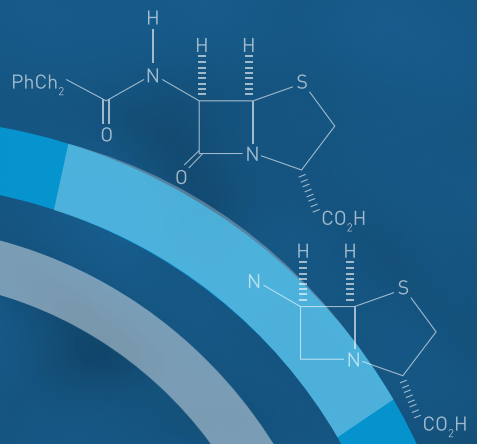
World Health Organization

European Region



WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network

AMC data 2022

Abstract

This report presents analyses of data on antimicrobial medicines consumption collected from non-European Union countries in the WHO European Region – 15 countries provided 2022 data. The analyses show the results for key metrics of antibiotic consumption, including total use, relative use of agents according to the WHO Access, Watch and Reserve (AWaRe) classification, and concordance with WHO monitoring indicators for responsible use of antibiotics. Analyses explore the consumption of antifungal agents, focusing on the consumption of agents used to treat invasive fungal disease.

Keywords

CONSUMPTION
SURVEILLANCE
ANTIBIOTICS
ANTIFUNGALS
RESPONSIBLE USE OF ANTIBACTERIALS
EASTERN EUROPE
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ABBREVIATIONS

AMC	Antimicrobial Medicines Consumption (Network)
AMR	antimicrobial resistance
ANOVA	analysis of variance (test)
ATC	Anatomical Therapeutic Chemical (classification system)
ATC3	ATC 3rd level
ATC5	ATC 5th level
AWaRe	WHO Access, Watch and Reserve (classification)
CAGR	compound annual growth rate
COVID-19	coronavirus disease 2019
DDD	defined daily doses
DID	defined daily doses per 1000 inhabitants per day
DU75%	drug utilization 75%
EML	WHO Model List of Essential Medicines for adults
EMLc	WHO Model List of Essential Medicines for children
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
EU	European Union
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GLASS-AMC	Global Antimicrobial Resistance and Use Surveillance System, Antimicrobial Medicines Consumption (module)
GLASS-IT	Global Antimicrobial Resistance and Use Surveillance System Information Technology (platform)
IFD	invasive fungal disease
IP	inhalation powder
IS	inhalation solution
IV	intravenous

Abbreviations of country names used in tables and figures

ALB	Albania
ARM	Armenia
AZE	Azerbaijan
BLR	Belarus
BIH	Bosnia and Herzegovina
GEO	Georgia
KAZ	Kazakhstan
KGZ	Kyrgyzstan
MDA	Republic of Moldova
MKD	North Macedonia
MNE	Montenegro
RUS	Russian Federation
SRB	Serbia
SWI	Switzerland
TJK	Tajikistan
TUR	Türkiye
UKR	Ukraine
UZB	Uzbekistan

EXECUTIVE SUMMARY

The WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network aims to support all Member States of the WHO European Region that are not part of the European Surveillance of Antimicrobial Consumption Network, which is coordinated by the European Centre for Disease Prevention and Control. The following Member States are currently engaged in the AMC Network: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, Türkiye, Ukraine and Uzbekistan.

This is the sixth AMC Network report, with analyses conducted using 2022 data from 15 AMC Network countries. The 2023 WHO Access, Watch and Reserve (AWaRe) classification of antibiotics is applied and the WHO national monitoring target of at least 60% of total consumption being Access agents is assessed. The utilization of antibacterial substances accounting for 75% of consumption (the drug utilization 75% (DU75%)), measured in defined daily doses, is calculated for oral and parenteral formulations separately. The consumption of antifungal agents is explored, focusing on agents used to manage invasive fungal disease (IFD).

Key findings

Data on total consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) classification group J01) were available for 15 countries in 2022. Consumption of J01 antibacterials ranged from 9.6 defined daily doses per 1000 inhabitants per day (DID) (Armenia) to 35.7 DID (Türkiye), with a median consumption of 16.8 DID and a population-weighted mean consumption of 20.7 DID. The comparable estimates for 2021 from 10 countries were 8.6–34.4 DID, a median consumption of 19.9 DID and a population-weighted mean consumption of 20.3 DID.

As in previous AMC reports, consumption according to formulation and pharmacological subgroup varied widely across the 15 countries. Parenteral formulations represented from 5% to 45% of total consumption of J01 antibacterials. Consumption of beta-lactam penicillins (J01C) ranged from 14% to 54% of total J01 consumption (the AMC Network population-weighted mean was 36%). Cephalosporin (J01D) consumption varied from 9% to 32%, quinolone (J01M) consumption varied from 8% to 21% and consumption of macrolides, lincosamides and streptogramins (J01F) ranged from 8% to 25%.

Thirteen countries had consumption estimates available for all years (2014–2022). Two showed statistically significant increases in consumption of J01 antibacterials over the nine years of data collection – Azerbaijan (compound annual growth rate (CAGR) +10.5%) and Bosnia and Herzegovina (CAGR +3.4%). Only one country, Switzerland, showed a statistically significant reduction in consumption over time (CAGR –1.1%). Trends towards decreasing consumption in some countries in earlier years were affected by changed consumption patterns during the coronavirus disease 2019 (COVID-19) pandemic.

Consumption of Access agents represented between 39% (Albania) and 68% (Belarus) of total antibacterial consumption in 2022. Access agents comprised 50% or more of total consumption in eight of 15 countries (53%). By comparison, Watch group agents represented between 30% (Belarus and Kyrgyzstan) and 61% (Albania) of total consumption. The 2022 population-weighted estimates

across the AMC Network were: Access agents 51%, Watch agents 47%, Reserve agents 0.3% and unclassified agents 1.7%.

In 2019, WHO proposed a global monitoring indicator that by 2023, 60% of all antibiotics consumed should come from Access, the group of antibiotics at lowest risk of resistance. Four countries – Belarus, Bosnia and Herzegovina, Kyrgyzstan and Switzerland – met the global monitoring target in 2022. Only one country, Switzerland, would have achieved this target in each of the five years (2018–2022).

The number of agents constituting the DU75% by oral substance in 2022 ranged from six to 10 across the 15 AMC Network countries. The Access agents amoxicillin and beta-lactamase inhibitor (ATC code J01CR02) and amoxicillin (J01CA04) ranked first and second for consumption in the population-weighted DU75%. The Watch agent azithromycin (J01FA10), a macrolide, was ranked third in the population-weighted DU75%. A second macrolide, clarithromycin (J01FA09), was fourth most consumed oral antibiotic. The Watch agent ceftriaxone (J01DD04) was ranked number one most consumed parenteral antibiotic across the Network.

Consumption data disaggregated by community and hospital sectors were available for five countries – Montenegro, the Russian Federation, Switzerland, Türkiye and Ukraine – with community consumption of J01 antibacterials comprising 86–96% of total consumption in 2022. Consumption estimates for North Macedonia are only for the community sector. Most consumption in the community sector was for oral antibacterial agents. Parenteral agents represented 1% of community consumption in Switzerland and Türkiye and 8% in Ukraine. In contrast, hospital consumption was dominated by parenteral formulations, ranging from 54% of consumption in Switzerland to 88% in Türkiye. Volumes of consumption in the hospital setting were low, varying from 1.0 DID in Switzerland to 2.0 DID in the Russian Federation.

Patterns of community consumption varied across the six countries. Beta-lactam antibacterials (J01C) represented from 18% to 45% of community consumption. Cephalosporins were widely consumed in Montenegro, North Macedonia and Türkiye (24–25% of community consumption) but less frequently in the Russian Federation and Switzerland (9% and 7% respectively). Agents from the macrolides, lincosamides and streptogramins (J01F) were widely consumed in Montenegro (24% of community consumption), Ukraine (24%) and the Russian Federation (23%). Quinolone antibacterials (J01M) constituted 18% of community consumption in the Russian Federation and 17% in Ukraine, but only 9–10% of consumption in the other four countries.

The substantial differences in patterns of consumption overall and at community level shown in these analyses suggest significant differences in management protocols and treatment guidelines at country level. Reasons for these differences should be investigated. Countries could consider a review of treatment algorithms and guidelines for common conditions against medicines recommended in the WHO AWaRe antibiotic book. This book is an evidence-based resource providing recommendations for first- and second-line treatment options for more than 30 of the most common clinical infections in children and adults managed in community and hospital settings.

Exploratory analyses for antifungal agents for systemic use were conducted for 12 countries. There was wide variability in total consumption in 2022, ranging from 2.6 DID in Azerbaijan to 0.16 DID in North Macedonia (community consumption only). The numbers of antifungal agents used varied from three agents in North Macedonia and Tajikistan to 13 in the Russian Federation.

Nystatin (A07AA02) was widely consumed as an intestinal anti-infective (11 countries). Ten countries reported consumption of terbinafine (D01BA02) for the systemic treatment of dermatological fungal infections.

Seven countries reported parenteral consumption of the polyene antibiotic amphotericin B for IFD (consumption from < 0.001 to 0.034 DID). The triazole fluconazole was the only agent with reported consumption in all 12 countries (ranging from 1.2 DID in Tajikistan to 0.1 DID in North Macedonia). Very low levels of consumption of the newer echinocandins – caspofungin, micafungin and anidulafungin – were reported in five countries (Belarus, the Russian Federation, Serbia, Switzerland and Türkiye). No country reported consumption of the antimetabolite flucytosine in 2022.

Estimates of the population-weighted mean consumption of antifungals were used to examine trends in consumption of antifungal agents between 2019 and 2022. Nystatin consumption as an intestinal anti-infective appears to be decreasing (population-weighted mean 0.233 DID in 2019 and 0.114 DID in 2022). The triazole fluconazole, consumed in all 12 countries, showed a trend towards increasing consumption over time (0.467 DID in 2019 to 0.54 DID in 2022). There was no evidence on increased consumption over time or increases in the numbers of countries reporting use of echinocandins.

1. INTRODUCTION

1.1 Background

Antimicrobial resistance (AMR) is threatening the sustainability and resilience of health systems and affecting country preparedness and responses to pandemics. Bacterial AMR in the WHO European Region caused over half a million deaths in 2019 (European Antimicrobial Resistance Collaborators, 2022), with estimated annual costs attributed to AMR in the European Union (EU) of €1.5 billion in health-care costs and productivity losses. Ensuring prudent antimicrobial use is a key priority in an effective response to the challenges of AMR. Regular surveillance of antibiotic consumption to identify potential overuse, underuse and inappropriate use can help identify potential targets for interventions to improve antibiotic utilization.

The WHO European Strategic Action Plan on Antibiotic Resistance (WHO Regional Office for Europe, 2011), which expired in 2020, and the WHO Global Action Plan on Antimicrobial Resistance (WHO, 2015) have guided the AMR agenda in the Region since 2015. At the 73rd session of the WHO Regional Committee for Europe in Astana, Kazakhstan in October 2023, Member States approved the *Roadmap on antimicrobial resistance for the WHO European Region 2023–2030* (WHO Regional Office for Europe, 2024). The purpose of the AMR roadmap is to inspire, guide and support countries in the Region to identify, prioritize, implement and monitor high-impact interventions to tackle AMR.

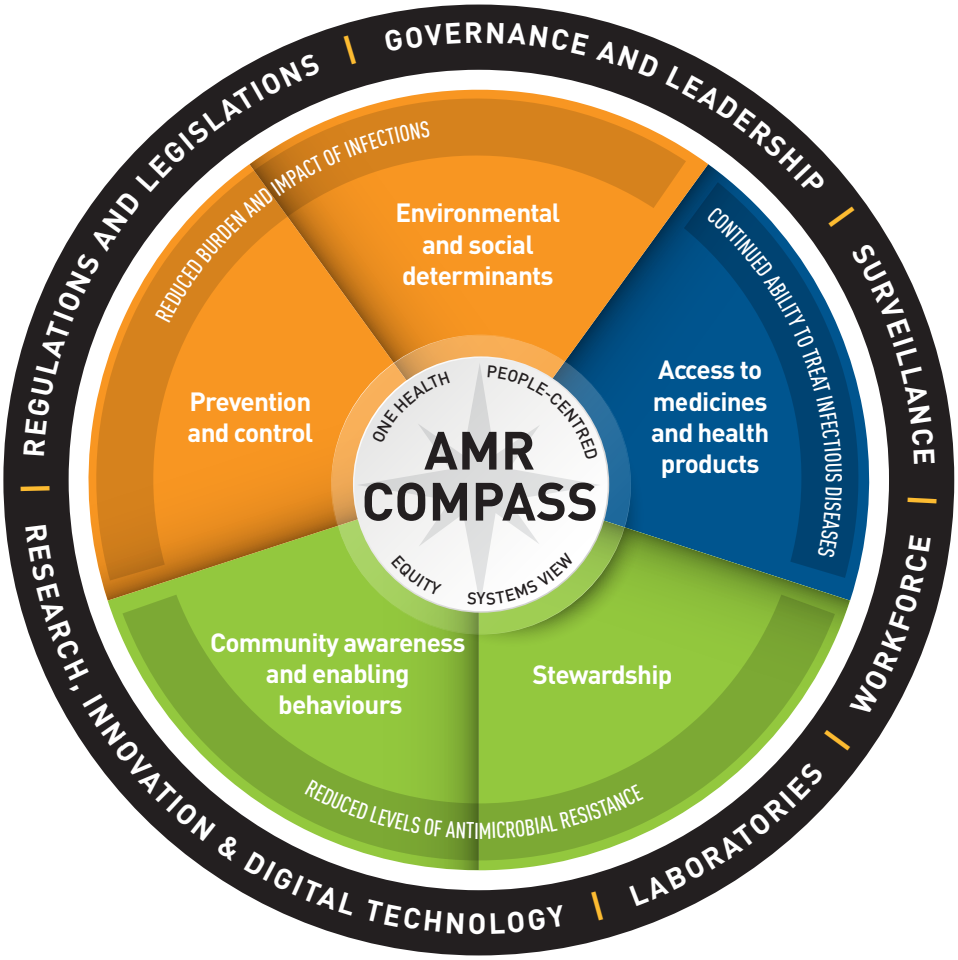
The roadmap is based around the AMR Compass (Fig. 1), which identifies the five action areas and six enablers based on a combination of the best available evidence and expert opinion (WHO Regional Office for Europe, 2024). Each action area and enabler has a set of high-impact interventions.

The five action areas are: (i) infection prevention and control and water, sanitation and hygiene; (ii) environmental and social determinants; (iii) stewardship; (iv) community awareness and enabling behaviours; and (v) access to medicines and health products.

The six enablers are: (i) regulations and legislations; (ii) governance and leadership; (iii) laboratories; (iv) workforce; (v) research, innovation and digital technology; and (vi) surveillance – data for action.

This report supports surveillance, providing data on antimicrobial medicines consumption in non-EU Member States of the WHO European Region.

Fig. 1 AMR Compass



Source: WHO Regional Office for Europe (2024).

1.2 The WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network

The WHO Regional Office for Europe AMC Network has been undertaking systematic surveillance of antimicrobial medicines consumption in 18 non-EU Member States of the WHO European Region since 2011 (WHO Regional Office for Europe, 2022). Data collection is based on the WHO Anatomical Therapeutic Chemical (ATC) classification system and defined daily doses (DDD) methodology (WHO Collaborating Centre for Drug Statistics Methodology, 2024).

The following Member States are currently engaged in the AMC Network: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, Türkiye, Ukraine and Uzbekistan.

1.3 Previous publications of AMC Network data

Five reports of AMC Network data have been published. The first report covered data for 2011–2014 and was published in 2017 (WHO Regional Office for Europe, 2017). An analysis of data for 2011–2017 for 17 Network members was published in 2020 (WHO Regional Office for Europe, 2020). A third report of AMC Network data for 2014–2018 was published in 2021 (WHO Regional Office for Europe, 2021) and a fourth of 2019 data for 14 AMC Network countries in 2022 (WHO Regional Office for Europe, 2022). The fifth report analysed 2020 and 2021 data for 13 countries and 10 countries respectively and was published in 2023 (WHO Regional Office for Europe, 2023).

Analyses of AMC Network data have also been presented in the peer-reviewed literature. A crossnational comparison of 2015 AMC data for 16 members of the AMC Network was published in 2019 (Robertson et al., 2019) and a comparison of AMC Network data with those of the European Surveillance of Antibiotic Consumption Network (ESAC-Net), which is coordinated by the European Centre for Disease Prevention and Control, using data for 2014–2019 was published in 2021 (Robertson et al., 2021).

1.4 Scope and aim of this report

This report extends the reporting of the AMC Network, presenting 2022 data for 15 countries from members that submitted data and gave permission for them to be published.

Crossnational comparisons are presented in this report. The analyses apply the 2023 WHO Access, Watch and Reserve (AWaRe) classification of antibiotics (WHO, 2021; 2023a; 2023b) and assess concordance with the WHO global/national target that 60% of total consumption is Access agents (WHO, 2018a). Analyses also report on the antibacterial substances accounting for 75% of consumption – the drug utilization 75% (DU75%) (Zarb et al., 2011). Exploratory analyses are presented on the consumption of antifungal agents.

2. METHODS

2.1 Data sources and data collection

2.1.1 Data sources

AMC Network countries mostly rely on import data, using customs records and declaration forms supplemented by sales records from market authorization holders, local manufacturing estimates, wholesaler records, commercial data and, in some cases, reimbursement data sources to derive estimates of consumption (Table 1). In some countries, data are not available for all years examined.

Table 1 Sources of data used for consumption estimates, 2014–2022

Country	2014	2015	2016	2017	2018	2019	2020	2021	2022
Albania	I	I	I	I	I	I	I	–	I
Armenia	I, M	I, M	I, M	I, M	I, M	I, M	I, M	I, M	I, M
Azerbaijan	I	I	I	I	I	I	I	I	I
Belarus	I, M	I, M	I, M	I, M	I, M	I, M	I, M[a]	I, M	I, M
Bosnia and Herzegovina	S, M	S, M	S, M	S, M	S, M	S, M	S, M	S, M	S, M
Georgia	I	I	I	I	I	I	I	–	I
Kazakhstan	–	S	S	S	S	–	–	–	–
Kyrgyzstan	–	I, S	I, S	I, S	I, S	I, S	I, S	I, S	I, S
Montenegro	S	S	S	S	S	S	S	S	S
North Macedonia[b]	R	R	R	R	R	R	R	R	R
Republic of Moldova	I, M	I, M	I, M	I, M	I, M	–	–	–	-
Russian Federation	S	S	S	S	S	S	S	S	S
Serbia	S	S	S	S	S	S	S	S	S
Switzerland[c]	S	S	S	S	S	S	S	S	S
Tajikistan	I, C	I, C	I, C	I, C	I, C	I, C	I, C	I, C	I, C
Türkiye[d]	S	S	S	S	S	S	S	S	S
Ukraine	S	S	S	S	S	S	S	S	S
Uzbekistan	–	–	I, S	I, S	I, S	I, S	–	–	–

C: certification records; I: import records; M: manufacturing records; R: reimbursement data; S: sales data.
[a] Alternative suppliers were used to procure some medicines during the coronavirus disease 2019 (COVID-19) pandemic. Data from these suppliers were not included in the analyses. Estimates of total consumption and consumption of specific agents used to manage COVID-19, including azithromycin, clarithromycin and oseltamivir, will therefore be underestimates of actual consumption. [b] Reimbursement data cover the community sector only.
[c] Estimates are derived from IQVIA[1] sell-in data (sales data from wholesalers to pharmacy), self-dispending doctors and hospitals, therefore covering outpatient and inpatient consumption. Data include consumption estimates for Liechtenstein due to the nature of the data source. [d] Türkiye uses wholesalers' records from the pharmaceutical track and trace system.
Source: AMC Network.

1 IQVIA is a human data science company that has assets in data, technology and advanced analytics with an interest in health care and human health.

2.1.2 Data collection

Data collection is based on a standardized protocol that is aligned with the *WHO methodology for a global programme on surveillance of antimicrobial consumption* (WHO, 2017) and the *GLASS methodology for surveillance of national antimicrobial consumption* (WHO, 2020) (GLASS stands for Global Antimicrobial Resistance and Use Surveillance System). Data are collected at product level (proprietary and generic products) and comprise information on the active substance(s) of the product, route of administration, strength per unit, number of units per package and total number of packages consumed. Data collection is facilitated by means of a standard Excel template with functions to calculate volume and consumption for each product.

2.2 ATC and DDD classification systems

The AMC Network uses the ATC classification system to distinguish between pharmacological subgroups and substance levels of antimicrobials and uses DDD as the primary measurement metric (WHO Collaborating Centre for Drug Statistics Methodology, 2024).

The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. A DDD is assigned only for medicines that have an ATC code. The DDD, however, is a technical unit of use and does not necessarily reflect the recommended or average prescribed daily dose. The DDDs for anti-infectives are as a rule based on use in infections of moderate severity, but some anti-infectives are used only in severe infections and their DDDs are assigned accordingly. There are no separate DDDs for children, which makes the DDD estimates for paediatric formulations more difficult to interpret. There are no DDDs for topical preparations.

Only medicines with an assigned ATC code and DDD are included in the analyses reported here. Various medicines without such codes are consumed by the populations of several countries of the AMC Network. Exclusion of these medicines means that data are missing in the numerator for the calculation, and the resulting DDD per 1000 inhabitants per day (DID) estimates will underestimate total antimicrobial consumption in the country.

2.2.1 Population estimates

Population-adjusted estimates of consumption are derived by dividing the total number of DDDs at the desired ATC code level by the relevant population. For total consumption, this is the national population, which is assumed to reflect the potential scope of usage of the product.

Since 2011, the AMC Network has applied population estimates from the World Bank for the calculations, except for North Macedonia, where the population eligible to receive medicines under the health insurance fund is used, and Switzerland and Türkiye, where national population estimates are applied. In the case of Switzerland, national estimates are used for the sake of consistency with the estimates published in their national reports; for Türkiye, national estimates account for the large refugee populations in that country that are not reflected in World Bank population estimates.

WHO launched GLASS in 2015 to foster harmonized antimicrobial resistance and use surveillance in all countries and thereby inform strategies to contain AMR. GLASS initially focused on surveillance data on human priority bacterial pathogens considered the most significant threat globally. The GLASS information technology (GLASS-IT) platform now incorporates surveillance data on antimicrobial medicines consumption (the GLASS Antimicrobial Medicines Consumption module (GLASS-AMC)). For global reporting using the GLASS-IT platform, WHO uses United Nations population statistics as

standardized population estimates for all Member States (United Nations Department of Economic and Social Affairs, Population Division, 2022).

For countries that have enrolled in GLASS-AMC, 2022 data were submitted and approved for publication using the GLASS-AMC platform. The remaining countries submitted data via the Regional Office data collection platform. For consistency, analyses in this report apply United Nations population estimates for the calculations. Exceptions are for Türkiye and Ukraine, where national population estimates are applied, and North Macedonia, where the population eligible for health insurance is used.

2.3 Antimicrobial agents included in this report

2.3.1 Antibacterial agents

The main analyses presented here are for the antibacterials for systemic use (ATC group J01) and related pharmacological subgroups. Data on additional antimicrobials outside the ATC J01 group are also included in the calculation of antimicrobial consumption according to the 2023 WHO AWaRe classification (WHO, 2023b). These comprise: neomycin (A07AA01), streptomycin oral (A07AA04), polymyxin B oral (A07AA05), kanamycin oral (A07AA08), vancomycin oral (A07AA09), colistin oral (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole oral (P01AB01), tinidazole oral (P01AB02), ornidazole oral (P01AB03) and secnidazole (P01AB07) (Table 2).

There were no new additions to the AWaRe classification in 2023, so the medicines included in the 2021 AWaRe index are unchanged. The 2023 Expert Committee on Selection of Essential Medicines did, however, add the Reserve agent ceftolozane/tazobactam to both the WHO Model List of Essential Medicines for adults (EML) (WHO, 2023b) and the WHO Model List of Essential Medicines for children (EMLc) and nominated the Reserve agent tedizolid phosphate as a therapeutic alternative to linezolid.

Table 2 Antibacterials included in the analyses

Class of agents	ATC code (medicine)
Antibacterials for systemic use	J01
Pharmacological subgroups of J01	
Tetracyclines	J01A
Amphenicols	J01B
Beta-lactam antibacterials, penicillins	J01C
Other beta-lactam antibacterials	J01D
Sulfonamides and trimethoprim	J01E
Macrolides, lincosamides and streptogramins	J01F
Aminoglycoside antibacterials	J01G
Quinolone antibacterials	J01M
Combinations of antibacterials	J01R
Other antibacterials	J01X
Antibiotics for intestinal tract	A07AA01 (neomycin) A07AA04 (streptomycin) A07AA05 (polymyxin B) A07AA08 (kanamycin) A07AA09 (vancomycin) A07AA10 (colistin) A07AA11 (rifaximin) A07AA12 (fidaxomicin) A07AA13 (rifamycin oral)
Antimycobacterials	J04AB02 (rifampicin) J04AB03 (rifamycin) J04AB04 (rifabutin)
Nitroimidazole derivatives	P01AB01 (metronidazole) P01AB02 (tinidazole) P01AB03 (ornidazole) P01AB07 (secnidazole)

2.3.2 Antifungal agents

Exploratory analyses are presented in this report for antifungals for systemic use.

Fungal infections (mycoses) can be classified as superficial, cutaneous, subcutaneous or systemic (deep) infections depending on the type and degree of tissue involvement and the host response to the pathogen. Superficial and cutaneous fungal infections typically affect the hair, nails and skin. Deep mycoses (invasive disease) can affect the circulatory system, brain, lungs, heart, liver, spleen and kidney, with the most common portals of entry being the respiratory and gastrointestinal tracts and blood vessels. Primary pathogens can establish infections in normal hosts. Opportunistic pathogens cause disease in individuals with compromised host defence mechanisms.

Cases of invasive fungal disease (IFD) are rising as the at-risk population expands (WHO, 2022a). Contributors to the increased risk include interventions that impair the immune system (chemotherapy and immunotherapy for cancer) and organ transplantation. Patients with chronic obstructive pulmonary disease, liver or kidney disease, viral respiratory tract infections such as influenza and those with prior non-tuberculous mycobacterial infections are at heightened risk. The global threats of IFD are compounded by the rapid emergence of antifungal resistance and limited access to quality diagnostics and treatment in many settings. Antifungal resistance generally leads to prolonged therapy and hospital stays and can require treatment with expensive second-line antifungal medicines that often are not available in low- and middle-income countries.

Currently, four classes of systemic antifungal medicines (polyenes, azoles, pyrimidines and echinocandins) are used in IFD. Agents from each of these groupings are included on the WHO EML for 2023 (see Table 3 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* (WHO, 2023b)). Echinocandins (anidulafungin, caspofungin and micafungin) are the newest class of antifungal drugs and act by inhibiting β (1, 3)-D-glucan synthase, an enzyme necessary for the integrity of the fungal cell wall. The main adverse effect is hepatotoxicity. The incidence of infusion-related adverse effects and nephrotoxicity is much lower than with amphotericin B, but the higher cost of these drugs in comparison to azole antifungals is likely to limit their use.

Table 3 lists antifungal agents available for systemic treatment of dermatological and intestinal infections, and for invasive disease. Topical preparations do not contribute to estimates of DIDs, as there are no standard measures and the quantity of topical preparations used will vary with the size of the area affected, the severity of infection and the duration of treatment. Topical antifungal preparations therefore are not considered further in this report.

Table 3 Antifungal agents for systemic use

ATC code	Agent	Common formulation types
Agents for systemic treatment of dermatological infections		
Anti-infectives and antiseptics for local oral treatment		
A01AB04	Amphotericin	Lozenge, suspension
A01AB10	Natamycin	Buccal tablet
Intestinal anti-infectives		
A07AA02	Nystatin	Lozenge, oral liquid, tablet
A07AA03	Natamycin	Tablet
A07AA07	Amphotericin	Tablet
A07AC01	Miconazole	Buccal tablet
Antifungals for dermatological use		
D01BA01	Griseofulvin	Oral liquid, tablet/capsule
D01BA02	Terbinafine	Tablet, granules
D01BA03	Fosravuconazole	Tablet
J02AB02	Ketoconazole	Tablet
J02AB01	Miconazole	Parenteral
Agents for the treatment of IFD		
Antibiotics (polyenes)		
J02AA01	Amphotericin B	Parenteral
Triazole and tetrazole derivatives		
J02AC01	Fluconazole	Parenteral, oral liquid, capsule
J02AC02	Itraconazole	Capsule, oral liquid
J02AC03	Voriconazole	Tablet, powder for oral liquid, parenteral
J02AC04	Posaconazole	Oral suspension, delayed-release tablet, parenteral
J02AC05	Isavuconazole	Capsule, parenteral
Anti-metabolites		
J02AX01	Flucytosine	Capsule, parenteral
Echinocandins		
J02AX04	Caspofungin	Parenteral
J02AX05	Micafungin	Parenteral
J02AX06	Anidulafungin	Parenteral

Medicines included in the EML 2023 (WHO, 2023b)
Source: WHO Collaborating Centre for Drug Statistics Methodology (2024).

2.4 Metrics and indicators reported

2.4.1 Measures of volume and relative consumption

Total numbers of DDDs for each product are aggregated to give the total number of DDDs at the desired ATC code level. The number of DDDs provides a measure of the extent of use, but for comparative purposes, these data are usually adjusted for population size or population group, depending on the medicines of interest and the level of disaggregation of data that is possible. For most antibacterials, DID is calculated for the total population, including all age and gender groups.

Patterns of consumption in 2022 by ATC 3rd level[2] (ATC3) of J01 antibacterial agents and J02 antifungal agents overall and by route of administration (oral and parenteral) were assessed. Both volumes in DID and measures of relative consumption, expressed as a percentage of total consumption of groups of antimicrobials, were derived for pharmacological subgroups of J01 and J02.

2.4.1.1 Total consumption in DID

The DID is the primary indicator of antibiotic consumption in countries as defined by the European Commission and WHO (European Centre for Disease Prevention and Control et al., 2017) and is a key indicator reported in the first WHO global report on antimicrobial consumption (WHO, 2018b).

2.4.1.2 Route of administration

Oral administration is generally regarded as the most acceptable and economical method of administration of antimicrobials. Oral medication is associated with fewer complications, lower health-care costs and earlier hospital discharge. It nevertheless must be recognized that there may be cultural and medical practice traditions that favour the use of parenteral formulations in some settings.

This report includes analyses of the use of oral and parenteral formulations for J01 and J02 medicines. Where consumption of parenteral formulations is comparatively high, there may be opportunities to increase the use of oral formulations without any loss of clinical efficacy. Consumption of inhalation solution (IS) and inhalation powder (IP) formulations is also reported.

2.4.1.3 Consumption of pharmacological subgroups (ATC3)

Absolute and relative consumption figures for pharmacological subgroups of J01 and J02 (ATC3) are presented in this report.

2.4.2 Trends in total consumption over time

To illustrate changes in rates in antimicrobial consumption over time, the compound annual growth rate (CAGR) of total antibiotic consumption of J01 antibacterials was calculated for each participating country. This reflects the average annual change as a proportion (percentage) of the consumption in the starting year. CAGRs were estimated for countries that had at least five years of data available.

2 In the ATC classification system, the active substances are classified in a hierarchy with five levels. The system has 14 main anatomical/pharmacological groups, or 1st levels. Each ATC main group is divided into 2nd levels which could be either pharmacological or therapeutic groups. The 3rd and 4th levels are chemical, pharmacological or therapeutic subgroups and the 5th level is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups (WHO Collaborating Centre for Drug Statistics Methodology, 2022).

Linear regression was used for presenting trends in consumption for each participating country and evaluated using analysis of variance (ANOVA) tests. *P* values of ≤ 0.05 were considered statistically significant.

2.4.3 WHO AWaRe classification

The AWaRe classification of antibiotics was developed in 2017 by the WHO Expert Committee on Selection and Use of Essential Medicines as a tool to support antibiotic stewardship efforts at local, national and global levels. Antibiotics are classified into three groups – Access, Watch and Reserve – taking into account the impact of different antibiotics and antibiotic classes on AMR to emphasize the importance of their appropriate use. The characteristics of these groups are shown in Table 4.

Subsequent updates to the AWaRe classification in 2019 and 2021 have resulted in the classification of 258 antibiotics. No medicines were added to the AWaRe classification in 2023 (WHO, 2023b).

The AWaRe classification is a useful tool for monitoring antibiotic consumption, defining targets and monitoring the effects of stewardship policies that aim to optimize antibiotic use and curb AMR. The WHO Thirteenth General Programme of Work 2019–2023 includes a country-level target of at least 60% of total antibiotic consumption being Access group antibiotics (WHO, 2018a; 2021).

The proportions of consumption (percentage) according to the AWaRe classification are presented in this report.

The agents listed in the 2023 AWaRe index are shown in the Annex.

Table 4 WHO categories of antibiotics – descriptions

Group	Definition
Access agents	This group includes 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 agents	This group includes antibiotics 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. Antibiotics in the Watch group should be prioritized as key targets of stewardship programmes and monitoring.
Reserve agents	This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms. Antibiotics in the Reserve group should be treated as last-resort options; they should be accessible, but their use should be tailored to highly specific patients and settings when all alternatives have failed or are not suitable. These medicines could be protected and prioritized as key targets of national and international stewardship programmes involving monitoring and utilization reporting to preserve their effectiveness.
Unclassified	These are medicines not specifically identified in the groups described above. Some unclassified agents are included in WHO's list of not-recommended antibiotics. The not-recommended agents are the fixed-dose combinations of multiple broad-spectrum antibiotics whose use is neither evidence-based nor recommended in high-quality international guidelines. WHO does not recommend their use in clinical practice.

2.4.4 WHO global monitoring indicator

WHO has proposed a global monitoring indicator that by 2023, 60% of all antibiotics consumed should come from the Access group, those at lowest risk of resistance (WHO, 2021).

The proportion of total consumption that comprised Access agents was calculated for each year of analysis from 2014 to 2022. The number of countries reaching the WHO global monitoring target in 2022 and across each of the years assessed is reported.

2.4.5 DU75%

The 10 most consumed oral formulations and 10 most consumed parenteral formulations were presented in the 2017 and 2020 AMC Network reports. These analyses, which were based on the observations of ESAC-Net and other analyses, suggest that consumption tended to be concentrated in a relatively small number of agents.

The DU75% was calculated in the 2021 AMC Network report. This metric was considered in the WHO global report on antimicrobial consumption (WHO, 2018b), where results were stratified by route of administration (oral and parenteral formulations) and reported by region. All substances that appeared on the DU75% lists in countries within a region were compiled into a region-specific list for oral substances and parenteral substances respectively.

The DU75% for 2018 was reported by country and across networks in the 2021 joint publication on AMC data from ESAC-Net and the WHO Regional Office for Europe (Robertson et al., 2021).

In this report, the DU75% is calculated for oral and parenteral formulations separately. Results are shown as the ranking of consumption at substance level (ATC 5th level (ATC5)). In addition to reporting the numbers of antibacterial agents in the DU75% segment, the report categorizes the agents in this segment according to the AWaRe classification. This facilitates identification of restricted and special-use antibacterials that may be consumed widely and be potential targets for stewardship activities.

2.4.6 Summary measures applied to crossnational comparisons

AMC Network summary data are presented using arithmetic and population-weighted mean estimates.

Arithmetic means for total consumption are derived by summing the national estimates for total consumption and dividing by the number of countries contributing data to the calculation.

Population-weighted estimates for total consumption are calculated by multiplying the DID for each country with the corresponding population, summing the country estimates and dividing the total DDDs by the total population of participating countries (European Centre for Disease Prevention and Control, 2021).

Using similar methods, population-weighted estimates are calculated for the relative consumption of AWaRe group agents and for components of the DU75% in the AMC Network.

2.4.7 Metrics reported in the analyses

The key metrics used in analyses and included in this report are summarized in Table 5.

Table 5 Metrics used in analyses and included in this report

Category	Unit
Estimates of volumes of consumption of antibacterials for systemic use (J01)	
Total consumption of J01 antibacterials by route of administration	DID
Total consumption of J01 antibacterials by pharmacological subgroup (ATC3): - tetracyclines (J01A) - amphenicols (J01B) - beta-lactam antibacterials, penicillins (J01C) - other beta-lactams (includes cephalosporins) (J01D) - sulfonamides and trimethoprim (J01E) - macrolides, lincosamides and streptogramins (J01F) - quinolone antibacterials (J01M) - other J01 antibacterials (J01G, J01R, J01X)	DID
Relative consumption of J01 antibacterials by subgroup	
Relative consumption of J01 antibacterials by pharmacological subgroup	%
Relative consumption of AWaRe antibiotics[a]	
Relative consumption of AWaRe group agents	%
Concordance with WHO global monitoring indicator	
Proportion of total consumption that is Access agents	%
DU75%	
DU75% – oral formulation	Rank
DU75% – parenteral formulation	Rank
Summary metrics reported in crossnational comparisons	
Arithmetic mean estimates of: - total consumption of J01 antibacterials - consumption of pharmacological subgroups (ATC3) - consumption of agents according to AWaRe classification	 DID DID, % DID, %
Population-weighted mean estimates of: - total consumption of J01 antibacterials - consumption of pharmacological subgroups (ATC3) - consumption of agents according to AWaRe classification - agents comprising the DU75%	 DID DID, % DID, % Rank

[a] Total consumption of antibiotics for this calculation includes: J01 antibacterials neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07).

Joint interpretation of these metrics will help to identify broad areas for national antibiotic stewardship and guideline development, even when information about indication is not available. Previous AMC Network reports have described several limitations to the data sources used. Even with these limitations, the variability of consumption patterns within and between countries provides a basis for further investigation to better understand how antibacterials are used in practice. The consumption data need to be interpreted with an understanding of the local context, taking account of changes in regulations (including enforcement of prescription-only access), data sources, resistance patterns and the potential impact of interventions to change practices.

Exploratory analyses for antifungal agents presented in this report will provide a platform for monitoring access to key agents and consumption patterns in following years. Metrics reported are total consumption of antifungals for systemic use (DID), consumption of individual antifungal agents (DID) and population-weighted mean consumption of individual antifungal agents (DID).

3. ANTIMICROBIAL MEDICINES CONSUMPTION ACROSS THE AMC NETWORK, 2022

In this chapter, comparisons are made across AMC Network members providing consumption data for 2022 from 15 countries. Where possible, comparisons with 2021 (10 countries) are provided.

3.1 Estimates of volumes of consumption of antibacterials for systemic use (J01)

3.1.1 Total consumption in 2022

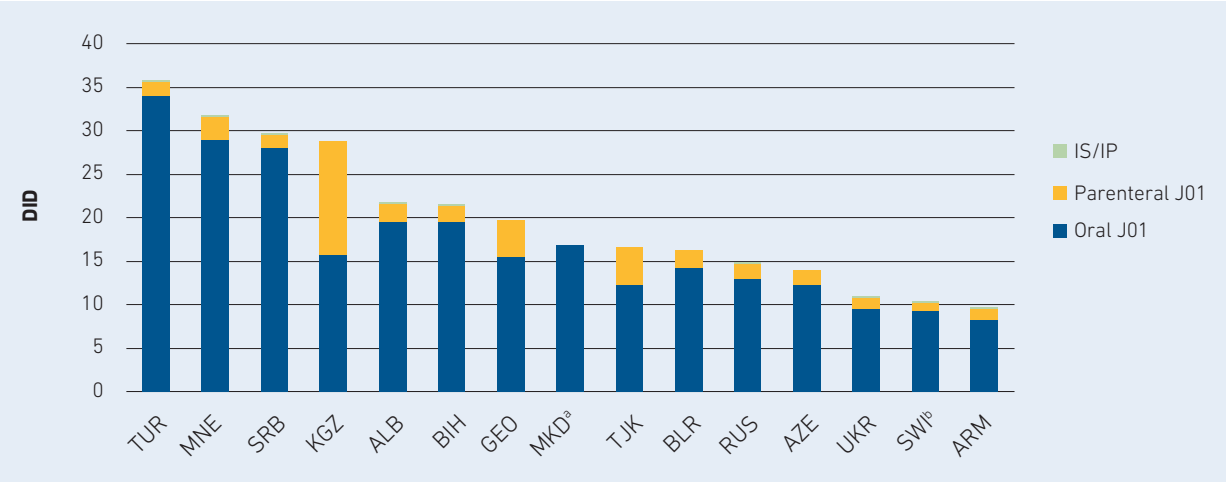
Consistent with previous analyses of AMC Network data, there is wide variability in reported total consumption of J01 antibacterials for systemic use (ATC class J01) for 2022 – ranging from 35.7 DID (Türkiye) to 9.6 DID (Armenia) (Fig. 2 and Table 6). This compares to a range of 34.4 DID (Serbia) to 8.6 DID (Switzerland) in 2021, based on data from 10 Network countries.

The median consumption in 2022 was 16.8 DID (in 2021 it was 19.3 DID across 10 Network members). The population-weighted mean total of J01 consumption in 2022 was 20.7 DID, compared to 20.3 DID in 2021.

3.1.2 Route of administration in 2022

The extent of consumption of parenteral formulations varied widely, from 5% in Serbia and Türkiye up to 45% in Kyrgyzstan (Table 6). North Macedonia data relate to community consumption of oral antibiotics only. There was very low consumption of IS and powder formulations of antibacterials in 2022.

Fig. 2 Total consumption of J01 antibacterials by route of administration, 2022



[a] Community consumption. [b] Estimates include consumption data of Liechtenstein.

Table 6 Total consumption of J01 antibacterials by route of administration, 2022

Route of administration	DID (% of total[a])															
	TUR	MNE	SRB	KGZ	ALB	BIH	GEO	MKD[b]	TJK	BLR	RUS	AZE	UKR	SWI[c]	ARM	WHO/AMC[d]
Oral J01	34.0 (95)	29.0 (92)	28.0 (95)	15.8 (55)	19.5 (90)	19.5 (91)	15.6 (79)	16.8 (100)	12.2 (73)	14.3 (88)	13.0 (88)	12.2 (87)	9.5 (87)	9.3 (91)	8.2 (85)	18.7 (90)
Parenteral J01	1.7 (5)	2.7 (8)	1.5 (5)	13.1 (45)	2.2 (10)	1.9 (9)	4.2 (21)	–	4.4 (27)	2.0 (12)	1.7 (12)	1.7 (13)	1.4 (13)	0.9 (9)	1.4 (15)	2.0 (10)
IS/IP	< 0.01 (0)	0.01 (0)	0.02 (0)	–	< 0.01 (0)	0.01 (0)	–	–	–	–	0.01 (0)	–	0.01 (0)	0.03 (0)	0.01 (0)	< 0.01 (0)
Total	**35.7**	**31.7**	**29.6**	**29.0**	**21.7**	**21.4**	**19.8**	**16.8**	**16.6**	**16.3**	**14.8**	**13.9**	**11.0**	**10.2**	**9.6**	**20.7**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] Estimates include consumption data of Liechtenstein.
[d] WHO/AMC population-weighted mean for countries of the AMC Network.

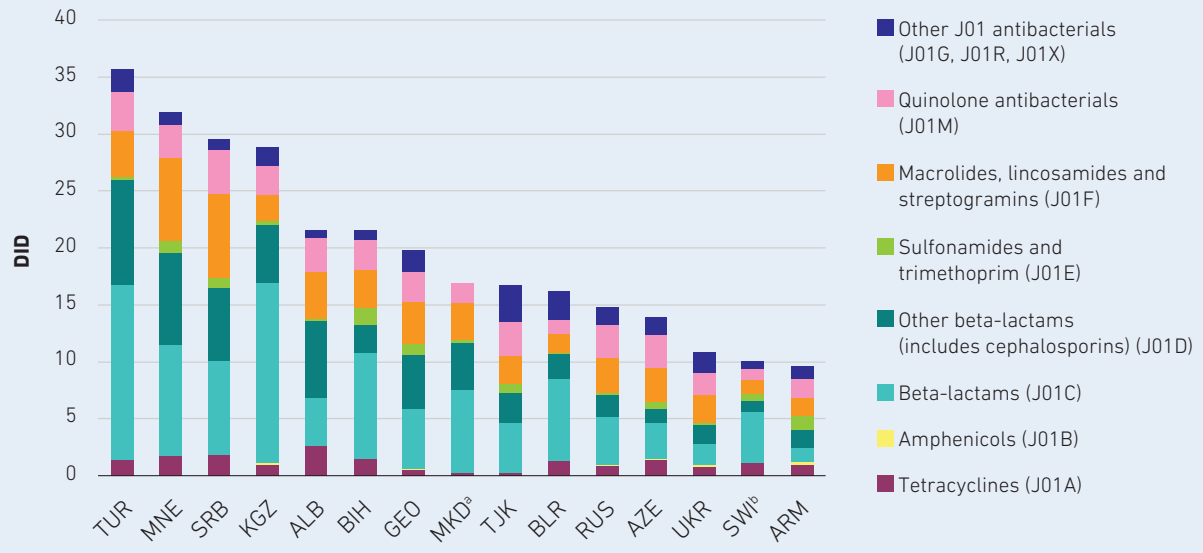
3.1.3 Pharmacological subgroups in 2022

In 2022, consumption of beta-lactam penicillins (J01C) ranged from 14% of total J01 consumption in Armenia to 54% of J01 consumption in Kyrgyzstan (Fig. 3 and Table 7). The AMC Network population-weighted mean was 36%.

Cephalosporin (J01D) consumption varied from 9% of J01 consumption in Azerbaijan to 32% in Albania (the AMC Network population-weighted mean was 20%). Quinolone (J01M) consumption varied from 8% in Belarus to 21% in Azerbaijan.

Consumption of macrolides, lincosamides and streptogramins (J01F) in 2022 ranged from 8% in Kyrgyzstan to 25% in Serbia.

Fig. 3 Total consumption of J01 antibacterials by pharmacological subgroup, 2022



[a] Community consumption. [b] Estimates include consumption data of Liechtenstein.

Table 7 Total consumption of J01 antibacterials by pharmacological subgroup, 2022

Class of agents	DID (% of total[a])															
	TUR	MNE	SRB	KGZ	ALB	BIH	GEO	MKD[b]	TJK	BLR	RUS	AZE	UKR	SWI[c]	ARM	WHO/AMC[d]
Tetracyclines (J01A)	1.4 (4)	1.8 (6)	1.8 (6)	1.0 (3)	2.6 (12)	1.5 (7)	0.5 (3)	0.3 (2)	0.2 (1)	1.3 (8)	0.9 (6)	1.4 (10)	0.8 (7)	1.2 (12)	1.0 (10)	**1.1 (5)**
Amphenicols (J01B)	–	–	<0.01 (0)	0.2 (1)	<0.01 (0)	–	0.1 (1)	–	0.1 (0)	<0.01 (0)	0.1 (1)	0.1 (1)	0.2 (2)	–	0.2 (2)	**0.1 (0)**
Beta-lactams (J01C)	15.4 (43)	9.7 (31)	8.3 (28)	15.7 (54)	4.2 (20)	9.3 (43)	5.3 (27)	7.3 (43)	4.4 (27)	7.2 (44)	4.2 (28)	3.2 (23)	1.8 (17)	4.4 (43)	1.3 (14)	**7.4 (36)**
Other beta-lactams (includes cephalosporins) (J01D)	9.2 (26)	8.1 (26)	6.4 (22)	5.1 (18)	6.8 (32)	2.5 (12)	4.7 (24)	4.1 (24)	2.6 (16)	2.2 (14)	1.9 (13)	1.2 (9)	1.7 (16)	1.0 (10)	1.6 (16)	**4.1 (20)**
Sulfonamides and trimethoprim (J01E)	0.3 (1)	1.0 (3)	0.9 (3)	0.4 (2)	0.2 (1)	1.5 (7)	1.0 (5)	0.2 (1)	0.8 (5)	0.1 (1)	0.2 (2)	0.6 (5)	0.2 (2)	0.6 (6)	1.2 (12)	**0.3 (2)**
Macrolides, lincosamides and streptogramins (J01F)	4.0 (11)	7.3 (23)	7.4 (25)	2.3 (8)	4.1 (19)	3.3 (15)	3.7 (19)	3.3 (19)	2.4 (14)	1.7 (11)	3.0 (21)	3.0 (21)	2.4 (22)	1.2 (12)	1.5 (16)	**3.2 (16)**
Quinolone antibacterials (J01M)	3.4 (10)	2.9 (9)	3.8 (13)	2.5 (9)	3.0 (14)	2.6 (12)	2.6 (13)	1.7 (10)	3.0 (18)	1.2 (8)	3.0 (20)	2.9 (21)	1.9 (17)	1.0 (10)	1.7 (18)	**2.9 (14)**
Other J01 antibacterials (J01G, J01R, J01X)	2.0 (6)	1.1 (3)	0.9 (3)	1.7 (6)	0.7 (3)	0.8 (4)	1.9 (10)	–	3.2 (19)	2.5 (15)	1.5 (10)	1.5 (11)	1.8 (17)	0.7 (7)	1.1 (12)	**1.7 (8)**
Total	**35.7**	**31.7**	**29.6**	**29.0**	**21.7**	**21.4**	**19.8**	**16.8**	**16.6**	**16.3**	**14.8**	**13.9**	**11.0**	**10.2**	**9.6**	**20.7**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] Estimates include consumption data of Liechtenstein.
[d] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.4 Trends 2014–2022

Table 8 shows the trends in total consumption of antibacterials for systemic use (ATC J01) for the years 2014–2022. The CAGR of total antibiotic consumption was calculated for each participating country. This reflects the average annual change as a proportion (%) of the consumption in the starting year. The CAGR was estimated for countries that had at least five years of data available. Linear regression was used for presenting trends in consumption and evaluated using ANOVA tests. *P* values of ≤ 0.05 were considered statistically significant.

Thirteen countries – Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Kyrgyzstan, Montenegro, North Macedonia, the Russian Federation, Serbia, Switzerland, Tajikistan, Türkiye and Ukraine – had consumption estimates for all years (2014–2022).

Two of these countries showed statistically significant increases in consumption of J01 antibacterials over the nine years of data collection – Azerbaijan (CAGR +10.5%) and Bosnia and Herzegovina (CAGR +3.4%). Only one country, Switzerland, showed a statistically significant reduction in consumption over this time frame (CAGR –1.1%). Trends towards decreasing consumption in some countries were subsequently affected by changed consumption patterns during the COVID-19 pandemic.

Table 8 Trends in consumption of J01 antibacterials, 2014–2022

Country	Total consumption of J01 antibacterials in DID									CAGR[a]	Trend line	Trend[b]
	2014	2015	2016	2017	2018	2019	2020	2021	2022			
ALB	19.6	16.3	16.4	18.7	18.9	17.0	31.8	–	21.7	8.4%		–
ARM	13.3	9.8	9.6	12.3	12.6	11.8	18.4	14.5	9.6	–3.9%		–
AZE	6.3	7.3	9.3	7.7	8.7	10.5	10.6	11.1	13.9	10.5%		↑
BIH	16.4	17.6	18.2	17.8	18.9	17.1	19.0	18.9	21.4	3.4%		↑
BLR	17.9	16.7	16.6	19.5	18.5	22.0	25.4	19.5	16.3	–1.1%		–
GEO	17.7	23.9	22.2	24.8	20.6	16.3	14.2	24.4	19.8	1.4%		–
KAZ	–	17.1	15.5	14.1	14.8	–	–	–	–	–	–	–
KGZ	33.2	16.8	21.6	17.1	11.4	22.3	35.1	21.3	29.0	–1.7%		–
MDA	17.8	14.0	18.4	19.1	16.0	–	–	–	–	–2.7%		–
MKD[c]	16.3	16.7	17.0	16.9	16.6	15.6	14.5	15.3	16.8	0.4%		–
MNE	26.2	28.5	28.5	26.7	26.6	26.8	27.4	31.3	31.7	2.4%		–
RUS	13.4	14.1	14.9	15.0	14.6	15.1	19.3	16.1	14.8	1.3%		–
SRB	23.9	29.3	24.7	20.1	21.4	24.9	27.4	32.3	29.6	2.7%		–
SWI[d]	11.2	11.2	11.0	10.6	10.7	10.6	9.0	8.6	10.2	–1.1%		↓
TJK	30.4	21.5	20.7	16.1	19.0	22.8	30.0	19.6	16.6	–7.3%		–
TUR	34.7	35.5	35.4	31.0	30.9	33.2	25.8	28.3	35.7	0.3%		–
UKR	9.5	12.2	8.8	11.3	12.3	19.0	17.0	13.3	11.0	1.8%		–
UZB	–	–	25.4	16.5	18.5	22.6	–	–	–	–		–
WHO/AMC[e]	19.0	19.4	19.8	18.3	18.4	20.9	21.1	19.4	20.7	1.1%		–

↑↓ indicates statistically significant change.
[a] The CAGR was only calculated where there were 5 years of data available for the country. [b] Linear regression analysis. [c] Community consumption.
[d] Estimates include consumption data of Liechtenstein. [e] WHO/AMC population-weighted mean for countries of the AMC Network.

3.2 Relative consumption of AWaRe groups of antibiotics

Analyses based on the WHO AWaRe groups of antibiotics can support antimicrobial stewardship efforts and focus attention on prescribing practices that should be reviewed further.

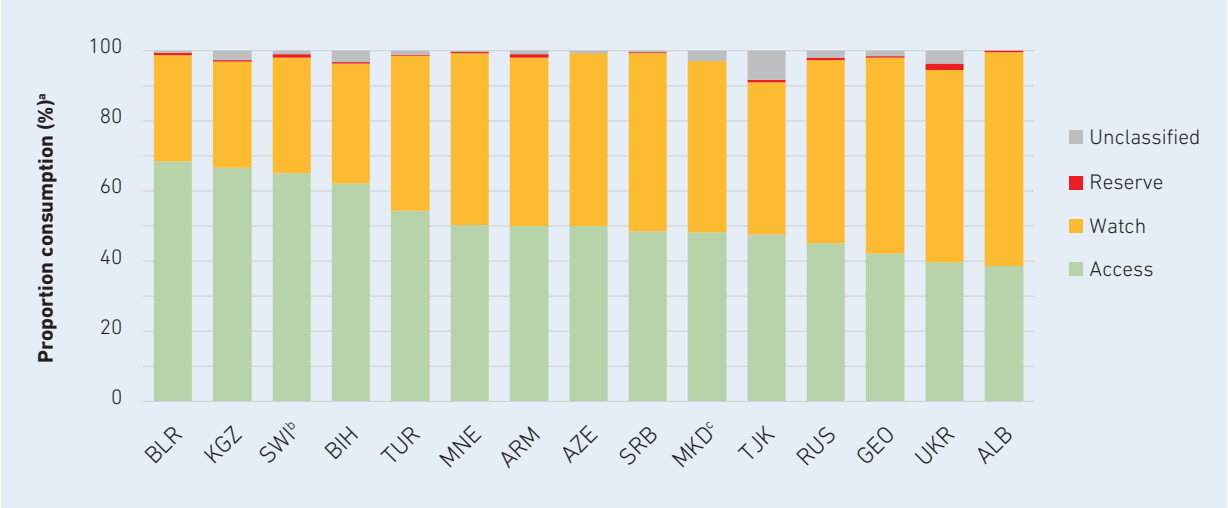
3.2.1 AWaRe 2022

The relative consumption of AWaRe group antibiotics in 2022 is shown in Fig. 4 and is summarized in Table 9.

Consumption of Access agents represented between 39% (Albania) and 68% (Belarus) of total antibacterial consumption in 2022 (Table 9). In eight of 15 countries (53%), Access agents comprised 50% or more of total antibacterial consumption. By comparison, Watch group agents represented between 30% (Belarus and Kyrgyzstan) and 61% (Albania) of total consumption.

The 2022 population-weighted estimates across the AMC Network were: Access agents 51%, Watch agents 47%, Reserve agents 0.3% and unclassified agents 1.7%. These results are similar to those reported in 2021 (Access agents 50%, Watch agents 49%, Reserve agents 0.3% and unclassified agents 1.4%).

Fig. 4 Relative consumption of antibacterials by WHO AWaRe classification as a proportion of total consumption, 2022



[a] Total consumption of antibiotics for this calculation includes J01 antibacterials neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [b] Estimates include consumption data of Liechtenstein. [c] Community consumption.

Table 9 Relative consumption of AWaRe classification antibacterials, 2022

Group of agents	Consumption according to 2023 WHO AWaRe classification[a] (% of total[b])															
	BLR	KGZ	SWI[c]	BIH	TUR	MNE	ARM	AZE	SRB	MKD[d]	TJK	RUS	GEO	UKR	ALB	WHO/AMC[e]
Access	11.5 (68)	20.0 (67)	6.9 (66)	13.6 (62)	20.4 (54)	16.5 (51)	5.1 (50)	7.3 (50)	14.8 (49)	8.2 (48)	8.0 (48)	7.0 (45)	8.5 (42)	4.4 (40)	8.6 (39)	11.0 (51)
Watch	5.1 (30)	9.1 (30)	3.5 (33)	7.5 (35)	16.6 (44)	16.1 (49)	4.9 (49)	7.2 (49)	15.5 (51)	8.3 (49)	7.3 (44)	8.1 (52)	11.3 (56)	6.1 (55)	13.6 (61)	10.2 (47)
Reserve	0.1 (0)	< 0.1 (0)	0.1 (1)	< 0.1 (0)	0.1 (0)	< 0.1 (0)	0.1 (1)	–	< 0.1 (0)	–	< 0.1 (0)	0.1 (0)	< 0.1 (0)	0.2 (2)	< 0.1 (0)	0.1 (0)
Unclassified	0.1 (1)	0.8 (3)	< 0.1 (0)	0.7 (3)	0.4 (1)	0.1 (0)	< 0.1 (0)	< 0.1 (0)	0.1 (0)	0.5 (3)	1.4 (8)	0.3 (2)	0.3 (2)	0.4 (3)	–	0.4 (2)
Total	**16.8**	**30.0**	**10.6**	**21.8**	**37.4**	**32.7**	**10.0**	**14.5**	**30.3**	**17.0**	**16.7**	**15.5**	**20.2**	**11.0**	**22.3**	**21.6**

[a] Total consumption of antibiotics for this calculation includes: J01 antibacterials neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [b] Total amounts and percentages may vary slightly due to rounding. [c] Estimates include consumption data of Liechtenstein. [d] Community consumption. [e] WHO/AMC population-weighted mean for countries of the AMC Network.

3.2.2 WHO global monitoring indicator

In 2019, WHO proposed a global monitoring indicator that by 2023, 60% of all antibiotics consumed should come from Access, the group of antibiotics at lowest risk of resistance (WHO, 2018b; 2019). Trends in the relative consumption of Access agents between 2014 and 2022 are shown in Table 10.

No country would have met the WHO target of at least 60% of total consumption being Access agents in all years (2014–2022) (Table 10). Only one country, Switzerland, met the WHO target in 2020 and would have achieved this target in each of the last five years (2018–2022). Four countries – Belarus, Bosnia and Herzegovina, Kyrgyzstan and Switzerland – met the global monitoring target in 2022.

Table 10 Countries achieving the target of 60% of total consumption being Access agents, 2014–2022

Country[a]	Access agents as proportion (%) of total consumption[b]								
	2014	2015	2016	2017	2018	2019	2020	2021	2022
ALB	61	48	51	44	40	37	45	–	39
ARM	67	68	57	66	63	57	47	50	50
AZE	58	61	50	56	62	71	46	40	50
BIH	69	69	70	68	66	63	53	58	62
BLR	57	60	56	62	61	67	47	66	68
GEO	32	46	60	64	43	54	53	36	42
KAZ	–	63	60	57	53	–	–	–	–
KGZ	53	72	56	50	34	54	54	61	67
MDA	49	56	47	49	51	–	–	–	–
MKD[c]	53	49	50	48	47	46	41	42	48
MNE	61	56	58	59	57	60	48	46	51
RUS	51	51	51	51	50	50	41	43	45
SRB	68	65	63	60	51	58	45	42	49
SWI[d]	55	56	58	58	60	61	63	64	66
TJK	65	58	62	46	43	55	41	49	48
TUR	45	45	47	48	51	51	53	56	54
UKR	46	37	51	42	40	34	19	35	40
UZB	–	–	31	42	30	35	–	–	–
WHO/AMC[e]	50	50	49	50	48	49	44	49	51

Country has met the 60% target

[a] Country estimates are rounded up. [b] Total consumption of antibiotics for this calculation includes: J01 antibacterials neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [c] Community consumption. [d] Estimates include consumption data of Liechtenstein. [e] WHO/AMC population-weighted mean for countries of the AMC Network.

3.3 DU75%

The DU75% represents the antibacterial substances accounting for 75% of consumption measured in DDD (Zarb et al., 2011). The DU75% is calculated for oral and parenteral formulations separately. Results are shown as the ranking of consumption at substance level (ATC5). In addition to reporting the numbers of antibacterial agents in the DU75% segment, the agents are categorized according to the AWaRe classification. This facilitates identification of restricted and special-use antibacterials that may be widely consumed and be potential targets for stewardship activities.

3.3.1 DU75% 2022

Table 11 (oral agents) and Table 12 (parenteral agents) show the ranking of consumption of antibacterial agents that comprised the DU75% in 2022.

The number of agents constituting the DU75% by oral substance ranged from six to 11 across the AMC Network countries (Table 11). There were nine agents in the population-weighted DU75% for the AMC Network.

Two Access group agents were the most consumed oral agents. Oral amoxicillin and beta-lactamase inhibitor (ATC code J01CR02) was included in the DU75% in 14 of 15 AMC Network countries, ranked first for consumption in six of those countries and first in the population-weighted DU75%. Amoxicillin (J01CA04) ranked second in the population-weighted DU75%, appeared in the DU75% for 14 countries and was ranked the most consumed oral antibiotic in four countries.

The Watch agent azithromycin (J01FA10), a macrolide, was included in the DU75% for 14 of the 15 AMC Network countries and was ranked first most consumed antibiotic in four countries and second in a further four countries. It ranked third in the population-weighted DU75% in 2022. In 2020, azithromycin was ranked first most consumed antibiotic in an analysis of data from 10 countries, consistent with the higher levels of use of this agent during the COVID-19 pandemic. Rankings post-pandemic are more in line with pre-pandemic patterns of consumption.

A second macrolide, clarithromycin (J01FA09), was fourth most consumed oral antibiotic in 2022.

Ciprofloxacin (J01MA02), a fluoroquinolone, was included in the DU75% for 12 of the 15 AMC Network countries and was ranked fifth in the population-weighted DU75%.

Two to six Watch agents appeared in the DU75% for each of the AMC Network countries and there were six Watch agents in the population-weighted Network estimate.

Two unclassified oral agents, furazidin (J01XE03) and ciprofloxacin and tinidazole (J01RA11), were included in the DU75% for two and one AMC Network countries respectively.

The Watch agent ceftriaxone (J01DD04) was ranked number one most consumed parenteral antibiotic in 11 countries and ranked second in three (Table 11). This analysis excludes North Macedonia, as only consumption data for oral agents is reported.

Table 11 Ranking of consumption of antibacterials at substance level (ATC5) that comprise the DU75% (oral use), 2022

Agent (ATC)[a]	Ranking of consumption of antibacterial agents that comprised the DU75%															Number of countries[c]	WHO/AMC[d]
	ALB	ARM	AZE	BIH	BLR	GEO	KGZ	MKD	MNE	RUS	SRB	SWI[b]	TJK	TUR	UKR		
Amoxicillin (J01CA04)	3	9	3	2	2	6	1	5	1	1	3	2	1		6	14	2
Amoxicillin and enzyme inhibitor (J01CR02)	2	3	4	1	1	1	4	1	4	3	2	1		1	2	14	1
Doxycycline (J01AA02)	6	6	5	6	4					7	6	3		5	4	10	7
Sulfamethoxazole and trimethoprim (J01EE01)		1	7	5		5						5	4		10	7	
Nitrofurantoin (J01XE01)		4	6		3	4	8					6			5	7	
Tetracycline (J01AA07)			8				7									2	
Cefalexin (J01DB01)									6		5					2	
Metronidazole (J01XD01)							5									1	
Azithromycin (J01FA10)	1	2	1	3	5	2	3	6	2	2	1	7	3		1	14	3
Ciprofloxacin (J01MA02)	9	5		4			2	4	5	5	8	4	2	4	8	12	5
Cefixime (J01DD08)	5	8		7			6	2	3	8	4			6	7	10	9
Levofloxacin (J01MA12)	7	7	2			3				4	7				3	7	8
Clarithromycin (J01FA09)								3		6				3		4	4
Cefuroxime (J01DC02)	4				6									2	11	3	6
Cefaclor (J01DC04)	8													7		2	
Cefdinir (J01DD15)														8		1	
Furazidin (J01XE03)													6		9	2	
Ciprofloxacin and tinidazole (J01RA11)													5			1	

Access agents. Watch agents. Unclassified

[a] Agents included in this analysis: J01 antibacterials neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [b] Estimates include consumption data of Liechtenstein. [c] Numbers of countries that have this agent in the DU75%. [d] WHO/AMC population-weighted mean for countries of the AMC Network.

Table 12 Ranking of consumption of antibacterials at substance level (ATC5) that comprise the DU75% (parenteral use), 2022

Agent (ATC)[a]	Ranking of consumption of antibacterial agents that comprised the DU75%														Number of countries[c]	WHO/AMC[d]
	ALB	ARM	AZE	BIH	BLR	GEO	KGZ	MNE	RUS	SRB	SWI[b]	TJK	TUR	UKR		
Metronidazole (J01XD01)		2	3	4	5				4	3		6		2	8	
Cefazolin (J01DB04)	2			3	6				5		5	4	2		7	2
Amikacin (J01GB06)								3		6		2			3	5
Ampicillin (J01CA01)							1					3			2	3
Ampicillin and enzyme inhibitor (J01CR01)			4										8		2	
Gentamicin (J01GB03)								2		2					2	7
Benzylpenicillin (J01CE01)							3								1	8
Benzathine benzylpenicillin (J01CE08)			5												1	
Flucloxacillin (J01CF05)											6				1	
Amoxicillin and enzyme inhibitor (J01CR02)											1				1	
Ceftriaxone (J01DD04)	1	1	1	2	1	1	2	1	1	1	2	1	1	1	14	1
Levofloxacin (J01MA12)	3		2		4				2	4				3	6	4
Meropenem (J01DH02)					2					5			3		3	6
Cefotaxime (J01DD01)					3				3						2	
Piperacillin and enzyme inhibitor (J01CR05)											4		5		2	
Moxifloxacin (J01MA14)													6		1	
Cefepime (J01DE01)					7										1	
Cefuroxime (J01DC02)											3				1	
Rifamycin (J04AB03)													4		1	9
Teicoplanin (J01XA02)													7		1	
Vancomycin (J01XA01)										7					1	
Combinations (J01CE30)				1											1	
Ceftriaxone, combinations (J01DD63)												5			1	

Access agents. Watch agents. Unclassified

[a] Agents included in this analysis: J01 antibacterials neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [b] Estimates include consumption data of Liechtenstein. [c] Numbers of countries that have this agent in the DU75%. [d] WHO/AMC population-weighted mean for countries of the AMC Network.

3.4 Estimates of volumes of consumption of antibacterials for systemic use (J01) – community

Few AMC Network countries currently analyse consumption data by community and hospital sectors separately. The 2020 AMC Network report (WHO Regional Office for Europe, 2020) showed consumption data for 2015–2017 by sectors for Kazakhstan, Montenegro, the Russian Federation and Türkiye, although no crossnational comparisons were presented. In this report, consumption data for the community sector are compared for Montenegro, the Russian Federation, Switzerland, Türkiye and Ukraine, along with consumption estimates for North Macedonia, where data only for the community sector are available.

3.4.1 Community consumption in 2022

Community consumption of J01 antibacterials comprised 86–96% of total consumption in 2022 (Table 13). Only data for the community sector are available for North Macedonia.

Table 13 Community consumption as a proportion of total consumption of J01 antibacterials, 2022

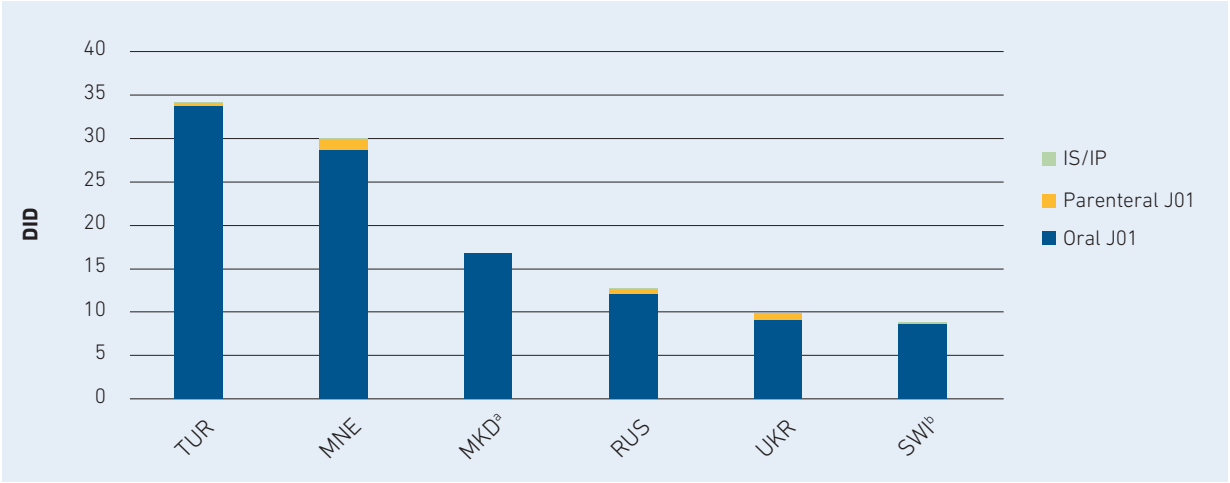
Setting	DID (% of total[a])					
	TUR	MNE	MKD	RUS	SWI[b]	UKR
Community J01	34.1 (96)	30.0 (95)	16.8 (100)	12.7 (86)	8.8 (86)	9.9 (91)
Hospital J01	1.6 (4)	1.7 (5)	–	2.1 (14)	1.4 (14)	1.0 (9)
Total J01	**35.7**	**31.7**	**16.8**	**14.8**	**10.2**	**11.0**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Estimates include consumption data of Liechtenstein.

3.4.2 Route of administration in 2022

Most consumption in the community sector is for oral antibacterial agents. Parenteral agents represented 1% of community consumption in Switzerland and Türkiye and 8% in Ukraine (Fig. 5 and Table 14). Consumption of IS and powder formulations of J01 antibacterials was very low.

Fig. 5 Community consumption of J01 antibacterials by route of administration, 2022



[a] Community consumption. [b] Estimates include consumption data of Liechtenstein.

Table 14 Community consumption of J01 antibacterials by route of administration, 2022

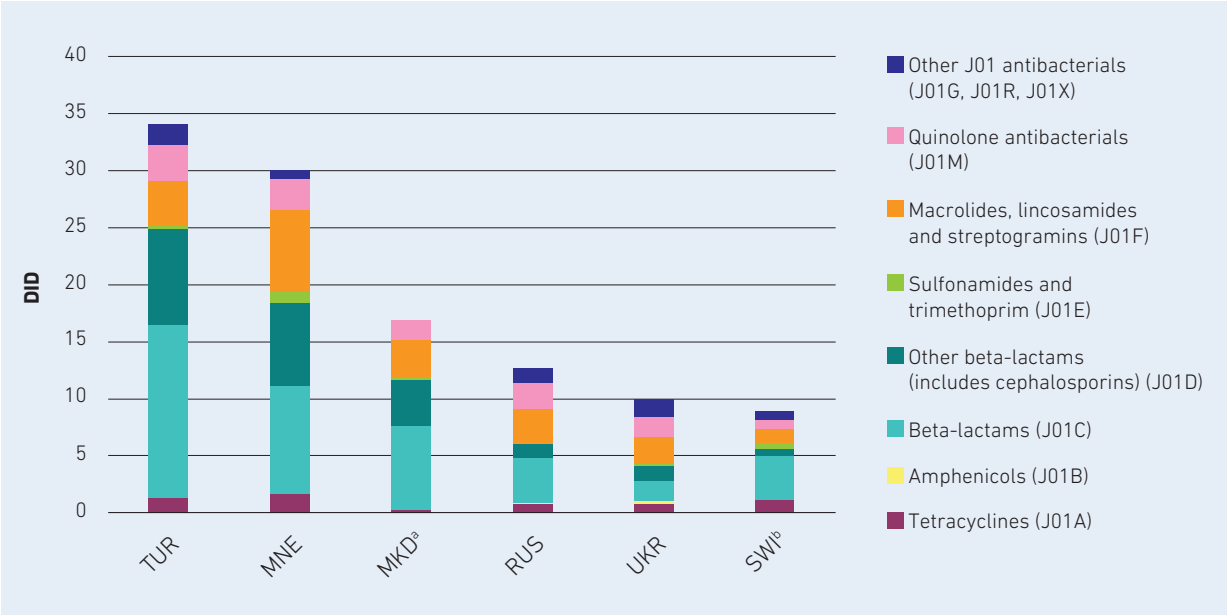
Route of administration	DID (% of total[a])					
	TUR	MNE	MKD	RUS	SWI[b]	UKR
Oral J01	33.8 (99)	28.6 (95)	16.8 (100)	12.2 (96)	8.7 (98)	9.1 (92)
Parenteral J01	0.3 (1)	1.4 (5)	–	0.5 (4)	0.1 (1)	0.8 (8)
IS/IP	< 0.01 (0)	0.01 (0)	–	0.01 (0)	0.02 (0)	< 0.01 (0)
Total	**34.1**	**30.0**	**16.8**	**12.7**	**8.8**	**9.9**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Estimates include consumption data of Liechtenstein.

3.4.3 Pharmacological subgroups in 2022

Patterns of consumption in the community varied across the six countries (Fig. 6 and Table 15). Beta-lactam antibacterials (J01C) were the most consumed pharmacological subgroup in all six countries, ranging from 18% in Ukraine to 45% in Türkiye. Cephalosporins were widely consumed in Montenegro, North Macedonia and Türkiye (24–25% of community consumption) but less frequently in the Russian Federation and Switzerland (9% and 7% respectively). Agents from the macrolides, lincosamides and streptogramins (J01F) were widely consumed in Montenegro (24% of community consumption), Ukraine (24%) and the Russian Federation (23%). Quinolone antibacterials (J01M) constituted 18% of community consumption in the Russian Federation and 17% in Ukraine, but only 9–10% of consumption in the other four countries.

Fig. 6 Community consumption of J01 antibacterials by pharmacological subgroup, 2022



[a] Community consumption. [b] Estimates include consumption data of Liechtenstein.

Table 15 Community consumption of J01 antibacterials by pharmacological subgroup, 2022

Class of agents	DID (% of total[a])					
	TUR	MNE	MKD[b]	RUS	SWI[c]	UKR
Tetracyclines (J01A)	1.3 (4)	1.7 (6)	0.3 (2)	0.8 (7)	1.2 (14)	0.8 (8)
Amphenicols (J01B)	–	–	–	0.1 (1)	–	0.2 (2)
Beta-lactams (J01C)	15.2 (45)	9.5 (32)	7.3 (43)	4.0 (31)	3.8 (43)	1.8 (18)
Other beta-lactams (includes cephalosporins) (J01D)	8.4 (25)	7.2 (24)	4.1 (24)	1.1 (9)	0.6 (7)	1.3 (14)
Sulfonamides and trimethoprim (J01E)	0.3 (1)	1.0 (3)	0.2 (1)	0.2 (2)	0.6 (7)	0.2 (2)
Macrolides, lincosamides and streptogramins (J01F)	3.9 (11)	7.2 (24)	3.3 (19)	2.9 (23)	1.1 (13)	2.4 (24)
Quinolone antibacterials (J01M)	3.2 (9)	2.7 (9)	1.7 (10)	2.3 (18)	0.9 (10)	1.7 (17)
Other J01 antibacterials (J01G, J01R, J01X)	1.8 (5)	0.7 (2)	–	1.3 (10)	0.7 (8)	1.6 (16)
Total	**34.1**	**30.0**	**16.8**	**12.7**	**8.8**	**9.9**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] Estimates include consumption data of Liechtenstein.

3.4.4 Trends 2016–2022

Table 16 shows trends in community consumption from 2016 to 2022. Trends for increases or decreases are more consistent in Montenegro (CAGR +2%) and Switzerland (–1.3%), although the changes were not statistically significant.

Table 16 Trends in community consumption of J01 antibacterials, 2016–2022

Country	Community consumption of J01 antibacterials in DID							CAGR[a]	Trend line	Trend[b]
	2016	2017	2018	2019	2020	2021	2022			
KAZ	–	11.2	11.8	–	–	–	–	–		–
MKD[c]	17.0	16.9	16.6	15.6	14.5	15.3	16.8	–0.2%		–
MNE	26.6	24.9	25.0	25.0	25.7	29.1	30.0	2.0%		–
RUS	12.7	12.3	12.1	12.9	16.2	13.2	12.7	0.1%		–
SWI[d]	9.5	9.0	9.2	9.1	7.6	7.3	8.8	–1.3%		–
TUR	34.2	29.8	30.5	31.8	24.4	27.0	34.1	0.0%		–
UKR	–	–	–	–	–	11.3	9.9	–		–

[a] The CAGR was only calculated where there were 5 years of data available for the country. [b] Linear regression analysis. [c] Community consumption.
[d] Estimates include consumption data of Liechtenstein.

3.5 Estimates of volumes of consumption of antibacterials for systemic use (J01) – hospital

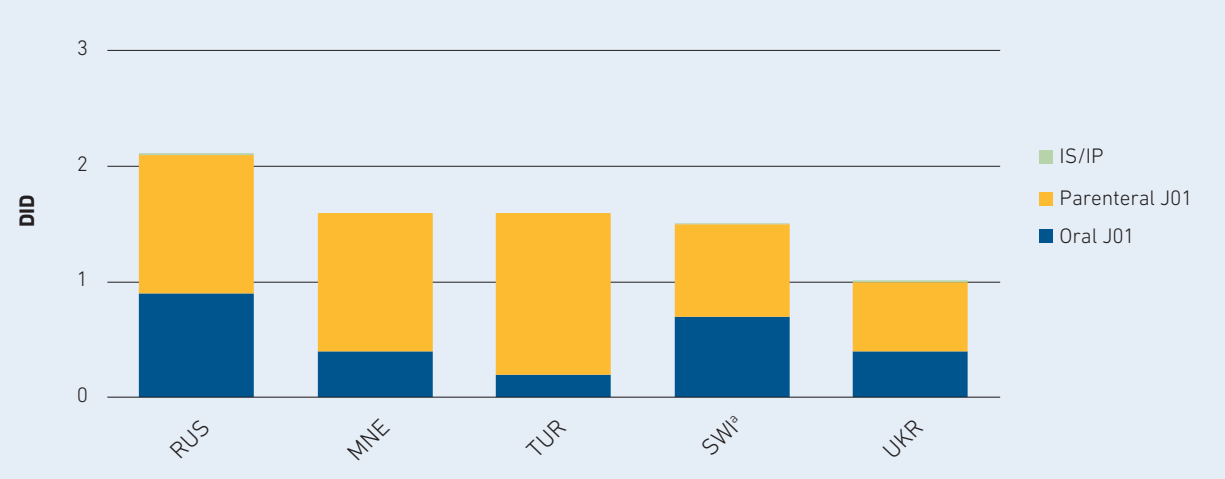
3.5.1 Hospital consumption in 2022

Consumption in the hospital setting was low, varying from 1.0 DID in Ukraine to 2.0 DID in the Russian Federation (Fig. 7 and Table 17).

3.5.2 Route of administration in 2022

Hospital consumption is dominated by parenteral formulations, which constitute from 54% of consumption in Switzerland to 88% in Türkiye.

Fig. 7 Hospital consumption of J01 antibacterials by route of administration, 2022



[a] Estimates include consumption data of Liechtenstein.

Table 17 Hospital consumption of J01 antibacterials by route of administration, 2022

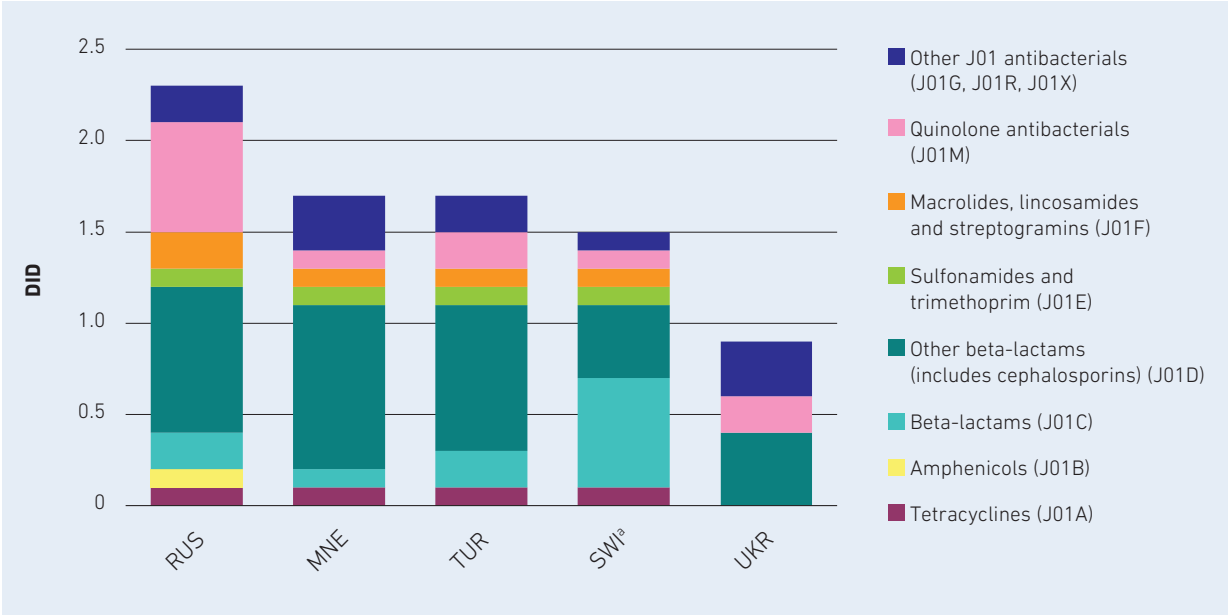
Route of administration	DID (% of total[a])				
	RUS	MNE	TUR	SWI[b]	UKR
Oral J01	0.9 (42)	0.4 (25)	0.2 (12)	0.7 (46)	0.4 (39)
Parenteral J01	1.2 (58)	1.2 (75)	1.4 (88)	0.8 (54)	0.6 (60)
IS/IP	< 0.01 (0)	–	–	< 0.01 (0)	0.01 (1)
Total	**2.0**	**1.7**	**1.6**	**1.4**	**1.0**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Estimates include consumption data of Liechtenstein.

3.5.3 Pharmacological subgroups in 2022

Patterns of consumption in the hospital setting varied across the five countries (Fig. 8 and Table 18). Beta-lactam antibacterials (J01C) were the most consumed pharmacological subgroup in Switzerland (44% of hospital consumption) but represented 4–12% of consumption in the other four countries. Cephalosporins were widely consumed, representing 56% of consumption in Montenegro and 51% in Türkiye. Quinolone antibacterials (J01M) constituted 31% of hospital consumption in the Russian Federation and 23% in Ukraine, but only 8–13% of consumption in the other three countries.

Fig. 8 Hospital consumption of J01 antibacterials by pharmacological subgroup, 2022



[a] Estimates include consumption data of Liechtenstein.

Table 18 Hospital consumption of J01 antibacterials by pharmacological subgroup, 2022

Class of agents	DID (% of total[a])				
	RUS	MNE	TUR	SWI[b]	UKR
Tetracyclines (J01A)	< 0.1 (2)	< 0.1 (2)	< 0.1 (2)	< 0.1 (3)	< 0.1 (1)
Amphenicols (J01B)	< 0.1 (0)	–	–	–	< 0.1 (0)
Beta-lactams (J01C)	0.2 (10)	0.1 (7)	0.2 (12)	0.6 (44)	< 0.1 (4)
Other beta-lactams (includes cephalosporins) (J01D)	0.8 (37)	0.9 (56)	0.8 (51)	0.4 (29)	< 0.1 (38)
Sulfonamides and trimethoprim (J01E)	< 0.1 (1)	< 0.1 (2)	< 0.1 (1)	< 0.1 (2)	< 0.1 (2)
Macrolides, lincosamides and streptogramins (J01F)	0.2 (8)	0.1 (7)	0.1 (5)	0.1 (7)	< 0.1 (5)
Quinolone antibacterials (J01M)	0.6 (31)	0.1 (8)	0.2 (13)	0.1 (8)	0.2 (23)
Other J01 antibacterials (J01G, J01R, J01X)	0.2 (11)	0.3 (21)	0.2 (15)	0.1 (6)	0.3 (27)
Total	**2.0**	**1.7**	**1.6**	**1.4**	**1.0**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Estimates include consumption data of Liechtenstein.

3.5.4 Trends 2016–2022

Table 19 shows trends in hospital consumption from 2016 to 2022. While there were trends for decreases in consumption over time in Montenegro, the Russian Federation and Switzerland, none of the reported changes were statistically significant. The increases seen in Türkiye (+5.4%) were not statistically significant.

Table 19 Trends in hospital consumption of J01 antibacterials, 2016–2022

Country	Hospital consumption of J01 antibacterials in DID							CAGR[a]	Trend line	Trend[b]
	2016	2017	2018	2019	2020	2021	2022			
KAZ	–	2.9	3.0	–	–	–	–	–		–
MNE	1.9	1.7	1.6	1.7	1.8	2.2	1.7	–1.9%		–
RUS	2.2	2.7	2.5	2.2	3.1	2.9	2.0	–1.2%		–
SWI[c]	1.5	1.6	1.6	1.6	1.5	1.3	1.4	–0.8%		–
TUR	1.1	1.1	0.5	1.3	1.4	1.3	1.6	5.4%		–
UKR	–	–	–	–	–	2.0	1.0	–		–

[a] The CAGR was only calculated where there were five years of data available for the country. [b] Linear regression analysis. [c] Estimates include consumption data of Liechtenstein.

4. EXPLORATORY ANALYSES – ANTIFUNGAL AGENTS

4.1 Estimates of volumes of consumption of antifungals for systemic use

Twelve countries were able to provide data on antifungal consumption for each of the years 2019 to 2022.

4.1.1 Total consumption in 2022

There is wide variability in reported consumption of antifungals for systemic use (ATC class J02, as well as selected agents from ATC classes A01, A07 and D01) for 2022 (Fig. 9 and Table 20).

Total consumption of antifungal agents varied across the 12 countries (Fig. 9). Highest total consumption was reported in Azerbaijan (2.6 DID in 2022), followed by Tajikistan (2.0 DID) and Türkiye (1.8 DID). Notably, total consumption in Tajikistan related to use of three agents – nystatin (0.7 DID) as an intestinal anti-infective, fluconazole for IFD (1.2 DID) and terbinafine (0.02 DID) for dermatological infections.

Nystatin consumption estimates were available for 11 countries, ranging from 0.7 DID in Tajikistan to 0.03 DID in Kyrgyzstan.

Ten countries reported consumption of terbinafine in 2022, ranging from 0.7 DID in Switzerland to 0.02 DID in Tajikistan.

Consumption data for the polyene antibiotic amphotericin B were provided for seven countries, although consumption was low (ranging from < 0.001 to 0.034 DID). There is no additional information on the extent of consumption of liposomal amphotericin B.

The triazole fluconazole was the only agent with reported consumption in all 12 countries, ranging from 1.2 DID in Tajikistan to 0.1 DID in North Macedonia. Two other triazole agents, itraconazole and voriconazole, were each consumed in nine countries.

There were limited consumption data for the newer echinocandins – caspofungin, micafungin and anidulafungin – with consumption reported in five countries (Belarus, the Russian Federation, Serbia, Switzerland and Türkiye). Volumes of consumption were very low in each case.

No country reported consumption of the antimetabolite flucytosine in 2022.

The numbers of antifungal agents used varied across the countries, from three agents in North Macedonia and Tajikistan to 13 in the Russian Federation.

Fig. 9 Consumption of antifungals for systemic use, 2022

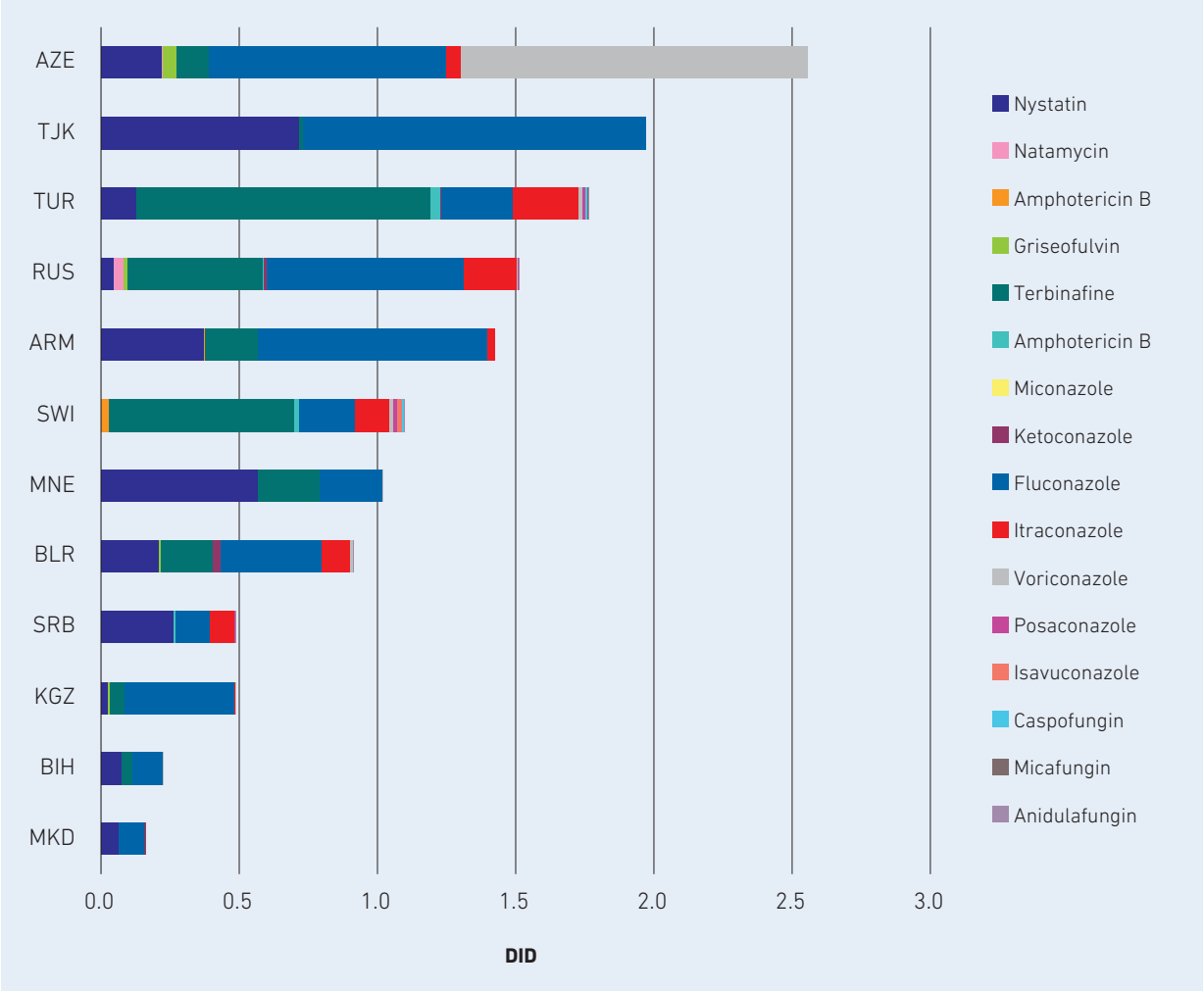


Table 20 Consumption of antifungals for systemic use, 2022

Agent (ATC)	Number of countries	Consumption of antifungals for systemic use in DID											
		AZE	TJK	TUR	RUS	ARM	SWI[a]	MNE	BLR	SRB	KGZ	BIH	MKD[b]
Intestinal anti-infectives													
Nystatin (A07AA02)	11	0.222	0.719	0.129	0.048	0.374	–	0.572	0.210	0.266	0.027	0.076	0.065
Natamycin (A07AA03)	3	0.002	–	–	0.036	0.003	–	–	–	–	–	–	–
Amphotericin B (A07AA07)	2	–	–	–	–	0.002	0.030	–	–	–	–	–	–
Systemic use for dermatological infections													
Griseofulvin (D01BA01)	4	0.051	–	–	0.015	–	–	–	0.007	–	0.008	–	–
Terbinafine (D01BA02)	11	0.116	0.015	1.063	0.488	0.190	0.671	0.218	0.190	< 0.001	0.052	0.040	–
Ketoconazole (J02AB02)	4	–	–	0.003	0.015	–	–	–	0.026	< 0.001	–	–	–
IFD													
Antibiotics (polyenes)													
Amphotericin B (J02AA01)	7	–	–	0.034	0.002	< 0.001	0.016	0.004	0.001	0.005	–	–	–
Triazole and tetrazole derivatives													
Fluconazole (J02AC01)	12	0.858	1.237	0.261	0.711	0.828	0.201	0.227	0.365	0.124	0.397	0.107	0.097
Itraconazole (J02AC02)	9	0.052	–	0.236	0.191	0.027	0.128	–	0.105	0.086	0.006	–	0.001
Voriconazole (J02AC03)	9	1.255	–	0.017	0.004	–	0.011	0.001	0.009	0.002	< 0.001	0.003	
Posaconazole (J02AC04)	4	–	–	0.010	0.001	–	0.017	–	–	0.004	–	–	–
Isavuconazole (J02AC05)	2	–	–	–	–	–	0.016	–	< 0.001		–	–	–
Echinocandins													
Caspofungin (J02AX04)	5	–	–	0.006	0.001	–	0.005	–	< 0.001	0.001	–	–	–
Micafungin (J02AX05)	5	–	–	0.003	0.001	–	< 0.001	–	< 0.001	0.001	–	–	–
Anidulafungin (J02AX06)	5	–	–	0.002	< 0.001	–	0.003	–	< 0.001	0.001	–	–	–
Number of agents consumed		**7**	**3**	**11**	**13**	**7**	**11**	**5**	**12**	**11**	**6**	**4**	**3**
Total DID[c] in 2022		**2.556**	**1.971**	**1.764**	**1.513**	**1.424**	**1.098**	**1.022**	**0.913**	**0.49**	**0.49**	**0.226**	**0.163**

[a] Community consumption. [b] Estimates include consumption data of Liechtenstein. [c] Total amounts and percentages may vary slightly due to rounding.

4.1.2 Trends 2019–2022

Table 21 shows the trends in population-weighted mean consumption of antifungals for systemic use across the 12 countries providing data for the years 2019–2022. Due to the sparseness of data, low levels of consumption for some agents and availability of data for only four years, the CAGR of total antifungal consumption was not calculated for these exploratory analyses.

There was no reported consumption of several antifungal agents in any of the four years – amphotericin B (A01AB04) and natamycin (A01AB10) for local oral treatment, miconazole (A07AC01, J02AB01) and fosravuconazole (D01BA03).

Overall, nystatin consumption as an intestinal anti-infective appears to be decreasing (0.23 DID in 2019 and 0.11 DID in 2022).

Terbinafine was the most consumed antifungal for systemic treatment of dermatological infections, both by volume (0.56 DID in 2022) and number of countries reporting use (11 countries).

Parenteral amphotericin B was used in seven or eight countries across the four years of data, although consumption was low.

The triazole fluconazole was consumed in all 12 countries and showed a trend towards increasing consumption over time. Population-weighted mean consumption ranged from 0.47 DID in 2019 to 0.54 DID in 2022.

Isavuconazole consumption was reported from one country in 2019 and 2020 and two countries in 2021 and 2022.

Flucytosine consumption was reported in only one of the 12 countries in the years 2019 to 2021; no country reported consumption of this agent in 2022.

There was no evidence on increased consumption over time or increases in the numbers of countries reporting use of this newest class of antifungal agents.

Table 21 Population-weighted mean consumption (DID) of oral and parenteral antifungals across 12 countries, 2019–2022

ATC	Population-weighted mean consumption (number of countries reporting some consumption of the agent)				
	Agent	2019	2020	2021	2022
Intestinal anti-infectives					
A07AA02	Nystatin	0.233 (10)	0.152 (10)	0.095 (10)	0.114 (11)
A07AA03	Natamycin	0.028 (5)	0.025 (4)	0.020 (4)	0.018 (3)
A07AA07	Amphotericin B (oral)	–	0.002 (1)	0.001 (1)	0.001 (2)
Systemic use for dermatological infections					
D01BA01	Griseofulvin	0.011 (3)	0.008 (3)	0.010 (3)	0.010 (4)
D01BA02	Terbinafine	0.625 (11)	0.514 (11)	0.534 (11)	0.595 (11)
J02AB02	Ketoconazole	0.014 (4)	0.004 (6)	0.008 (4)	0.009 (4)
Invasive fungal disease					
Antibiotics (polyenes)					
J02AA01	Amphotericin B (parenteral)	0.009 (7)	0.009 (7)	0.014 (8)	0.012 (7)
Triazole and tetrazole derivatives					
J02AC01	Fluconazole	0.467 (12)	0.478 (12)	0.493 (12)	0.540 (12)
J02AC02	Itraconazole	0.212 (9)	0.159 (8)	0.170 (9)	0.176 (9)
J02AC03	Voriconazole	0.006 (7)	0.006 (8)	0.051 (8)	0.052 (9)
J02AC04	Posaconazole	0.003 (4)	0.004 (4)	0.004 (4)	0.004 (4)
J02AC05	Isavuconazole	< 0.001 (1)	0.001 (1)	< 0.001 (2)	< 0.001 (2)
Antimetabolites					
J02AX01	Flucytosine	< 0.001 (1)	< 0.001 (1)	< 0.001 (1)	–
Echinocandins					
J02AX04	Caspofungin	0.002 (4)	0.002 (4)	0.002 (4)	0.002 (5)
J02AX05	Micafungin	0.001 (5)	0.001 (5)	0.001 (5)	0.002 (5)
J02AX06	Anidulafungin	0.001 (4)	0.001 (4)	0.001 (5)	0.001 (5)

5. DISCUSSION

The analyses in this report focus on crossnational comparisons of consumption data for 2022 from 15 AMC Network countries. Primary analyses relate to J01 antibacterials, where consumption patterns mirror the variability shown in earlier reports. Total consumption ranged from 9.6 to 35.7 DID in 2022 compared to 8.6 to 34.4 DID from 10 countries in 2021. The population-weighted mean consumption across the Network was 20.7 DID in 2022 (20.3 DID in 2021). Relative consumption of parenteral formulations varied widely (range 5–45% of total consumption) as did patterns of consumption of pharmacological subgroups.

Thirteen countries had consumption estimates available for all years (2014–2022). Two showed statistically significant increases in consumption of J01 antibacterials over the nine years – Azerbaijan (CAGR +10.5%) and Bosnia and Herzegovina (CAGR +3.4%). Only one country, Switzerland, showed a statistically significant reduction in consumption over time (CAGR –1.1%). Trends towards decreasing consumption in some countries in earlier years are likely to have been affected by changed consumption patterns during the COVID-19 pandemic.

Consumption of Access agents represented between 39% and 68% of total antibacterial consumption in 2022. The population-weighted estimates across the AMC Network were: Access agents 51%, Watch agents 47%, Reserve agents 0.3% and unclassified agents 1.7%. This compares to Access agent consumption across the Network of 50% in 2019, 46% in 2020 and 50% in 2021 (WHO Regional Office for Europe, 2023). It suggests a slow return towards pre-pandemic patterns of antibacterial prescribing and is further supported by the findings that the Watch agent azithromycin, which was used widely during the COVID-19 pandemic, fell in ranking from second to third most consumed oral antibacterial across the Network in 2022. Further years of data are needed to confirm these trends. In 2022, the Access agents amoxicillin and beta-lactamase inhibitor and amoxicillin ranked first and second for consumption in the population-weighted DU75% for oral antibacterials. As in previous analyses, the Watch agent ceftriaxone was ranked number one most consumed parenteral antibiotic across the Network.

Five countries (Montenegro, the Russian Federation, Switzerland, Türkiye and Ukraine) were able to provide consumption data disaggregated to community and hospital sectors separately. Community sector data were also available for North Macedonia. Community consumption of J01 antibacterials comprised 86–96% of total consumption in 2022 (100% for North Macedonia). Most community consumption was for oral antibacterial agents, with only 1–8% consumption of parenteral agents. Conversely, consumption in the hospital setting was low (1.0–2.0 DID), with consumption dominated by parenteral formulations (54–88% of consumption).

Analyses of patterns of consumption of pharmacological subgroups in community and hospital settings showed wide variations between countries in choice of agents used. Beta-lactam antibacterials (J01C) represented from 18% to 45% of community consumption. These agents comprised 44% of hospital consumption in one country, but only 4–12% of hospital consumption in the other four countries. Similarly, cephalosporins varied from 7–25% of consumption in community settings and 29–56% of hospital consumption.

The substantial differences in patterns of consumption of J01 antibacterials overall and at community and hospital levels shown in these analyses suggest significant differences in management protocols and treatment guidelines at country level. Reasons for these differences should be investigated. Countries could consider a review of treatment algorithms and guidelines for common conditions against medicines recommended in the WHO AWaRe antibiotic book (WHO, 2022b).

The AWaRe book is an evidence-based resource providing recommendations for first- and second-line treatment options for more than 30 of the most common clinical infections in children and adults managed in community and hospital settings. The antibiotic treatment recommendations are based on reviews of the evidence undertaken for the 2017, 2019 and 2021 updates of the EML and EMLc and provide guidance on how to best use these antibiotics based on the principles of the AWaRe framework. Each chapter on a clinical infection includes background information (pathophysiology, epidemiology, global burden, most common pathogens and how to make the clinical diagnosis, including assessing disease severity), diagnostic tools that may be clinically helpful where available and treatment recommendations. The empiric antibiotic recommendations are based on clinical signs and symptoms. Guidance is given where appropriate for "no antibiotic care", including symptomatic management for low-risk patients with minor infections who do not need antibiotic treatment. First- and second-choice antibiotic options are given where relevant based on the EML, EMLc and AWaRe system and other WHO guidance documents.

To facilitate use, each chapter provides an infographic that contains a short summary of the most important information (clinical presentation, diagnostic tests and treatment). These infographics are available in downloadable format for use at country level (WHO, 2022c). AMC Network countries should consider a review of national treatment guidelines and protocols against the AWaRe book recommendations. The evidence-based guidance of the book can facilitate rapid update of local guidelines and protocols. The infographics can be adapted and promoted for local use to improve the quality of prescribing of antibacterial agents.

Exploratory analyses for antifungal agents for systemic use were conducted for 12 countries. There was wide variability in total consumption in 2022, ranging from 2.6 DID in Azerbaijan to 0.16 DID in North Macedonia (community consumption only). The numbers of antifungal agents used varied from three agents in North Macedonia and Tajikistan to 13 in the Russian Federation.

Nystatin was widely consumed as an intestinal anti-infective (11 countries). Ten countries reported consumption of terbinafine for the systemic treatment of dermatological fungal infections. Of the agents to treat IFD, the triazole fluconazole was the only agent with reported consumption in all 12 countries (range 0.1–1.2 DID). Consumption levels of the newer echinocandins – caspofungin, micafungin and anidulafungin – reported in five countries were very low. None of the 12 countries reported consumption of the antimetabolite flucytosine in 2022.

Estimates of the population-weighted mean consumption of antifungals was used to examine trends in consumption between 2019 and 2022. Nystatin consumption as an intestinal anti-infective appears to be decreasing (population-weighted mean 0.23 DID in 2019 and 0.11 DID in 2022). Fluconazole showed a trend towards increasing consumption over time (0.47 DID in 2019 to 0.54 DID in 2022). There was no evidence of increased consumption over time or increases in the numbers of countries reporting use of echinocandins.

The 2022 WHO priority fungal agents report (WHO, 2022a) noted that while existing antifungal medicines are effective, they are associated with a range of adverse effects, lengthy courses of treatment and drug–drug interactions. Additionally, affordable access to quality medicines and diagnostic tests is unevenly distributed, meaning many fungal infections go undiagnosed and untreated.

The analyses of antifungal agents presented in this report is a first attempt to collate data from AMC Network countries. The results provide a platform for monitoring changes in consumption – both volumes of consumption and choice of agents – over time. Given the low levels of consumption of many of the agents used to treat IFD shown in this report, an important next step for Network countries could be to review the registration status of key antifungal agents, particularly those included on the WHO EML and EMLc. This applies particularly to the echinocandins group of medicines. The incidence of infusion-related adverse effects and nephrotoxicity with these medicines is much lower than with amphotericin B, but their higher cost in comparison to azole antifungals is likely to limit their use.

Micafungin was added to the complementary list of the WHO EML in 2021 with a square-box listing, nominating anidulafungin and caspofungin as alternatives. As countries update their national essential medicines lists, special attention should be given to a review of antifungal agents. Medicines on the list should align with those recommended in treatment guidelines and be included in national procurement programmes to ensure equitable and affordable access to quality antifungal agents.

As noted in previous analyses, the limitations of some of the data have implications for interpretation of results. Only medicines with an assigned ATC code and DDD are included in the analyses. Where medicines without codes are consumed by the population, DID estimates will be underestimated. While import records have limitations, they will include the over-the-counter supply of antibacterials without prescription that occurs in some countries. Without information on indications for treatment, some results are difficult to interpret. A fuller interpretation of the consumption data requires an understanding of the local context.

These limitations do not diminish the importance of regular analysis of local data, its dissemination to relevant health-care professionals and communities, and its use to inform decision-making. The quality of the data is unlikely to improve unless the data are seen as relevant and useful for policy development and implementation. Missing information may provide the impetus for commitments to improve the scope and completeness of data collection. Dissemination of information on antibacterial consumption to clinicians and the public will heighten awareness of inappropriate use and problem prescribing and dispensing practices. Substantial differences in the volumes and patterns of consumption between countries that have been reported in consecutive AMC Network reports suggest there are many targets for further studies, both quantitative and qualitative, to understand better the use of these medicines in clinical practice.

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ANNEX. AGENTS INCLUDED IN THE 2023 ACCESS, WATCH AND RESERVE (AWaRe) INDEX

Access antibiotics for 2023 are shown in Table A.1, Watch in Table A.2 and Reserve in Table A.3.

Table A.1 Access antibiotics 2023

Antibiotic	Class	ATC code	Listed in EML 2023
Amikacin	Aminoglycosides	J01GB06	Yes
Amoxicillin	Penicillins	J01CA04	Yes
Amoxicillin/clavulanic-acid	Beta-lactam/beta-lactamase inhibitor	J01CR02	Yes
Ampicillin	Penicillins	J01CA01	Yes
Ampicillin/sulbactam	Beta-lactam/beta-lactamase inhibitor	J01CR01	No
Azidocillin	Penicillins	J01CE04	No
Bacampicillin	Penicillins	J01CA06	No
Benzathine-benzylpenicillin	Penicillins	J01CE08	Yes
Benzylpenicillin	Penicillins	J01CE01	Yes
Brodimoprim	Trimethoprim derivatives	J01EA02	No
Cefacetrile	First-generation cephalosporins	J01DB10	No
Cefadroxil	First-generation cephalosporins	J01DB05	No
Cefalexin	First-generation cephalosporins	J01DB01	Yes
Cefaloridine	First-generation cephalosporins	J01DB02	No
Cefalotin	First-generation cephalosporins	J01DB03	No
Cefapirin	First-generation cephalosporins	J01DB08	No
Cefatrizine	First-generation cephalosporins	J01DB07	No
Cefazedone	First-generation cephalosporins	J01DB06	No
Cefazolin	First-generation cephalosporins	J01DB04	Yes
Cefradine	First-generation cephalosporins	J01DB09	No
Cefroxadine	First-generation cephalosporins	J01DB11	No
Ceftezole	First-generation cephalosporins	J01DB12	No
Chloramphenicol	Amphenicols	J01BA01	Yes
Clindamycin	Lincosamides	J01FF01	Yes
Clometocillin	Penicillins	J01CE07	No
Cloxacillin	Penicillins	J01CF02	Yes

Table A.1 contd

Antibiotic	Class	ATC code	Listed in EML 2023
Dicloxacillin	Penicillins	J01CF01	No
Doxycycline	Tetracyclines	J01AA02	Yes
Epicillin	Penicillins	J01CA07	No
Flucloxacillin	Penicillins	J01CF05	No
Furazidin	Nitrofuran derivatives	J01XE03	No
Gentamicin	Aminoglycosides	J01GB03	Yes
Hetacillin	Penicillins	J01CA18	No
Mecillinam	Penicillins	J01CA11	No
Metampicillin	Penicillins	J01CA14	No
Meticillin	Penicillins	J01CF03	No
Metronidazole – IV	Imidazoles	J01XD01	Yes
Metronidazole – oral	Imidazoles	P01AB01	Yes
Nafcillin	Penicillins	J01CF06	No
Nifurtoinol	Nitrofuran derivatives	J01XE02	No
Nitrofurantoin	Nitrofuran derivatives	J01XE01	Yes
Ornidazole – IV	Imidazoles	J01XD03	No
Ornidazole – oral	Imidazoles	P01AB03	No
Oxacillin	Penicillins	J01CF04	No
Penamecillin	Penicillins	J01CE06	No
Phenoxymethylpenicillin	Penicillins	J01CE02	Yes
Pivampicillin	Penicillins	J01CA02	No
Pivmecillinam	Penicillins	J01CA08	No
Procaine-benzylpenicillin	Penicillins	J01CE09	Yes
Propicillin	Penicillins	J01CE03	No
Secnidazole	Imidazoles	P01AB07	No
Spectinomycin	Aminocyclitols	J01XX04	Yes
Sulbactam	Beta-lactamase inhibitors	J01CG01	No
Sulfadiazine	Sulfonamides	J01EC02	No
Sulfadiazine/tetroxoprim	Sulfonamide–trimethoprim combinations	J01EE06	No
Sulfadiazine/trimethoprim	Sulfonamide–trimethoprim combinations	J01EE02	No
Sulfadimethoxine	Sulfonamides	J01ED01	No
Sulfadimidine	Sulfonamides	J01EB03	No
Sulfadimidine/trimethoprim	Sulfonamide–trimethoprim combinations	J01EE05	No
Sulfafurazole	Sulfonamides	J01EB05	No
Sulfaisodimidine	Sulfonamides	J01EB01	No
Sulfalene	Sulfonamides	J01ED02	No
Sulfamazone	Sulfonamides	J01ED09	No
Sulfamerazine	Sulfonamides	J01ED07	No
Sulfamerazine/trimethoprim	Sulfonamide–trimethoprim combinations	J01EE07	No

Table A.1 contd

Antibiotic	Class	ATC code	Listed in EML 2023
Sulfamethizole	Sulfonamides	J01EB02	No
Sulfamethoxazole	Sulfonamides	J01EC01	No
Sulfamethoxazole/trimethoprim	Sulfonamide–trimethoprim combinations	J01EE01	Yes
Sulfamethoxypyridazine	Sulfonamides	J01ED05	No
Sulfametomidine	Sulfonamides	J01ED03	No
Sulfametoxydiazine	Sulfonamides	J01ED04	No
Sulfametrole/trimethoprim	Sulfonamide–trimethoprim combinations	J01EE03	No
Sulfamoxole	Sulfonamides	J01EC03	No
Sulfamoxole/trimethoprim	Sulfonamide–trimethoprim combinations	J01EE04	No
Sulfanilamide	Sulfonamides	J01EB06	No
Sulfaperin	Sulfonamides	J01ED06	No
Sulfaphenazole	Sulfonamides	J01ED08	No
Sulfapyridine	Sulfonamides	J01EB04	No
Sulfathiazole	Sulfonamides	J01EB07	No
Sulfathiourea	Sulfonamides	J01EB08	No
Sultamicillin	Beta-lactam/beta-lactamase inhibitor	J01CR04	No
Talampicillin	Penicillins	J01CA15	No
Tetracycline	Tetracyclines	J01AA07	No
Thiamphenicol	Amphenicols	J01BA02	No
Tinidazole – IV	Imidazoles	J01XD02	No
Tinidazole – oral	Imidazoles	P01AB02	No
Trimethoprim	Trimethoprim derivatives	J01EA01	Yes

ATC: Anatomical Therapeutic Chemical (classification system).
EML: WHO Model List of Essential Medicines for adults.
IV: intravenous.

Table A.2 Watch antibiotics 2023

Antibiotic	Class	ATC code	Listed in EML 2023
Arbekacin	Aminoglycosides	J01GB12	No
Aspoxicillin	Penicillins	J01CA19	No
Azithromycin	Macrolides	J01FA10	Yes
Azlocillin	Penicillins	J01CA09	No
Bekanamycin	Aminoglycosides	J01GB13	No
Biapenem	Carbapenems	J01DH05	No
Carbenicillin	Penicillins	J01CA03	No
Carindacillin	Penicillins	J01CA05	No
Cefaclor	Second-generation cephalosporins	J01DC04	No
Cefamandole	Second-generation cephalosporins	J01DC03	No
Cefbuperazone	Second-generation cephalosporins	J01DC13	No
Cefcapene-pivoxil	Third-generation cephalosporins	J01DD17	No
Cefdinir	Third-generation cephalosporins	J01DD15	No
Cefditoren-pivoxil	Third-generation cephalosporins	J01DD16	No
Cefepime	Fourth-generation-cephalosporins	J01DE01	No
Cefetamet-pivoxil	Third-generation-cephalosporins	J01DD10	No
Cefixime	Third-generation cephalosporins	J01DD08	Yes
Cefmenoxime	Third-generation cephalosporins	J01DD05	No
Cefmetazole	Second-generation cephalosporins	J01DC09	No
Cefminox	Second-generation cephalosporins	J01DC12	No
Cefodizime	Third-generation cephalosporins	J01DD09	No
Cefonicid	Second-generation cephalosporins	J01DC06	No
Cefoperazone	Third-generation cephalosporins	J01DD12	No
Ceforanide	Second-generation cephalosporins	J01DC11	No
Cefoselis	Fourth-generation cephalosporins	to be assigned	No
Cefotaxime	Third-generation cephalosporins	J01DD01	Yes
Cefotetan	Second-generation cephalosporins	J01DC05	No
Cefotiam	Second-generation cephalosporins	J01DC07	No
Cefoxitin	Second-generation cephalosporins	J01DC01	No
Cefozopran	Fourth-generation cephalosporins	J01DE03	No
Cefpiramide	Third-generation cephalosporins	J01DD11	No
Cefpirome	Fourth-generation cephalosporins	J01DE02	No
Cefpodoxime-proxetil	Third-generation cephalosporins	J01DD13	No
Cefprozil	Second-generation cephalosporins	J01DC10	No
Cefsulodin	Third-generation cephalosporins	J01DD03	No
Ceftazidime	Third-generation cephalosporins	J01DD02	Yes
Cefteram-pivoxil	Third-generation cephalosporins	J01DD18	No
Ceftibuten	Third-generation cephalosporins	J01DD14	No

Table A.2 contd

Antibiotic	Class	ATC code	Listed in EML 2023
Ceftizoxime	Third-generation cephalosporins	J01DD07	No
Ceftriaxone	Third-generation cephalosporins	J01DD04	Yes
Cefuroxime	Second-generation cephalosporins	J01DC02	Yes
Chlortetracycline	Tetracyclines	J01AA03	No
Cinoxacin	Quinolones	J01MB06	No
Ciprofloxacin	Fluoroquinolones	J01MA02	Yes
Clarithromycin	Macrolides	J01FA09	Yes
Clofoctol	Phenol derivatives	J01XX03	No
Clomocycline	Tetracyclines	J01AA11	No
Delafloxacin	Fluoroquinolones	J01MA23	No
Demeclocycline	Tetracyclines	J01AA01	No
Dibekacin	Aminoglycosides	J01GB09	No
Dirithromycin	Macrolides	J01FA13	No
Doripenem	Carbapenems	J01DH04	No
Enoxacin	Fluoroquinolones	J01MA04	No
Ertapenem	Carbapenems	J01DH03	No
Erythromycin	Macrolides	J01FA01	No
Fidaxomicin	Macrolides	A07AA12	No
Fleroxacin	Fluoroquinolones	J01MA08	No
Flomoxef	Second-generation cephalosporins	J01DC14	No
Flumequine	Quinolones	J01MB07	No
Flurithromycin	Macrolides	J01FA14	No
Fosfomycin – oral	Phosphonics	J01XX01	No
Fusidic-acid	Steroid antibacterials	J01XC01	No
Garenoxacin	Fluoroquinolones	J01MA19	No
Gatifloxacin	Fluoroquinolones	J01MA16	No
Gemifloxacin	Fluoroquinolones	J01MA15	No
Grepafloxacin	Fluoroquinolones	J01MA11	No
Imipenem/cilastatin	Carbapenems	J01DH51	No
Isepamicin	Aminoglycosides	J01GB11	No
Josamycin	Macrolides	J01FA07	No
Kanamycin – IV	Aminoglycosides	J01GB04	No
Kanamycin – oral	Aminoglycosides	A07AA08	No
Lascufloxacin	Fluoroquinolones	J01MA25	No
Latamoxef	Third-generation cephalosporins	J01DD06	No
Levofloxacin	Fluoroquinolones	J01MA12	No
Levonadifloxacin	Fluoroquinolones	J01MA24	No
Lincomycin	Lincosamides	J01FF02	No
Lomefloxacin	Fluoroquinolones	J01MA07	No

Table A.2 contd

Antibiotic	Class	ATC code	Listed in EML 2023
Loracarbef	Second-generation cephalosporins	J01DC08	No
Lymecycline	Tetracyclines	J01AA04	No
Meropenem	Carbapenems	J01DH02	Yes
Metacycline	Tetracyclines	J01AA05	No
Mezlocillin	Penicillins	J01CA10	No
Micronomicin	Aminoglycosides	To be assigned	No
Midecamycin	Macrolides	J01FA03	No
Minocycline – oral	Tetracyclines	J01AA08	No
Miocamycin	Macrolides	J01FA11	No
Moxifloxacin	Fluoroquinolones	J01MA14	No
Nemonoxacin	Quinolones	J01MB08	No
Neomycin – IV	Aminoglycosides	J01GB05	No
Neomycin – oral	Aminoglycosides	A07AA01	No
Netilmicin	Aminoglycosides	J01GB07	No
Norfloxacin	Fluoroquinolones	J01MA06	No
Ofloxacin	Fluoroquinolones	J01MA01	No
Oleandomycin	Macrolides	J01FA05	No
Oxolinic-acid	Quinolones	J01MB05	No
Oxytetracycline	Tetracyclines	J01AA06	No
Panipenem	Carbapenems	J01DH55	No
Pazufloxacin	Fluoroquinolones	J01MA18	No
Pefloxacin	Fluoroquinolones	J01MA03	No
Penimepicycline	Tetracyclines	J01AA10	No
Pheneticillin	Penicillins	J01CE05	No
Pipemidic-acid	Quinolones	J01MB04	No
Piperacillin	Penicillins	J01CA12	No
Piperacillin/tazobactam	Beta-lactam/beta-lactamase inhibitor, anti-pseudomonal	J01CR05	Yes
Piromidic-acid	Quinolones	J01MB03	No
Pristinamycin	Streptogramins	J01FG01	No
Prulifloxacin	Fluoroquinolones	J01MA17	No
Ribostamycin	Aminoglycosides	J01GB10	No
Rifabutin	Rifamycins	J04AB04	No
Rifampicin	Rifamycins	J04AB02	No
Rifamycin – IV	Rifamycins	J04AB03	No
Rifamycin – oral	Rifamycins	A07AA13	No
Rifaximin	Rifamycins	A07AA11	No
Rokitamycin	Macrolides	J01FA12	No
Rolitetracycline	Tetracyclines	J01AA09	No
Rosoxacin	Quinolones	J01MB01	No

Table A.2 contd

Antibiotic	Class	ATC code	Listed in EML 2023
Roxithromycin	Macrolides	J01FA06	No
Rufloxacin	Fluoroquinolones	J01MA10	No
Sarecycline	Tetracyclines	J01AA14	No
Sisomicin	Aminoglycosides	J01GB08	No
Sitafloxacin	Fluoroquinolones	J01MA21	No
Solithromycin	Macrolides	J01FA16	No
Sparfloxacin	Fluoroquinolones	J01MA09	No
Spiramycin	Macrolides	J01FA02	No
Streptoduocin	Aminoglycosides	J01GA02	No
Streptomycin – IV	Aminoglycosides	J01GA01	No
Streptomycin – oral	Aminoglycosides	A07AA04	No
Sulbenicillin	Penicillins	J01CA16	No
Tazobactam	Beta-lactamase inhibitors	J01CG02	No
Tebipenem	Carbapenems	J01DH06	No
Teicoplanin	Glycopeptides	J01XA02	No
Telithromycin	Macrolides	J01FA15	No
Temafloxacin	Fluoroquinolones	J01MA05	No
Temocillin	Penicillins	J01CA17	No
Ticarcillin	Penicillins	J01CA13	No
Tobramycin	Aminoglycosides	J01GB01	No
Tosufloxacin	Fluoroquinolones	J01MA22	No
Troleandomycin	Macrolides	J01FA08	No
Trovafloxacin	Fluoroquinolones	J01MA13	No
Vancomycin – IV	Glycopeptides	J01XA01	Yes
Vancomycin – oral	Glycopeptides	A07AA09	Yes

ATC: Anatomical Therapeutic Chemical (classification system).
EML: WHO Model List of Essential Medicines for adults.
IV: intravenous.

Table A.3 Reserve antibiotics 2023

Antibiotic	Class	ATC code	Listed in EML 2023
Aztreonam	Monobactams	J01DF01	No
Carumonam	Monobactams	J01DF02	No
Cefiderocol	Other cephalosporins	J01DI04	Yes
Ceftaroline-fosamil	Fifth-generation cephalosporins	J01DI02	No
Ceftazidime/avibactam	Third-generation cephalosporins	J01DD52	Yes
Ceftobiprole-medocaril	Fifth-generation cephalosporins	J01DI01	No
Ceftolozane/tazobactam[a]	Fifth-generation cephalosporins	J01DI54	Yes
Colistin – IV	Polymyxins	J01XB01	Yes
Colistin – oral	Polymyxins	A07AA10	No
Dalbavancin	Glycopeptides	J01XA04	No
Dalfopristin/quinupristin	Streptogramins	J01FG02	No
Daptomycin	Lipopeptides	J01XX09	No
Eravacycline	Tetracyclines	J01AA13	No
Faropenem	Penems	J01DI03	No
Fosfomycin – IV	Phosphonics	J01XX01	Yes
Iclaprim	Trimethoprim derivatives	J01EA03	No
Imipenem/cilastatin/relebactam	Carbapenems	J01DH56	No
Lefamulin	Pleuromutilin	J01XX12	No
Linezolid[b]	Oxazolidinones	J01XX08	Yes
Meropenem/vaborbactam	Carbapenems	J01DH52	Yes
Minocycline – IV	Tetracyclines	J01AA08	No
Omadacycline	Tetracyclines	J01AA15	No
Oritavancin	Glycopeptides	J01XA05	No
Plazomicin	Aminoglycosides	J01GB14	Yes
Polymyxin-B – IV	Polymyxins	J01XB02	Yes
Polymyxin-B – oral	Polymyxins	A07AA05	No
Tedizolid	Oxazolidinones	J01XX11	No
Telavancin	Glycopeptides	J01XA03	No
Tigecycline	Glycylcyclines	J01AA12	No

ATC: Anatomical Therapeutic Chemical (classification system).
EML: WHO Model List of Essential Medicines for adults.
IV: intravenous.
[a] New addition to EML 2023. [b] Tedizolid phosphate is listed as a therapeutic alternative to linezolid.

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