

Drug costs and antibiotic stewardship in a tertiary care hospital in Kazakhstan: ABC/VEN, 2022–2025

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Abstract

Introduction: Multi-year hospital-level data on drug expenditure in Kazakhstan are scarce, although antimicrobial resistance and the growing use of high-cost biologics require expenditure monitoring tools. This study aimed to quantify four-year trends in drug expenditure, formulary structure and antibiotic spending in a multidisciplinary tertiary care hospital.

Methods: Annual pharmacy dispensing ledgers for 2022–2025 were analyzed retrospectively. Each item was assigned an International Nonproprietary Name and an Anatomical Therapeutic Chemical code. ABC analysis and vital, essential and non-essential classification were performed by nonproprietary name, and antibacterials were mapped to the World Health Organization Access, Watch and Reserve groups. Expenditure was normalized per bed-day.

Results: The number of nonproprietary names dispensed decreased from 194 to 172, whereas expenditure increased by 40.6% to 523.8 million Kazakhstani tenge and expenditure per bed-day by 35.1%. The share of immunosuppressants rose from 2.9% to 22.8%; ustekinumab and vedolizumab accounted for 20.3% of expenditure in 2025. Group A comprised 15.1–19.1% of names and 80.0–80.8% of expenditure; no non-essential medicine entered group A, but non-essential expenditure increased to 1.9% in 2025. Antibacterial expenditure rose by 66.6% in 2025; Watch agents accounted for 75.5–78.1% and Reserve agents for 10.3–14.4% of antibacterial spending.

Conclusions: Formulary contraction coincided with a shift of the budget toward biologics and Watch and Reserve antibiotics. The findings are limited by the single-center design, nominal prices and the absence of consumption metrics based on defined daily doses; expenditure-based Access, Watch and Reserve signals should be combined with such metrics in multicenter studies.

Keywords: drug costs, drug utilization, anti-bacterial agents, antimicrobial stewardship, tertiary care centers, formulary management.

Introduction

Rational use of medicines (RUM) is a core objective of the health system of Kazakhstan. Under Order of the Minister of Health No. KR DSM-179/2020, healthcare organizations must perform an annual internal evaluation of RUM, and its results are reviewed by the formulary commission [1].

The Anatomical Therapeutic Chemical (ATC) classification is the World Health Organization (WHO)-recommended standard for grouping medicines in drug utilization research, and the defined daily dose (DDD) is its companion unit of consumption; together they allow comparison across settings independently of brand, pack size and price [2,3]. ABC analysis applies

the Pareto principle to the concentration of expenditure, whereas the VEN classification ranks medicines as vital (V), essential (E) or non-essential (N) according to clinical priority [4-6]. The presence of non-essential medicines in ABC group A is a recognized marker of inefficient procurement [5,6].

Kazakhstan has developed a national formulary infrastructure, including the Kazakhstan National Formulary (KNF), the Guaranteed Volume of Free Medical Care (GVFMC) and compulsory social health insurance [7-9]. Published studies from hospitals in Kazakhstan have examined antibiotic use in a nephrology department and during the COVID-19 pandemic [10,11]. However, multi-year, hospital-wide analyses that combine ATC, ABC/VEN and antibiotic stewardship indicators remain uncommon for tertiary centers.

Antimicrobial resistance (AMR) is a global health priority [12], and surveillance and stewardship capacity in post-Soviet countries, including Kazakhstan, remains fragmented [13-15]. The WHO AWaRe (Access, Watch, Reserve) classification of antibiotics is the recommended framework for monitoring antibiotic portfolios [16] and has been applied to describe patterns of hospital antibiotic use [17]. Growth in expenditure on Watch and Reserve agents does not prove inappropriate prescribing, but it is an actionable signal for prospective audit and feedback.

To our knowledge, this is the first study from Kazakhstan to combine, over four consecutive years, ATC, ABC/VEN and AWaRe analyses of complete hospital pharmacy ledgers at the level of International Nonproprietary Names (INNs), with activity-based denominators and item-level calculations available for verification. The aim was to (i) describe the portfolio and expenditure dynamics per bed-day and per discharged patient; (ii) assess procurement rationality with ABC/VEN analysis; and (iii) characterize antibiotic expenditure using the AWaRe classification.

Methods

Study design and setting

A retrospective observational drug utilization study of annual drug dispensing was conducted in a single multidisciplinary tertiary care hospital in Kazakhstan (identified on the separate title page in accordance with the journal's double-blind review policy). Reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [18]. The analysis covered calendar years 2022–2025.

Data source and eligibility

The data source was the annual pharmacy material ledgers (incoming and outgoing records, .xlsx format), which contain the trade name, unit, quantity dispensed and expenditure in Kazakhstani tenge (KZT) for each item and year. All items of the “Medications” section were included. Non-medicinal items recorded in that section were excluded: surgical suture material in 2022 (KZT 64.3 million) and one enteral nutrition product and one intra-articular medical device in 2025 (KZT 3.1 million). Medical devices, consumables, chemical reagents and infant formula, which are recorded in separate ledger sections, were not analyzed. Items listed in a ledger with zero quantity and zero expenditure were not counted as dispensed. Bed-days (86,363; 84,712; 81,522 and 89,878 in 2022–2025) and the number of discharged patients (11,312; 11,056; 11,289 and 11,963) were obtained from the official bed-utilization form of the hospital.

ATC classification and denominators

Each trade-name item was assigned an INN and a fifth-level ATC code according to the WHO ATC/DDD Index 2024 [3]. Expenditure on all trade names sharing one INN was summed. ATC levels 1 and 2 were used to describe the structure of expenditure. Drug expenditure per bed-day and per discharged patient was used as a volume-normalized metric. Because the ledgers record quantities in heterogeneous pack units, DDD-based consumption was not calculated.

ABC analysis

For each year, INNs were ranked in descending order of expenditure, and cumulative shares were calculated. Group A included the INNs that accounted for the first 80% of expenditure, group B the next 15% (cumulative 95%) and group C the remaining 5% [1,5,6].

VEN analysis

The VEN category was assigned per INN, with the KNF (<https://knf.kz>) as the primary reference, complemented by the WHO Model List of Essential Medicines (EML), 23rd list [19], the GVFMC list and WHO essential medicines criteria [4]. The same category was applied to an INN in all years. Vital (V) included agents for resuscitation and emergency cardiovascular care, anticoagulants, antidotes and hemostatics, blood-volume and electrolyte infusions, general and local anesthetics and neuromuscular blockers, insulin and systemic corticosteroids for emergencies, Reserve-group antibiotics and carbapenems. Essential (E) included agents with proven efficacy for elective or specialized therapy, including radiocontrast media, biologics and Access- and Watch-group antibiotics other than carbapenems. Non-essential (N) included agents without established efficacy in the KNF and EML, such as metabolic, “hepatoprotective” and “neuroprotective” agents and parenteral vitamins. The classification was approved by the Formulary Commission. An ABC/VEN matrix was constructed for each year.

AWaRe classification of antibiotics

All antibacterials for systemic use (ATC J01) were classified according to the WHO AWaRe classification of antibiotics, 2023 [16], as Access, Watch, Reserve or Not recommended. Antimycotics for systemic use (ATC J02) are reported separately because the AWaRe classification applies to antibiotics only. Topical and ophthalmic antibacterials were excluded. Because DDD and days of therapy (DOT) were not available, AWaRe results are reported as expenditure-based financial proxies: a high share of Watch or Reserve expenditure may reflect high unit costs, high consumption or both.

Statistical analysis

Absolute values, shares and year-on-year relative changes were calculated. Percentages and totals were calculated from unrounded values; because tables show values rounded to one decimal place, rounded rows may not sum exactly to the totals, and percentages recalculated from rounded values may differ by up to 0.2 percentage points. A control calculation comparing both approaches for Tables 6–8 is provided in Supplementary File S1 (sheet Rounding_check). Given the descriptive design, no hypothesis testing was planned. Analyses were performed in Python 3.11.15 with the pandas 3.0.2 and openpyxl 3.1.5 libraries; all tables were reproduced with spreadsheet formulas in Supplementary File S1.

Ethical considerations

The analysis used de-identified aggregated data on medicine dispensing without patient-level information. The Local Bioethics Committee of the study hospital confirmed that ethical review was not required (Protocol No. 053/CT-91 of 30 April 2026). The full name of the committee is given on the separate title page in accordance with the journal's double-blind review policy. Individual informed consent was not required.

Results

Portfolio and total expenditure

The number of INNs dispensed decreased from 194 in 2022 to 176 in 2023–2024 and to 172 in 2025 (trade-name items: 271, 238, 231 and 236). Total drug expenditure decreased by 7.7% in 2023 (from KZT 372.6 million to 343.9 million), then increased by 11.7% in 2024 (to 384.3 million) and by 36.3% in 2025 (to 523.8 million); the cumulative nominal increase in 2022–2025 was 40.6% (Table 1).

Drug expenditure per bed-day was KZT 4,314, 4,060, 4,714 and 5,828 (+35.1% over the period), and expenditure per discharged patient was KZT 32,936, 31,109, 34,042 and 43,788 (+32.9%). In 2025, bed-days increased by 10.3%, whereas expenditure increased by 36.3%. Expenditure on antibacterials (J01) per bed-day increased from KZT 381 in 2024 to 576 in 2025 (+51.1%), and expenditure on immunosuppressants (L04) per bed-day increased from KZT 547 to 1,327 (+142.8%).

Expenditure by ATC group

Five ATC level 2 groups – contrast media (V08), blood substitutes and perfusion solutions (B05), antithrombotic agents (B01), immunosuppressants (L04) and antibacterials

Table 2

Drug expenditure by ATC level 2 group, 2022–2025, KZT million (% of annual expenditure)

ATC level 2 group	2022	2023	2024	2025
V08 Contrast media	78.2 (21.0)	74.5 (21.7)	64.9 (16.9)	78.3 (15.0)
B05 Blood substitutes and perfusion solutions	59.5 (16.0)	66.8 (19.4)	72.3 (18.8)	86.6 (16.5)
B01 Antithrombotic agents	60.3 (16.2)	47.2 (13.7)	48.1 (12.5)	50.3 (9.6)
L04 Immunosuppressants	10.9 (2.9)	16.2 (4.7)	44.6 (11.6)	119.3 (22.8)
J01 Antibacterials for systemic use	36.1 (9.7)	38.2 (11.1)	31.1 (8.1)	51.8 (9.9)
C01 Cardiac therapy	24.9 (6.7)	15.3 (4.4)	16.7 (4.3)	22.8 (4.4)
N01 Anesthetics	20.1 (5.4)	10.9 (3.2)	24.5 (6.4)	18.5 (3.5)
A02 Drugs for acid related disorders	10.2 (2.7)	11.1 (3.2)	8.6 (2.2)	13.3 (2.5)
B02 Antihemorrhagics	13.1 (3.5)	8.2 (2.4)	8.5 (2.2)	5.7 (1.1)
Other ATC level 2 groups	59.2 (15.9)	55.5 (16.1)	65.1 (16.9)	77.1 (14.7)
Total	372.6 (100.0)	343.9 (100.0)	384.3 (100.0)	523.8 (100.0)

ATC – Anatomical Therapeutic Chemical classification; KZT – Kazakhstani tenge. The nine ATC level 2 groups with the highest cumulative 2022–2025 expenditure are shown. Percentages were calculated from unrounded values; columns may not sum exactly because of rounding.

for systemic use (J01) – accounted for 65.8% of expenditure in 2022 and 73.8% in 2025 (Table 2). L04 expenditure increased from KZT 10.9 million (2.9%) in 2022 to 119.3 million (22.8%) in 2025; ustekinumab and vedolizumab together accounted for KZT 106.5 million (20.3% of total expenditure) in 2025. The share of B01 decreased from 16.2% to 9.6%, and that of V08 from 21.0% to 15.0%.

ABC analysis

Group A contained 37 INNs (19.1%) in 2022 and 26 INNs (15.1%) in 2025, while accounting for 80.0–80.8% of

Table 1

Main indicators of drug supply, 2022–2025

Indicator	2022	2023	2024	2025
Number of INNs dispensed	194	176	176	172
Number of trade-name items dispensed	271	238	231	236
Total drug expenditure, KZT million	372.6	343.9	384.3	523.8
Change from previous year, %	–	–7.7	+11.7	+36.3
J01: number of INNs	24	20	20	18
J01: expenditure, KZT million	36.1	38.2	31.1	51.8
J02: expenditure, KZT million	2.9	4.7	3.4	2.8
J01 + J02: share of total expenditure, %	10.5	12.5	9.0	10.4
L04: expenditure, KZT million	10.9	16.2	44.6	119.3
L04: share of total expenditure, %	2.9	4.7	11.6	22.8
Bed-days	86,363	84,712	81,522	89,878
Discharged patients	11,312	11,056	11,289	11,963
Drug expenditure per bed-day, KZT	4,314	4,060	4,714	5,828
Drug expenditure per discharged patient, KZT	32,936	31,109	34,042	43,788
J01 expenditure per bed-day, KZT	419	451	381	576
L04 expenditure per bed-day, KZT	126	191	547	1,327

INN – International Nonproprietary Name; J01 – antibacterials for systemic use; J02 – antimycotics for systemic use; KZT – Kazakhstani tenge; L04 – immunosuppressants. An INN or trade-name item was counted as dispensed if its expenditure in the given year was above zero. Percentages were calculated from unrounded values. “–” – not applicable: 2022 is the baseline year of the analysis, so no change from the previous year is calculated.

Table 3

ABC analysis at INN level, 2022–2025

Indicator	2022	2023	2024	2025
Group A: number of INNs (% of INNs)	37 (19.1)	30 (17.0)	31 (17.6)	26 (15.1)
Group A: expenditure, KZT million (% of total)	299.3 (80.3)	276.0 (80.3)	307.5 (80.0)	423.2 (80.8)
Group B: number of INNs (% of INNs)	40 (20.6)	40 (22.7)	43 (24.4)	37 (21.5)
Group B: expenditure, KZT million (% of total)	54.7 (14.7)	51.3 (14.9)	58.2 (15.1)	75.3 (14.4)
Group C: number of INNs (% of INNs)	117 (60.3)	106 (60.2)	102 (58.0)	109 (63.4)
Group C: expenditure, KZT million (% of total)	18.6 (5.0)	16.6 (4.8)	18.6 (4.9)	25.3 (4.8)

ABC – classification of medicines by cumulative share of expenditure; INN – International Nonproprietary Name; KZT – Kazakhstani tenge. Criteria: INNs were ranked by annual expenditure in descending order; group A – INNs accounting for the first 80% of expenditure; group B – the next 15% (cumulative 95%); group C – the remaining 5%. Percentages were calculated from unrounded values; columns may not sum exactly because of rounding.

expenditure each year (Table 3). The contraction of group A indicates an increasing concentration of expenditure on fewer high-cost INNs rather than broader formulary coverage.

VEN analysis

The share of expenditure on vital medicines decreased from 50.8% (KZT 189.4 million) in 2022 to 39.3% (KZT 206.1 million) in 2025, whereas the share of essential medicines increased from 48.7% to 58.8% (KZT 308.0 million) (Table 4). The number of non-essential INNs increased from 6 to 16, and their share of expenditure from 0.4% to 1.9% (KZT 1.6 million and 9.7 million); in 2025 this increase was driven by ademetionine (KZT 3.8 million), fructose-1,6-diphosphate (1.9 million), ornithine aspartate (1.2 million) and thioctic acid (1.0 million), all of which were in ABC group B. No non-essential INN entered group A in any year. The share of vital medicines in group A expenditure decreased from 55.0% to 39.8%, reflecting the entry of high-cost essential biologics and radiocontrast media into group A.

Table 4 VEN analysis at INN level, 2022–2025

VEN category	2022	2023	2024	2025
V: number of INNs (% of INNs)	58 (29.9)	52 (29.5)	50 (28.4)	50 (29.1)
V: expenditure, KZT million (% of total)	189.4 (50.8)	157.0 (45.6)	179.0 (46.6)	206.1 (39.3)
E: number of INNs (% of INNs)	130 (67.0)	118 (67.0)	116 (65.9)	106 (61.6)
E: expenditure, KZT million (% of total)	181.6 (48.7)	185.7 (54.0)	202.8 (52.8)	308.0 (58.8)
N: number of INNs (% of INNs)	6 (3.1)	6 (3.4)	10 (5.7)	16 (9.3)
N: expenditure, KZT million (% of total)	1.6 (0.4)	1.3 (0.4)	2.5 (0.7)	9.7 (1.9)
ABC group A: V / E / N INNs	18 / 19 / 0	11 / 19 / 0	15 / 16 / 0	11 / 15 / 0
V share of ABC group A expenditure, %	55.0	44.9	48.4	39.8

ABC – classification of medicines by cumulative share of expenditure; E – essential; INN – International Nonproprietary Name; KZT – Kazakhstani tenge; N – non-essential; V – vital; VEN – vital, essential, non-essential classification. Percentages were calculated from unrounded values.

Leading INNs

Table 5 lists the ten INNs with the highest cumulative expenditure in 2022–2025. Iohexol ranked first in 2022–2024 (KZT 47.5, 44.1 and 45.9 million). In 2025, ustekinumab ranked first (KZT 67.0 million), followed by albumin and vedolizumab (KZT 39.5 million each); ustekinumab and vedolizumab were already dispensed in 2022 (KZT 4.5 and 6.4 million, respectively).

Table 5 Ten INNs with the highest cumulative expenditure, 2022–2025, KZT million

INN	ATC code	VEN	2022	2023	2024	2025	2022–2025
Iohexol	V08AB02	E	47.5	44.1	45.9	35.7	173.3
Enoxaparin	B01AB05	V	27.7	23.1	23.6	34.8	109.2
Ustekinumab	L04AC05	E	4.5	6.6	22.2	67.0	100.4
Albumin (human)	B05AA01	V	13.5	20.4	25.0	39.5	98.5
Sodium chloride 0.9% (infusion)	B05BB01	V	21.9	21.1	21.9	23.8	88.8
Vedolizumab	L04AA33	E	6.4	9.6	18.5	39.5	73.9
Sevoflurane	N01AB08	V	14.5	7.0	16.3	11.6	49.4
Iopromide	V08AB05	E	8.5	11.5	3.2	18.8	42.1
Meropenem	J01DH02	V	9.9	13.3	6.1	12.6	41.8
Gadobutrol	V08CA09	E	4.8	8.6	8.1	12.4	33.9

ATC – Anatomical Therapeutic Chemical classification; E – essential; INN – International Nonproprietary Name; KZT – Kazakhstani tenge; V – vital; VEN – vital, essential, non-essential classification. Selection criterion: the ten INNs with the highest cumulative 2022–2025 expenditure; expenditure on all trade names of one INN was summed. Sodium chloride 0.9% solution for infusion (B05BB01) is shown; sodium chloride solutions for injection (B05XA03) are counted separately.

Antibiotics and AWaRe signals

The number of antibacterial INNs decreased from 24 in 2022 to 20 in 2023–2024 and to 18 in 2025 (Table 1). Expenditure on J01 and J02 agents was KZT 39.1, 42.9, 34.5 and 54.6 million (+58.4% in 2025 compared with 2024), and J01 expenditure alone was KZT 36.1, 38.2, 31.1 and 51.8 million (+66.6% in 2025). Expenditure by INN is shown in Table 6 (Watch group) and Table 7 (Access, Reserve and Not recommended groups).

Table 6 Expenditure on Watch-group antibacterials (J01) by INN, 2022–2025, KZT million

INN	ATC code	AWaRe group	2022	2023	2024	2025
Meropenem	J01DH02	Watch	9.9	13.3	6.1	12.6
Piperacillin/tazobactam	J01CR05	Watch	2.5	3.3	6.7	14.8
Ceftriaxone	J01DD04	Watch	3.2	3.4	6.5	10.3
Cefuroxime	J01DC02	Watch	3.8	5.1	<0.1	–
Vancomycin	J01XA01	Watch	1.8	0.7	0.9	1.9
Ceftazidime	J01DD02	Watch	2.1	1.4	1.5	–
Ciprofloxacin	J01MA02	Watch	0.5	0.6	0.6	0.6
Levofloxacin	J01MA12	Watch	0.7	0.2	1.1	0.1
Cefepime	J01DE01	Watch	0.8	0.4	0.4	–
Imipenem/cilastatin	J01DH51	Watch	1.5	–	–	–
Doripenem	J01DH04	Watch	0.8	0.3	–	–
Azithromycin	J01FA10	Watch	<0.1	0.3	0.2	–
Clarithromycin	J01FA09	Watch	0.1	<0.1	<0.1	<0.1
Moxifloxacin	J01MA14	Watch	0.2	–	–	–
Total Watch			27.9	28.9	24.2	40.4

ATC – Anatomical Therapeutic Chemical classification; AWaRe – WHO Access, Watch, Reserve classification of antibiotics (2023); INN – International Nonproprietary Name; J01 – antibacterials for systemic use; KZT – Kazakhstani tenge; WHO – World Health Organization. Expenditure is the value dispensed according to the pharmacy ledger; “–” – not dispensed; “<0.1” – below KZT 0.1 million. The AWaRe group is shaded in the WHO color coding (Watch – yellow). Rows are ordered by cumulative expenditure. Totals were calculated from unrounded values; rounded rows may differ from the total by up to 0.2 (Supplementary File S1, sheet Rounding_check).

Table 7

Expenditure on Access-, Reserve- and Not recommended antibacterials (J01) by INN, 2022–2025, KZT million

INN	ATC code	AWaRe group	2022	2023	2024	2025
Amoxicillin/ clavulanic acid	J01CR02	Access	1.8	1.9	0.2	0.4
Metronidazole	J01XD01	Access	0.8	0.8	0.8	1.5
Cefazolin	J01DB04	Access	1.3	0.8	0.5	0.5
Amikacin	J01GB06	Access	0.1	0.4	0.8	1.8
Gentamicin	J01GB03	Access	0.1	0.1	0.1	0.1
Amoxicillin	J01CA04	Access	–	–	<0.1	<0.1
Sulfamethoxazole/ trimethoprim	J01EE01	Access	<0.1	–	–	–
Total Access			4.2	4.1	2.4	4.4
Colistin	J01XB01	Reserve	2.8	2.9	3.2	1.9
Linezolid	J01XX08	Reserve	0.5	2.2	1.3	0.5
Ceftazidime/ avibactam	J01DD52	Reserve	–	–	–	4.0
Ceftaroline fosamil	J01DI02	Reserve	–	–	–	0.5
Tigecycline	J01AA12	Reserve	0.4	–	–	–
Polymyxin B	J01XB02	Reserve	–	–	–	<0.1
Total Reserve			3.7	5.0	4.5	7.0
Cefoperazone/ sulbactam	J01DD62	Not recom- mended	0.4	0.3	0.1	–
Total Not recommended			0.4	0.3	0.1	–

ATC – Anatomical Therapeutic Chemical classification; AWaRe – WHO Access, Watch, Reserve classification of antibiotics (2023); INN – International Nonproprietary Name; J01 – antibacterials for systemic use; KZT – Kazakhstani tenge; WHO – World Health Organization. “–” – not dispensed; “<0.1” – below KZT 0.1 million. AWaRe groups are shaded in the WHO color coding (Access – green, Reserve – red); cefoperazone/sulbactam is classified by WHO as Not recommended. Rows are ordered by cumulative expenditure within each group. Totals were calculated from unrounded values (see note to Table 6).

Table 8

Distribution of J01 expenditure by AWaRe group and expenditure on antimycotics (J02), 2022–2025, KZT million (%)

Group / INN	2022	2023	2024	2025
Access	4.2 (11.5)	4.1 (10.6)	2.4 (7.6)	4.4 (8.4)
Watch	27.9 (77.1)	28.9 (75.5)	24.2 (77.8)	40.4 (78.1)
Reserve	3.7 (10.3)	5.0 (13.2)	4.5 (14.4)	7.0 (13.5)
Not recommended	0.4 (1.1)	0.3 (0.7)	0.1 (0.2)	–
Total J01	36.1 (100.0)	38.2 (100.0)	31.1 (100.0)	51.8 (100.0)
Amphotericin B (lipid complex) (J02AA01)	2.0	4.4	3.0	2.6
Caspofungin (J02AX04)	0.7	0.1	0.2	–
Fluconazole (J02AC01)	0.3	0.2	0.2	0.2
Total J02	2.9	4.7	3.4	2.8
Total J01 + J02	39.1	42.9	34.5	54.6

AWaRe – WHO Access, Watch, Reserve classification of antibiotics (2023); INN – International Nonproprietary Name; J01 – antibacterials for systemic use; J02 – antimycotics for systemic use; KZT – Kazakhstani tenge; WHO – World Health Organization. For AWaRe groups, values are KZT million (% of J01 expenditure); for J02, KZT million. The AWaRe classification applies to antibiotics only; antimycotics are therefore shown separately. AWaRe groups are shaded in the WHO color coding (Access – green, Watch – yellow, Reserve – red). “–” – not dispensed. Percentages were calculated from unrounded values and may differ by up to 0.2 percentage points from those recalculated from the rounded values shown (e.g., Watch, 2022: $27.9/36.1 = 77.3\%$, compared with 77.1% from unrounded values); control calculation: Supplementary File S1, sheet Rounding_check.

Watch agents accounted for 77.1%, 75.5%, 77.8% and 78.1% of J01 expenditure in 2022–2025, Reserve agents for 10.3%, 13.2%, 14.4% and 13.5%, and Access agents for 11.5%, 10.6%, 7.6% and 8.4% (Table 8). Cefoperazone/sulbactam, classified by WHO as Not recommended, accounted for 1.1% in 2022 and was not dispensed in 2025. The increase in 2025 was driven by piperacillin/tazobactam (KZT 14.8 million in 2025 compared with 6.7 million in 2024), meropenem (12.6 and 6.1 million, respectively) and ceftriaxone (10.3 and 6.5 million) and by the introduction of the Reserve agents ceftazidime/avibactam (KZT 4.0 million), ceftaroline fosamil (0.5 million) and polymyxin B (<0.1 million). Colistin (KZT 1.9–3.2 million per year) and linezolid (0.5–2.2 million) were dispensed in every year. Among antimycotics, lipid-complex amphotericin B accounted for KZT 2.0, 4.4, 3.0 and 2.6 million (Table 8).

Discussion

This four-year analysis of complete pharmacy ledgers shows a contraction of the hospital formulary together with a reallocation of expenditure toward high-cost biologics and toward Watch and Reserve antibiotics. The absence of non-essential medicines from ABC group A indicates procurement discipline for the highest-cost items, whereas the growth of non-essential expenditure in 2025 and the expansion of biologic and antibiotic expenditure are the main management challenges.

The increase in L04 expenditure from 2.9% to 22.8% of the drug budget marks a substantial change in tertiary-care pharmacotherapy. Biological medicines are recognized drivers of pharmaceutical expenditure growth in European health systems, where biosimilar uptake and related policies are used to contain this growth [20]. Ustekinumab and vedolizumab alone accounted for one fifth of expenditure in 2025. These agents are effective in moderate-to-severe inflammatory bowel disease [21], but their cost requires governance: indication-based prescribing, monitoring of treatment outcomes and pharmacoeconomic evaluation. European experience shows that pricing, reimbursement and procurement policies can improve affordable access to high-cost medicines [22]; comparable institutional and national mechanisms are warranted in Kazakhstan.

The ABC/VEN results show that group A remained free of non-essential medicines, but the share of vital medicines within group A decreased because high-cost essential biologics and radiocontrast media entered this group. The increase in non-essential expenditure in 2025, mainly on metabolic and “hepatoprotective” agents, was small in absolute terms but is directly actionable by the formulary commission. VEN categories should be revalidated regularly against the updated EML and KNF [19].

The 66.6% nominal increase in J01 expenditure in 2025, concentrated in Watch and Reserve agents, represents a substantial fiscal reallocation toward higher-tier antimicrobials. Because the ledgers lack DDD and DOT denominators, this trend cannot be interpreted as proof of excessive consumption or inappropriate prescribing; rather, it identifies agents that should be prioritized for prospective audit and feedback. The WHO target of at least 60% Access use refers to consumption at national level and is therefore not directly comparable with hospital expenditure shares [16]. In Central Asia, where the AMR burden is documented and antimicrobial stewardship (AMS) infrastructure is still developing [13–15,23], such financial signals can help formulary commissions target limited stewardship resources. Future analyses should link expenditure

to DDD or DOT metrics to separate price effects from consumption intensity.

Compared with earlier studies from Kazakhstan, which were limited to one department or to the pandemic period [10,11], the present analysis covers the complete medication ledger of a tertiary hospital over four years, uses INN-level classification and activity denominators, and provides item-level calculations for verification. At the institutional level, structured dashboards combining ABC/VEN and AWaRe indicators could give formulary commissions actionable data to balance clinical need against financial sustainability; at the national level, the approach can be reproduced in other hospitals with routinely available ledgers and could support multicenter benchmarking.

Limitations

First, this is a single-center study, and generalizability to other hospitals in Kazakhstan is limited. Second, the ledgers record dispensing from the central pharmacy to wards rather than administration to patients and INN and ATC assignment was performed by the authors from trade names. Third, expenditure-normalized metrics per bed-day were reported, but DDD- or DOT-based consumption could not be calculated. Fourth, VEN assignment was performed institutionally with reference to the EML and KNF and may differ from that of other institutions or specialty cohorts. Fifth, all monetary indicators are nominal KZT values, not adjusted for inflation or converted to purchasing power parity; given the cumulative growth of consumer and pharmaceutical prices in Kazakhstan in 2022–2025, the real increase in expenditure is smaller than the nominal 40.6%. Sixth, the ledgers do not record clinical indications or appropriateness of use. Seventh, the AWaRe classification was applied to expenditure shares rather than consumption volumes, so the predominance of Watch-group spending may reflect the high acquisition cost of newer beta-lactam/beta-lactamase inhibitor combinations rather than high prescribing volume. AWaRe results should therefore be regarded as financial proxies for stewardship prioritization, not as direct measures of prescribing quality.

Implications

For tertiary hospitals, we recommend (1) structured AMS programs with AWaRe dashboards; (2) pharmacoeconomic review of high-cost L04 medicines; (3) continued ABC/VEN monitoring with zero tolerance for non-essential medicines in group A and review of non-essential expenditure; and (4) multicenter ATC networks to enable national benchmarking.

Conclusion

In 2022–2025, the study hospital reduced its formulary from 194 to 172 INNs, while nominal drug expenditure increased by 40.6% and expenditure per bed-day by 35.1%. This growth was driven mainly by biologics, which changed the structure of the drug budget, and by increased spending on Watch and Reserve antibiotics.

The ABC/VEN analysis showed that expenditure remained concentrated in high-cost therapeutic groups and that non-essential medicines were absent from group A, although non-essential expenditure increased in 2025. The shift toward Watch and Reserve agents supports expenditure-based AWaRe monitoring as a prioritization tool for stewardship.

These conclusions are limited by the single-center design, nominal prices and the absence of DDD-based consumption data.

Integrated pharmacoeconomic monitoring at the institutional level and multicenter pharmacoepidemiological studies with consumption metrics are needed to establish national benchmarks and to inform rational medicine use policies in Kazakhstan.

Supplementary materials

The Supplementary information includes:

- Supplementary File S1. Primary data and calculations underlying Tables 1–8.

Supplementary File S1 (Excel) contains all 1,132 rows of the “Medications” section of the 2022–2025 ledgers with the assigned INN, ATC code, VEN category, AWaRe group and reason for exclusion, and reproduces Tables 1–8 with spreadsheet formulas; the sheet `Rounding_check` compares totals and percentages derived from unrounded and rounded values for Tables 6–8.

These supplementary materials have been provided by the authors to give readers additional information about their work.

The file can be accessed using: https://www.editorialpark.com/download/article-suppl/792/JCMK-48096-2026-R4_Supplementary_File_S1_4.xlsx.

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Data availability statement: Item-level data and all calculations underlying Tables 1–8 are provided in Supplementary File S1. The original pharmacy ledgers contain commercially sensitive procurement details and are available from the corresponding author on reasonable request and with institutional approval.

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