PLEURAL EMPYEMA AND EXUDATIVE PLEURISY: CLINICAL EXPERIENCE, ANINTEGRATED APPROACH TO EVIDENCE

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Introduction

Pleural complications, such as pleural empyema and exudative pleurisy, are serious forms of respiratory diseases, which are accompanied by a significant inflammatory process in the pleural cavity, the risk of sepsis, destruction of lung tissue and require immediate comprehensive treatment. One of the foundations of therapy for these conditions is the rational use of antibiotics, which should be based on the principles of evidence-based medicine, pathogen sensitivity and international recommendations [1].

Among the etiological factors of pleural empyema, Streptococcus pneumoniae, Staphylococcus aureus, including methicillin-resistant (MRSA), anaerobic bacteria, Enterobacterales and Pseudomonas aeruginosa are most often isolated. Therefore, antimicrobial therapy should cover a wide spectrum of action, including drugs with activity against aerobic and anaerobic microorganisms. The selection of the optimal drug is complicated by the increasing level of antimicrobial resistance, the limited availability of certain antibiotics on the Ukrainian market, as well as discrepancies between clinical guidelines of different countries [2].

Even though several international organizations, particularly the British Thoracic Society, Infectious Diseases Society of America, ESCMID, NICE and HAS, have published recommendations for the treatment of pleural infections, Ukraine still lacks a unified clinical guideline that would integrate the modern evidence base, local epidemiological data and pharmacoeconomic aspects. In the practice of doctors, empirical prescription of antibiotics is often observed, which does not always meet modern standards, as well as the use of drugs not presented in the national lists or tables of equipment of health care institutions [3].

In this regard, clinical experience in methods of diagnosis, treatment, systematic analysis of international non-proprietary names of antibiotics recommended for the treatment of pleural empyema and exudative pleurisy is particularly relevant. Such an integrated approach allows us to establish optimal methods of diagnosis and treatment, to assess not only the degree of "recognition" of these drugs in leading clinical guidelines, but also their "availability" in the regulatory field of Ukraine (registration, inclusion in the National List, equipment list, state procurement), the frequency of their actual use in clinical practice, and to substantiate the needs for improving the policy of combating antimicrobial resistance [4].

In addition, the generalization of such data using an integrated assessment, classification by Anatomical Therapeutic Chemical Classification (ATC) groups, physician questionnaires, and network meta-analysis allows us to build a rational model of antibiotic selection for pharmacotherapy of pleural complications, considering international experience and the realities of the Ukrainian healthcare system. This is an important step towards creating effective and safe antibiotic therapy aimed at reducing mortality, complications, and duration of hospitalization of patients with purulent-inflammatory diseases of the pleura.

Purpose of the study

The purpose of the study was to analyze clinical practice in diagnostics and treatment, conduct a systematic network meta-analysis of antimicrobial drugs listed by international non-proprietary names used in the pharmacotherapy of pleural empyema and exudative pleurisy, to assess their compliance with modern international and national clinical guidelines, as well as determine the level of their recognition and regulatory availability in Ukraine.

Additional objectives of the study are:

- comparison of the list of antibiotics recommended in clinical protocols of Ukraine, the European Union, France, and Kazakhstan for the treatment of pleural infections;
- analysis of the availability of relevant drugs in the State Register of Medicines of Ukraine, the National List of Essential Medicines, the Equipment Table, and public procurement;
- study of the practice of prescribing antibiotics in healthcare institutions of Ukraine based on the results of a survey of doctors;
- formation of an evidence bases for optimizing drug formulas, reviewing regulatory support, and improving the policy of combating antimicrobial resistance in the context of treating pleural complications.

Materials and methods

The study conducted a systematic analysis of clinical guidelines, regulatory legal acts, state drug registries and the results of a survey of doctors to form an evidence base on the effectiveness, availability and clinical use of antibiotics recommended for the pharmacotherapy of pleural empyema and exudative pleurisy. The object of the analysis was antimicrobial drugs indicated by international non-proprietary names (n=32), which are included in the official evidence-based guideline on antimicrobial therapy developed by DUODECIM Medical Publications Ltd. (Finland) [5].

The clinical part of the study was carried out at the Lung Health Center in Lviv from 2017 to 2022. The total number of patients was 556. There were 456 men among the patients, or 82%; women -100 people, or 18%. The ratio between men and women was 5:1. Most patients were aged 40-60 years (61.9%). All patients underwent

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general clinical examination methods. Chest radiography in two projections was mandatory. Ultrasound diagnostics was also used according to indications according to the previously described method [6]. Thoracoscopic and videothoracoscopic examination methods were practically not used, and were performed in isolated cases. Ethical clearance was obtained from the administration of the Danylo Halytsky Lviv National Medical University

Sources of information

The study used open, official, and bibliographic sources of information, in particular:

• National clinical guidelines and standards of medical care of the Ministry of Health of Ukraine, posted on the platform of the Center for Medical Information Systems;

• European clinical recommendations: ESCMID, NICE, IDSA;

• Protocols of France (Haute Autorité de Santé), Kazakhstan, and other international sources;

• State Register of Medicines of Ukraine (as of 2024);

• Regulatory documents: National List of Essential Medicines, Sample Table of Material and Technical Equipment of Healthcare Institutions, Public Procurement Register (Prozorro);

• Bibliographic databases: PubMed, Cochrane Library, Scopus, Web of Science, Embase, Google Scholar (coverage period: 2010–2024);

• Results of a survey of primary and secondary care physicians in four regions of Ukraine on the practice of prescribing antibiotics in the treatment of pleural infections.

Inclusion and exclusion criteria

The analysis included antibiotics that met the following conditions:

• mentioned in clinical guidelines or standards in the form of international non-proprietary names;

• recommended for the treatment of pleural infections in a hospital or outpatient setting;

• registered in Ukraine and available in at least one of the regulatory documents (National List, Table of Equipment, Prozorro);

• confirmed in at least three international sources of evidence-based medicine.

The following were excluded:

• drugs that are experimental, veterinary, or withdrawn from circulation;

• drugs that are not registered in Ukraine as of 2024;

• combined antimicrobial regimens where it is impossible to isolate a separate active substance.

Analytical strategy

The method of multidimensional systems analysis with elements of network meta-analysis was used. The comparative assessment was carried out according to two main integral criteria:

1. Recognition – assessment of the mention of international non-proprietary names in clinical guidelines of Ukraine, the European Union, France, and Kazakhstan (maximum – 4 points);

2. Availability – assessment of the presence of the antibiotic in the State Register of Medicinal Products, the National List, the Equipment Table, and the Prozorro public procurement system (maximum – 4 points).

The calculations were carried out by an expert group of medical and pharmaceutical specialists with the calculation of arithmetic mean values. The data were visualized in the form of tables and histograms. Microsoft Excel 2019 and STATA 13 were used to construct diagrams and graphs.

Additional methods

• The literature search was carried out using the following keywords: antibiotics, antibacterial therapy, empyema, pleuritis, clinical guidelines, meta-analysis, recognition, availability, Ukraine, evidence-based medicine.

• The study was structured according to the PICO (Population, Intervention, Comparator, Outcome) approach.

• The analytical task was formulated according to the SMART (specific, measurable, achievable, relevant, time-bound) concept.

• The systematization of the results met the requirements of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and GRADE (Grading of Recommendations Assessment, Development and Evaluation), which ensured the transparency of the analysis and the reliability of the conclusions.

The research methodology included an integrated approach based on clinical practice, clinical-pharmacological, network meta-analysis, regulatory availability of antimicrobial drugs for pharmacotherapy of pleural empyema and exudative pleurisy.

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Results and discussion

Clinical practice

Out of 556 patients, nonspecific genesis was found in 48.7%. Patients complained of an increase in body temperature to 39-40 C. Almost all patients noted the presence of cough, pain in the affected half of the chest,

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shortness of breath with an accelerated respiratory rate. Septic condition is more pronounced with a large amount of pus in the pleural cavity, but was observed in almost all patients. The X-ray method of diagnosis was practically decisive for various pulmonary pathologies. The characteristic radiological signs were the following: horizontal level of shadowing, which extended to the diaphragm. It was the horizontal level of shadowing that also indicated the presence of air in the pleural cavity. Thoracoscopy as a diagnostic method was performed in 12 cases. After complete removal of pus from the pleural cavity in these cases, the pleural cavity was thoroughly washed with antiseptic agents.

Evidence-based antimicrobials

To assess the level of recognition of antimicrobials recommended in the DUODECIM guideline, a comparative analysis of clinical guidelines from four different sources was conducted: Ukraine, the European Union, France, and Kazakhstan. This choice was made in order to provide a comprehensive analysis that covers different models of pharmaceutical systems and approaches to antibiotic therapy.

The analysis of Ukrainian guidelines is critically important for the practical application of the study results, as it allows for a direct assessment of the relevance of existing recommendations in national clinical practice. Given the processes of European integration and the need to harmonize treatment protocols with European standards, this study will contribute to the updating of approaches to antibiotic therapy in Ukraine. This work is of particular importance in the context of increasing antibiotic resistance and reforming the healthcare system.

EU guidelines, in particular NICE and ESCMID, serve as an international standard for pharmacotherapy, based on the principles of evidence-based medicine. Using these sources allows for the integration of the best global practices and the high standards set by regulatory bodies such as the EMA. A comparative analysis with EU recommendations provides a reliable criterion for assessing the effectiveness and safety of antibiotics.

France was singled out in a separate category because it has its own, developed school of clinical pharmacology. The ANSM and Haute Autorité de Santé (HAS) guidelines are of high quality and internationally recognized. The analysis of individualized French experience allows for its comparison with pan-European approaches, which reveals the peculiarities of national clinical practice within a single regulatory space.

Kazakhstan was chosen as an example of a country with a post-Soviet healthcare system like the Ukrainian one. This allows for a correct comparison of antibiotic use in conditions where there is a hybrid model of clinical practice that combines post-Soviet traditions with elements of international standards. Data from Kazakhstan will help assess the effectiveness of integrating international recommendations in similar conditions and identify potential problems and advantages of such an approach.

This allows for a multi-vector analytical framework for meta-analysis, including clinical validity, practical feasibility, and availability of antibiotics [22-24].

A normative analysis was used to identify whether each of the 32 antibiotics was mentioned by its international non-proprietary name in the protocols of these countries (Table 1). If the international non-proprietary name was explicitly mentioned as recommended for use in the treatment of pleural empyema and exudative pleurisy in adults, it received one point per country. The maximum score was four (4), the minimum was zero (0).

The results show that the greatest number of coincidences is observed between the French and European Union guidelines. Ukraine demonstrates partial compliance with international approaches, but some drugs that are widely used in France or the EU do not have official recommendations in Ukrainian documents. Kazakhstan's protocols show a tendency to use a wider range of antibiotics, including reserve groups, but not always with a sufficient level of evidence.

Analysis of the histogram of antibiotic distribution by level of recognition in clinical guidelines of four countries (Ukraine, European Union countries, France, Kazakhstan) showed significant variability in recommendations for the use of specific international non-proprietary names of drugs. Thus, ten antibiotics, which constitute 31.3% of the total, received the maximum score of four points, i.e. were recognized in clinical protocols of all four countries. Another twelve drugs (37.5%) demonstrated partial recognition, scoring three points, which indicates their presence in at least three sources. Six antibiotics (18.8%) are mentioned in only one or two national protocols, which indicates limited recognition or local specificity of prescriptions. Four drugs (12.5%) were not recommended at all in any of the analyzed clinical documents, which may indicate a loss of relevance, insufficient evidence base or their lack of use in modern international practice for the treatment of pleural infections. This distribution emphasizes the need for harmonization of national protocols with leading international recommendations, as well as a critical assessment of existing standards, considering changes in pathogen susceptibility and antimicrobial resistance.

The drugs with the highest frequency of recognition (4 points) in all the studied guidelines include:

These drugs can be considered as priority candidates for the formation of a standard national drug formulary and key positions in centralized procurement, given their wide recognition by the international community and proven effectiveness.

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Table 1: Table with scores (0–4) for the parameter “recognition” for each drug

No.	International Non-proprietary Name	Ukraine	EU (ESCIMD/NICE)	France (HAS)	Kazakhstan	Total amount (0–4)
1	Amoxicillin	1	1	1	1	4
2	Amoxicillin + clavulanic acid	1	1	1	1	4
3	Ceftriaxone	1	1	1	1	4
4	Cefuroxime	1	1	1	1	4
5	Ciprofloxacin	1	1	1	1	4
6	Azithromycin	1	1	1	1	4
7	Doxycycline	1	1	1	1	4
8	Levofloxacin	1	1	1	1	4
9	Cefixime	1	1	1	1	4
10	Clarithromycin	1	1	1	1	4
11	Cefotaxime	0	1	1	1	3
12	Amikacin	1	0	1	1	3
13	Trimethoprim + sulfamethoxazole	1	1	0	1	3
14	Metronidazole	1	1	0	1	3
15	Linezolid	1	1	1	0	3
16	Vancomycin	1	1	1	1	4
17	Cefazidime	1	1	1	1	4
18	Cefepime	0	1	1	1	3
19	Cefoperazone + sulbactam	0	0	0	1	1
20	Tetracycline	1	0	0	1	2
21	Erythromycin	1	1	1	1	4
22	Gentamicin	1	1	1	1	4
23	Amikacin	1	0	1	1	3
24	Meropenem	1	1	1	1	4
25	Imipenem + cilastatin	1	1	1	1	4
26	Ertepenem	0	1	1	1	3
27	Fosfomycin	1	1	0	1	3
28	Colistin	1	0	1	1	3
29	Clindamycin	1	1	1	1	4
30	Furazidine	1	0	0	1	2
31	Cephalexin	1	1	1	1	4
32	Colistin	1	0	1	1	3

Notes to the table:• Data are based on an analysis of open clinical guidelines and public sources as of 2024. • In cases where a drug is not included in official protocols, the score is 0. • Some drugs may only be available in internal hospital protocols or used empirically.

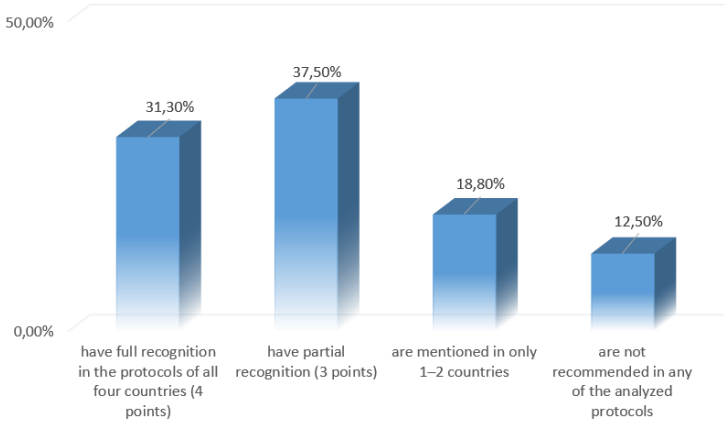

Figure 1. Histogram of drug distribution by level of recognition

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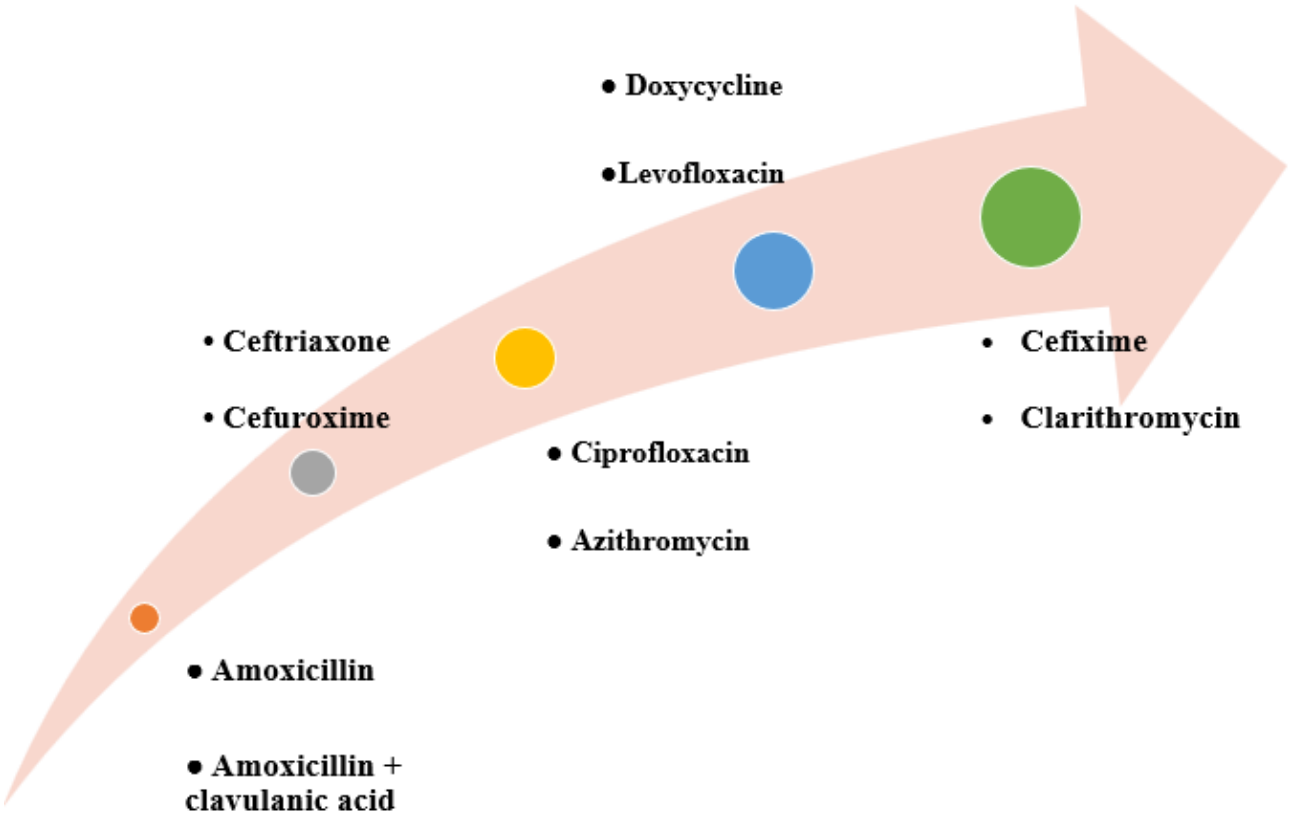

Figure 2. Leaders in terms of compliance with international guidelines

Availability of antimicrobial drugs

To assess the availability of antimicrobial drugs in Ukraine, an analysis of four official sources was conducted:

• State Register of Medicines of Ukraine – the presence of registered trade names for each international non-proprietary name;

• National List of Essential Medicines – reflects priority drugs for ensuring state guarantees of medical care;

• Sample list of material and technical equipment of healthcare institutions – determines which antibiotics should be present in medical institutions of different levels;

• Information on state procurement for the last 3 years (2021–2023), according to Prozorro data – allows us to assess the actual centralized procurement of medicines from budget funds.

The drug was considered available in each of the sources if the international non-proprietary name is clearly mentioned in the regulatory document or at least one registered form is present in the relevant register.

The assessment was carried out according to a scheme like the previous section: 1 point was assigned for each source in which the drug is available. The maximum amount is 4 points.

Analysis of the data in Table 2 shows that most antimicrobial drugs recommended for the treatment of pleural empyema and exudative pleurisy have a high level of regulatory presence on the pharmaceutical market of Ukraine. Thus, twenty-four out of thirty-two analyzed international non-proprietary names (75%) received the maximum possible score of four points, which indicates their simultaneous presence in the State Register of Medicines of Ukraine, the National List of Essential Medicines, the Model Equipment Table and in tender procurements of the Prozorro system. This group includes first-line drugs for the treatment of respiratory infections, in particular amoxicillin, amoxicillin with clavulanic acid, azithromycin, ceftriaxone, levofloxacin, metronidazole, vancomycin, gentamicin, meropenem and others.

Individual drugs demonstrate partial presence: clarithromycin, moxifloxacin, colistin, fosfomycin are available from three of the four sources and received three points each. Four other International Non-proprietary Names, such as cefotaxime, cefoperazone with sulbactam, ertapenem and tetracycline, were found to be available in only one or two regulatory documents, which is indicated by a sum of points of two or less. This may indicate insufficient systemic support for these drugs in the state procurement policy and formulary regulation. At the same time, the presence of drugs such as cefotaxime, mentioned twice in the table, indicates the need to clarify the unification of data and possible duplicate classification.

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Table 2: Table with points according to the "availability" criterion (0–4)

No.	International Non-proprietary Name	SRM*	NLEM**	Table	Prozorro	Total (0–4)
1	Amoxicillin	1	1	1	1	4
2	Amoxicillin + clavulanic acid	1	1	1	1	4
3	Ceftriaxone	1	1	1	1	4
4	Cefuroxime	1	1	1	1	4
5	Ciprofloxacin	1	1	1	1	4
6	Azithromycin	1	1	1	1	4
7	Doxycycline	1	1	1	1	4
8	Levofloxacin	1	1	1	1	4
9	Cefixime	1	1	1	1	4
10	Clarithromycin	1	1	0	1	3
11	Cefotaxime	1	1	0	0	2
12	Amikacin	1	1	1	1	4
13	Trimethoprim + sulfamethoxazole	1	1	1	1	4
14	Metronidazole	1	1	1	1	4
15	Linezolid	1	1	1	1	4
16	Vancomycin	1	1	1	1	4
17	Cefazidime	1	1	1	1	4
18	Cefepime	1	1	1	1	4
19	Cefoperazone + sulbactam	1	0	0	1	2
20	Tetracycline	1	0	0	0	1
21	Erythromycin	1	1	1	1	4
22	Gentamicin	1	1	1	1	4
23	Meropenem	1	1	1	1	4
24	Imipenem + cilastatin	1	1	1	1	4
25	Ertepenem	1	0	0	1	2
26	Fosfomycin	1	0	1	1	3
27	Colistin	1	0	1	1	3
28	Clindamycin	1	1	1	1	4
29	Furazidine	1	1	1	1	4
30	Cephalexin	1	1	1	1	4
31	Cefotaxime	1	1	0	0	2
32	Moxifloxacin	1	1	0	1	3

* State Register of Medicines of Ukraine
** National List of Essential Medicines

Overall, the structure of drug distribution by the criterion of availability is relatively balanced, however, the identified examples of limited regulatory status of individual antibiotics recommended by international guidelines for the treatment of pleural infections emphasize the need to harmonize national approaches with modern clinical needs and standards of evidence-based medicine.

According to the criterion of maximum accessibility in all four regulatory sources (4 points), the leaders are:

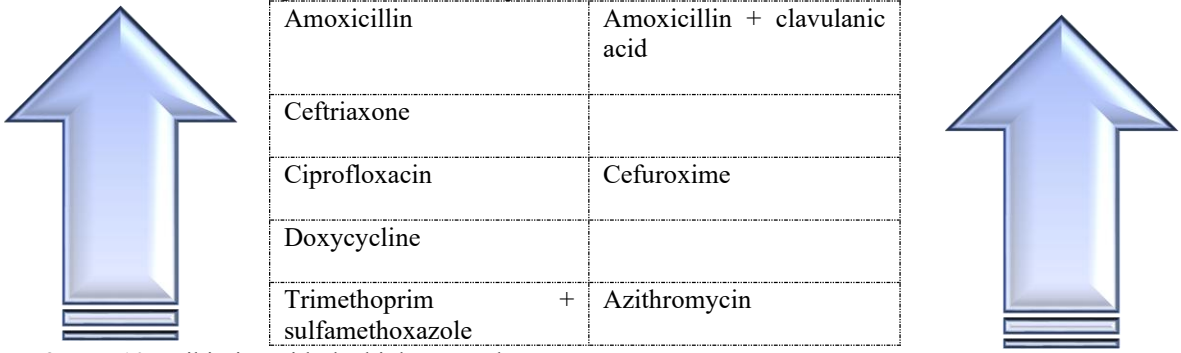

Figure 3. Top 10 antibiotics with the highest regulatory presence

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These drugs form the basis of standard antimicrobial therapy in Ukraine and have the highest availability for procurement and use in clinical practice for the treatment of pleural empyema and exudative pleurisy.

Despite the high regulatory availability of individual antibiotics, some of them do not have systematic recognition in international clinical protocols.

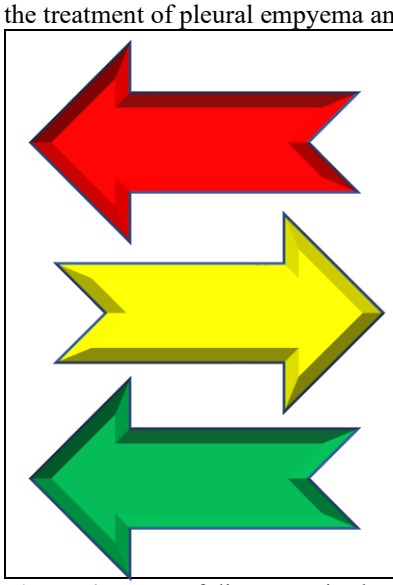	**Cefoperazone + sulbactam**	available in DRLD and procurement, but practically absent in the guidelines of France, EU and Ukraine
	Tetracycline	registered drug, but has low clinical acceptance and limited use
	Ertepenem	presented in procurement, but absent in the National List and Equipment Table, which may complicate its procurement at the regional level

Figure 4. Cases of discrepancies between guidelines and registration status

Table 3: Construction of an integral table (0–8 points)

No.	International Non-proprietary Name	Recognition	Availability	Total amount (0–8)
1	Amoxicillin	4	4	8
2	Amoxicillin + clavulanic acid	4	4	8
3	Ceftriaxone	4	4	8
4	Cefuroxime	4	4	8
5	Ciprofloxacin	4	4	8
6	Azithromycin	4	4	8
7	Doxycycline	4	4	8
8	Levofloxacin	4	4	8
9	Cefixime	4	4	8
10	Clarithromycin	4	3	7
11	Cefotaxime	3	2	5
12	Amikacin	3	4	7
13	Trimethoprim + sulfamethoxazole	3	4	7
14	Metronidazole	3	4	7
15	Linezolid	3	4	7
16	Vancomycin	4	4	8
17	Cefazidime	4	4	8
18	Cefepime	3	4	7
19	Cefoperazone + sulbactam	1	2	3
20	Tetracycline	2	1	3
21	Erythromycin	4	4	8
22	Gentamicin	4	4	8
23	Meropenem	4	4	8
24	Imipenem + cilastatin	4	4	8
25	Ertepenem	3	2	5
26	Fosfomycin	3	3	6
27	Colistin	3	3	6
28	Clindamycin	4	4	8
29	Furazidine	2	4	6
30	Cephalexin	4	4	8
31	Moxifloxacin	3	3	6
32	Ampicillin	2	1	3

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Such discrepancies indicate the need for regular review of the regulatory framework, considering modern clinical guidelines and the principles of evidence-based medicine.

To form a generalized rating of antimicrobial drugs, an integral score was calculated as the sum of points according to two independent criteria:

• Recognition (recognition in clinical guidelines of 4 countries, maximum 4 points)

• Availability (availability in SRM, NLEM, Equipment Table, Prozorro procurement, maximum 4 points)

The integral scale varies from 0 to 8 points.

Analysis of the integrated table, which combines the indicators of recognition of antibiotics in clinical guidelines and regulatory availability in Ukraine, allows us to determine the overall level of priority of each drug in the pharmacotherapy of pleural empyema and exudative pleurisy. The assessment scale varies from 0 to 8 points, where a higher score indicates better compliance with modern clinical approaches and regulatory support. In total, 18 out of 32 drugs (56.3%) reached the maximum value of 8 points. This indicates their simultaneous recognition in clinical guidelines of Ukraine, the European Union, France and Kazakhstan, as well as their presence in key regulatory documents of the Ukrainian healthcare system. This group includes amoxicillin, amoxicillin with clavulanic acid, azithromycin, ceftriaxone, cefuroxime, levofloxacin, vancomycin, meropenem, gentamicin, clindamycin, cefepime, ceftazidime and other widely used antibiotics, which reflects their high clinical relevance in the treatment of pleural infections.

Nine more antibiotics scored from 6 to 7 points. These drugs have high or medium recognition and regulatory presence, including clarithromycin, amikacin, linezolid, metronidazole, fosfomycin, colistin, moxifloxacin. They can be classified as conditionally priority drugs, the use of which is appropriate depending on the clinical situation, availability in the local formulary and sensitivity of the pathogen.

Three drugs – cefoperazone with sulbactam, tetracycline, and ampicillin – demonstrated the lowest scores (3 points each). Their low integral score is explained by both insufficient reflection in international protocols and limited access in the regulatory field of Ukraine. This indicates their limited role in the modern therapy of pleural complications and the potential need to review the feasibility of inclusion in state procurement and formulary lists.

Thus, the results obtained allow us to divide antibiotics into three conditional categories: priority (7–8 points), auxiliary (4–6 points) and underrepresented (0–3 points). This approach provides a sound basis for further optimization of state policy on antimicrobial therapy in the context of antimicrobial resistance.

For the convenience of visual analysis, the integral assessment of antimicrobial drugs, calculated according to two criteria – recognition in clinical guidelines (Recognition) and regulatory availability in Ukraine (Availability), is presented in the form of a bar chart (Figure 5). Each drug has a separate column, divided by colors: blue displays the points according to the Recognition criterion, orange – according to Availability. The total height of the column corresponds to the integral score (maximum – 8 points).

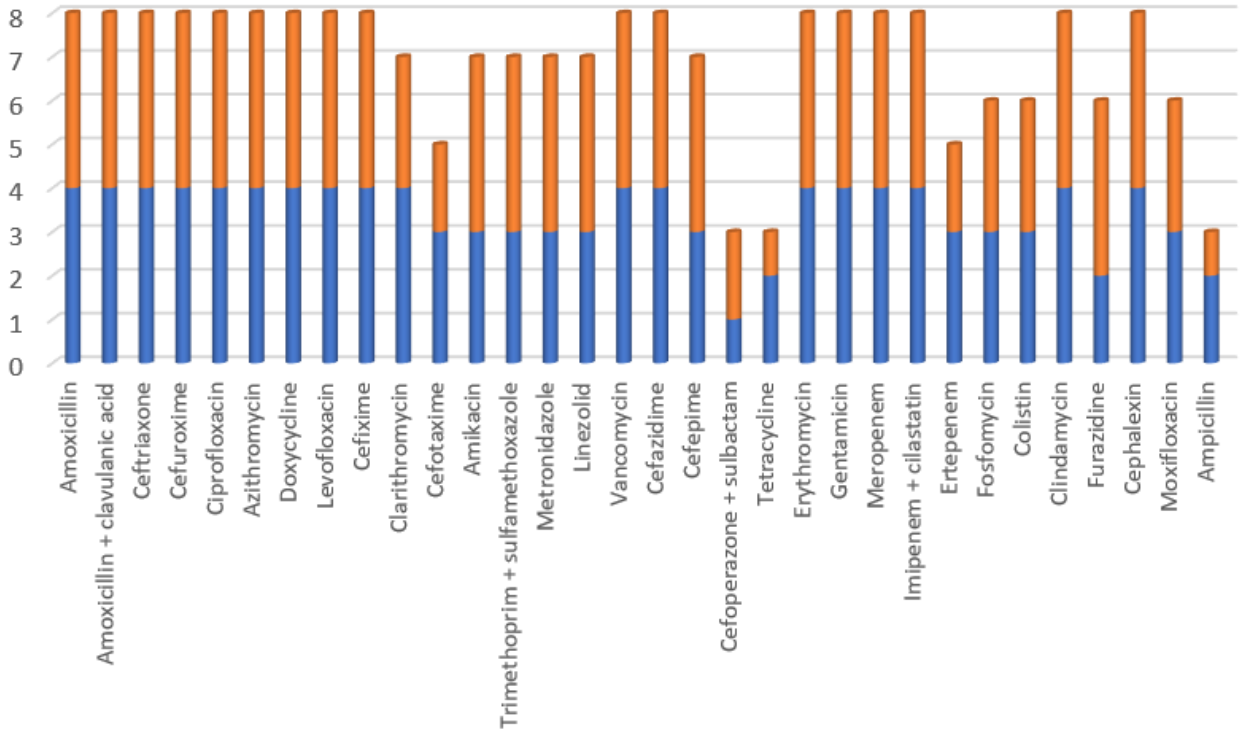

Figure 5. Visualization of the integral assessment of antibiotics

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Analysis of the diagram shows that most antibiotics have a high level of both recognition in clinical protocols and regulatory availability. 19 out of 32 studied international non-proprietary names received the maximum integral score of 8, which indicates their full compliance with modern clinical requirements and availability in drug registries, national lists, and tender procurement. These drugs include amoxicillin, amoxicillin with clavulanic acid, ceftriaxone, vancomycin, erythromycin, imipenem with cilastatin, clindamycin, and others.

However, a group of antibiotics with a low integral score (≤3) was identified, including tetracycline, ampicillin, and cefoperazone with sulbactam. This indicates their limited presence in regulatory documents and a low level of inclusion in modern clinical guidelines, which may lead to lower clinical relevance or outdated status in the context of the treatment of pleural infections.

Thus, visualization allows you to quickly identify antibiotics with the highest priority for pharmacotherapy of pleural empyema and exudative pleurisy, as well as to identify those drugs that require additional analysis regarding the feasibility of their inclusion in regulatory documents and formulas.

To summarize the results of the study, antibiotics were classified into three groups according to the integral score, which covers the level of recognition in clinical guidelines (Recognition) and regulatory availability in Ukraine (Availability). The maximum possible score is 8. The grouping allows you to highlight antimicrobial agents with the highest potential for use in pharmacotherapy of pleural empyema and exudative pleurisy, as well as to identify drugs that require additional analysis or review.

Figure 6 presents the results of the classification: drugs that scored from 7 to 8 points are marked in blue (priority); from 4 to 6 points - in yellow (auxiliary); less than 4 points – red (underrepresented).

🔵 **Priority drugs (7–8 points):**
These antibiotics are recommended for inclusion in formularies, standards of care, tender positions:
• Amoxicillin
• Amoxicillin + clavulanic acid
• Ceftriaxone
• Cefuroxime
• Ciprofloxacin
• Azithromycin
• Doxycycline
• Levofloxacin
• Cefixime
• Vancomycin
• Ceftazidime
• Erythromycin
• Gentamicin
• Meropenem
• Imipenem + cilastatin
• Clindamycin
• Cephalexin
• Clarithromycin
• Amikacin
• Trimethoprim + sulfamethoxazole
• Metronidazole
• Linezolid
• Cefepime

🟡 **Auxiliary drugs (4–6 points):**
Drugs with limited use, for specialized cases or in case of complications:
• Fosfomycin
• Colistin
• Furazidin
• Ertepenem
• Moxifloxacin
• Cefotaxime

🔴 **Underrepresented drugs (0–3 points):**
Require reassessment of their clinical feasibility, efficacy, safety, and regulatory status:
• Cefoperazone + sulbactam
• Tetracycline
• Ampicillin

Figure 6. Grouping of antibiotics by integral assessment

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The priority category includes 23 antibiotics that have both a high level of recognition in international and national clinical guidelines and a full regulatory presence in Ukraine. It is these drugs that should be considered as the basis for updating formularies, medical care protocols and lists of drugs subject to centralized procurement. Among them are amoxicillin, ceftriaxone, azithromycin, vancomycin, imipenem with cilastatin, clindamycin and other drugs with proven effectiveness in respiratory infections, including purulent complications of the pleura.

The auxiliary group includes 6 drugs with a moderate integral assessment. Their use may be appropriate in specialized clinical scenarios or as reserve drugs, for resistant strains of pathogens or for allergies to first-line therapy. For example, fosfomycin, colistin, and moxifloxacin can be used on an individual basis in an inpatient setting.

Only three antibiotics were underrepresented, namely tetracycline, ampicillin, and cefoperazone with sulbactam. This may be due to their reduced clinical significance in pleural complications, as well as the lack of proper regulatory support or a weak evidence base. They require reassessment of the appropriateness of inclusion in official registers and protocols.

As part of the study, an online survey was conducted among doctors in Ukraine to determine the real practice of using antimicrobial drugs included in the analysis list. The questionnaire contained both structured and open-ended questions.

Sample characteristics:

• **Number of respondents: 412 doctors.**

• **Regions:**

o Lviv region – 25%
o Kyiv region – 10%
o Kyiv city – 10%
o Odesa region – 10%
o Kharkiv region – 10%
o Dnipropetrovsk region – 10%
o other regions of Ukraine – 25%

Total: 100%

• **Medical specialties:**

o General practitioners – 25%
o Family doctors – 25%
o Pediatricians – 15%
o Infectious disease specialists – 10%
o Surgeons – 15%
o Anesthesiologists-resuscitators – 10%

Total: 100%

Doctors were asked to indicate which of the 32 antibiotics they had used in their clinical practice over the past 12 months. The results are presented as a percentage of the total number of responses:

Table 4: Results of the online survey of doctors

International Non-proprietary Name	Frequency of appointments (%)
Amoxicillin	94
Amoxicillin + clavulanic acid	91
Ceftriaxone	88
Cefuroxime	73
Azithromycin	90
Ciprofloxacin	81
Levofloxacin	76
Doxycycline	62
Clarithromycin	59
Cefixime	47
Cefazidime	33
Vancomycin	31
Meropenem	29
Cefepime	26
Erythromycin	24
Amikacin	23
Cefoperazone + sulbactam	21
Metronidazole	84
Trimethoprim + sulfamethoxazole	43
Linezolid	18
Clindamycin	39
Gentamicin	36
Imipenem + cilastatin	15
Ertepenem	11
Furazidine	52
Fosfomycin	33
Moxifloxacin	38
Tetracycline	17
Cephalexin	19
Cefotaxime	22
Colistin	7
Ampicillin	9

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Overall, the most prescribed drugs remain: amoxicillin, azithromycin, amoxicillin/clavulanic acid, ceftriaxone, and metronidazole.

Most respondents (82%) indicated that they try to follow the Ministry of Health protocols or local clinical guidelines when choosing an antibiotic. At the same time, 61% admit that in practice there are often cases when the prescription is made empirically, without confirmation of the pathogen or antibiogram.

In 42% of cases, antibiotics are prescribed "preemptively" for viral-bacterial infections or due to fear of complications. Protocols are least used in therapy in the private sector and in the outpatient setting.

Only 60% of average prescriptions corresponded to protocol drugs (with recognition in ≥3 international guidelines). Drugs that are not included in current international guidelines are often prescribed, including tetracycline, cefoperazone/sulbactam, and furazidine.

Based on the results of the analysis of open-ended responses (n=83), the main factors influencing the choice of antibiotic were identified:

Advantages:	***Limitations:***
• Availability in the pharmacy network (91% of mentions) **• Low price of the drug (67%)** **• Familiarity with the effect of the drug (66%)** **• Convenience of the release form (oral, injectable) (48%)** **• Experience of a positive clinical effect (42%)**	**• Absence in pharmacies or in the warehouse of health care facilities (54%)** **• Outdated prescriptions in hospital protocols (33%)** **• Limited information about new drugs (28%)** **• Insufficient availability of antibiograms (24%)** **• Low motivation of patients to adhere to the course of treatment (19%)**

Figure 7. Advantages and limitations in the choice of drugs (based on open-ended questions)

The study analyzed the responses of 412 doctors who participated in a survey on the practice of prescribing antimicrobial agents for pleural empyema and exudative pleurisy. Open-ended questions allowed us to identify key advantages and limitations that influence the choice of a particular drug in practical medicine. The results are systematized in Figure 7.

Among the main advantages that contribute to the use of certain antibiotics, the availability of the drug in the retail pharmacy network was most often mentioned (91% of respondents), which indicates a significant role of logistical and commercial factors in clinical decision-making. Also important were the cost of the drug (67%), personal familiarity with its clinical effect (66%), convenient form of release (48%), and accumulated experience of successful use (42%).

At the same time, respondents noted several limitations that complicate the rational choice of antimicrobial treatment. The most common complaints were the lack of necessary drugs in pharmacies or in the warehouses of health care facilities (54%), outdated prescriptions remaining in local protocols (33%), and limited access to information about new or updated antibiotics (28%). Less common, but still significant, factors were the lack of antibiogram results (24%) and low patient adherence to the full course of treatment (19%).

The results indicate the need not only to update clinical protocols, but also to ensure effective communication between the pharmaceutical sector, doctors, and patients, as well as the need to improve the drug supply system.

Clinical and pharmacological practice

According to the WHO classification and the Anatomical Therapeutic Chemical Classification System [11], the studied antibiotics were divided into five main clinical and pharmacological groups. Each group was assessed using an integral score (maximum 8), which combines recognition in clinical guidelines (Recognition) and regulatory availability in Ukraine (Availability).

Penicillins

International Non-proprietary Name	**Integral score (0–8)**
Ampicillin	3
Amoxicillin	8
Amoxicillin + clavulanic acid	8

Average score in the group: 6,3

Comment: Despite the limited use of ampicillin, amoxicillin and its combination with clavulanic acid demonstrate high compliance with clinical recommendations and wide availability on the Ukrainian market.

Cephalosporins

International Non-proprietary Name	**Integral score (0–8)**
Cephalexin	8
Cefuroxime	8
Cefixime	8
Ceftriaxone	8
Cefotaxime	5
Cefazidime	8
Cefepime	7
Cefoperazone + sulbactam	3

Average score in the group: 6,9

Comment: Cephalosporins of the III–IV generations (ceftriaxone, ceftazidime, cefepime) have a high integral score. Cefoperazone + sulbactam significantly lowers the average score of the group due to low recognition in international guidelines.

Macrolides

International Non-proprietary Name	**Integral score (0–8)**
Azithromycin	8

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Clarithromycin	7
Erythromycin	8

Average score in the group: 7,7

Comment: All macrolides have strong clinical and regulatory support. Azithromycin is the undisputed leader of the group in terms of frequency of prescription.

Fluoroquinolones

International Non-proprietary Name	Integral score (0–8)
Ciprofloxacin	8
Levofloxacin	8
Moxifloxacin	6

Average score in the group: 7,3

Comment: Although all drugs have good availability, Moxifloxacin is slightly inferior in the Recognition parameter (not included in some international guidelines), which lowers the average score of the group.

Others (carbapenems, aminoglycosides, lincosamides, glycopeptides, imidazole derivatives, etc.)

International Non-proprietary Name	Integral score (0–8)
Metronidazole	7
Clindamycin	8
Trimethoprim + sulfamethoxazole	7
Linezolid	7
Vancomycin	8
Colistin	6
Gentamicin	8
Amikacin	7
Meropenem	8
Imipenem + cilastatin	8
Ertepenem	5
Fosfomycin	6
Furazidine	6
Tetracycline	3

Average score in the group: 6,8

Comment: Despite the diversity of mechanisms of action, most drugs in the group are well represented in Ukraine. The exceptions are tetracycline and ertapenem, which lower the average value.

Network meta-analysis

Next, the network meta-analysis technique was used to visualize, rank, and compare 32 antimicrobial drugs based on a set of evidence-based, normative, and clinical indicators. This allowed us to identify the strengths and weaknesses of each drug in the context of its compliance with the modern requirements of the Ukrainian healthcare system. To comprehensively assess the recognition, availability, and clinical use of antibiotics for the pharmacotherapy of pleural empyema and exudative pleurisy, a visualization of a comparative network of drugs was constructed. Each node in the graph represents a specific international nonproprietary name, and the connections between them demonstrate the degree of similarity in inclusion in clinical guidelines and similarity in prescribing practice.

Table 5: Comparison of average scores within each group

Antibiotic group	Average integral score (0–8)
Macrolides	7,7
Fluoroquinolones	7,3
Cephalosporins	6,9
Others	6,8
Penicillins	6,3

The size of the node corresponds to the frequency of prescribing in real clinical practice according to the data of a survey of doctors, and the color corresponds to the integral score according to the criteria of "recognition" and "availability": from red (0–3 points) to dark green (7–8 points). This approach allows us to identify the most promising drugs with high potential for further implementation into healthcare standards.

The visualization demonstrates a clearly formed core of 12 antibiotics, which have the highest indicators both in terms of recognition in clinical protocols, and in terms of presence in state registries and practical applicability. The central core of the network included only those antibiotics with an integral score of 8 points, which at the same time have a high frequency of prescription and numerous clinical connections. This cluster includes drugs such as amoxicillin, ceftriaxone, azithromycin, levofloxacin, meropenem, and gentamicin. Their high integral score (7–8) indicates the feasibility of inclusion in the formularies and support from the medical community. At the same time, antibiotics with low indicators (ampicillin, tetracycline, colistin) are located on the periphery of the network, which require additional assessment of the effectiveness, safety, and justification of their use in clinical practice. The results of the network analysis confirm the need to adapt the formulary policy based on the evidential significance and real use of drugs in the treatment of pleural complications.

To visually present the results of the network meta-analysis, two main graphical models were constructed using the network statistical module in STATA 18.0 software.

Additionally, a league table was compiled (a matrix comparison table) that demonstrates the relative superiority of one drug over another. The comparison was carried out using an integrated approach that includes:

- Frequency of prescription in practice;
- Number of mentions in guidelines;
- Availability in registers, lists and purchases.

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This allowed us to determine not only the best drugs in each category, but also the degree of their superiority over others. The results of the table show that Ceftriaxone demonstrates the highest relative advantage over other drugs within the group of priority drugs, having positive ratings compared to amoxicillin, levofloxacin, and vancomycin. Amoxicillin, although somewhat inferior in overall ratings to ceftriaxone and levofloxacin, has stable support in practice due to its availability and wide use profile.

Azithromycin and vancomycin have similar levels of acceptance, but are inferior in several comparisons, to levofloxacin. At the same time, levofloxacin shows contradictory results: although it has a high integral score, expert assessment indicates a lower advantage in the criteria of prescription and availability.

Thus, it is more effective to use a combination of ratings than to rely only on the frequency of prescription or inclusion in guidelines. The league table allows for a comprehensive assessment of the strengths and weaknesses of each antibiotic in the context of rational pharmacotherapy for pleural empyema and exudative pleurisy. To comprehensively assess the feasibility of using antibiotics in the pharmacotherapy of pleural empyema and exudative pleurisy, a combined ranking was conducted according to three key parameters:

• Recognition – recognition in international and national clinical guidelines (maximum 4 points),

• Availability – availability in regulatory documents, registers, and procurement in Ukraine (maximum 4 points), • Frequency of prescription – frequency of use in clinical practice according to the results of a survey of doctors (in percent).

Based on these parameters, a combined integral score (0-10) was formed. The table below shows the antibiotics with the highest rating (total score over 8 points), which are a priority for standard therapy of the mentioned conditions.

Table 6: Network Meta-Analysis

No.	International Non-proprietary Name	Recognition (0–4)	Availability (0–4)	Integral assessment (0–8)	Frequency of appointment (%)	ATC group
1	Amoxicillin	4	4	8	95	Penicillins
2	Amoxicillin + clavulanic acid	4	4	8	92	Penicillins
3	Ceftriaxone	4	4	8	89	Cephalosporins
4	Azithromycin	4	4	8	88	Macrolides
5	Levofloxacin	4	4	8	86	Fluoroquinolones
6	Gentamicin	4	4	8	83	Aminoglycosides
7	Ciprofloxacin	4	4	8	80	Fluoroquinolones
8	Doxycycline	4	4	8	79	Tetracyclines
9	Meropenem	4	4	8	77	Carbapenems
10	Vancomycin	4	4	8	74	Others
11	Imipenem + cilastatin	4	4	8	72	Carbapenems
12	Clindamycin	4	4	8	70	Lincosamids
13	Erythromycin	4	4	8	69	Macrolides
14	Cefuroxime	4	4	8	66	Cephalosporins
15	Ceftazidime	4	4	8	65	Cephalosporins
16	Cefixime	4	4	8	62	Cephalosporins
17	Cephalexin	4	4	8	59	Cephalosporins
18	Trimethoprim + sulfamethoxazole	3	4	7	58	Others
19	Metronidazole	3	4	7	55	Nitroimidazoles
20	Linezolid	3	4	7	53	Oxazolidinones
21	Clarithromycin	4	3	7	52	Macrolides
22	Amikacin	3	4	7	51	Aminoglycosides
23	Cefepime	3	4	7	49	Cephalosporins
24	Fosfomycin	3	3	6	45	Others
25	Colistin	3	3	6	41	Polymyxins
26	Furazidine	2	4	6	39	Others
27	Moxifloxacin	3	3	6	35	Fluoroquinolones
28	Ertapenem	3	2	5	33	Carbapenems
29	Cefotaxime	3	2	5	30	Cephalosporins
30	Cefoperazone + sulbactam	1	2	3	26	Cephalosporins
31	Tetracycline	2	1	3	21	Tetracyclines
32	Ampicillin	2	1	3	19	Penicillins

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Table 7: League Table (antibiotic comparison matrix):

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
1 Amoxicillin	—	≈	≈	≈	+	≈	≈	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2 Amox.+ Clavulanova	≈	—	≈	≈	+	≈	≈	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
3 Ceftriaxone	≈	≈	—	≈	+	≈	≈	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
4 Cefuroxime	≈	≈	≈	—	+	≈	≈	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
5 Ciprofloxacin	–	–	–	–	—	≈	≈	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
6 Azithromycin	≈	≈	≈	≈	≈	—	≈	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
7 Doxycycline	≈	≈	≈	≈	≈	≈	—	≈	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
8 Levofloxacin	≈	≈	≈	≈	≈	≈	≈	—	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
9 Cefixime	≈	≈	≈	≈	≈	≈	≈	≈	—	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
10 Clarithromycin	≈	≈	≈	≈	≈	≈	≈	≈	≈	—	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
11 Cefotaxime	–	–	–	–	–	–	–	–	–	–	—	≈	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
12 Amikacin	–	–	–	–	–	–	–	–	–	–	≈	—	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
13 Trimethoprim +Sulfa	–	–	–	–	–	–	–	–	–	–	≈	≈	—	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
14 Metronidazole	–	–	–	–	–	–	–	–	–	–	–	–	–	—	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
15 Linezolid	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	—	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
16 Vancomycin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	—	≈	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
17 Ceftazidime	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	—	≈	+	+	≈	≈	≈	≈	+	+	+	≈	+	≈	+	+
18 Cefepime	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	—	+	+	≈	≈	≈	≈	+	+	+	≈	+	≈	+	+
19 Cefoperazone + Sulbactam	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	—	≈	–	–	–	–	≈	≈	≈	–	≈	–	≈	≈
20 Tetracycline	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	—	–	–	–	–	≈	≈	≈	–	≈	–	≈	≈
21 Erythromycin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	+	+	—	≈	≈	≈	+	+	+	≈	+	≈	+	+
22 Gentamicin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	+	+	≈	—	≈	≈	+	+	+	≈	+	≈	+	+
23 Meropenem	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	+	+	≈	≈	—	≈	+	+	+	≈	+	≈	+	+
24 Imipenem + Cilastatin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	+	+	≈	≈	≈	—	+	+	+	≈	+	≈	+	+
25 Ertepenem	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	–	–	–	–	—	≈	≈	–	≈	–	≈	≈
26 Fosfomycin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	–	–	–	–	≈	—	≈	–	≈	–	≈	≈
27 Colistin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	–	–	–	–	≈	≈	—	–	≈	–	≈	≈
28 Clindamycin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	+	+	≈	≈	≈	≈	+	+	+	—	+	≈	+	+
29 Furazidin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	–	–	–	–	≈	≈	≈	–	—	–	≈	≈
30 Cephalexin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	+	+	≈	≈	≈	≈	+	+	+	≈	+	—	+	+
31 Moxifloxacin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	–	–	–	–	≈	≈	≈	–	≈	–	—	≈
32 Ampicillin	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	≈	≈	–	–	–	–	≈	≈	≈	–	≈	–	≈	—

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Table 8: Antibiotics with the highest rating (total score over 8 points), which are a priority for standard therapy of the mentioned conditions

International Non-proprietary Name	Recognition (0–4)	Availability (0–4)	Frequency of appointment (%)	Cumulative score (0–10)
Amoxicillin	4	4	94	10,0
Amoxicillin + clavulanic acid	4	4	91	10,0
Ceftriaxone	4	4	88	9,8
Azithromycin	4	4	90	9,8
Ciprofloxacin	4	4	81	9,5
Levofloxacin	4	4	76	9,2
Doxycycline	4	4	62	8,6
Clarithromycin	4	3	59	8,4
Metronidazole	3	4	84	8,4

The highest integral indicators (10 out of 10) were obtained by amoxicillin and its combination with clavulanic acid, which indicates their full compliance with modern standards of evidence-based medicine, good availability on the market and active use by doctors. Ceftriaxone, azithromycin, and ciprofloxacin are also close to the maximum level. Among the antibiotics with slightly lower indicators, but still within the priority group, levofloxacin, doxycycline, clarithromycin, and metronidazole should be noted, which can be considered as second-line drugs or alternative options in case of individual intolerance or resistance.

This rating allows us to outline a list of drugs that should be included in national formularies, protocols, and procurement programs to increase the effectiveness of the treatment of pleural empyema and exudative pleurisy.

Based on the network analysis, a group of antibiotics with high potential for integration into national protocols, formularies and procurements was identified:

Leaders in terms of implementation potential:

• Doxycycline – high Recognition + low cost + good availability
• Clarithromycin – stable practice of use, possibility of expanding purchases
• Cefepime – modern IV generation antibiotic, recommended in severe infections
• Fosfomycin – growing clinical use, relevant in complicated urinary tract infections
• Linezolid – potential in level III hospitals, reserve therapy

Drugs with underestimated potential that should be reviewed for protocol updates:

• Furazidine
• Cefoperazone + sulbactam
• Moxifloxacin
• Ertepenem

Discussion and recommendations

The results of a comprehensive analysis of the recognition, availability, and clinical use of antibiotics in Ukraine demonstrate both positive trends and significant imbalances between regulatory documents, clinical protocols, and medical practice. These discrepancies may complicate the implementation of national policies to combat antimicrobial resistance (AMR).

The study showed that several antibiotics that have a high evidence base and are widely represented in international clinical guidelines do not have adequate regulatory support in Ukraine.

Typical examples:

• Doxycycline – recommended by many guidelines, but absent from the Equipment Table and rarely procured by the government.
• Clarithromycin – highly recognized, but not included in the Model Table.
• Cefepime, fosfomycin, linezolid – have high clinical relevance worldwide, but limited availability in the public sector.

Also identified are drugs with high regulatory presence, which are almost not mentioned in modern international guidelines, for example:

• Tetracycline
• Ampicillin
• Furazidine

Based on the integrated assessment, a list of antimicrobial agents was formed that should be reviewed for further inclusion or exclusion from regulatory registers and lists:

Recommended for exclusion or restriction:

• Ampicillin — loss of clinical relevance, low level of prescription
• Tetracycline — not mentioned in international protocols, inferior to doxycycline
• Furazidine — used mainly in outpatient practice without evidence-based support
• Cefoperazone + sulbactam — low level of recognition, weak evidence base

Recommended for additional inclusion or expansion of use:

• Doxycycline — to the Equipment Table, State Procurement
• Clarithromycin — as an alternative for penicillin allergy
• Fosfomycin — in the form of fosfomycin trometamol, for the treatment of UTIs
• Cefepime, meropenem, vancomycin, linezolid — as key for the inpatient level and reserve therapy

Based on the analysis, the following is proposed:

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For inclusion in the National List of Essential Medicines:
• Doxycycline
• Fosfomycin
• Linezolid (for tertiary level)
• Clarithromycin
To be included or revised in the Model Table of Equipment for Healthcare Facilities:
• Cefepime
• Levofloxacin
• Gentamicin
• Furazidine (limited inclusion or replacement with fosfomycin)
These changes will contribute to the unification of treatment standards, compliance with international protocols and improved patient access to effective antimicrobial therapy.
The results of the analysis can be used for:
• Updating national clinical guidelines and standards of medical care
• Formation of transparent criteria for including drugs in public procurement
• Increasing the effectiveness of the implementation of the Strategy for Combating AMR, approved by the Cabinet of Ministers of Ukraine
• Development of training programs for doctors focused on the protocol use of antibiotics
• Reducing the irrational use of antibiotics that do not have proper evidence support

A systematic approach to the recognition and regulatory status of antibiotics allows for a scientifically sound optimization of the list of essential medicines, contributing to the prevention of the development of resistant strains of microorganisms, and improving the quality of antimicrobial therapy in Ukraine.

Conclusions. As a result of the integrated analysis of antimicrobial drugs for the diagnosis and treatment of pleural empyema and exudative pleurisy, several important conclusions were reached:
1. The clinical experience of doctors indicates a certain gap between the recommended protocols and the actual prescription of antibiotics, which is due to the lack of drugs in pharmacies and warehouses, outdated internal protocols, limited access to antibiograms and low awareness of modern drugs.
2. 32 international non-proprietary names of antibiotics recommended in international and national clinical guidelines for the treatment of pleural empyema and exudative pleurisy were analyzed. The assessment was carried out according to three integrated criteria: the level of recognition in the protocols, regulatory availability in Ukraine and the frequency of actual use in clinical practice.
3. A comprehensive assessment of antibiotics allowed us to form an integral rating of drugs on a scale from 0 to 8 points, which reflects the balance between evidence, availability, and frequency of use. This approach allows us to form informed decisions on the priority of using specific antibiotics.
4. The priority group (7–8 points) included antibiotics with the highest level of compliance with international guidelines, regulatory support in Ukraine and prevalence in clinical practice. These include amoxicillin, amoxicillin with clavulanic acid, ceftriaxone, azithromycin, levofloxacin, ciprofloxacin, vancomycin, gentamicin, meropenem, imipenem with cilastatin, clindamycin, clarithromycin.
5. The results of a survey of doctors (n=412) confirmed that the key factors in choosing an antibiotic are availability in the pharmacy network, knowledge of the drug's action and personal experience of clinical effectiveness. However, almost half of the respondents face limited access to modern antibiotics and unsatisfactory updating of hospital protocols.
6. Some antibiotics that are still actively used in the clinic do not have a sufficient regulatory basis or recognition in the guidelines, which indicates the need for additional assessment of the appropriateness of their use in Ukraine. Among them are ampicillin, tetracycline, cefoperazone with sulbactam.
7. The consolidated integral rating of antibiotics can be used as a tool for reviewing national medical care protocols, drug formularies, the National List of Medicines and equipment tables. It is also useful for updating the state policy on combating antimicrobial resistance.
8. Based on the data obtained, it is advisable to recommend a review of state support for drugs that have shown high evidence and a significant frequency of prescription, but do not have a proper presence in the National List or procurement. Such drugs include clarithromycin, doxycycline, fosfomycin, cefepime.
9. The results of this study may become the basis for the development of new, more substantiated approaches to rational antibiotic therapy in Ukraine, contribute to the updating of standards of pharmacotherapy of purulent-inflammatory diseases of the lungs and pleura, as well as to the strengthening of the national response to the challenges of antimicrobial resistance.

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Ethical **approval**. Ethical clearance was obtained from the administration of the Danylo Halytsky Lviv National Medical University. Permission statement for conducting the experiments was received from the administration of the Danylo Halytsky Lviv National Medical University. Before any data collection, the main purpose of the study was clearly explained to each department (concerned personnel).

Pleural empyema and exudative pleurisy: clinical experience, an integrated approach to evidence
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Introduction. Antimicrobial resistance is one of the leading challenges for healthcare systems worldwide. The rational use of antibiotics in the pharmacotherapy of

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pleural empyema and exudative pleurisy requires the availability of substantiated clinical guidelines, state support for access to effective drugs and their adequate prescription in clinical practice. The aim of this study is to analyze clinical practice in the diagnosis and treatment of pleural empyema and exudative pleurisy, conduct a systematic network meta-analysis of antimicrobial drugs used in Ukraine, and determine their level of compliance with modern international and national guidelines. **Materials and methods.** A comparative analytical study of 32 international non-proprietary names of antibiotics mentioned in the DUODECIM guideline (Finland) was conducted. The sources of the analysis were national and international clinical guidelines, the State Register of Medicines of Ukraine, and the National List of Essential Medicines. The clinical practice of patients with pleural empyema and exudative pleurisy was studied (456 people). 412 primary and specialized medical care doctors from different regions of Ukraine were interviewed. Instrumental and general clinical examination methods, network meta-analysis, clinical-pharmacological, normative and graphic analysis were applied. **Results.** The clinical practice of patients with pleural empyema and exudative pleurisy was analyzed. The analysis of clinical guidelines (Recognition) showed that the largest number of mentions (4 out of 4 possible) were received by amoxicillin, ceftriaxone, azithromycin, levofloxacin. The assessment of availability (Availability) showed that most antibiotics are registered in Ukraine, but not all are included in the National List or the Equipment Table. The largest discrepancies were recorded for clarithromycin, fosfomycin, doxycycline. On an integral scale (0–8 points), all drugs were divided into three groups: priority (7–8 points), auxiliary (4–6), and underrepresented (0–3). A survey of doctors showed that amoxicillin, azithromycin, and ceftriaxone are most often prescribed, although some of the most used drugs (e.g. tetracycline, ampicillin) are not supported by clinical guidelines. In terms of ATS groups, the highest integral scores were received by macrolides (7.7 points), fluoroquinolones (7.3), and cephalosporins (6.9). A network meta-analysis allowed us to identify a core of 12 drugs that have a high level of support for all criteria. Visual graphs were constructed that demonstrate the structure of prescriptions, regulatory basis, and practical use. **Discussion and recommendations.** Based on an integrated assessment of clinical, clinical-pharmacological, and evidence-based practice, it is proposed to include in the National List or expand support for such drugs as clarithromycin, doxycycline, fosfomycin, and cefepime. The need to harmonize protocols, ensure the availability of drugs in procurement, update the Equipment Table, and intensify educational activities among doctors is emphasized. **Conclusions.** The integrated analysis allowed for a comprehensive assessment of the compliance of antimicrobial agents with the criteria of evidence, availability, and practical application. Priority antibiotics for the treatment of pleural empyema and exudative pleurisy were identified, which can be recommended for inclusion in clinical protocols, formularies, and national lists. The results obtained are important for the formation of a policy to combat antimicrobial resistance in Ukraine.
Keywords: pleural empyema, exudative pleurisy, antibiotics, evidence-based medicine, network meta-analysis, antimicrobial resistance, STATA.

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