

Adherence to the Pharmacist's Protocol of sore throat symptomatic treatment in Ukraine and problems of harmonization with international guidelines

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Background: Good pharmaceutical counselling in the sore throat symptomatic treatment is an important component of the health care first line, timely detection of infectious diseases, provision of qualified assistance, prevention of complications, and correct use of medications.

Methods: The study included a self-assessment of adherence of Ukrainian pharmacists to the Pharmacist Protocol through a survey, evaluation of the level of awareness of Ukrainian pharmacists with international standards for the symptomatic treatment of sore throat, assessing prospects and finding ways to harmonize the Ukrainian standard with international ones.

Results: A high level of commitment of pharmacists to the proper detection of the patient's problem, high fluctuations in adherence to the detection of specific "alarm" symptoms, an average level of proper information about the medications, a low level of awareness of international approaches to the sore throat symptomatic treatment with nonsteroidal anti-inflammatory drugs were established. Based on the results of the assessment of prospects, it was determined that there are basement and opportunities for Ukrainian Pharmacist's Protocol harmonization with international guidelines.

Conclusions: Based on the conducted research, proposals for changes to the Pharmacist's Protocol were developed.

Key words: Ukrainian pharmacists, sore throat, self-medication, standards, harmonization.

Dodržování Protokolu lékárníka pro symptomatickou léčbu bolesti v krku na Ukrajině a problémy harmonizace s mezinárodními pokyny

Úvod: Kvalitní farmaceutické poradenství při symptomatické léčbě bolesti v krku je důležitou součástí primární zdravotní péče, včasného rozpoznání infekčních onemocnění, poskytování kvalifikované pomoci, prevence komplikací a správného užívání léčiv.

Metody: Studie zahrnovala sebehodnocení dodržování Protokolu lékárníka ukrajinskými lékárníky prostřednictvím dotazníkového šetření, hodnocení úrovně jejich povědomí o mezinárodních standardech pro symptomatickou léčbu bolesti v krku, posouzení perspektiv a hledání způsobů harmonizace ukrajinského standardu s mezinárodními pokyny.

Výsledky: Byla zjištěna vysoká míra angažovanosti lékárníků ve správném rozpoznání problému pacienta, výrazné kolísání v dodržování postupů při rozpoznávání specifických varovných příznaků, průměrná úroveň správného informování o léčivých přípravcích a nízká úroveň povědomí o mezinárodních přístupech k symptomatické léčbě bolesti v krku nesteroidními protizánětlivými léky. Na základě hodnocení perspektiv bylo zjištěno, že existují základy a příležitosti pro harmonizaci ukrajinského Protokolu lékárníka s mezinárodními pokyny.

Závěry: Na základě provedeného výzkumu byly vypracovány návrhy na změny v Protokolu lékárníka.

Klíčová slova: ukrajínští lékárníci, bolest v krku, samoléčba, standardy, harmonizace.

Introduction

A sore throat is a symptom of an upper respiratory tract infection and a continual topic of discussion in the medical community. Most of the discussed issues are devoted to the diagnosis of the cause of sore throat and the early detection of beta-hemolytic streptococcus A, approach to antibacterial therapy, risk of antibiotic resistance, physical, microbiological and immunological balance of the mucous membrane of the oral cavity, cause-effect relations between the state of the oral cavity microbiota and the risks for systemic disease development (1, 2, 3, 4).

However, sore throat is a symptom not only of bacterial but mostly viral infection, as well as non-infectious lesions. Pain in the throat can be accompanied by hoarseness of the voice, negatively affects its height and strength. Such condition reduces a person's communicative abilities, undermines their opportunities to interact in everyday life, thereby adding social factors to the deterioration of the quality of life (5).

A sore throat of viral and non-infectious nature is usually treated symptomatically. A large number of over-the-counter (OTC) drugs based on non-steroidal anti-inflammatory drugs (NSAIDs), anaesthetics, antiseptics, and natural remedies have been introduced into medical practice. Existing international (European, British, American) guidelines are unanimous in their recommendations of analgesics-antipyretics and NSAIDs for the sore throat symptomatic treatment (6, 7).

Today, in Ukraine, in the circumstances of a full-scale war with Russia and the increased burden on the medical component of health care, the pharmacist's participation in primary care support is more important than ever. Pharmacist's Protocols for the symptomatic treatment of mild ailments, including sore throat, have been developed in Ukraine (first version in 2010, final in 2022) (8).

The content, destination, purposes, and structure of the Pharmacist's Protocol for dispensing over-the-counter medicines titled „Symptomatic treatment of sore throat” were presented in our previous work (9). However, there is a lack of data about the level of adherence of Ukrainian pharmacists to the Standard, as well as perspectives and approaches to harmonizing the Standard with international guidelines.

The purpose of our study was to investigate the level of adherence of pharmacists in Ukraine to the Pharmacist's Protocols for dispensing OTC medicines titled „Symptomatic treatment of sore throat”, assess the prospects and elaborate the approaches to harmonize the Protocol with international guidelines, taking into account its focus on pharmacists and the concept of responsible self-medication.

Materials and Methods

The study included the following steps:

- Questionnaire development and pharmacists' survey providing.
- Clinical and pharmaceutical analysis of paracetamol- and ibuprofen-containing medicines registered in Ukraine.
- Assessment of prospects and elaboration of approaches for harmonization of the Pharmacist's Protocol with international guidelines.

With the onset of the COVID-19 epidemic and, especially, the beginning of the full-scale military aggression of the Russian Federation against sovereign Ukraine, methods of communication using IT tech-

nologies are actively being used in Ukraine. Therefore, the first stage of the research was conducted as a web-survey (December 2023).

The questionnaire was developed taking into account the structure of the Pharmacist's Protocol for dispensing OTC medicines „Symptomatic treatment of sore throat” (8) and includes three parts:

- Social indicators (city, pharmacists' age, position in the pharmacy, work experience) and competence level regarding the document regulating pharmaceutical care in the sore throat symptomatic treatment.
- Assessment of the level of pharmacists' adherence to the Pharmacist's Protocol for dispensing OTC medicines „Symptomatic treatment of sore throat” according to the Protocol's paragraphs.
- Evaluation of the level of Ukrainian pharmacists' vision of international guidelines for sore throat symptomatic treatment and opinions about the reasonability of harmonization of the Ukrainian Pharmacist's Protocol with them.

For pharmacists' better understanding and convenience, they answered the questionnaire based on 4-point Likert scale (10) with the options: „Never”, „Rather No”, „Rather Yes”, and „Always”. Data from the self-assessment were documented in Microsoft Excel 2021. Descriptive statistics were used.

The analysis of paracetamol- and ibuprofen-containing medicines registered in Ukraine was carried out during January – April 2024 on the basis of data from the State Register of Medicines (11) and instructions for medical use of medicines located there. The inclusion criteria were the keywords „paracetamol” and „ibuprofen” in the category „Composition of active substances”. According to them, a list of registered drugs was obtained. The criteria for exclusion from the list were: belonging to a group of substances, double registration due to a change of the registration term, manufacturer's name and address, instruction's content. Topical paracetamol- and ibuprofen-containing medicaments (creams, gels, vaginal solutions) and combinations with glucosamine and chondroitin sulphate were also excluded. The final list of paracetamol- and ibuprofen-containing medicines was studied based on the content of the instructions for medical use. The composition, dosage form, a note of indications for use in „sore throat”, „pharyngotonsillitis”, „rhinopharyngitis”, approval for use in children, specific side effects, special warnings, and precautions for use were evaluated.

Based on the results of the first two steps, the perspectives were assessed, and approaches for harmonization of the Pharmacist's Protocol with international guidelines were elaborated.

Ethical consideration and informed consent

In accordance with Article 2(c) of Directive 2001/20/EC of the European Parliament and Council, the present study was classified as a non-interventional, observational trial, therefore, it did not require the approval of the bioethical committee of the National University of Pharmacy (Kharkiv, Ukraine) and Poznan University of Medical Sciences (Poland). The present survey research was associated with minimal risk. In addition, there was no procedure for which written informed consent was required. In this case, the completion of the data collection form by the pharmacists was accepted as consent to participate in the study.

Tab. 1. Adherence to the Pharmacist's Protocol for dispensing OTC medicines „Symptomatic treatment of sore throat” (n = 35)

	Never	Rather No	Rather Yes	Always
Assessment of a patient/ patient's representative needs				
who has a problem (patient, family members, familiars – children or adults)	–	3	11	21
when the illness started and duration	–	1	13	21
what measures were taken before addressing the pharmacy	–	6	10	19
what medicines have already been used	–	2	13	20
Subtotal:	0 0 %	12 8.5 %	47 33.6 %	81 57.9 %
Adherence to the algorithm of pharmaceutical care and clarification of factors that influence the recommendation for the proper medicine choice				
the presence of alarm symptoms that require immediate medical attention	–	–	18	17
the presence of infectious factors which contribute to pain	–	8	14	13
presence of physical and chemical factors (environment, bad habits)	3	13	9	10
presence of chronic diseases in a patient	–	10	14	11
pregnancy (in women)	–	4	12	19
Subtotal:	3 1.7 %	35 20.0 %	67 38.3 %	70 40.0 %
Information provision				
non-medicinal approaches to the sore throat symptomatic treatment	5	15	9	6
the proper technique of the medicinal product application			12	23
possible side effects of the medicinal product		3	24	8
the risk of an adverse reaction and/or ineffectiveness of the medicinal product in case of it incorrect use	–	3	18	14
monitoring of information assimilation by the patient/patient's representative	1	6	19	9
Subtotal:	6 3.4 %	27 15.4 %	82 46.9 %	60 34.3 %
TOTAL:	9 3.4 %	74 15.1 %	196 40.0 %	211 34.3 %

Results

Initially, 45 pharmacy employers from different cities in Ukraine took part in the web survey. However, according to the indicators of the residence place and pharmacy's position, the persons who were abroad or on maternity leave or held the „cashier”, „hall administrator”, „procurement manager” positions at the time of the survey, respectively, were excluded. The final number of surveyed pharmacists was 35 people.

Young people under the 25-years age (68.6 %) with 1–5 years of work experience (65.6 %) predominated among pharmaceutical respondents.

The geographic location of the respondents covered almost the entire territory of Ukraine, including border cities and regions that are under constant threat of missile attacks. Pharmacists from the eastern and northern territories (Kyiv, Chernihiv, Sumy, Kharkiv, Donetsk) accounted for 51.4% of the respondents, western and central (Ivano-Frankivsk, Lutsk, Rivne, Vinnytsia, Poltava) – 28.6 %, southern (Odesa, Mykolaiv) – 18.6 %.

100% of respondents confirmed that they are aware of the Pharmacist's Protocol for dispensing OTC medicines „Symptomatic treatment of sore throat”. Pharmacists informed that patients' requests for help with a complaint of a sore throat can be divided in the following way: a vague complaint about a symptom (17.1 %) or request to release a specific medicine (8.6 %) or to recommend any for the sore throat treatment (74.3 %). Based on this ratio, the necessity for the pharmacist to possess the skills of primary assessment of the patient's condition and to provide quality pharmaceutical care when choosing a proper medicine for the sore throat treatment remains important.

The next step of our research was to assess the level of pharmacists' adherence to comply with the Protocol's thesis (Tables 1 and 2).

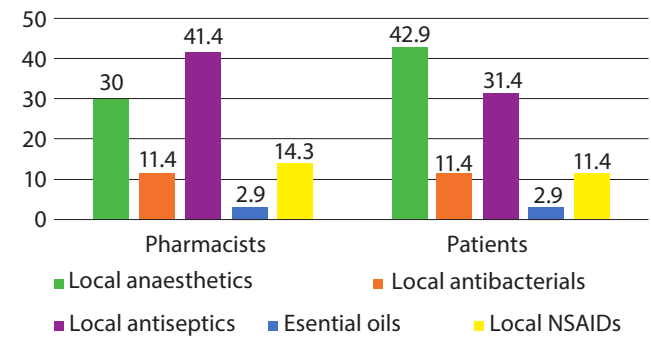
In general, the pharmacists demonstrated a high level of adherence (91.5 %) to comply with the first part of the Protocol, which deals with assessing the patient's needs and making a decision about the acceptability of responsible self-medication. However, there were pharmacists who admitted that the procedure for finding out the factors that influence the recommendation for the proper medicinal product choice is carried out “rather no” (20.0 %) or “never” (1.7 %).

The commitment to the identification of individual “alarm” symptoms fluctuates quite significantly in our sample. Pharmacists more often ask about fever (97.1 %), swallowing disorders (82.9 %), and the

Tab. 2. Adherence to the alarm symptoms identification according to the Pharmacist's Protocol for dispensing OTC medicines „Symptomatic treatment of sore throat” (n = 35)

Alarm symptom	Number / %
1) laboured (hard to breathe) breathing, being unable to say several words between inspirations	21 / 60.0 %
2) inability to swallow saliva	29 / 82.9 %
3) sharp tonsil enlargement, plaque, and tonsil ulceration	26 / 74.3 %
4) bright «blazing» throat redness	24 / 68.6 %
5) lymph node enlargement and soreness during palpation	18 / 51.4 %
6) temperature increase to 38.5–39 °C	34 / 97.1 %
7) sore throat associated with a skin rash	11 / 31.4 %
8) sore throat associated with severe headache, ear pain, and stomach ache	18 / 51.4 %
9) sore throat associated with urine colour change	5 / 14.3 %
10) pain persists after 2 days of sore throat symptomatic treatment	30 / 85.7 %
MEAN±SD:	21.6±8.9 / 61.7±25.5 %

Fig. 1. Preference (%) of pharmacists and patients (based on pharmacists' opinion) to a certain pharmacological group of medicines in the sore throat symptomatic treatment



duration of the symptom of sore throat on the background of symptomatic treatment (85.7 %), and much less about the presence of a rash (31.4 %) or changes in urine colour (14.3 %). In other words, signs of local disorders and bacterial infection are checked, but systemic consequences or infection complications, such as kidney damage, are of less interest (Tab. 2).

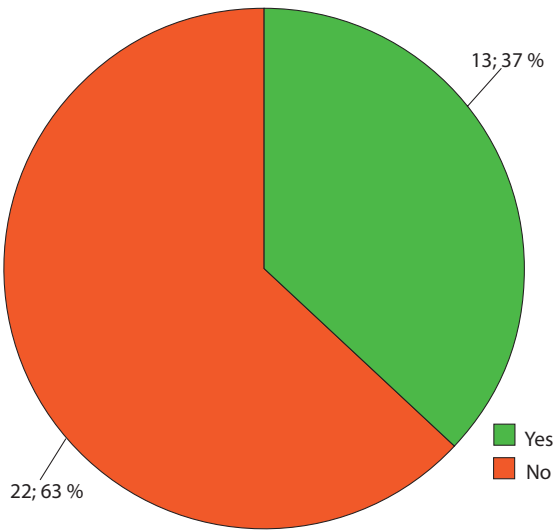
In case of alarm symptoms identification, 100 % of pharmacists refer patients to a doctor. However, 74.3 % of respondents admitted that they additionally recommend a remedy for temporary relief of sore throat, which does not contradict the rules of the Pharmacist's Protocols in Ukraine. The pharmacists' preferences to recommend a medicine of a certain pharmacological group are presented in Figure 1. The data about patients' preferences according to the pharmacists' opinion are also given.

In pharmacists' recommendations the local antiseptics (recommended by 41.4 % of respondents) and local anaesthetics (recommended by 30 % of respondents) are the leading among the five pharmacological groups. However, according to pharmacists' opinions, patients' preferences are the opposite. 42.9 % of pharmacists claim that patients more often ask about anaesthetics, and 31.4 % about antiseptics. The detected low level of pharmacists' recommendations and patients' requests for NSAIDs, antibacterial agents, and essential oils for local use calls attention to itself in this survey.

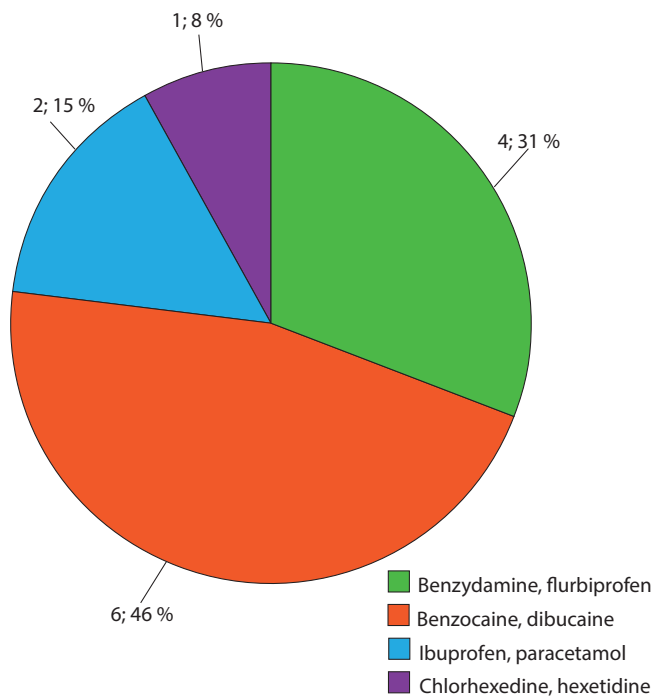
According to the opinion of 94.3% of pharmacists, patients prefer mouth dissolving solid dosage forms for sore throat treatment (tablets or lozenges). Therefore, the use of systemic medicines that must be swallowed will require additional explanation to the patient about the feasibility of their use.

Fig. 2. Level of pharmacists' awareness about international (in particular, European) guidelines for the sore throat symptomatic treatment

A. Are you familiar with international (in particular, European) guidelines for the sore throat treatment?



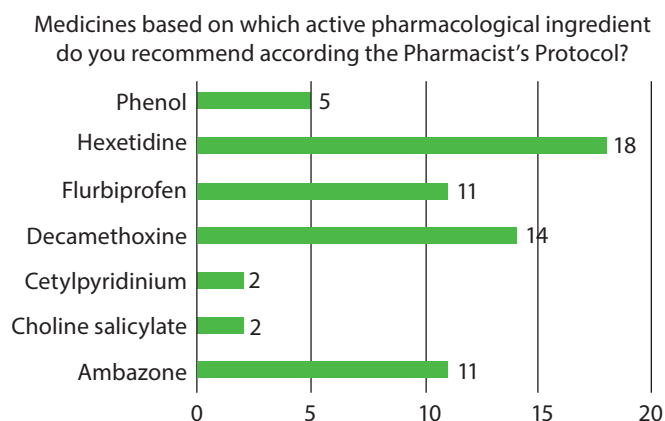
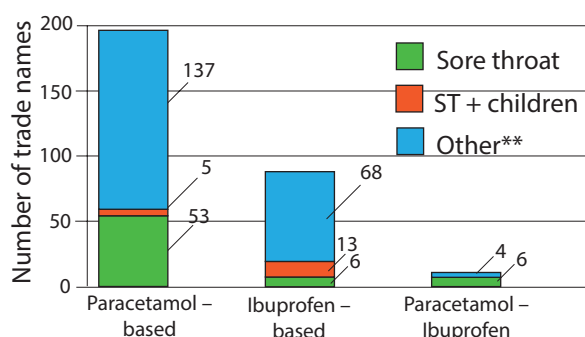
B. What medicines are recommended in Europe for the sore throat symptomatic treatment?



Tab. 3. Active pharmacological ingredients are included in the Pharmacist's Protocol for the dispensing OTC medicines Symptomatic treatment of sore throat"

INN	ATC index. Group name	Registered trade names
Ambazone	R02AA01. Throat preparations	5 / mono – 5
Cetylpyridinium	R02AA06. Throat preparations	9 / combinations – 9
Choline salicylate	N02BA03. Other analgesics and antipyretics. Salicylic acid and derivatives	17 / combinations – 17
Decamethoxine	D08AJ10. Antiseptics and disinfectants. Quaternary ammonium compounds	2 / mono – 2
Flurbiprofen	R02AX01. Throat preparations. Other throat preparations	9 / mono – 9
Hexetidine	A01AB12. Stomatological preparations. Anti-infectives and antiseptics for local oral treatment	19 / combinations – 18 + mono – 1
Phenol	R02AA19. Throat preparations	2 / mono – 2

Registered trade names are presented in total number / mono-component or(and) combined medicines. Dosage forms with ambazone, flurbiprofen, decamethoxin, phenol contain one API. Hexetidine is used, both alone and in combination with cholinosalicylate/chlorobutanol or chlorobutanol/racemic camphor/menthol (levomenthol)/eucalyptus oil. Hence, cholinosalicylate is combined with hexetidine and chlorobutanol. Cetylpyridinium is included in combinations with either lysozyme or benzydamine

Fig. 3. The rating of active pharmacological ingredients according Ukrainian pharmacist's survey**Fig. 4.** The ratio of paracetamol- and ibuprofen-containing medicinal products approved for sore throat treatment and in children in total number

* – approval to use in children is noted in the trade name of medicine; ** – without indication to use in sore throat treatment or in children

International guidelines (European, British, German, FIP etc.) recommend paracetamol or ibuprofen to relieve the symptom of sore throat (6, 12, 13, 14). The next task of our survey was to find out whether Ukrainian pharmacists are familiar with the international principles of symptomatic treatment of sore throat. The results are presented in Figure 2.

Thirteen pharmacists (37%) gave a positive answer to the question, but their level of knowledge was low, because only 15% (2 out of 13)

Tab. 4. Present accordance, perspectives and necessity of harmonization of Ukrainian approaches with international guidelines

	No	Rather No	Rather Yes	Yes
Recommendation of systemic application of paracetamol or ibuprofen (per os)	15	10	8	2
The patient's consent to systemic use paracetamol or ibuprofen	13	12	9	1
The awareness about the presence of "sore throat" indication in the instructions for medicinal use of paracetamol or ibuprofen	10	11	11	3
Worthwhileness of harmonization of the Ukrainian Pharmacist's Protocol with international (European) guidelines	0	3	20	12
TOTAL:	38 27.1 %	36 25.7 %	48 34.3 %	18 12.9 %

correctly named paracetamol and ibuprofen as medicines recommended in Europe for the sore throat symptomatic treatment.

Today, 7 active pharmacological ingredients are included in the Ukrainian Pharmacist's Protocol for dispensing OTC medicines "Symptomatic treatment of sore throat" as the first line. They only remotely correspond to international approaches to the sore throat symptomatic relief (Tab. 3) (6, 8, 9, 12, 13, 14).

Figure 3 shows that among the active pharmacological ingredients prescribed by Protocol, the interviewed pharmacists most often recommend the antiseptics hexetidine and decamethoxine. The anti-inflammatory drug flurbiprofen takes the third place.

The final step of our survey was a question regarding the accordance of Ukrainian approaches to the sore throat symptomatic treatment with international guidelines and necessity of their harmonization (Tab. 4).

It was determined that pharmacists in Ukraine rarely recommend systemic paracetamol or ibuprofen for the symptomatic treatment of sore throat (10 vs. 25). The same ratio is observed regarding patients' consent to use systemic paracetamol or ibuprofen. Most of the interviewed pharmacists are unaware that the possibility to use paracetamol or ibuprofen for sore throat treatment is indicated by instructions for the medical use (21 vs. 14). However, the absolute majority of respondents consider it expedient to harmonize the Ukrainian Pharmacist's Protocol with international (European) guidelines (32 against 3).

The next stage was the study of clinical and pharmaceutical features of paracetamol- and ibuprofen-containing medicinal products in Ukraine regarding the possibility of their use for sore throat symptomatic treatment.

The search of medicinal products was carried out based on the database of State Register of medicinal products of Ukraine (15) by the keyword of the active pharmaceutical ingredient „paracetamol“, „ibuprofen“. Clinical and pharmaceutical features were studied in accordance with the instructions for medical use located on the website of the State Register of medicinal products of Ukraine (15) and the website <https://likicontrol.com.ua/>. The results are presented in Figure 4 and Table 5.

At the time of our research, 292 medicinal products with paracetamol (mostly combined) and ibuprofen (including combined) were registered in Ukraine. Relatively, only 58 (20 %) paracetamol-, 19 (6.5 %) ibuprofen- and 6 (2 %) both-containing medicines had a clear indication, which was formulated as „sore throat“ or „pharyngotonsillitis“ or „rhinopharyngitis“ and all of them were products of systemic action for oral application (powder for oral solution, tablets, effervescent tablets, syrup, granules for oral solution, soft capsules, suspensions etc.).

Among ibuprofen-containing medicinal products that have a clear indication according above-mentioned key words, 94.5 % are medicines approved for use in children aged 3 (or 6) months to 12 years. Two-thirds of these medicines are marked by words „baby“, „kids“, „for children“ in their trade name (13/68 %), emphasizing the possibility of use in the first year of life.

Tab. 5. Paracetamol- and ibuprofen-containing medicinal products, which have a prescribed indication to use in sore throat treatment

Dosage form	Paracetamol, dose	Other active pharmacological ingredients	Trade name numbers	Approved age
Paracetamol-containing				
Syrup	30 ml / 600 mg	Dextromethorphan 15 mg Doxylamine 7.5 mg	1	≥ 15 years
	5 ml / 120 mg	—	2	3 or 6 months – 12 years
Granules for oral solution	750 mg	Phenylephrine HCl 10 mg Ascorbic acid 60 mg	6	≥ 12 years
	650 mg	Phenylephrine bitartrate 15.58 mg Chlorpheniramine maleate 4 mg	1	≥ 14 years
Powder for oral solution	1 000 mg	Phenylephrine HCl 12.2 mg	2	≥ 16 years
	1 000 mg	Phenylephrine HCl 10 mg Ascorbic acid 70 mg	1	≥ 12 years
	1 000 mg	Phenylephrine HCl 10 mg Ascorbic acid 40 mg	1	≥ 12 years
	750 mg	Phenylephrine HCl 10 mg Ascorbic acid 60 mg	3	≥ 12 years
	650 mg	Phenylephrine HCl 10 mg	2	≥ 16 years
	650 mg	Phenylephrine HCl 10 mg Chlorpheniramine maleate 4 mg	1	≥ 12 years
	600 mg	Phenylephrine HCl 10 mg Ascorbic acid 40 mg	1	≥ 12 years
	500 mg	Phenylephrine HCl 12.2 mg	1	≥ 16 years
	500 mg	Pheniramine maleate 25 mg Ascorbic acid 200 mg	7	≥ 15 years
	500 mg	Phenylephrine HCl 10 mg Guaifenesin 200 mg	3	≥ 12 years
	280 mg	Pheniramine maleate 10 mg Ascorbic acid 100 mg	1	≥ 6 years
	280 mg	Pheniramine maleate 10 mg Ascorbic acid 100 mg	1	≥ 6 years
Tablets	650 mg	Caffeine 50 mg	1	≥ 12 years
	500 mg	Caffeine 50 mg	1	≥ 12 years
	500 mg	Diclofenac sodium 50 mg	2	≥ 14 years, Rx
	500 mg	Caffeine 30 mg Codeine phosphate 8 mg	1	≥ 18 years, Rx
	500 mg	Caffeine 25 mg Phenylephrine HCl 5 mg Terpin hydrate 20 mg Ascorbic acid 30 mg	1	≥ 12 years
	500 mg	Caffeine anhydrous 30 mg Phenylephrine HCl 10 mg Chlorpheniramine maleate 2 mg	1	≥ 12 years
Film-coated tablets	500 mg	Diclofenac potassium 50 mg Serratiopeptidase 15 mg	1	≥ 14 years, Rx
	500 mg	Diclofenac sodium 50 mg Chlorzoxazone 250 mg	1	≥ 14 years, Rx
	500 mg	Diclofenac potassium 50 mg	1	≥ 14 years, Rx
	500 mg	Caffeine 65 mg	1	≥ 12 years
	500 mg	—	1	≥ 12 years
	500 mg	Pseudoephedrine HCl 30 mg Dextromethorphan HBr 15 mg Ascorbic acid 60 mg	1	≥ 12 years Rx
Soluble tablets	500 mg	Caffeine 30 mg Codeine phosphate 8 mg	1	≥ 18 years, Rx
Coated tablets	500 mg	Caffeine 65 mg	2	≥ 12 years
Effervescent tablets	500 mg	Caffeine 65 mg	3	≥ 12 years
	500 mg	—	1	≥ 6 years
Suspension	5 ml / 120 mg	—	3	3 months – 12 years
	5 ml / 160 mg	Cetirizine HCl 2.5 mg Chlorpheniramine maleate 1 mg Dextromethorphan HBr 5 mg	1	≥ 4 years
Capsules	500 mg	Caffeine 30 mg Codeine phosphate 8 mg	1	≥ 12 years, Rx
Ibuprofen-containing				
Film-coated tablets	—	Ibuprofen 200 mg Phenylephrine 10 mg	1	≥ 12 years

Suspension	–	Ibuprofen 5 ml / 200 mg	9	6 months–12 years
	–	Ibuprofen 5 ml / 100 mg	9	3 months–12 years
Paracetamol + Ibuprofen				
Film-coated tablets	500 mg	Ibuprofen 200 mg	4	≥ 18 years
Soft capsules	500 mg	Ibuprofen 200 mg	2	≥ 18 years

Rx – prescription only medicine.

In the analogous group of paracetamol-containing medicinal products, the amount of medicines approved for use in children of various ages gains 96.5 %. Only 5 (8.6 %) of them pay attention to the possibility of use in children first year of life („for children,” „baby”) in their trade name.

It should be accented that indications for use in sore throat/pharyngitis/rhinopharyngitis are prescribed for numerous paracetamol-containing medicinal products combined with vasoconstrictor, psycholeptic, narcotic, vitamin, expectorant, antitussive and hypnotic APIs (88 %).

The share of monocomponent medicines is 30 % in total (from 83 trade names), with a large majority of ibuprofen-containing products (22 %).

The powders for oral solution (23 paracetamol-containing combined medicines, 28 %) and suspensions (4 paracetamol and 18 ibuprofen-containing medicines, 26.5 %) prevail among the dosage forms of medical products that have a clear indication to use in sore throat treatment.

In the evaluated list, we identified 9 prescribed medicines, which are combinations of paracetamol with the NSAID diclofenac, the narcotic codeine, the muscle relaxant chlorzoxazone, as well as the adreno- and sympathomimetic with psychotropic activity pseudoephedrine.

Discussion

Pharmaceutical care standards were implemented in Ukraine at the national level in 2010, when the first edition of the Pharmacist's Protocols was approved. Since then, the Protocols have been constantly revised and updated. When performing improvement and development procedures, it is recommended to rely on the principles of evidence-based medicine, international experience and take into account Ukrainian features and opportunities. However, the issue of adherence to the Protocols by pharmacists, as well as the harmonization of the Protocols with international guidelines, remains an important problem.

Since requests from pharmacy customers are characterized by vague wording, the relevance of pharmacists' possession of the skills to primarily assess the needs and condition of the patient/patient representative (16) was confirmed at the first stage of the presented research.

A fairly high level (83.1 %) of adherence to the Protocol for the dispensing of OTC medicines "Symptomatic treatment of sore throat" among pharmacists' representatives of most regions of Ukraine, including direct front-line zone, was established. Ukrainian pharmacists pay special attention to identifying "alarm" symptoms, signs of local disorders and bacterial infection, to clarifying the features of a specific patient's condition, which fully corresponds to the algorithms of international guidelines (17). However, a problem is the low level of adherence

to questions that refer to systemic effects or complications of infection, such as kidney damage (14.3 %). Considering that glomerulonephritis or acute rheumatic fever are systemic diseases with severe consequences (18, 19, 20), this protocol's thesis needs attention and effort to increase the level of pharmacists' adherence.

100% adherence to referral for a doctor's consultation due to "alarm" symptoms was found. The compliance with international guidelines (17), the lack of exceeding their authority and understanding of responsibility for untimely provision of further specialized medical advice were demonstrated by the interviewed pharmacists.

In the part of the study of pharmacists' commitment to recommend/patients to demand the medicine of certain pharmacological groups, it was found that the preferences are opposite. Pharmacists tend to recommend first of all local antiseptics for the sore throat symptomatic treatment, then local anaesthetics, and patients vice versa. So, the pharmacists follow the recommendations of the Protocol for dispensing OTC medicines "Symptomatic treatment of sore throat," where 5 of the 7 recommended active substances belong to antiseptics. Regarding patient preference for local anaesthetics, it can be assumed that patients value their ability to provide rapid, almost instantaneous pain relief (21, 22, 23). It is noteworthy that both pharmacists and patients do not apply for the symptomatic treatment of sore throat with systemic NSAIDs, as recommended by international guidelines (6, 12, 13, 14). Local usage of NSAIDs also has a low level of adherence by both pharmacists and patients (from 11.4% to 14.3 %).

About 2/3 of registered OTC medicines for the sore throat symptomatic treatment in Ukraine are presented by solid dosage forms (tablets, lozenges) (15). Lozenges offer many advantages to formulation pharmacists. They are convenient to use and store. They can be given to those patients who have difficulty in swallowing; easy to administer to geriatric and paediatric population; pleasant taste. It extends the time of drug in the oral cavity to elicit a specific effect; easy to prepare, with minimum amount of equipment and time; do not require water intake for administration; technique is non-invasive, as is the case with parenterals (24). Perhaps these factors explain the high adherence of patients to solid dosage forms for absorption (according to the opinion of the vast majority of surveyed pharmacists, 94.3 %).

The level of pharmacists' awareness about international approaches to sore throat symptomatic treatment is unfortunately low, as only 3 people out of 35 respondents indicated paracetamol and ibuprofen as the recommended medicines (6). It could be explained by the lack of international experience harmonization with the content of the relevant education courses for pharmacists in Ukraine (25) and the content of the relevant Pharmacist's Protocol (8). The necessity for such harmonization is admitted by the majority (91.5 %) of respondents.

There are real backgrounds for the harmonization of the Ukrainian Protocol with international approaches to the sore throat symptomatic treatment: 1) systemic paracetamol- and ibuprofen-containing preparations are available (292 trade names), 2) 28 % (83 trade names) of the medicines are approved for the sore throat treatment – the clear indications “sore throat”, “pharyngotonsillitis”, “rinotonsillitis” are pointed in instructions for medical use, 3) approved preparations are presented in convenient oral dosage forms, 4) most medicines (90 %) are approved for use in children, including 28 % in children of the first year of life, which indicates their high level of safety.

However, in our opinion, there is a necessity to detail for the pharmacist and the patient the possibility of using certain paracetamol- and ibuprofen-containing medicines for the sore throat symptomatic treatment. For example, it was established that for this purpose, 9 prescribed combinations of paracetamol with diclofenac/codeine/chlorzoxazone/pseudoephedrine are allowed to be used in Ukraine today. We believe that there should be clearly defined grounds for the use of these remedies, as well as strict supervision by a doctor, because the risk of developing undesirable reactions may significantly exceed the benefits of use. The dangers of gastro- and cardiotoxicity of diclofenac (26), narcotic and psychotropic activity of codeine and pseudoephedrine are widely known (27, 28).

The application of OTC combined anti-cold medicines also, in our opinion, requires clarification of the possibility of sore throat symptomatic treatment. Complex action is not always desirable, especially when the severity of one symptom prevails over others. The benefit of using a combination has in the same time a high risk for the development of unwanted reactions. Various combinations of paracetamol with decongestants (chlorpheniramine, pheniramine, cetirizine), psycholeptics (caffeine), vasoconstrictors (phenylephrine), antitussives (dextromethorphan), expectorants (guaifenesin, terpinhydrate), hypnotic ingredients (doxylamine) increase the risk of interaction with other active pharmacological ingredients, strengthening/weakening of pharmacological action, development of toxic and allergic reactions. First of all, the central nervous system (excessive sleepiness, dizziness or, on the contrary, insomnia and increased excitability) and cardiovascular (tachycardia, arterial hypertension) systems can be targeted. Another disadvantage in the use of combined anti-cold agents is their dosage form (powder or granules for the preparation of an oral solution), which requires additional circumstances for preparation, as well as the impossibility of dose correction, especially when the dose of paracetamol reaches 1 000 mg.

From this point of view, tablets and capsules seem to be more attractive for adult patients due to comprehensibility, convenience and accuracy of application, as soon as ready-made suspensions for children and people with swallowing problems.

Thus, when adapting the Ukrainian Pharmacist's Protocol with international guidelines for the sore throat symptomatic treatment, it is recommended to focus on systemic paracetamol and ibuprofen dosage forms for oral use.

Paracetamol and ibuprofen are characterized by a high level of analgesic activity and safety, the possibility of use in special groups of

patients (children, including the first year of life, the elderly, patients with chronic diseases), the absence of dysbiotic disorders in the oral cavity and a low risk of allergic reactions/methglobinemia in comparison with local antiseptics and anaesthetics (29, 30, 31, 32).

It is reasonable to prefer the monocomponent medicines. The combination of paracetamol with caffeine, which provides synergism of the analgesic effect, is acceptable as well.

In order to increase the level of safety when using paracetamol and ibuprofen, the Pharmacist's Protocol should include information on dosage approaches and warnings about unwanted effects of the medicines.

Conclusion

The conducted study demonstrated a high level of adherence of pharmacists to the Ukrainian standard of pharmaceutical care, an insufficient level of their awareness of modern trends in the sore throat symptomatic treatment, the willingness of pharmacists to adapt and harmonize their work with international guidelines, and the existence of grounds for harmonization. The outcome of the performed work are the proposals for harmonizing the Pharmacist's Protocol „Symptomatic treatment of sore throat” with international guidelines.

Proposals

- Implement the following changes to the Pharmacist's Protocol for dispensing OTC medicines „Symptomatic treatment of sore throat”:
 - Add to paragraph 4 “List of over-the-counter medicines for the symptomatic treatment of sore throat” the next active pharmaceutical ingredients:
 - Analgesics and antipyretics: Paracetamol.
 - Nonsteroidal anti-inflammatory drugs: Ibuprofen.
- Add the following to paragraph 5 „Providing proper information about medicines for responsible self-medication”:
 - Analgesics and antipyretics. Nonsteroidal anti-inflammatory drugs.
 - systemic oral monocomponent ibuprofen- or paracetamol-containing medicines or a combination of paracetamol with caffeine can be used for sore throat symptomatic treatment;
 - when paracetamol is contraindicated, ibuprofen is the medicine of choice;
 - to use liquid forms of monocomponent ibuprofen- and paracetamol-containing medicines for children from the first year of life to 12 years;
 - the maximum dose of paracetamol should not exceed 60 mg/kg per day (maximum single dose 1 g and maximum daily dose 4 g); frequency of administration – 3–4 times a day with at least 4 hour interval;
 - the maximum dose of ibuprofen should not exceed 1 200 mg/day for adults and 600 mg/day for children; frequency of administration – 2–3 times a day with at least 6 hour interval;
 - paracetamol-containing medicines have a small therapeutic window (the toxic dose exceeds the maximum therapeutic

dose by only 2–3 times), so it is necessary to adhere to the prescribed dose;

- ibuprofen in the syrup dosage form is approved for use in children from 3 months of age;
- paracetamol is used with caution in liver diseases;
- ibuprofen is contraindicated in the stomach and duodenum peptic ulcer, inflammatory diseases of the digestive tract, tendency to bleeding and blood coagulation disorders, bronchospastic conditions, asthma, it is applied with caution in liver and/or kidney failure, arterial hypertension;
- ibuprofen reduces the effect of thiazide diuretics and antihypertensive agents;
- ibuprofen can cause dizziness, so it is not prescribed to people whose activities require high concentration of attention and speed of psychomotor reactions;
- not combine the analgesics-antipyretics and NSAIDs with alcohol (the ulcerogenic effect of ibuprofen, and the hepatotoxic effect, especially of paracetamol, increase);
- the suspension with ibuprofen must be shaken thoroughly before use.

- Risk control and prevention of therapy duplication — check whether the patient is using other paracetamol- or ibuprofen-containing medicines.
- Spread the information about the possibility of symptomatic treatment of sore throat with paracetamol and ibuprofen among pharmacists of the undergraduate and postgraduate training levels, during special courses/webinars on pharmaceutical care, by printing or online publication of special practical guidelines.

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Conflict of interest statement

No potential conflicts of interest were reported by the authors.

Authors' contributions

VP and SM contributed to the literature search of the topic, design of the paper, and the writing of the manuscript. SM collected the data. VP analysed the data. All authors contributed to the article and approved the submitted version.

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