UKRAINIAN JOURNAL
OF MEDICINE, BIOLOGY AND SPORTS
Volume 10, No. 1. 2025

Journal homepage: https://uajmbs.com.ua/en
Article's History: Received: 18.10.2024; Revised: 28.01.2025; Accepted: 06.03.2025

UDC 615.24:339.13.021:339.138 **DOI:** 10.63341/ujmbs/1.2025.08

Analysis of outpatient consumption of propulsives in Ukraine compared with Norway and the Baltic states

Olga Gerasymova
PhD in Pharmaceutical Sciences, Associate Professor
National University of Pharmacy
61002, 53 H. Skovoroda Str., Kharkiv, Ukraine
https://orcid.org/0000-0003-0278-5705

Larysa Iakovlieva
Doctor of Pharmaceutical Sciences, Professor
National Technical University "Kharkiv Polytechnic Institute"
61002, 2 Kyrpichova Str., Kharkiv, Ukraine
https://orcid.org/0000-0002-9961-4664

Oksana Tkachova*
Doctor of Pharmaceutical Sciences, Professor
National University of Pharmacy
61002, 53 H. Skovoroda Str., Kharkiv, Ukraine
https://orcid.org/0000-0003-4646-0400

Abstract. Disorders involving impaired gastrointestinal peristalsis are widely prevalent both globally and in Ukraine. Propulsives drugs, which enhance the motor activity of the gastrointestinal tract and prevent antiperistaltic contractions of the intestinal smooth muscle, are used in the treatment of such conditions. This study aimed to assess the outpatient consumption of medicinal products classified under group A03F propulsives in Ukraine between 2020 and 2022, in comparison with published data on the use of the same drug group in Norway, Estonia, Lithuania, and Latvia. Consumption volumes were determined using the ATC/DDD methodology and expressed in DDDs per 1,000 inhabitants per day (DIDs). The results were compared with corresponding published statistical data from Norway and the Baltic countries. The findings indicated that the consumption of medicines in group A03F ranged from 0.98 to 1.21 DIDs over the study period, with a decrease observed in 2022. Ukraine differed only slightly from Norway and the Baltic states in terms of the consumption levels of these medicines. The leading position in the consumption of A03F group medicines varied by year: in 2020 – Norway; in 2021 – both Ukraine and Norway; and in 2022 – Lithuania. The lowest consumption volumes were recorded in Estonia. During the study period, domperidone was the most commonly used propulsives in Ukraine, while metoclopramide was most widely used in Norway and the Baltic countries. A comparative assessment of approaches to the use of propulsives in these countries was conducted. The findings may be used to determine the level of access in Ukraine to essential medicines for patients with gastrointestinal motility disorders and to support decision-making by healthcare authorities regarding regulatory measures

Keywords: pharmaceutical market; ATC/DDD methodology; medicine consumption; gastrointestinal motility disorders; metoclopramide; domperidone; itopride hydrochloride; mosapride

Introduction

Disorders of peristalsis play a significant role in the patho-genesis of many gastrointestinal (GI) diseases and conditions. According to the Rome Foundation Global Epidemiology Study (RFGES), the global prevalence of functional GI disorders averages 40.3%. These conditions have substantial economic implications for healthcare systems

Suggest Citation:
Gerasymova O, Iakovlieva L, Tkachova O. Analysis of outpatient consumption of propulsives in Ukraine compared with Norway and the Baltic states. Ukr J Med Biol Sport. 2025;10(1):08–15. DOI: 10.63341/ujmbs/1.2025.08

*Corresponding author

and adversely affect patients' quality of life [1]. As reported by A. Vernon-Roberts *et al.* [2], functional GI disorders account for approximately 5% of visits to primary care physicians and are a common reason for referrals to tertiary care services for further investigation or to exclude serious organic diseases. A. Fikree *et al.* [3] note that such disorders are associated with 30% of outpatient gastroenterology consultations and represent 12% of the workload in primary care. Motor function disorders occur in patients of various ages and sexes, although they are more frequently observed in women than in men. According to Y.V. Karulina [4], such disorders are present in over 30% of paediatric patients with digestive system pathologies. These findings highlight the relevance of investigating the population-level consumption of medicines used to treat gastrointestinal peristalsis disorders.

Propulsives are the treatment of choice for GI motility disorders. Through various mechanisms of action, they enhance GI motor activity, prevent antiperistaltic contractions of the intestinal smooth muscle, and are used as part of first-line therapy for functional GI disorders. According to V.V. Chernyavskyi & L.L. Pavlovskyi [5], medicines from this group are considered a cornerstone of pharmacotherapy and are prioritised in the treatment of functional dyspepsia with predominant postprandial distress syndrome. In a study on approaches to prokinetic therapy for gastric motility disorders conducted by M. Camilleri *et al.* [6], it was found that propulsives are prescribed as the first pharmacological option following dietary advice, due to their ability to improve gastric emptying and alleviate symptoms of gastroparesis. An expert review by the European Society of Neurogastroenterology and Motility and the American Neurogastroenterology and Motility Society, as presented by S. Bor *et al.* [7], emphasised that medicines in this group improve GI motility both regionally and throughout the intestine. Each agent has specific advantages and limitations, as well as a distinct safety profile. These findings are supported by research conducted by Y.V. Nikiforova [8], which explored the clinical use of propulsives. In particular, the study highlighted the role of domperidone in the treatment of functional dyspepsia and gastro-oesophageal reflux disease, as well as its potential use following gastric resection, during cytostatic therapy, and in diabetic gastroparesis.

Available literature provides limited data on the consumption of medicines from the A03F group, propulsives. The existing data, obtained using the ATC/DDD methodology, are primarily the results of previous studies conducted on outpatient consumption of medicines from this group in Ukraine and selected other countries during 2016-2018 [9]. Comparable studies on the consumption of propulsives, expressed in DDDs per 1,000 inhabitants per day, conducted outside Ukraine are not found in the currently accessible literature. Only hospital consumption data for the broader A03 group, Drugs for functional gastrointestinal disorders, are available – specifically for Romania (1998-2018), as reported by M. Pană *et al.* [10], and for Moldova (2009-2013), as documented by E.P. Bernaz [11].

Given the growing global relevance of gastrointestinal motility disorders, continued investigation into the consumption of A03F group medicines in Ukraine is warranted, along with a comparative analysis of their use in other countries. This study aimed to assess the outpatient consumption of A03F propulsives in Ukraine between 2020 and 2022, in comparison with published data on the same group of medicines in Norway, Estonia, Lithuania, and Latvia.

Materials and Methods

The study period (2020-2022) was selected based on the most recent available statistical data on outpatient consumption of A03F group medicines, propulsives, in the countries chosen for comparison. Data from the pharmaceutical market research system "Proxima Research"/"Morion" provided by Morion Ltd were used to analyse the range and volume of these medicines. This included information on the number of international non-proprietary names (INNs), trade names (TNs), and units of medicine sold.

To assess outpatient medicine consumption, the ATC/DDD methodology was employed. This method is recognised by the World Health Organization (WHO) as the international standard in this field. The ATC/DDD methodology is based on the Anatomical Therapeutic Chemical (ATC) classification system and the assumed average maintenance dose per day for a medicine used for its main indication in adults (Defined Daily Dose – DDD) [12, 13]. Compared to other approaches that measure consumption in physical units (e.g. number of packages), the ATC/DDD methodology calculates a relative indicator and is considered the most reliable for evaluating whether the structure of medicine use aligns with the needs of the healthcare system. It also allows for meaningful cross-country comparisons.

The DDD values for the INNs of the medicines were obtained from the WHO website [14]. Where DDDs were not available, the Prescribed Daily Dose (PDD) was calculated using the official instructions for medical use. To determine the volume of A03F propulsives consumed in Ukraine, the number of DDDs for each medicine was calculated for each study year, followed by the calculation of DDDs per 1,000 inhabitants per day (DIDs). This relative indicator made it possible to estimate the number of DDDs consumed daily by every 1,000 people in the population over the study period. For the calculation of DIDs, population data from the State Statistics Service of Ukraine [15] were used, reflecting the available population as of 1 January for each respective year: 2020 – 41,902.4 thousand; 2021 – 41,588.4 thousand; 2022 – 41,167.3 thousand. The formula applied for the calculation was:

$$DIDs = DDDs \times 1{,}000 / Population\ of\ Ukraine \times 365\ days, \quad (1)$$

where *DDDs* is the number of defined daily doses consumed in Ukraine in a given year.

To compare the volume, structure, and dynamics of outpatient consumption of A03F group medicines in Ukraine during 2020-2022 with other countries, Norway

and the Baltic states (Lithuania, Latvia, and Estonia) were selected. The selection criterion for these countries was the availability of statistical data on outpatient consumption of A03F medicines during the same period, calculated using the ATC/DDD methodology, as published for Norway [16], Estonia [17], Lithuania [18], and Latvia [19].

Results and Discussion

At the first stage of the study, the range of A03F propulsives available on the Ukrainian pharmaceutical market during 2020-2022 was analysed, and the number of INNs and TNs recorded within the study period was determined. The findings are presented in Table 1. Analysis of the Ukrainian pharmaceutical market revealed that medicines in the A03F group were represented by four INNs between 2020 and 2022: domperidone, metoclopramide, itopride hydrochloride, and mosapride. The number of TNs for prokinetic agents varied slightly over the years, ranging from 33 to 34. Domperidone products accounted for the majority (18-20 TNs), while mosapride was represented by only one TN. Throughout the study period, the market was predominantly composed of Ukrainian-produced A03F medicines. Notably, no Ukrainian-manufactured trade names of mosapride were present during this time. The price range per pack for TNs of metoclopramide, domperidone, and itopride hydrochloride was broad, providing options suitable for patients with varying levels of purchasing power.

Table 1. Range of A03F propulsives on the Ukrainian pharmaceutical market in 2020-2022

ATC code, INN of medicines	Number of TN of medicines			Number of Ukrainian/ imported TNof medicines			Price range per package of medicine, UAH		
	2020	2021	2022	2020	2021	2022	2020	2021	2022
A03FA01 Metoclopramide	7	7	7	5/2	5/2	5/2	38.24-533.16	40.91-576.59	48.89-620.87
A03FA03 Domperidone	20	18	18	14/6	12/6	12/6	11.67-189.77	21.68-199.70	26.87-245.35
A03FA07 Itopride hydrochloride	6	7	8	1/5	2/5	2/6	111.59-641.80	115.39-656.51	133.39-855.36
A03FA09 Mosapride	1	1	1	0/1	0/1	0/1	158.68	173.73	217.81
Total	34	33	34	20/14	19/14	19/15	11.67-641.80	21.68-656.51	26.87-855.36

Source: compiled by the authors based on original research

In Ukraine, the use of prokinetic agents is regulated by current unified clinical protocols for the medical management of patients with gastro-oesophageal reflux disease and dyspepsia [20, 21], as well as the new clinical protocol "Guidelines 00172. Nausea and Vomiting", developed by international experts [22]. Trade names of metoclopramide, a representative of this pharmacological group, are included in the Affordable Medicines programme, according to the List of Medicinal Products subject to reimbursement under the state-guaranteed healthcare scheme [23]. The next stage of the study involved calculating DDDs per 1,000 inhabitants per day (DIDs) for A03F propulsives available on the Ukrainian pharmaceutical market during the study period, with the aim of assessing the volume, structure and trends in their outpatient use. The results showed that consumption levels of A03F propulsives in Ukraine over 2020-2022 were as follows: 2020 – 1.08 DIDs; 2021 – 1.21 DIDs; 2022 – 0.98 DIDs. Consumption figures for this medicine group varied annually, with the lowest value recorded in 2022 compared to previous years. Based on these findings, calculated per 1,000 Ukrainian inhabitants, it can be concluded that approximately 0.10%-0.12% of the Ukrainian population consumed one Defined Daily Dose (DDD) of a propulsives each day throughout the respective years. The consumption volumes of the INN of medicines belonging to the A03F group in Ukraine during 2020-2022 are shown in Figure 1.

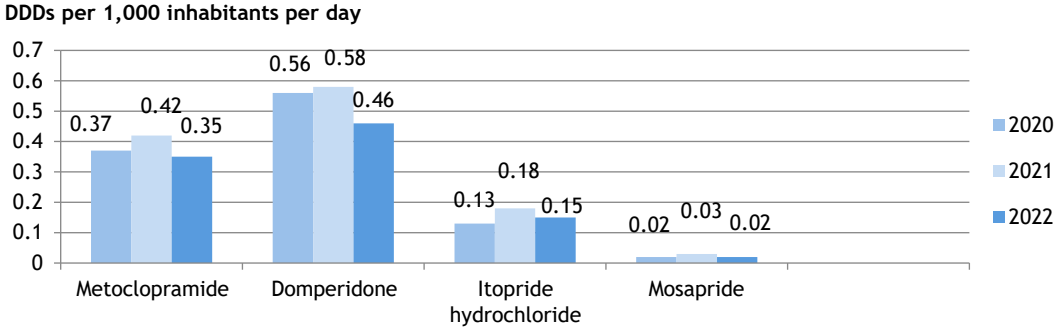

Figure 1. Outpatient consumption of A03F propulsives in Ukraine by INN, 2020-2022

Source: compiled by the authors based on original research

The highest consumption volumes in 2020-2022 were recorded for domperidone, which accounted on average for 49% of the total consumption of A03F medicines. This can be attributed to the wide availability of low-cost generics in the Ukrainian pharmaceutical market. These findings are consistent with data from the "PharmXplorer" market research system by Proxima Research, which listed domperidone among the top 10 most frequently prescribed INNs by gastroenterologists for digestive disorders in 2022 [24]. The lowest consumption volumes were observed for mosapride. During 2020-2021, the consumption of all A03F propulsives increased, but in 2022, there was a decline, coinciding with the onset of russia's full-scale invasion of Ukraine. This decrease may be linked to the significant migration of the Ukrainian population to other countries.

The next stage of the study involved comparing the results of outpatient consumption of A03F propulsives in Ukraine with published statistical data for 2020-2022 from Norway, Estonia, Lithuania and Latvia. The results are presented in Table 2.

Table 2. Volume and structure of consumption (DDDs per 1,000 inhabitants per day) of A03F propulsives in Ukraine, Norway, Estonia, Lithuania, Latvia in 2020-2022

No.	ATC code,INN of medicines	Indicator (DDDs per 1,000 inhabitants per day - DIDs)/country/years														
		Ukraine			Norway			Estonia			Lithuania			Latvia		
		2020	2021	2022	2020	2021	2022	2020	2021	2022	2020	2021	2022	2020	2021	2022
1	A03FA01 Metoclopramide	0.37	0.42	0.35	1.13	1.20	1.26	0.80	0.84	0.89	0.87	0.85	0.96	0.70	0.74	0.76
2	A03FA03 Domperidone	0.56	0.58	0.46	0.01	0.01	0.01	0.01	0.02	0.02	0.17	0.19	0.22	0.31	0.31	0.31
3	A03FA07 Itopride hydrochloride	0.13	0.18	0.15	-	-	-	-	-	-	-	-	0.24	-	-	-
4	A03FA09 Mosapride	0.02	0.03	0.02	-	-	-	-	-	-	-	-	-	-	-	-
	Total	1.08	1.21	0.98	1.14	1.21	1.27	0.81	0.86	0.91	1.04	1.04	1.42	1.01	1.05	1.07

Source: compiled by the authors based on original research and data [16-19]

During the study period, a nearly identical proportion of the population in each of the countries examined consumed 1 DDD of one of the prokinetic agents daily: Norway – between 0.11% and 0.13%, Lithuania – between 0.10% and 0.14%, Latvia – between 0.10% and 0.11%, and Estonia – between 0.08% and 0.09%. Leadership in the volume of A03F propulsives consumption shifted across countries during the period: in 2020, Norway ranked highest; in 2021, Ukraine and Norway shared the lead; and in 2022, Lithuania recorded the highest levels. Estonia consistently reported the lowest consumption volumes throughout the entire study period. Across all countries, the consumption of A03F propulsives fluctuated over time. In 2022, a decrease in consumption was observed in Ukraine, while Norway, Estonia, Latvia, and Lithuania recorded increases. Notably, Lithuania experienced a 1.3-fold increase in 2022 compared with 2020 and 2021, possibly due to an expansion in the range of available INNs of prokinetic agents in that year.

An analysis of the consumption structure of this group of medicinal products revealed that four substances were used in Ukraine (metoclopramide, domperidone, itopride hydrochloride, and mosapride). According to published statistical data from Norway [16], Estonia [17], and Latvia [19], only two INNs (domperidone and metoclopramide) were recorded over the three-year study period. In Lithuania, only two INNs (domperidone and metoclopramide) were used during 2020-2021, while in 2022, data on the consumption of three INNs (domperidone, metoclopramide, and itopride hydrochloride) were reported [18]. In Ukraine, domperidone was the clear leader in terms of consumption volume, whereas in the other four European countries studied, metoclopramide was most frequently used. This indicates differing national approaches to the use of A03F propulsives.

Ambulatory consumption of A03F group medicinal products has been the subject of relatively limited academic investigation. Available literature includes data only from a previous study by the authors on the use of this group of medicinal products in 2016-2018 in Ukraine and selected European countries (Norway, Estonia, Lithuania, and Latvia) [9], with no additional research findings reported by other scholars.

A comparison of the results of propulsives consumption in Ukraine during 2020-2022, as presented in the current study, with those from the earlier analogous study [9], indicates that there were no significant changes in consumption levels of this group of medicinal products over the six-year observation period: 1.03 in 2016, 1.15 in 2017, 1.27 in 2018 [9], 1.08 in 2020, 1.21 in 2021, and 0.98 in 2022. While Ukraine led in the consumption of these medicines among the studied European countries in 2018, it held lower positions in the rankings in 2016-2017 and 2020-2022. However, the overall differences in consumption volumes across the countries were relatively minor. Estonia consistently recorded the lowest values for DDDs per 1,000 inhabitants per day for this group of medicines across both study periods (2016-2018 and 2020-2022). Over time, the proportion of the population taking 1 DDD of a propulsives daily remained largely unchanged in Ukraine, Norway, and the Baltic states, ranging from 0.10% to 0.12% in Ukraine during both the 2016-2018 and 2020-2022 periods. Norway recorded a daily consumption rate of 0.11% during 2016-2018, increasing slightly to between 0.11% and 0.13% in 2020-2022. In Lithuania, the proportion ranged from 0.12% to 0.14% in 2016-2018, and from 0.10% to 0.14% in 2020-2022. In Latvia, it varied between 0.11% and 0.13% during 2016-2018 and between 0.10% and 0.11% in 2020-2022.

Estonia consistently showed the lowest values, from 0.08% to 0.09%, across both periods. Notably, changes in the approach to the use of A03F propulsives were observed only in Lithuania. In 2022, the use of itopride hydrochloride was introduced in the country, which may be attributed to its favourable safety profile compared with other propulsives. This advantage was explicitly highlighted in the Rome IV criteria for functional gastrointestinal disorders [25]. The leading substances by the number of consumed DDDs remained unchanged in 2020-2022: in Ukraine, domperidone was predominant, while in Norway and the Baltic states, metoclopramide maintained its leading position. These two medicines are the most widely known and well-researched representatives of the propulsives [5, 6].

Metoclopramide and domperidone are both dopamine receptor antagonists; however, they differ in chemical structure, and consequently in their safety profiles and clinical applications [26-28]. Metoclopramide inhibits central dopamine D2 and serotonin 5-HT3 receptors, blocks intestinal D2 and muscarinic receptors, and acts as an agonist at peripheral 5-HT4 serotonin receptors. According to V.V. Chernyavskyi & L.L. Pavlovskyi [5], who examined the use of propulsives in the management of functional gastroduodenal disorders, metoclopramide is primarily employed as an anti-nausea and antiemetic agent. In the opinion of S.M. Tkach & A.E. Dorofieiev [26], who conducted a comparative analysis of the efficacy and safety of dopamine receptor antagonists in gastrointestinal disorders, metoclopramide is considered a weak stimulant of intestinal peristalsis and is most frequently prescribed for gastroparesis of various origins. According to M.A. Kalas *et al.* [27], who investigated the mechanism of action and safety profile of metoclopramide, it is regarded as the only medicine approved by the FDA in the past 40 years specifically for the treatment of gastroparesis.

According to a study by Y.V. Nikiforova [8] on the role and place of domperidone in contemporary clinical practice, domperidone is considered the treatment of choice for managing peristaltic disorders and is included in combination therapy regimens for GI disease. Domperidone belongs to the benzimidazole class and acts as a peripheral D2-receptor antagonist. These receptors mediate dopamine's predominantly inhibitory effect on smooth muscle by interacting with the cholinergic system [26]. As reported by H.V. Osiodlo & O.O. Fedorova [25], domperidone does not cross the blood-brain barrier and therefore does not cause many of the central adverse effects associated with metoclopramide, such as extrapyramidal disorders, headache, dizziness or drowsiness. According to V.V. Chernyavskyi & L.L. Pavlovskyi [5], the most clinically significant adverse reactions associated with domperidone involve the cardiovascular system. These include sudden cardiac death, QT interval prolongation, severe ventricular arrhythmias and torsade de pointes tachycardia. As a result, the use of domperidone has been restricted in many countries [26], prompting numerous clinical studies on its cardiovascular safety. These studies have supported its continued use with strict precautions. A cohort study by A. Cowan *et al.* [28] found a low risk of hospitalisation due to ventricular arrhythmia following a 30-day course of outpatient treatment with domperidone. No significant difference in risk levels was identified between domperidone and metoclopramide. According to other researchers [25], significant adverse effects associated with domperidone include elevated serum prolactin levels and the development of gynaecomastia, galactorrhoea and amenorrhoea. It is recommended that domperidone be used at the lowest effective dose for the shortest duration necessary to control symptoms. This approach helps minimise the risk of adverse effects, as demonstrated in the study by S. Alkhowaiter *et al.* [29], which investigated the treatment of chronic GI motility disorders in patients with systemic sclerosis. These adverse effects may have influenced the level of domperidone consumption observed in Norway, Estonia, Lithuania and Latvia, as established in the present study. In Ukraine, the use of domperidone is regulated by the current unified clinical protocols for the management of patients with gastro-oesophageal reflux disease and dyspepsia [20, 21].

The differences identified in the use of propulsives between Ukraine and the studied European countries highlight the need for further investigation into the medical, social, economic and political factors that affect the consumption and therapeutic use of this group of medicines across different countries. Relevant areas for exploration include clinical prescribing practices, the structure and policies of national healthcare systems, regulatory frameworks for medical care, medicine availability, patient awareness of treatment, and adherence to prescribed therapies. The findings from such studies could be valuable for healthcare policymakers and may contribute to improving medical and pharmaceutical care for patients with GI motility disorders.

Conclusions

Using the ATC/DDD methodology, an assessment was conducted of outpatient consumption of medicines in the A03F group, propulsives, in Ukraine during 2020-2022. The results were compared with published data on the consumption of this group of medicines in Norway and the Baltic countries. During the study period, four INNs from this group (metoclopramide, domperidone, itopride hydrochloride, and mosapride) were available on the Ukrainian pharmaceutical market, represented by 33 to 34 TN of medicines, mostly produced by Ukrainian manufacturers. Outpatient consumption volumes of propulsives, measured by the number of DDDs consumed, varied in Ukraine during the study period, with a 19% decrease recorded in 2022 compared to 2021. This decline may be attributed to the mass migration of the population abroad following the outbreak of full-scale war in the country.

The level of outpatient consumption of propulsives in Ukraine during 2020-2022 differed only slightly from that in Norway and the Baltic countries. Throughout the study period, the consumption of medicines in this group

fluctuated across all these countries, with the highest levels recorded in different countries in different years – Norway, Ukraine, and Lithuania. The lowest level of consumption during 2020-2022 was observed in Estonia. In contrast to Ukraine, a general upward trend in outpatient consumption of propulsives was noted in Norway and the Baltic countries, possibly reflecting gradual improvements in the diagnosis of functional bowel disorders and increased attention to patients' quality of life.

In terms of structure, outpatient consumption of medicines in the A03F propulsives in Ukraine differed significantly from that in Norway and the Baltic countries. In Ukraine, domperidone was the most commonly prescribed, whereas metoclopramide predominated in Norway and the Baltic states. Unlike Ukraine, clinical practice in Norway, Estonia, and Latvia was limited to TNs based on only two INNs (domperidone and metoclopramide), while in Lithuania, three INNs (domperidone, metoclopramide, and itopride hydrochloride) were used. These differences reflect varying approaches to the treatment of conditions associated with gastrointestinal motility disorders and the use of this group of medicines across the studied countries, which are shaped by national clinical guidelines, medical traditions, and medicine availability.

The study findings may contribute to the development of pharmaceutical policy and reimbursement systems for A03F group medicines in Ukraine within the framework of outpatient care for gastrointestinal motility disorders. Given the widespread prevalence of such conditions among the population of Ukraine and other countries, as well as the observed variation in the use of propulsives across different nations, further research into the volume of A03F medicine consumption in Ukraine, and comparisons with other countries in terms of consumption volume and structure, would be beneficial.

Acknowledgements
None.

Funding
This study received no funding.

Conflict of Interest
None.

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Аналіз амбулаторного споживання стимуляторів перистальтики в Україні у порівнянні з Норвегією та країнами Балтії

Ольга Герасимова
Кандидат фармацевтичних наук, доцент
Національний фармацевтичний університет
61002, вул. Григорія Сковороди, 53, м. Харків, Україна
https://orcid.org/0000-0003-0278-5705

Лариса Яковлєва
Доктор фармацевтичних наук, професор
Національний технічний університет «Харківський політехнічний інститут»
61002, вул. Кирпичова, 2, м. Харків, Україна
http://orcid.org/0000-0002-9961-4664

Оксана Ткачова
Доктор фармацевтичних наук, професор
Національний фармацевтичний університет
61002, вул. Григорія Сковороди, 53, м. Харків, Україна
http://orcid.org/0000-0003-4646-0400

Анотація. Захворювання з розладами перистальтики шлунково-кишкового тракту значно поширені серед населення як в світі, так і в Україні. При їх лікуванні застосовують препарати стимуляторів перистальтики, які посилюють моторну активність шлунково-кишкового тракту і запобігають антиперистальтичним скороченням гладкої мускулатури в кишечнику. Метою роботи була оцінка амбулаторного споживання лікарських засобів групи A03F «Стимулятори перистальтики» у 2020-2022 роках в Україні у порівнянні з аналогічними опублікованими даними щодо споживання лікарських засобів цієї ж групи в таких країнах, як Норвегія, Естонія, Литва та Латвія. Обсяги споживання препаратів визначали за ATC/DDD-методологією у показниках «DDDs/1000 жителів/день» (або DIDs). Отримані дані порівнювали з аналогічними опублікованими статистичними даними Норвегії та країн Балтії. Основні результати дослідження показали, що обсяги споживання лікарських засобів групи A03F «Стимулятори перистальтики» протягом досліджуваного періоду становили 0,98-1,21 DIDs та в 2022 році зменшились. Україна незначно відрізнялась від Норвегії та країн Балтії за рівнем споживання цих препаратів. Позицію лідера за обсягами споживання лікарських засобів досліджуваної групи A03F обіймали різні країни: 2020 рік – Норвегія, 2021 рік – Україна та Норвегія, 2022 рік – Литва. Найменші обсяги споживання встановлені в Естонії. Лідером за обсягами споживання у досліджуваний період в Україні був домперидон, в Норвегії та країнах Балтії – метоклопрамід. Проведена порівняльна оцінка підходів до використання стимуляторів перистальтики в цих країнах. Отримані дані можуть бути використані для встановлення рівня забезпеченості в Україні пацієнтів з захворюваннями, які супроводжуються порушеннями перистальтики шлунково-кишкового тракту, базовими препаратами для їх корекції, і для прийняття відповідних регуляторних рішень організаторами охорони здоров'я

Ключові слова: фармацевтичний ринок; ATC/DDD-методологія; споживання лікарських засобів; порушення перистальтики шлунково-кишкового тракту; метоклопрамід; домперидон; ітоприду гідрохлорид; мозаприд