/tetroxoprim	Sulfonamide-trimethoprim-combinations	Oral	No
Sulfadiazine/trimethoprim	Sulfonamide-trimethoprim-combinations	Oral	No
Sulfadimethoxine	Sulfonamides	Oral	No
Sulfadimidine	Sulfonamides	Oral	No
Sulfadimidine/trimethoprim	Sulfonamide-trimethoprim-combinations	Oral	No
Sulfafurazole	Sulfonamides	Oral	No
Sulfaisodimidine	Sulfonamides	Oral	No
Sulfalene	Sulfonamides	Oral	No
Sulfamazone	Sulfonamides	Oral	No
Sulfamerazine	Sulfonamides	Oral	No
Sulfamerazine/trimethoprim	Sulfonamide-trimethoprim-combinations	Oral	Yes
Sulfamethizole	Sulfonamides	Oral	No
Sulfamethoxazole	Sulfonamides	Oral	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Sulfamethoxazole/trimethoprim	Sulfonamide-trimethoprim-combinations	Oral	Yes
Sulfamethoxypyridazine	Sulfonamides	Oral	No
Sulfametomidine	Sulfonamides	Oral	No
Sulfametoxydiazine	Sulfonamides	Oral	No
Sulfametrole/trimethoprim	Sulfonamide-trimethoprim-combinations	Oral	No
Sulfamoxole	Sulfonamides	Oral	No
Sulfamoxole/trimethoprim	Sulfonamide-trimethoprim-combinations	Oral	No
Sulfanilamide	Sulfonamides	Oral	No
Sulfaperin	Sulfonamides	Oral	No
Sulfaphenazole	Sulfonamides	Oral/IV	No
Sulfapyridine	Sulfonamides	Oral	No
Sulfathiazole	Sulfonamides	Oral/IV	No
Sulfathiourea	Sulfonamides	Oral	No
Sultamicillin	Beta-lactam/beta-lactamase-inhibitor	Oral	No
Talampicillin	Penicillins	Oral	No
Tetracycline	Tetracyclines	Oral	No
Thiamphenicol	Amphenicols	Oral	No
Tinidazole	Imidazoles	Oral/IV	No
Trimethoprim	Trimethoprim- derivatives	Oral	No

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Watch Category

Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Arbekacin	Aminoglycosides	Oral/IV	No

Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Azithromycin	Macrolides	Oral/IV	Yes
Azlocillin	Penicillins	Oral/IV	No
Aspoxicillin	Penicillins	Oral/IV	No
Bekanamycin	Aminoglycosides	IV/Topical	No
Biapenem	Carbapenems	IV	No
Carbenicillin	Penicillins	Oral	No
Carindacillin	Penicillins	Oral	No
Cefacetrile	First-generation-cephalosporins	IV	No
Cefaclor	Second-generation-cephalosporins	Oral	No
Cefamandole	Second-generation-cephalosporins	IV	No
Cefbuperazone	Second-generation-cephalosporins	Oral/IV	No
Cefcapene-pivoxil	Third-generation-cephalosporins	Oral	No
Cefdinir	Third-generation-cephalosporins	Oral	No
Cefditoren-pivoxil	Third-generation-cephalosporins	Oral	No
Cefepime	Fourth-generation-cephalosporins	IV/IM	No
Cefetamet-pivoxil	Third-generation-cephalosporins	Oral	No
Cefixime	Third-generation-cephalosporins	Oral	Yes
Cefmenoxime	Third-generation-cephalosporins	IV/IM	No
Cefmetazole	Second-generation-cephalosporins	IV/IM	No
Cefminox	Second-generation-cephalosporins	IV/IM	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Cefodizime	Third-generation-cephalosporins	IV/IM	No
Cefonicid	Second-generation-cephalosporins	IV/IM	No
Cefoperazone	Third-generation-cephalosporins	IV/IM	No
Ceforanide	Second-generation-cephalosporins	IV/IM	No
Cefoselis	Fourth-generation-cephalosporins	IV	No
Cefotaxime	Third-generation-cephalosporins	IV	Yes
Cefotetan	Second-generation-cephalosporins	IV/IM	No
Cefotiam	Second-generation-cephalosporins	IV/IM	No
Cefoxitin	Second-generation-cephalosporins	IV	No
Cefozopran	Fourth-generation-cephalosporins	IV	No
Cefpiramide	Third-generation-cephalosporins	IV/IM	No
Cefpirome	Fourth-generation-cephalosporins	IV/IM	No
Cefpodoxime-proxetil	Third-generation-cephalosporins	Oral	No
Cefprozil	Second-generation-cephalosporins	Oral	No
Cefsulodin	Third-generation-cephalosporins	IV/IM	No
Ceftazidime	Third-generation-cephalosporins	IV	Yes
Cefteram-pivoxil	Third-generation-cephalosporins	Oral	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Ceftibuten	Third-generation-cephalosporins	Oral	No
Ceftizoxime	Third-generation-cephalosporins	IV/Suppository	No
Ceftriaxone	Third-generation-cephalosporins	IV	Yes
Cefuroxime	Second-generation-cephalosporins	Oral/IV	Yes
Chlortetracycline	Tetracyclines	Oral/IV/Topical	No
Cinoxacin	Quinolones	Oral	No
Ciprofloxacin	Fluoroquinolones	Oral/IV/Topical	Yes
Clarithromycin	Macrolides	Oral	Yes
Clofoctol	Phenol derivatives	Oral/Rectal	No
Clomocycline	Tetracyclines	Oral	No
Delafoxacin	Fluoroquinolones	Oral/IV	No
Demeclocycline	Tetracyclines	Oral	No
Dibekacin	Aminoglycosides	IV/IM	No
Dirithromycin	Macrolides	Oral	No
Doripenem	Carbapenems	IV	No
Enoxacin	Fluoroquinolones	Oral	No
Ertapenem	Carbapenems	IV/IM	No
Erythromycin	Macrolides	Topical	Yes
Fidaxomicin	Macrolides	Oral	No
Fleroxacin	Fluoroquinolones	Oral/IV	No
Flomoxef	Second-generation-cephalosporins	IV	No
Flumequine	Quinolones	Oral/IV	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Flurithromycin	Macrolides	Oral	No
Fosfomycin	Phosphonics	Oral/IV	No
Fusidic-acid	Steroid antibacterials	Topical	Yes
Garenoxacin	Fluoroquinolones	Oral	No
Gatifloxacin	Fluoroquinolones	Topical	No
Gemifloxacin	Fluoroquinolones	Oral	No
Grepafloxacin	Fluoroquinolones	Oral	No
Imipenem/cilastatin	Carbapenems	IV	No
Isepamicin	Aminoglycosides	IV/IM	No
Josamycin	Macrolides	IM	No
Kanamycin	Aminoglycosides	IV	Yes
Lascufloxacin	Fluoroquinolones	IV	No
Latamoxef	Third-generation-cephalosporins	IV/IM	No
Levofloxacin	Fluoroquinolones	Oral	Yes
Levonadifloxacin	Fluoroquinolones	Oral/IV	No
Lincomycin	Lincosamides	Oral	No
Lomefloxacin	Fluoroquinolones	Oral	No
Loracarbef	Second-generation-cephalosporins	Oral	No
Lymecycline	Tetracyclines	Oral/IV	No
Meropenem	Carbapenems	IV	Yes
Metacycline	Tetracyclines	Oral	No
Mezlocillin	Penicillins	IV/IM	No
Micronomicin	Aminoglycosides	Topical	No
Midecamycin	Macrolides	Oral	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Minocycline	Tetracyclines	Oral/Topical	No
Miocamycin	Macrolides	Oral	No
Moxifloxacin	Fluoroquinolones	Oral	Yes
Nemonoxacin	Quinolones	Oral	No
Neomycin	Aminoglycosides	IV/Oral/Topical	No
Netilmicin	Aminoglycosides	Topical	No
Norfloxacin	Fluoroquinolones	Oral	No
Ofloxacin	Fluoroquinolones	Oral	No
Oleandomycin	Macrolides	Oral	No
Oxolinic-acid	Quinolones	Oral	No
Oxytetracycline	Tetracyclines	IV	No
Panipenem	Carbapenems	IV	No
Pazufloxacin	Fluoroquinolones	IV	No
Pefloxacin	Fluoroquinolones	Oral	No
Penimepicycline	Tetracyclines	Oral/IM	No
Pheneticillin	Penicillins	IV/Oral	No
Pipemidic-acid	Quinolones	Oral	No
Piperacillin	Penicillins	IV	No
Piperacillin/ tazobactam	Beta-lactam/beta-lactamase-inhibitor_ anti-pseudomonal	IV	Yes
Piromidic-acid	Quinolones	Oral	No
Pristinamycin	Streptogramins	Oral	No
Prulifloxacin	Fluoroquinolones	Oral	No
Ribostamycin	Aminoglycosides	Oral	No
Rifabutin	Rifamycins	Oral	Yes

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Rifampicin	Rifamycins	Oral	Yes
Rifamycin	Rifamycins	IV/Oral	No
Rifaximin	Rifamycins	Oral	No
Rokitamycin	Macrolides	Oral	No
Rolitetracycline	Tetracyclines	Oral	No
Rosoxacin	Quinolones	Oral	No
Roxithromycin	Macrolides	Oral	No
Rufloxacin	Fluoroquinolones	Oral	No
Sarecycline	Tetracyclines	Oral	No
Sisomicin	Aminoglycosides	Oral	No
Sitafloxacin	Fluoroquinolones	Oral	No
Solithromycin	Macrolides	Oral	No
Sparfloxacin	Fluoroquinolones	Oral	No
Spiramycin	Macrolides	IV	No
Streptoduocin	Aminoglycosides	IV	No
Streptomycin	Aminoglycosides	Oral	Yes
Sulbenicillin	Penicillins	IV	No
Tazobactam	Beta-lactamase-inhibitors	IV	No
Tebipenem	Carbapenems	Oral	No
Teicoplanin	Glycopeptides	IV/IM	No
Telithromycin	Macrolides	Oral	No
Temafloxacin	Fluoroquinolones	Oral	No
Temocillin	Penicillins	IV	No

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Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Ticarcillin	Penicillins	IV	No
Tobramycin	Aminoglycosides	IV/IM/Topical/ Inhalational	No
Tosufloxacin	Fluoroquinolones	Oral	No
Troleandomycin	Macrolides	Oral	No
Trovaflaxacin	Fluoroquinolones	IV/Oral	No
Vancomycin	Glycopeptides	IV/Oral	Yes

Reserve Category

Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Aztreonam	Monobactams	IV/IM	No
Carumonam	Monobactams	IV/IM	No
Cefiderocol	Other- cephalosporins	IV	No
Ceftaroline-fosamil	Fifth-generation cephalosporins	IV	No
Ceftazidime/avibactam	Third-generation- cephalosporins	IV	No
Ceftobiprole-medocaril	Fifth-generation cephalosporins	IV	No
Ceftolozane/tazobactam	Fifth-generation cephalosporins	IV	No
Colistin	Polymyxins	IV/Oral	No
Dalbavancin	Glycopeptides	IV	No
Dalfopristin/quinupristin	Streptogramins	IV	No
Daptomycin	Lipopeptides	IV	No
Eravacycline	Tetracyclines	IV	No

Antibiotic	Class	Route of Administration	Listed on EML 2022 (ICMR)
Faropenem	Penems	Oral	No
Fosfomycin	Phosphonics	IV	No
Iclaprim	Trimethoprim- derivatives	IV	No
Imipenem/cilastatin/ relebactam	Carbapenems	IV	No
Lefamulin	Pleuromutilin	Oral	No
Linezolid	Oxazolidinones	Oral	Yes
Meropenem/ vaborbactam	Carbapenems	IV	No
Minocycline_IV	Tetracyclines	IV/Oral	No
Omadacycline	Tetracyclines	IV/Oral	No
Oritavancin	Glycopeptides	IV	No
Plazomicin	Aminoglycosides	IV	No
Polymyxin-B	Polymyxins	IV/Oral	No
Tedizolid	Oxazolidinones	IV/Oral	No
Telavancin	Glycopeptides	IV	No
Tigecycline	Glycylcyclines	IV	No

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Conclusion

Rational, safe, and evidence-based use of antibiotics is imperative to combat antimicrobial resistance. By adhering to clinical guidelines, implementing antimicrobial stewardship programs, conducting regular audits, and educating both healthcare providers and the public, we can significantly reduce the misuse/overuse of antibiotics and the subsequent rise in Antimicrobial Resistance (AMR).

1. Web Annex C. WHO AWaRe (access, watch, reserve) classification of antibiotics for evaluation and monitoring of use, 2023. In: The selection and use of essential medicines 2023: Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines, 24 – 28 April 2023. Geneva: World Health Organization; 2023 (WHO/MHP/HPS/EML/2023.04).
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