ANTITUSSIVE CODEINE MEDICINES IN UKRAINE: CLINICAL AND PHARMACOLOGICAL, MARKETING, REGULATORY ASPECTS, AND FORECASTS

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Introduction

In the previous study, a pharmacoeconomic analysis of codeine medicines was conducted using the ABC and VED methods [1].

Antitussive drugs play an important role in the treatment of respiratory diseases accompanied by cough. A special niche among such drugs is occupied by codeine medicines. Codeine is a semisynthetic opioid that has been used in medicine for more than a century. Codeine has a unique mechanism of action: it affects the cough center in the medulla oblongata, suppressing the cough reflex, which makes it indispensable in the treatment of dry, debilitating cough. However, along with proven effectiveness, codeine medicines have several features that affect their use in clinical practice [2-7].

Globally, codeine medicines are the subject of significant attention from regulatory authorities due to the risk of addiction, abuse, and side effects. In many countries, their circulation is strictly controlled, including restrictions on access to non-prescription drugs and the establishment of quotas for production and sales. In Ukraine, this problem is also relevant, as codeine abuse among the population leads to social and medical complications, in particular the development of addiction and side effects. At the same time, such drugs remain important in pharmacotherapy due to their high effectiveness [8-10].

Regulatory aspects of the use of codeine medicines in Ukraine deserve special attention. On the one hand, there is a need to ensure the availability of these drugs for patients who really need them. On the other hand, it is important to minimize the risks of uncontrolled use. As of today, Ukraine has introduced strict restrictions on the dispensing of codeine medicines - they are available only by prescription. In addition, work is ongoing to improve the regulatory framework for their circulation, which meets international standards [11-13].

The epidemiological situation also affects the use of codeine medicines. The increase in the number of diseases accompanied by cough, such as influenza, COVID-19 and other acute respiratory infections, increases the demand for antitussives. At the same time, the pandemic has highlighted weaknesses in the supply chain of medicines, including codeine medicines, in particular problems with organization, storage, and availability for end users [14, 15].

Codeine abuse is a significant problem, especially among young people. Cases of using codeine medicines for non-medical purposes, such as achieving a euphoric effect, pose serious health risks and require active action by the state and the medical community. In this context, preventive measures aimed at raising public awareness of the dangers of abuse and strengthening control over the circulation of such medicines are important [16, 17].

From a marketing point of view, codeine medicines have a stable demand on the pharmaceutical market of Ukraine. However, competition between manufacturers forces them to look for new ways to attract consumers, through the introduction of new forms of release, increasing the availability of information about medicines and ensuring high product quality. At the same time, pharmaceutical companies face challenges related to regulatory restrictions and the need for transparency of the entire production and sales process [18, 19].

No less important are the forecasts for the further use of codeine medicines in Ukraine. It is expected that regulatory policy will become stricter, especially regarding circulation control and prescription dispensing. At the same time, there is a trend in the world to search for alternatives to codeine, synthetic or herbal remedies that provide similar efficacy, but have a lower risk of addiction [20]. The study utilized the following registries: European Convention on Drug Control, 1986. Council of Europe, International Convention on Narcotic Drugs and Psychotropic Substances, 1988. UN, WHO Drug Control System, World Health Organization, 2019, and Convention on Narcotic Drugs, 1961. UN.

Thus, antitussive codeine medicines remain an important component of pharmacotherapy, but their use is accompanied by several challenges. The relevance of this issue is due not only to medical aspects, but also to social, economic, and regulatory factors. Further study of these medicines will contribute to improving their use, increasing the safety and effectiveness of treatment.

Purpose of the study

The purpose of this article is to study the features of codeine medicines and analyze their role in modern medicine. The article aims to:

1. Describe the clinical and pharmacological properties of codeine – to reveal the mechanism of its action, antitussive, analgesic effects, and explain how these properties contribute to the treatment of various diseases.
2. Consider the features of the composition and forms of release of codeine medicines – to demonstrate the diversity of medicines, their combinations with other active substances, as well as the advantages of each form in different clinical situations.
3. Analyze the codeine medicines market in Ukraine – to provide an idea of the main manufacturers, and to study the development trends of this segment of the pharmaceutical market.
4. Assess the regulatory aspects of the circulation of codeine medicines – to study the rules of registration,

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release and control that operate on the Ukrainian market, and to compare them with international standards.
5. Warn about the risks of abuse – emphasize the danger of developing addiction if recommendations are not followed and consider measures that help minimize such risks.
This article is aimed at comprehensively highlighting the role of codeine medicines in pharmacotherapy, as well as providing recommendations for their rational and safe use.

Materials and methods
The following materials and methods were used to conduct this study:
Research materials
1. Codeine medicines registration data
Information from the State Register of Medicines of Ukraine, containing information about codeine medicines, their composition, release forms, manufacturers, and registration dates.
Current pharmacopoeial and regulatory documents related to the production, circulation, and control of codeine medicines.
2. Scientific literature
Publications on pharmacology, toxicology and clinical medicine related to the use of codeine.
Analytical reviews and studies devoted to the medicines market in Ukraine and the world.
The following databases were used in the study:
State Register of Medicines
State Formulary of Medicines
ATC/DDD Index 2024, WHO Collaborating Centre for Drug Statistics Methodology
ATC/DDD Index 2023, WHO Collaborating Centre for Drug Statistics Methodology
ATC classification, Compendium
Review of the pharmaceutical market of Ukraine
Analytical reviews of the market – Weekly APTEKA
Analysis of the pharmaceutical market in Ukraine, 2023 – Pro-Consulting
Pharmaceutical market of Ukraine – analytical review
Pharmacies of the world – 2023: digital initiatives and their impact on the pharmaceutical market
Global pharmaceutical industry outlook, 2023 and beyond
Global use of medicines: status and trends
Pharmaceutical market – Pharmaceutical Encyclopedia
World forecasts and trends – Weekly APTEKA
Research methods
1. Analytical method. The composition of codeine medicines, their release forms and compliance with modern pharmacopoeial requirements were analyzed. The features of combinations of codeine with other active substances were studied.
2. Statistical method. Data processing was carried out on the number of registered codeine medicines in Ukraine, the dynamics of their sales and popularity among patients and doctors.
3. Comparative analysis. Regulatory requirements for the circulation of codeine medicines in Ukraine were compared with international standards. Differences in release forms and dosages of medicines in different markets were studied.
4. Documentary analysis of scientific sources. A critical analysis of scientific works was conducted that consider the effectiveness, safety, and risks of the use of codeine medicines.
5. Expert assessment. The conclusions of practicing physicians, pharmacologists and regulatory specialists were involved to assess the safety of use and prospects for the development of the codeine medicines market.
Research limitations
The study is based on available public sources and statistical data. Limitations may include incomplete data on unofficial consumption of codeine medicines or unavailability of information on clinical trials in private companies.
The use of the above methods allowed to provide a comprehensive approach to the analysis of codeine medicines, their role in medicine and the pharmaceutical market of Ukraine.
The research of the article is a fragment of research works of Private Scientific Institution "Scientific and Research University of Medical and Pharmaceutical Law" and Danylo Halytsky Lviv National Medical University on the topic "Diagnosis, treatment, pharmacotherapy of inflammatory, traumatic and onco-thoracic pathology using instrumental methods" (state registration number 0125U000071, implementation period 2025-2031); Lviv Medical Institute on the topic of "Improving the system of circulation of drugs during pharmacotherapy on the basis of evidentiary and forensic pharmacy, organization, technology, biopharmacy and pharmaceutical law" (state registration number 0120U105348, implementation period 2021-2026); Private Scientific Institution "Scientific and Research University of Medical and Pharmaceutical Law" on the topic “Multidisciplinary research of post-traumatic stress disorders during war among patients (primarily combatants)” (state registration number 0124U002540, implementation period 2024-2028).

Results and discussion
1. Description of the pharmacological properties of codeine
Codeine is an alkaloid of the opium poppy, which belongs to the group of semi-synthetic opioids. It is widely used in medicine as an analgesic, antitussive and weak sedative. The main pharmacological properties of codeine include:
Anesthetic action
Codeine interacts with μ-opioid receptors in the central nervous system, which reduces the transmission of pain impulses. Its analgesic effect is weaker than that of morphine, but sufficient to relieve moderate pain.
Antitussive effect
Codeine suppresses the cough reflex by acting on the cough centers in the medulla oblongata. Due to this, it is used in the treatment of unproductive cough, especially in cases where the symptom is debilitating for the patient.
Weak sedative effect
Codeine has a sedative effect, which is due to its effect on the central nervous system. In small doses, it rarely causes severe drowsiness, which allows its use in outpatient practice.
Metabolism and pharmacokinetics

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After oral administration, codeine is rapidly absorbed from the gastrointestinal tract.
In the liver, it is partially metabolized to morphine by the enzyme CYP2D6, which provides its analgesic effect.
The half-life of codeine is about 3-4 hours.
Side effects and risks
Codeine can cause several side effects, including:
Nausea, vomiting, and constipation.
Decreased respiratory rate at high doses.
Potential dependence with prolonged use due to its effect on opioid receptors.
Comparison with other opioid medicines
Codeine has a weaker analgesic effect compared to other opioids such as morphine or fentanyl, but its safety profile makes it suitable for short-term use in a wide range of patients.

2. Overview of the composition and release forms of registered codeine medicines in Ukraine

For a more detailed analysis of the pharmacological properties and characteristics of codeine, as well as for assessing the features of registered codeine medicines, a systematization of the available information was carried out. Table 1 shows the key parameters that allow comparing different dosage forms, dosages, and other aspects of the use of codeine medicines in Ukraine.

Table 1. Codeine medicines available on the pharmaceutical market of Ukraine.

No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Composition of active substances	ATC code
1.	CODEINE PHOSPHATE	tablets of 0.03 g N.10	1 tablet contains Codeine phosphate 30 mg	R05DA04
2.	CODEPSIN	tablets N. 10	1 tablet contains: terpine hydrate 250 mg, sodium bicarbonate 250 mg, codeine phosphate 8 mg	R05FA02
3.	CODETERP	tablets N. 10	1 tablet contains 8 mg of codeine phosphate, 250 mg of terpene hydrate, and 250 mg of sodium bicarbonate	R05FA02
4.	PARACOD IC	tablets N. 10	1 tablet contains paracetamol 500 mg and codeine phosphate 8 mg	N02BE51
5.	CODETERP H	tablets N.10	1 tablet contains codeine phosphate in terms of codeine 4 mg, terpine hydrate 125 mg and sodium bicarbonate 125 mg	R05FA02
6.	CODESAN IC	tablets N. 10	1 tablet contains codeine phosphate 9.5 mg, thermopsis dry extract (Herba Thermopsidis Lanceolatae) 20 mg, licorice root (Liquiritiae radix) (chopped) 200 mg, sodium bicarbonate 200 mg	R05FA02
7.	CODTERPIN IC	tablets N. 10	1 tablet contains codeine phosphate 10.9 mg, terpine hydrate 250 mg, sodium bicarbonate 250 mg	R05FA02
8.	COFEX	60 ml of syrup	5 ml of syrup contain: chlorpheniramine maleate 4 mg, codeine phosphate 10 mg	R05DA
9.	BIFOK IC	tablets N. 10	1 tablet contains ibuprofen 200 mg, codeine phosphate 10 mg	M01AE51
10.	CODEFEMOL H	syrup, 100 ml or 200 ml in a bottle	5 ml of syrup contains paracetamol 60 mg, pseudoephedrine	R05DA20

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No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Composition of active substances	ATC code
			hydrochloride 7.5 mg, codeine phosphate 5 mg	
11.	CAFFETIN	tablets N. 10	1 tablet contains paracetamol 250 mg, propifenazone 210 mg, caffeine 50 mg, codeine 7.1 mg	N02BE51
12.	PYATIRCHATKA IC	tablets N. 10	1 tablet contains metamizole sodium 300 mg, paracetamol 200 mg, sodium caffeine benzoate 50 mg, phenobarbital 10 mg, codeine phosphate 9.5 mg	N02BB72
13.	PENTALGIN IC	tablets N. 10	1 tablet contains metamizole sodium 300 mg, paracetamol 200 mg, sodium caffeine benzoate 50 mg, phenobarbital 10 mg, codeine phosphate 9.5 mg	N02BB72
14.	PENTALGIN-FS	tablets N. 10	1 tablet contains: paracetamol 300 mg, metamizole sodium monohydrate 300 mg, caffeine 50 mg, phenobarbital 10 mg, codeine phosphate 8 mg	N02BB72
15.	SOLPALGIN	capsules N. 10 capsules	1 capsule contains paracetamol 500 mg, caffeine 30 mg, codeine phosphate 8 mg	N02BE51
16.	PENTALGIN FS EXTRA CAPSULES	capsules N.10 capsules	1 capsule contains paracetamol 150 mg, metamizole sodium 150 mg, caffeine 25 mg, phenobarbital 5 mg, codeine phosphate 4 mg	N02BB72
17.	SOLPADEIN	tablets N.12	1 tablet contains 500 mg of paracetamol, 30 mg of caffeine, 8 mg of Codeine phosphate	N02BE51
18.	SOLPADEIN	soluble tablets N.2	1 tablet contains paracetamol 500 mg, caffeine 30 mg, codeine phosphate 8 mg	N02BE51
19.	PENTASET	tablets in bulk: N. 1000 or 5000 tablets	1 tablet contains paracetamol 210 mg, propifenazone 210 mg, caffeine 50 mg, phenobarbital 20 mg, codeine phosphate 10 mg	N02BB74
20.	PENTALGIN-Zdorovya	tablets N. 10	1 tablet contains paracetamol 210 mg, propifenazone 210 mg, caffeine 50 mg, phenobarbital 20 mg, codeine phosphate 10 mg	N02BB74
21.	OMNOPON NEO	solution for injections of 1 ml in ampoule N.5	1 ml of solution contains morphine hydrochloride 11.5 mg; noscapine - 5.4 mg;	N02AA51

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No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Composition of active substances	ATC code
			papaverine hydrochloride in – 0.72 mg; codeine in – 1.44 mg	
22.	OMNOPON-ZN	solution for injection; 1 ml each in ampoule N.5	1 ml of solution contains morphine hydrochloride – 11.5 mg; noscapine - 5.4 mg; papaverine hydrochloride – 0.72 mg; codeine – 1.44 mg; thebaine – 0.1 mg	N02AA51
23.	PENTASET	tablets N. 10	1 tablet contains paracetamol 210 mg, propifenazone 210 mg, caffeine 50 mg, phenobarbital 20 mg, codeine phosphate 10 mg	N02BB74

Preparations with codeine are mainly combined. They account for 95.83% of the total. Only 4.17% are monocomponent, containing only codeine as an active substance. This indicates the widespread use of combined forms to provide multifunctional action. For example, in the treatment of cough or pain, due to the constructive interaction of codeine with other active ingredients.

The following active pharmaceutical ingredients are used in combinations with codeine:

1. Terpin hydrate - used to relieve cough and reduce inflammatory processes.
2. Sodium bicarbonate – helps reduce acidity in the stomach, making breathing easier in bronchial diseases.
3. Paracetamol – an analgesic and antipyretic medicine, often used together with codeine to enhance the analgesic effect.
4. Ibuprofen – a non-steroidal anti-inflammatory medicine that reduces inflammation and pain.
5. Thermopsis dry extract – a plant component that promotes expectoration and relieves cough symptoms.
6. Licorice root (Liquiritiae radix) – used to relieve coughs and reduce inflammation in the respiratory tract.
7. Chlorpheniramine maleate – an antihistamine medicine used to reduce allergy symptoms such as nasal congestion and cough.
8. Pseudoephedrine hydrochloride – a medicine that reduces nasal congestion, used to make breathing easier for colds.
9. Metamizole sodium monohydrate – an analgesic and antipyretic medicine used to reduce pain.
10. Caffeine sodium benzoate – a stimulant medicine that helps fight fatigue and reduces drowsiness.
11. Phenobarbital – a sedative medicine used to treat nervous disorders and as an auxiliary component in painkillers.
12. Propyphenazone – an analgesic medicine used to relieve pain of various origins.
13. Morphine hydrochloride is a powerful painkiller medicine, used in combination medicines for severe pain.
14. Noscapine is a medicine used to relieve cough and reduce spasms in the respiratory tract.
15. Papaverine hydrochloride is an antispasmodic that reduces spasms in smooth muscles, including the muscles of the gastrointestinal tract and blood vessels.
16. Thebaine is an alkaloid used to enhance the effect of painkillers medicines, in combinations with codeine.

These ingredients in combinations with codeine help to achieve an effective therapeutic effect in diseases of the respiratory tract, analgesic, and anti-inflammatory measures, as well as to relieve cough.

Dosage forms of codeine medicines are presented in various versions. Allows to provide effective treatment depending on the type of disease and the required method of administration (Fig. 1).

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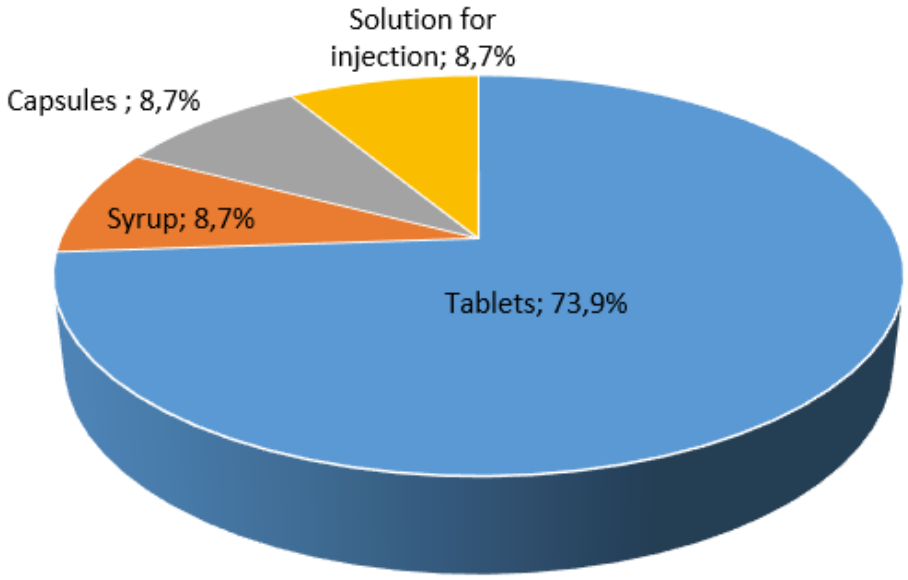

Fig. 1. Dosage forms of codeine medicines.

The most common are tablets (73.9%), which are used for oral administration. This form is convenient for patients, as it does not require special conditions for use and can be used in outpatient settings. Tablets often contain codeine in combination with other active substances (paracetamol or metamizole). It allows you to relieve pain of various origins, including headache, toothache, and pain during colds.

A smaller share among the dosage forms is occupied by syrups (8.7%), which contain codeine and are used to treat cough. Syrups are usually used in pediatrics and in the treatment of respiratory diseases, as they have a pleasant taste and are convenient for children, which makes it easier to take medicines.

In some cases, capsules (8.7%) are used, which also contain codeine and are intended for oral administration. Capsules are convenient for dosing and faster absorption of active ingredients compared to some other forms.

A special role is played by solutions for injection (8.7%) – Omnopon. It is used for injections for severe pain or in medical institutions where it is necessary to achieve a rapid analgesic effect. This form of medicines provides high bioavailability and is used mainly for intravenous or subcutaneous administration.

Thus, the variety of dosage forms of codeine medicines allows doctors to choose the optimal treatment option for each patient depending on individual needs and medical indications.

Distribution of codeine medicines by ATC groups:

The distribution of codeine medicines by ATC groups allows to assess their use according to therapeutic areas. This classification is based on an internationally recognized system that provides a standardized approach to the analysis of the pharmacological properties of medicines. The data demonstrate which groups of codeine medicines are in greatest demand and are used for various therapeutic purposes, such as pain relief, cough treatment or combined purposes.

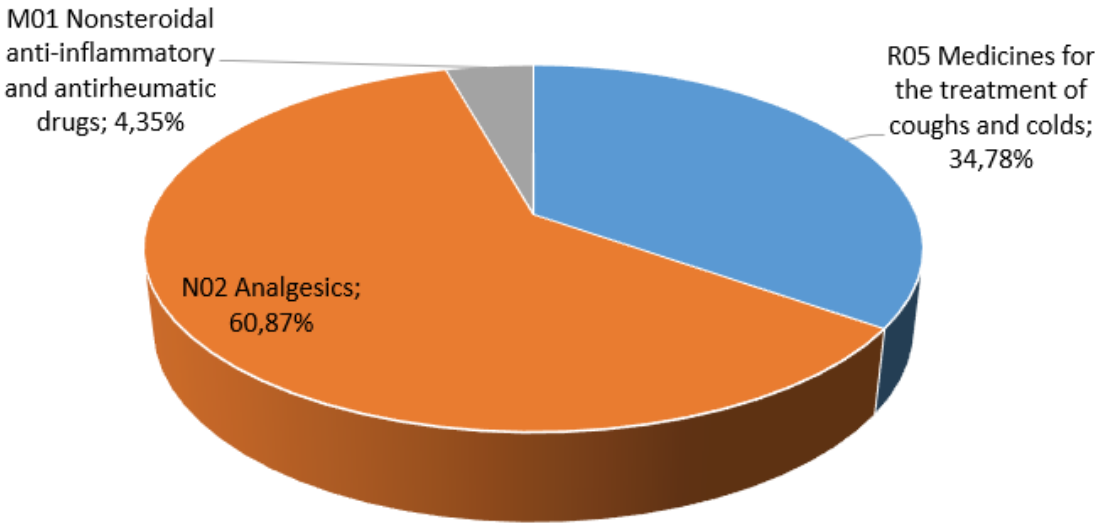

Fig. 2. Distribution of codeines medicine by ATC groups.

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Group R05 covers medicines used to treat cough and other symptoms of colds. This group includes subgroups: mucolytics (R05DA) and combined antitussives (R05FA). These medicines help to thin sputum, facilitate its discharge, and reduce irritation of the respiratory tract mucosa. They are used to treat both acute and chronic conditions associated with cough.

Analgesics occupy the largest share. They account for 60.87% of the total number of codeines medicines. This group includes combined analgesics (N02BE), which often contain codeine in combination with other active substances (paracetamol or ibuprofen). They are effective for relieving pain of varying intensity, from mild to moderate. Due to the synergistic effect of the components, these medicines provide rapid and long-lasting pain relief.

Group M01 includes nonsteroidal anti-inflammatory medicines, which make up 4.35% of codeine medicines. These medicines are used to relieve pain and inflammation accompanying rheumatic diseases, injuries, or other conditions. Medicines from this group provide a complex effect, combining analgesic and anti-inflammatory action, which makes them effective in cases where it is necessary to eliminate both pain and accompanying inflammation.

3. Codeine medicines market in Ukraine

The codeine medicines market in Ukraine has its own characteristics due to restrictions on the circulation of narcotic drugs, which include codeine. Codeine, as an opioid, is limited in circulation and is available only by prescription, which determines its use and availability on the pharmaceutical market. However, there is still a demand for codeine medicines in Ukraine. Especially in the context of pain relief and treatment of respiratory diseases. Here is a detailed analysis of the main aspects of this segment of the pharmaceutical market.

Table 2. Pharmaceutical market codeine medicines.

No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Manufacturer
1.	CODEINE PHOSPHATE	tablets of 0.03 g N.10	"INTERCHIM" Limited Liability Company, Ukraine
2.	CODEPSIN	tablets N. 10	"Pharma Start" LLC, Ukraine
3.	CODETERP	tablets N. 10	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
4.	PARACOD IC	tablets N. 10	"INTERCHIM" Limited Liability Company, Ukraine
5.	CODETERP H	tablets N.10	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
6.	CODESAN IC	tablets N. 10	"INTERCHIM" Limited Liability Company, Ukraine
7.	CODTERPIN IC	tablets N. 10	The company with additional responsibility "INTERCHEM" is the manufacturer responsible for the production of the series; quality control tests (physical/chemical, microbiological purity), storage of finished products; production, storage (finished products, raw materials); quality control tests (physical/chemical), Ukraine
8.	COFEX	60 ml of syrup	Jenom Biotech Pvt. Ltd., India
9.	BIFOK IC	tablets N. 10	"INTERCHIM" Limited Liability Company, Ukraine
10.	CODEFEMOL H	syrup, 100 ml or 200 ml in a bottle	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
11.	CAFFETIN	tablets N. 10	ALKALOID AD Skopje, Republic of North Macedonia
12.	PYATIRCHATKA IC	tablets N. 10	"INTERCHIM" Limited Liability Company, Ukraine

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No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Manufacturer
13.	PENTALGIN IC	tablets N. 10	"INTERCHIM" Limited Liability Company, Ukraine
14.	PENTALGIN-FS	tablets N. 10	"Pharma Start" LLC, Ukraine
15.	SOLPALGIN	capsules N. 10 capsules	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
16.	PENTALGIN FS EXTRA CAPSULES	capsules N.10 capsules	"Pharma Start" LLC, Ukraine
17.	SOLPADEIN	tablets N.12	GlaxoSmithKline Dungarvan Limited, Ireland
18.	SOLPADEIN	soluble tablets N.2	GlaxoSmithKline Dungarvan Limited, Ireland
19.	PENTASET	tablets in bulk: N. 1000 or 5000 tablets	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
20.	PENTALGIN-Zdorovya	tablets N. 10	Limited liability company "Pharmaceutical company "Zdorovya" (packaging from "in bulk" drug of the manufacturer company LLC "Kharkiv pharmaceutical enterprise "Zdorovya narodu", Ukraine), Ukraine
21.	OMNOPON NEO	solution for injections of 1 ml in ampoule N.5	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
22.	OMNOPON-ZN	solution for injection; 1 ml each in ampoule N.5	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine
23.	PENTASET	tablets N. 10	Limited Liability Company "Kharkiv Pharmaceutical Enterprise "People's Health", Ukraine

The main manufacturers of codeine medicines in Ukraine

There are both domestic and foreign manufacturers on the codeine medicines market in Ukraine. Among the domestic companies, the main ones are:

1. Pharmaceutical company "Darnitsa". "Darnitsa" is one of the leaders in the pharmaceutical market of Ukraine and produces several codeine medicines. Medicines of this company are in demand among doctors and patients due to their high quality and affordable price. Their range includes analgesic and combined codeine medicines.
2. Interhim. The company "Interhim" is also one of the main manufacturers of codeine medicines. It produces both analgesic and combined codeine medicines for the treatment of cough.
3. Oltech. Another domestic company that produces codeine medicines. It specializes in the manufacture of medicines for pain relief and the treatment of respiratory diseases.

From the side of foreign manufacturers, the Ukrainian market also has a significant presence of international companies:

1. AbbVie. Manufacturer of the drug "Omnopon", which contains Codeine. Popular on the Ukrainian market among medical institutions. It is used for pain relief and in the treatment of respiratory diseases.
2. Sanofi. One of the world's largest manufacturers of pharmaceutical medicines. Offers codeine medicines mainly for the treatment of cough and pain relief.

Trends in the development of the codeine medicines market in Ukraine

The codeine medicines market in Ukraine is characterized by certain trends that affect its development:

1. Strengthening control over the circulation of narcotic drugs. Since codeine is a narcotic drug, strict rules for its sale and release are imposed on it. This limits the availability of codeine medicines codeine medicine. Provides control from the state, but at the same time creates obstacles for patients who need these drugs.
2. Demand for combined medicines. The trend towards combined codeine medicines continues to grow. The combination of codeine with paracetamol, diphenhydramine or phenobarbital allows you to achieve more effective results in the treatment of pain and cough. Makes such medicines popular among doctors.
3. Growing demand for painkillers. Among the main reasons for the growth in demand for codeine medicines is

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the increase in the incidence of chronic pain and respiratory diseases. This creates additional opportunities for the development of the codeine medicines market. It also increases the responsibility for their proper prescription and use.

4. Innovations in production. Progressive production technologies and new research in the field of pharmaceuticals allow the development of new forms of codeine medicines. This may include more effective tablets, syrups or even medicines for inhalers that reduce side effects and increase the effectiveness of treatment.

5. Changes in legislation. It is expected that over time, changes in legislative acts regulating the circulation of narcotic drugs may occur in the pharmaceutical market. This may contribute to both strengthening control and reducing bureaucratic barriers, which will make medicines more accessible.

Thus, the codeine medicines market in Ukraine is at a stage of stable development with the prospect of increasing demand for painkillers and cough medicines. However, strict state control over their circulation and use remains important.

4. Regulatory aspects of the circulation of codeine medicines

Regulation of the circulation of codeine medicines in Ukraine is an important component of pharmaceutical practice, since codeine is a narcotic drug that requires special control to prevent abuse and ensure patient safety. The rules for registration, dispensing and control of such medicines are strictly regulated by law. They exist both at the national level and at the international level, within which Ukraine also participates.

Let's consider the key regulatory aspects of the circulation of codeine medicines in Ukraine and compare them with international standards.

Registration of codeine medicines in Ukraine

The process of registering codeine medicines in Ukraine is quite complicated. It is regulated by state bodies, in particular the Ministry of Health of Ukraine and the State Medical Service. Key stages of registering codeine medicines:

1. Submission of an application. To register codeine medicines, the manufacturer or distributor submits an application for registration to the Ministry of Health of Ukraine. Since codeine is a narcotic drug, in addition to the standard documentation (clinical trial reports, product characteristics, proof of efficacy and safety), an additional package of documents is submitted, confirming the compliance of the medicines with all safety requirements for the circulation of narcotic drugs.

2. Verification of documents and testing. Medicines undergo quality, efficacy, and safety checks. Special bodies check whether the medicines meet the requirements specified by Ukrainian legislation, as well as international standards for the control of narcotic drugs.

3. Issuance of a registration certificate. After successful testing and verification of all documentation, medicines receive permission for registration. An important requirement is to indicate in the registration documents the category of medicines as a narcotic drug.

Thus, the registration of codeine medicines in Ukraine is a procedure that includes additional control measures, compared to other clinical and pharmacological, classification and legal and nomenclature and legal groups of medicines.

Dispensing codeine medicines

In Ukraine, codeine medicines are dispensed exclusively on prescription. This is the main requirement to prevent abuse of such drugs, since codeine has the potential to develop addiction. According to Ukrainian legislation, there are several important aspects that regulate the dispensing of these codeine medicines:

1. Prescription and control over its execution. Codeine medicines can be purchased only on prescription, which must be issued by a doctor. Prescriptions for such medicines are subject to special control. Prescriptions must be drawn up in accordance with the requirements relating to the circulation of narcotic drugs. Doctors must justify the need to prescribe such medicines. In addition, pharmacists are obliged to check the compliance of the prescription.

2. Quantity limit. For each prescription for codeine medicine, there are restrictions on the quantity that can be dispensed to a patient. This helps to limit the possibility of drug abuse and control the circulation of narcotic drugs.

3. Special storage requirements. Codeine medicines must be stored in pharmacies under special conditions to ensure their safety and prevent unauthorized access.

Control over the circulation of codeine medicines

Control over the circulation of codeine medicines in Ukraine is carried out at several levels:

1. Ministry of Health of Ukraine is the main state body that regulates and controls the use of narcotic drugs. According to Ukrainian legislation, it issues licenses to manufacturers and also controls the distribution of codeine medicines.

2. State Service for Control over Medicines and Drugs. This body is responsible for supervising compliance with regulatory acts relating to the circulation of medicines, including narcotic drugs. They monitor pharmacies and hospitals, check the correctness of prescribing and storage of narcotic drugs.

3. International standards and agreements. Ukraine is a party to international agreements regulating the circulation of narcotic drugs, such as the European Convention on Drug Control and the International Convention against Traffic in Narcotic Drugs and Psychotropic Substances (1971). These agreements provide for strict control of narcotic drugs, including Codeine, and ensure that Ukrainian legislation complies with international requirements.

Comparison with international standards

In Ukraine, the circulation of codeine medicines is regulated in accordance with international standards, but with some peculiarities. According to international rules, such as the Drug Control System defined by the WHO and the 1961 Convention on Narcotic Drugs, Codeine is classified as a narcotic drug. Therefore, countries, including Ukraine, have an obligation to ensure strict control over its circulation, restrict its release only by prescription and provide special monitoring.

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At the international level, there are also different options for regulating the circulation of codeine. In some countries, such as the UK or the USA, codeine may be available without a prescription in low doses. While in Ukraine it is subject to strict control even in small doses. Accordingly, Ukraine is characterized by stricter control compared to some other countries.

Regulatory aspects of the circulation of codeine medicines in Ukraine generally comply with international standards. However, in Ukraine there are some additional restrictions aimed at ensuring the safety of the population and preventing drug abuse. This includes mandatory registration of medicines, prescription, and strict control by state authorities. The trend towards stricter rules for the circulation of codeine corresponds to the global trend of strengthening control over narcotic drugs.

The following is information about the names of medicines, their dosage forms, dosages, registration certificates and registration validity periods. This allows you to easily navigate the available products and their characteristics for further use in medical practice.

Table 3. Data on the registration of codeine medicines in Ukraine.

No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Registry No.	Expiry date from/to
1.	CODEINE PHOSPHATE	tablets of 0.03 g N.10	UA/11811/01/01	unlimited from 12/22/2016
2.	CODEPSIN	tablets N. 10	UA/11812/01/01	unlimited since November 3, 2016
3.	CODETERP	tablets N. 10	UA/3563/01/01	unlimited from 04/09/2020
4.	PARACOD IC	tablets N. 10	UA/12054/01/01	unlimited since March 20, 2017
5.	CODETERP H	tablets N.10	UA/3563/01/02	05/26/2020-05/26/2025
6.	CODESAN IC	tablets N. 10	UA/8687/01/01	unlimited from 01.10.2018
7.	CODTERPIN IC	tablets N. 10	UA/8689/01/01	unlimited from 04.10.2018
8.	COFEX	60 ml of syrup	UA/0711/02/01	unlimited since March 20, 2017
9.	BIFOK IC	tablets N. 10	UA/14315/01/01	unlimited from 06.03.2020
10.	CODEFEMOL H	syrup, 100 ml or 200 ml in a bottle	UA/12779/01/01	unlimited from 10/31/2019
11.	CAFFETIN	tablets N. 10	UA/0742/01/01	unlimited from 04/06/2020
12.	PYATIRCHATKA IC	tablets N. 10	UA/8698/01/01	unlimited from 05.12.2018
13.	PENTALGIN IC	tablets N. 10	UA/8694/01/01	unlimited from 11/30/2018
14.	PENTALGIN-FS	tablets N. 10	UA/2617/01/01	unlimited from 05.12.2019
15.	SOLPALGIN	capsules N. 10 capsules	UA/12311/01/01	unlimited since June 12, 2017
16.	PENTALGIN FS EXTRA CAPSULES	capsules N.10 capsules	UA/10881/01/01	unlimited from 07/08/2020
17.	SOLPADEIN	tablets N.12	UA/4740/03/01	unlimited from March 13, 2018
18.	SOLPADEIN	soluble tablets N.2	UA/4740/01/01	unlimited from 06/09/2021
19.	PENTASET	tablets in bulk: N. 1000 or 5000 tablets	UA/14529/01/01	unlimited since 12/22/2016

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No.	Name of the medicine	Release form (pharmaceutical form, potency (dosage), packaging	Registry No.	Expiry date from/to
20.	PENTALGIN-Zdorovya	tablets N. 10	UA/14757/01/01	unlimited from 15.10.2020
21.	OMNOPON NEO	solution for injections of 1 ml in ampoule N.5	UA/17471/01/01	unlimited from 15.01.2024
22.	OMNOPON-ZN	solution for injection; 1 ml each in ampoule N.5	UA/5179/01/01	unlimited from 05.03.2021
23.	PENTASET	tablets N. 10	UA/5787/01/01	unlimited since 22.03.2016

Table 3 shows that:

- 95.65% of drugs have an unlimited shelf life.
- 4.35% of drugs have a specific shelf life (until 26.05.2025).

5. Warning about the risks of abuse

One of the biggest threats when using medicines that have a high potential for abuse is the development of physical and mental dependence. It is important to understand that if the recommendations for taking such medicines are not followed, the risk of developing addiction increases significantly. This is especially true for medicines that have a sedative, analgesic, or psychoactive effect.

Risk of developing addiction

Abuse of medicines can lead to serious consequences, such as the formation of addiction, which is accompanied by a persistent desire to continue taking the medicine, even in the absence of medical indications. This can lead to such negative consequences as:

Physical dependence: the body begins to adapt to the medicine; to achieve the same effect it is necessary to increase the dose. Canceling the medicine or reducing the dose can lead to withdrawal symptoms, which are expressed in the form of anxiety, body aches, sleep disturbances and other physical manifestations.

Psychological dependence: the mental attitude towards the medicine changes in such a way that it becomes necessary to overcome stress, anxiety, or depression. This can lead to constant use of the medicine without control.

Negative social consequences: people suffering from addiction may experience difficulties in personal relationships, at work, and also have problems with legal status, in particular due to the use of prohibited medicines.

Measures that help minimize risks

To prevent abuse and the development of addiction, several important measures should be taken:

1. Strict adherence to the doctor's recommendations: the patient should strictly follow the doctor's instructions regarding the dosage and frequency of taking the medicine. The doctor should explain to the patient the possible risks and side effects that may occur if the dosage is exceeded or the patient changes the dosage regimen on his own.
2. Monitoring and evaluation of treatment effectiveness: Regular monitoring of the patient by the doctor helps to detect signs of addiction or abuse in time. Assessment of the patient's condition allows for adjustment of treatment and determination of the optimal therapeutic approach.
3. Use of drugs based on low dosage: In cases where the possibility of abuse exists, it is better to prescribe medicines with fewer active ingredients or in less concentrated forms to minimize the potential for abuse.
4. Psychological support and counseling: For patients who are at risk or already prone to addiction, it is important to provide access to psychological help and support. Counselors can help the patient understand the importance of proper treatment and provide support if necessary.
5. Educational programs for patients and health professionals: It is important to conduct educational campaigns for patients about the potential risks of abuse and dependence of medicines. Health professionals should be properly trained in the safe use of such medicines.
6. Restricting access to medicines: In some cases, restricting access to certain medicines can be an effective measure to prevent misuse. This may include prescription-only sales, monitoring purchases, or other restrictions to prevent uncontrolled use.

Warning about the risks of abuse and dependence is a key element of the safe use of medicines. It is important that patients and healthcare professionals actively cooperate in the treatment process, following recommendations and ensuring control over the treatment process. Increasing awareness of potential dangers and implementing risk-minimizing measures will help to preserve the health of patients and avoid serious negative consequences.

Conclusions.

1. Codeine medicines remain an important component of pharmacotherapy due to their effectiveness and variety of release forms, which meets a wide range of medical needs. At the same time, responsible use of such medicines should be under the supervision of a doctor and with strict adherence to recommended doses. Although codeine has a less pronounced analgesic effect compared to other opioids, its safety profile allows it to be used in the treatment of patients, especially for short-term use.
2. The vast majority of codeine medicines (95.83%) are combined, which indicates their use for the treatment of several conditions at the same time, such as pain and cough. Only 4.17% of medicines contain exclusively codeine. This trend emphasizes the widespread use of combined codeine medicines used together with other

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active substances, which allows achieving better treatment results.
3. The codeine medicines market in Ukraine is developing steadily, with the prospect of increasing demand for painkillers and cough medicines. However, a system of control over their circulation remains important, ensuring patient safety and minimizing the risks of abuse.
4. Regulatory measures for the circulation of codeine medicines in Ukraine comply with international standards, with additional restrictions aimed at ensuring safety. The control system provides for the registration of medicines, prescription, and strict control by state authorities. This practice corresponds to global trends in strengthening control over narcotic drugs.
5. An important aspect of the safe use of codeine medicines is warning about the risks of abuse and addiction. To do this, it is necessary to actively cooperate between patients and medical professionals, adhering to all recommendations and ensuring control over treatment. Raising awareness of possible dangers and implementing measures to minimize them will help preserve the health of patients and avoid serious negative consequences.

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Data availability statement. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Antitussive codeine medicines in Ukraine: clinical and pharmacological, marketing, regulatory aspects, and forecasts

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Introduction. The circulation and use of codeine-containing medicines require strict regulation to ensure effective pain and cough treatment while minimizing misuse risks. In Ukraine, the availability of such medicines is subject to regulatory measures aimed at balancing accessibility and safety. This study examines the effectiveness, diversity of pharmaceutical forms, and regulatory aspects of codeine-containing medicines in compliance with international standards. **Materials and methods.** The study is based on a systematic review of scientific literature and regulatory documents regarding the circulation and use of codeine-containing medicines in Ukraine. Data analysis included the assessment of pharmaceutical forms, prescription regulations, and restrictions designed to prevent misuse. The study also considered statistical data on the prevalence of codeine-containing medicines and their therapeutic applications in clinical practice. **Results and discussion.** The study identified a significant variety of codeine-containing pharmaceutical forms, with combination formulations demonstrating advantages in pain and cough management. Strict regulatory measures are in place, including mandatory registration, prescription-only dispensing, and expiration date restrictions. The research highlighted that 95.83% of codeine medicines are combination drugs, which indicates their use for treating multiple conditions simultaneously, such as pain and cough. Only 4.17% of medicines contain exclusively codeine, emphasizing the preference for combination therapy. Additionally, the market for codeine medicines in Ukraine is developing steadily, with an increasing demand for painkillers and cough medicines. However, ensuring patient safety and minimizing the risks of abuse remain essential aspects of regulation. Despite the comprehensive regulatory framework, there are still gaps in public awareness regarding misuse risks and the need for enhanced collaboration between patients and healthcare providers. **Conclusions.** Codeine medicines remain an important component of pharmacotherapy due to their effectiveness and variety of release forms, which meet a wide range of medical needs. At the same time, responsible use of such medicines should be under the supervision of a doctor and with strict adherence to recommended doses. Although codeine has a less pronounced analgesic effect compared to other opioids, its safety profile allows it to be used in the treatment of patients, especially for short-term use. The vast majority of codeine medicines (95.83%) are combined, which indicates their use for the treatment of several conditions at the same time, such as pain and cough. Only 4.17% of medicines contain exclusively codeine. This trend emphasizes the widespread use of combined codeine medicines used together with other active substances, which allows achieving better treatment results. The codeine medicines market in Ukraine is developing steadily, with the prospect of increasing demand for painkillers and cough medicines. However, a system of control over their circulation remains important, ensuring patient safety and minimizing the risks of abuse. Regulatory measures for the circulation of codeine medicines in Ukraine comply with international standards, with additional restrictions aimed at ensuring safety. The control system provides for the registration of medicines, prescription, and strict control by state authorities. This practice corresponds to global trends in strengthening control over narcotic drugs. An important aspect of the safe use of codeine medicines is warning about the risks of abuse and addiction. To do this, it is necessary to actively cooperate between patients and medical professionals, adhering to all recommendations and ensuring control over treatment. Raising awareness of possible dangers and implementing measures to minimize them will help preserve the health of patients and avoid serious negative consequences.

Keywords: cough, codeine, codeines medicines, pharmacology, marketing, pharmacotherapy, regulatory barriers, safety.

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