Musculoskeletal Health Systematic Review: Clinical and Pharmacological, Organizational and Legal, Administration and Pharmaceutical Management Aspects

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Abstract. This article examines current aspects of musculoskeletal health and pharmacotherapy of disorders of the human musculoskeletal system. An objective review of disorders of the musculoskeletal system was conducted in the areas of administration, clinical and pharmacological, organizational and legal, pharmaceutical management. The results of the systematic review show that the availability of diagnoses in the section "Orthopedics and traumatology" on the platform of the state expert center of the Ministry of Health of Ukraine is limited. It is necessary and urgent to expand the scientific base for practicing doctors. The study confirmed the importance of using new clinical protocols in medical and pharmaceutical practice for the implementation of evidence-based medicine and evidence-based pharmacy in Ukraine. Gradual improvement of medical and pharmaceutical practice allows to increase the quality, efficiency, safety, availability of pharmacotherapy for patients with disorders of the musculoskeletal system. The paper examines guidelines developed on the basis of health evidence provided by Duodecim Medical Publications. The study shows the availability of a wide range of treatment methods and helps to determine optimal therapy strategies in the field of orthopedics. It was found that non-steroidal anti-inflammatory drugs and analgesics are more often prescribed for the pharmacotherapy of disorders of the musculoskeletal system, which emphasizes the perspective of further clinical and pharmacological, organizational and legal researches in the pharmaceutical development and management of new drugs.

Keywords: evidence-based medicine, evidence-based pharmacy, ICD-11, musculoskeletal health, musculoskeletal disorders, administration, management, pharmacotherapy.

Introduction. Statistical data of the World Health Organization indicate the widespread distribution of disorders of the musculoskeletal system among the population of the whole world. Their number is estimated at approximately 1.71 billion people. These disorders are the leading cause of disability in most countries. Yes, lower back pain is particularly relevant for 160 countries. Disturbances of the musculoskeletal system significantly affect the quality of life, limit mobility, dexterity, lead to early retirement from work and a decrease in the level of well-being. WHO is actively responding to this burden by implementing programs in various areas. The health of the musculoskeletal system is determined by the condition of muscles, bones, joints, and adjacent tissues. Violations of this system encompass more than 150 different disorders. They are usually accompanied by constant pain, limitation of mobility, which significantly impairs the quality of life and people's ability to participate in social life [1].

An analysis of 2019 Global Burden of Disease (GBD) data found that approximately 1.71 billion people worldwide live with musculoskeletal disorders (low back pain, neck pain, fractures, osteoarthritis, amputations, rheumatoid arthritis, other injuries). High-income countries were the most affected by the number of patients – 441 million. They are followed by the countries of the Western Pacific region of WHO – 427 million and the region of Southeast Asia – 369 million patients [2].

Musculoskeletal disorders are a significant burden on the global economy and health care system. The search for new medical technologies, medicines and methods of their delivery remains relevant. It plays a key role in the musculoskeletal field, affects the restoration of degenerated and damaged tissues of the musculoskeletal system. Despite significant progress, many challenges regarding new drug delivery methods for the treatment of musculoskeletal disorders remain open [3].

While the prevalence of musculoskeletal disorders increases with age, younger people also suffer from them, often during the peak income period. For example, children's autoimmune

inflammatory diseases (juvenile arthritis) affect children's development. And lower back pain is the main reason for premature dismissal from work. The impact of early retirement on society in terms of direct health care costs and indirect costs (i.e., absence of work or reduced productivity) is enormous [4].

Musculoskeletal disorders are also the largest factor in the overall need for rehabilitation. Musculoskeletal disorders make up the largest share of rehabilitation care in children and about two-thirds in adults. Musculoskeletal disorders often coexist with other non-communicable diseases, increasing the risk of developing other non-communicable diseases, such as cardiovascular diseases. Patients with disorders of the musculoskeletal system also have a higher risk of developing mental problems [5].

The purpose of the study was to conduct a comprehensive review of disorders of the musculoskeletal system and included administration, clinical and pharmacological, organizational and legal, pharmaceutical management. The research of the author of the article is a continuation of the regular review of the ICD-11 [6, 7].

Materials and methods. The methodology for researching disorders of the human locomotor system was based on the theoretical principles of pharmaceutical and medical law in the areas of: administration of prescriptions, risk management and safety of pharmacotherapy.

The article reviewed the scientific sources of the world's leading scientists on disorders of the musculoskeletal system and related diagnoses. Studied: regulatory and legal framework, clinical protocols, guidelines, standards of treatment of disorders of the musculoskeletal system associated with drug addiction, drugs, instructions for medical use, other local documents. Methods of the research – administration, management, organizational and legal, normative, documentary, clinical and pharmacological, comparative, graphic analysis were used in the study. The basic concepts of evidence-based medicine and evidence-based pharmacy will be observed in the study. Researchers: evaluate literature data, examine the disorders of the musculoskeletal system codes, determine clinical and pharmacological groups of drugs in the pharmacotherapy of disorders of the musculoskeletal system, determine directions of professional reintegration, develop research design. Level of evidence for the expected results: grade B, level 3. Evidence based on data from at least one study with a high degree of quality, in which there was a control group – evidence will be based on clinical and pharmacological, classification and legal, nomenclature data – legal, social, organizational and legal, forensic and pharmaceutical, technological research. The degree of proven effectiveness and expediency of conducting the research: class I, level C (consensus of the beliefs of experts based on the results of research and practice) – the results of the research will be analyzed and compared with the data of other authors.

The research of the article is a fragment of research works of Lviv Medical Institute LLC 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); Kharkiv Medical Academy of Postgraduate Education on "Improving the organizational and legal procedure for providing patients with drugs from the standpoint of forensic pharmacy, organization and management of pharmacy" (state registration number 0116U003137, terms 2016-2020) and "Pharmaceutical and medical law: integrated approaches to the system of drug circulation from the standpoint of forensic pharmacy and organization of pharmaceutical business" (state registration number 0121U000031, terms 2021-2026); Luhansk State Medical University "Conceptual interdisciplinary approaches to pharmaceutical provision and availability of drugs, taking into account organizational and legal, technological, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, marketing, social and economic competencies" (state registration number 0123U101632, terms 2023-2027); Petro Mohyla Black Sea National University on the topic "Conceptual interdisciplinary approaches to the drug circulation system, taking into account organizational and legal, technological, biopharmaceutical, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, pharmacotherapeutic aspects" (state registration number 0123U100468, implementation period 2023-

2028); 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. Musculoskeletal health is relevant throughout a person's life, from childhood to old age. Musculoskeletal disorders can be sudden and short-term (e.g., fractures, sprains) or long-term (e.g., chronic primary low back pain and osteoarthritis). Low back pain is the main cause of the total burden of diseases of the musculoskeletal system (7.5% of cases worldwide). Other musculoskeletal disorders include fractures (26%), osteoarthritis (19%), neck pain (22%), amputations (5.5%), rheumatoid arthritis (18%), gout (1.7%) [8].

Systematic review International Classification of Diseases of the 11th revision (ICD-11).

In the 15th section of ICD-11, disorders of the musculoskeletal system are indicated [9]:

- injury, poisoning or some other consequences of external causes (NA00-NF2Z);
- diseases of the endocrine system, nutritional disorders, and metabolic disorders (5A00-5D46);
- some infectious and parasitic diseases (1A00-1H0Z);
- diseases of the temporomandibular joint (DA0E.8);
- selected conditions arising in the perinatal period (KA00-KD5Z);
- complications of pregnancy, childbirth, and the puerperium (JA00-JB6Z).

Classified in other headings:

- monogenic autoinflammatory syndromes (4A60);
- musculoskeletal symptoms (ME80-MF1Y);
- structural anomalies of skeletal development (LB70-LB9Z);
- connective tissue syndromes (LD28);
- syndromes with skeletal abnormalities (LD24).

In Ukraine, treatment protocols are established on the platform of the State Expert Center of the Ministry of Health of Ukraine [10].

Systematic review of diagnoses from the section “Orthopedics and traumatology” Ukraine.

The name of the diagnosis, the type of document in which the treatment is described and the registry number of the document are given (Table 1).

Table 1. Systematic review from the section “Orthopedics and traumatology”.

No.	Name	Type of document	Registration number
1.	Anaerobic infection (gas gangrene)	Guideline	KN 2016-777
		Order	MOZ 2016-777
		Protocol	GS 2016-777
2.	Dysplasia of the hip joints	Guideline	KNp 2017-114
3.	Osteoarthritis	Guideline	KNp 2017-105
4.	Rheumatoid arthritis	Protocol	GS 2014-263
		Guideline	KN 2014-263
		Order	MOZ 2014-263
5.	Ewing's sarcoma	Guideline	KN 2023-1142
		Стандарт	SMD 2023-1142
		Order	MOZ 2023-1142
6.	Vascular anomalies in children	Protocol	GS 2016-813
		Guideline	KN 2016-813
		Order	MOZ 2016-813
7.	Gaucher disease	Protocol	GS 2023-12
		Guideline	KN 2023-12
		Order	MOZ 2023-12

On the platform of the state expert center of the Ministry of Health of Ukraine, only 7 diagnoses from the section "Orthopedics and traumatology" are listed.

The use of new clinical protocols is one of the most important ways of implementing evidence-based medicine. On April 28, 2017, the Order of the Ministry of Health of Ukraine No. 1422 of December 29, 2016, which allows Ukrainian doctors to use international clinical protocols in their work [11], entered into force. According to the order, doctors can use sources of international clinical guidelines: universal, national, cardiovascular diseases, injuries, cancer, emergency medical care.

Next, it was of interest to study the guidelines of Duodecim Medical Publications, Ltd. on the basis of evidence-based medicine. [12].

Systematic review of guidelines from the Orthopedics section of Duodecim Medical Publications.

Systematic review of instructions from the section "Orthopedics" is given in the Table 2.

Table 2. Systematic review of guidelines based on evidence-based medicine from the section "Orthopedics".

No.	Name	Instruction number
1.	Amputation of the lower limb	00434
2.	Achilles tendon	00430
3.	Pain in the lower legs	00100
4.	Pain in the area of the hip joint in children	00657
5.	Pain in the hip joint and buttocks	00417
6.	Groin pain	00416
7.	Back pain in children	00660
8.	Pain in the neck and shoulder joint	00398
9.	Knee pain	00421
10.	Backache	00435
11.	Pain in the heel	00432
12.	Painful conditions in the area of the ankle and foot in children and adolescents	00431
13.	Painful conditions in the area of the ankle and foot in adults	00996
14.	Bursitis	00394
15.	Valgus deformity of the first toe	00433
16.	Shoulder dislocation	00352
17.	Congenital dislocation of the hip joint	00589
18.	Hygroma	00410
19.	Diseases of the spinal cord	00783
20.	Nerve entrapment and compression disorders	00779
21.	Baker's cyst	00427
22.	Clinical examination of patients with joint inflammation in primary care	00438
23.	Complex regional pain syndrome	00455
24.	Dupuytren's contracture	00412
25.	Wing-shaped scapula (scapula alata)	00402
26.	Lameness	00662
27.	Lateral and medial epicondylitis of the elbow joint	00407
28.	Treatment of diabetic foot syndrome	00497
29.	Lunatomalacia (Kinbeck's disease)	00413
30.	Muscular compartment syndrome	00429
31.	Examination of the shoulder joint	00404

32.	Osteoarthritis	00396
33.	Osteoporosis	00419
34.	Paresthetic meralgia	00415
35.	Damage to the ligaments of the ankle	00362
36.	Damage to biceps tendons	00406
37.	Bone tumors	00420
38.	Radiculopathy	00782
39.	Disorders of the rotator cuff of the shoulder joint	00405
40.	Tears of the meniscus	00425
41.	Dissecting osteochondritis of the knee joint	00426
42.	Frozen shoulder syndrome	01013
43.	Upper thoracic aperture syndrome	00401
44.	Carpal tunnel syndrome	00411
45.	Snapping finger syndrome	01053
46.	Tietze syndrome	00400
47.	Knee complaints in children	00659
48.	Musculoskeletal pain	00984
49.	Scoliosis and kyphosis	01010
50.	Specific signs and symptoms in patients with inflammatory joint diseases	00440
51.	Stenosis of the spinal canal in the lumbar region	00436
52.	Stress fractures	00348
53.	Structural abnormalities in children	00590
54.	Complications after joint replacement surgery	00397
55.	De Quervain's disease	00408
56.	Surgical treatment of rheumatoid arthritis	01120
57.	Chondromalacia of the patella	00422

It was found that the treatment of 57 diagnoses is described in the international evidence-based guidelines in the "Orthopedics" section.

Musculoskeletal health.

Musculoskeletal health suggests that doctors prescribe the following tests:

- blood test;
- computer tomography;
- magnetic resonance imaging;
- x-ray.

Pharmacotherapy may include acetaminophen, nonsteroidal anti-inflammatory drugs, prescription drugs (eg, opioids).

Musculoskeletal health will depend on the underlying cause of musculoskeletal pain. General methods of medical and pharmaceutical care include: acupuncture, manual correction, occupational therapy, analgesics, steroids, physiotherapy, therapeutic massage.

Certain conditions can increase your risk of musculoskeletal pain. Arthritis: causes chronic inflammation of the joints, pain, and stiffness of the joints. Fibromyalgia: A chronic disease with widespread whiteness in the muscles, tendons, ligaments, and fatigue. "Tunnel" syndromes: compression or pinching of nerves (carpal tunnel syndrome, ulnar tunnel syndrome, and metatarsal tunnel syndrome). These conditions are often caused by overuse injuries [13].

Musculoskeletal health is important for society and individual patients against the background of the spread of infectious diseases. A large number of the population develops diseases of the joints or muscles in connection with the aging process. Autoimmune diseases of joints, connective tissue and muscles can have a devastating effect even on young people. For example, rheumatoid arthritis can occur together with osteoarthritis or steroid-induced myopathies [14-21].

As life expectancy increases, the number of patients facing various diseases increases. Approximately 60% of patients seeking help with chronic pain have musculoskeletal disorders. Pharmacotherapy of these disorders is necessary to improve the quality of life [22-26].

Pharmacotherapy of disorders of the locomotor system includes analgesics (paracetamol, non-steroidal anti-inflammatory drugs, opioids). Long-term use of opioids can lead to addiction and other unwanted effects. Some drugs used to treat muscle disorders can cause muscle spasms, convulsions, or dystonia, which should be considered when prescribing.

Musculoskeletal health in sports medicine involves pain management. It is crucial for athletes with a lot of physical activity. However, there are some gaps in the scientific evidence regarding the use of analgesics in sports injuries. Solving these problems requires high-quality research on the development of new drugs, taking into account the experience of the author of the article and anti-doping rules [27-32].

Pharmaceutical provision of sports medicine for disorders of the musculoskeletal system.

- Paracetamol is one of the most common drugs for mild and moderate pain, it can be used both alone and in combination with other drugs.
- A combination of paracetamol and non-steroidal anti-inflammatory drugs may be more effective in relieving pain.
- NSAIDs are also widely used to treat sports pain.
- Methods of administration of non-steroidal anti-inflammatory drugs are a problem.
- Opioids should only be used in major injuries when other treatments are ineffective.
- The guidelines state that the prescription of opioids should be limited and temporary because they can cause dependence and addiction.

Musculoskeletal health involves rehabilitation in the treatment of pain in sports. Physical therapy can help reduce pain and improve physical function. In addition, pharmacotherapy should complement rehabilitation measures, and not interfere with them.

In general, pain management in sports requires a comprehensive approach that combines clinical and pharmacological, pharmaceutical, and non-pharmacological methods of treatment. Further research is needed to develop the most effective treatment strategy [33].

The musculoskeletal system is a critical component in providing support, stability, and movement. Disorders of the locomotor system can lead to serious consequences. In recent years, considerable attention has been paid to the development of methods of local drug delivery for pharmacotherapy.

One of the most common methods in the pharmacotherapy of disorders of the locomotor system is a complex of the use of drugs and surgical interventions. Local delivery of medicines has gained considerable popularity. The drugs are directed directly to the affected area. Systemic side effects of drugs are minimized. There is an increase in the effectiveness of treatment.

New advances in the field of local musculoskeletal drug delivery include the development of new drugs, improved delivery methods, and the introduction of innovative approaches. These new technologies allow more precise and effective treatment of diseases of the musculoskeletal system.

It can be noted that local drug delivery has great potential in the field of treatment and rehabilitation of the musculoskeletal system. Further research in this area can lead to the development of even more effective and safe methods of treatment, which will help reduce the burden of diseases of the musculoskeletal system on society and improve the quality of life of patients.

Musculoskeletal health involves the correct choice of medical and pharmaceutical technologies for the effective treatment of disorders of the musculoskeletal system. Recently, it has become increasingly evident that, in addition to surgery, the safety and efficacy of pharmacotherapy play an important role in patient health.

Traditional treatment methods, such as systemic administration of drugs, have their limitations. Most drugs are not released in a sustained manner or are not released at the correct site of the lesion. For example, local drug delivery allows for high concentrations of drugs in the right places, minimizing toxicity and negative side effects.

Musculoskeletal health in the application of local drug delivery is already carried out in clinical practice. For the treatment of chronic diseases, such as osteoarthritis, intra-articular administration of drugs is widely used. For injuries and muscle disorders, intramuscular or subcutaneous approaches are extremely effective. For tissue regeneration after damage or fracture, it is better to use implants or three-dimensional (3D) frameworks covered with drugs.

However, there are several challenges associated with local delivery of drugs through the musculoskeletal system. Some means of delivery have limited carrying capacity or short-term release, which complicates their practical application. In addition, the mechanical properties of some vehicles may not be sufficient for efficient function. It is also important to consider biological aspects, such as the metabolism and clearance of drugs, which may influence their effectiveness.

Despite these challenges, local drug delivery is a promising direction in the pharmacotherapy of musculoskeletal disorders. Further research and development of new therapeutics and delivery methods will help maximize the benefits of this approach and improve patient outcomes.

Musculoskeletal health includes an overview of advances in prescription, management, pharmacotherapy, and pharmaceutical care. Using 3D printing technology to create frames provides effective control over their structure, properties, and functions. This facilitates the development of materials that can be used for tissue regeneration and drug delivery. Synthetic, natural, and extracellular matrix-based biomaterials show significant potential in this context.

The next step is to develop delivery systems that can simultaneously use multiple drugs and control their release. This is especially important in the pharmacotherapy of disorders of the musculoskeletal system. There is an increase in therapeutic efficiency, a decrease in risks, and toxicity. Therefore, drug delivery is an effective strategy.

Small molecule and gene therapy has become another important strategy to repair and regenerate musculoskeletal tissue. It attracts attention due to its low toxicity and economic efficiency.

Musculoskeletal health is ensured by the use of tissue engineering and stem cell engineering.

The specified methods and methods of pharmacotherapy stimulate the healing of damaged tissues, show significant potential in improving clinical results for the musculoskeletal system [34].

A review of current advances in drug delivery for the treatment of musculoskeletal disorders reflects the great interest and active progress in this field. Thanks to the development of new drugs, innovative tools, and delivery strategies, it has been possible to develop effective methods of pharmacotherapy for various parts of the musculoskeletal system, such as bones, joints, cartilage, tendons, and skeletal muscles [35].

One of the key directions for musculoskeletal health is the pharmaceutical development of new drugs, such as genes, small molecule therapeutics and stem cells, used to treat diseases of the musculoskeletal system. In parallel, innovative tools such as 3D printing and tissue engineering techniques are developing to help develop new delivery strategies.

Significant progress in materials chemistry and drug delivery has led to the creation of sophisticated delivery systems using well-designed structures. Various delivery strategies such as calcium phosphate cements, microcapsules, biodegradable polymer scaffolds, and modified implants have been studied at the material level and in in vitro studies, showing improved outcomes in the treatment of various musculoskeletal disorders.

However, many new drug delivery methods are still in in vitro or early in vivo studies, and only a few have progressed to clinical trials. This may be due to difficulties in the design of complex delivery systems and their clinical development.

Further research for musculoskeletal health is necessary, relevant, and timely. It is necessary to combine experience in the field of pharmaceutical development of new drugs, nanotechnology, materials science, genetics, medicine, tissue engineering, proper GxP practices according to the principles of evidence-based medicine, evidence-based pharmacy [36-57]. Innovations cover a wide range of conditions affecting various components of the musculoskeletal system:

- joints: osteoarthritis, rheumatoid arthritis, psoriatic arthritis, gout, spondyloarthritis;
- bones: osteoporosis, osteopenia, associated fragility fractures;
- muscles: sarcopenia;

❖ various body sites and systems: including regional (e.g., back and neck pain) and widespread (e.g., fibromyalgia) pain conditions, inflammatory diseases that have musculoskeletal manifestations.

Based on the results of a systematic review of national and international clinical guidelines for the pharmacotherapy of disorders of the musculoskeletal system, the author of the article systematized the clinical and pharmacological groups of drugs (Fig. 1).

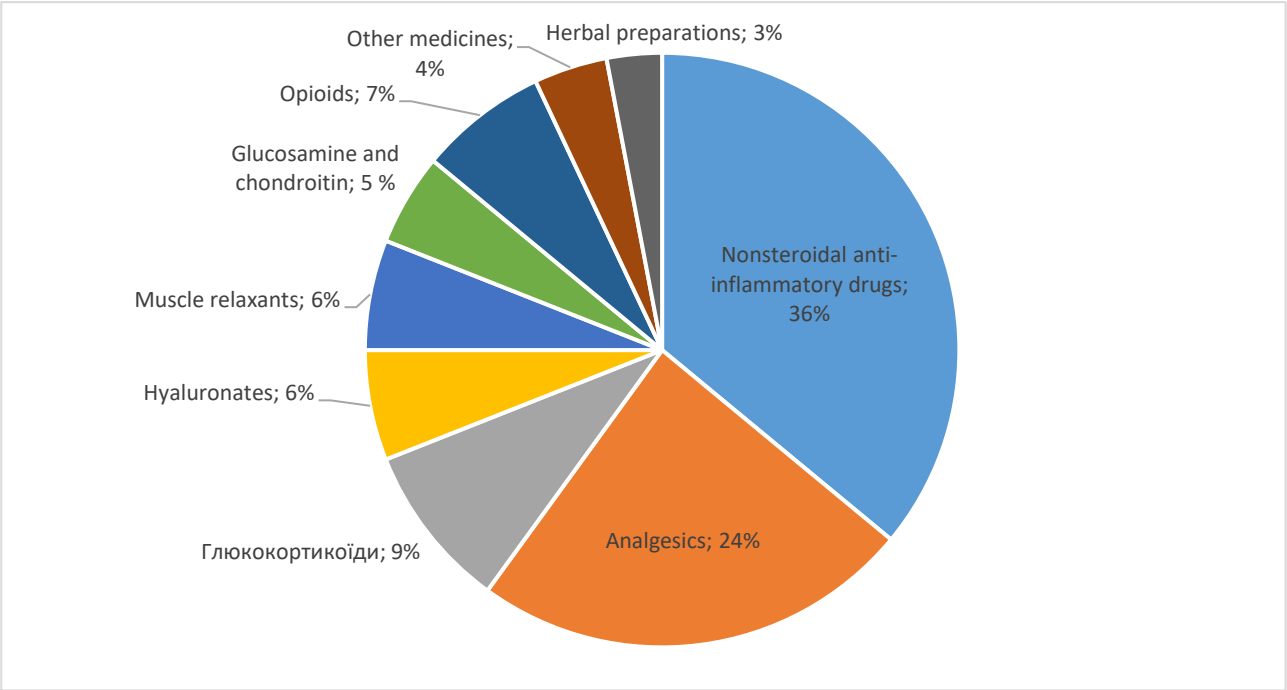

Fig. 1. Clinical and pharmacological groups of drugs for pharmacotherapy of disorders of the musculoskeletal system.

For the pharmacotherapy of disorders of the human locomotor system, the following clinical and pharmacological groups of drugs are most often used:

1. Nonsteroidal anti-inflammatory drugs (36%) are drugs that reduce inflammation, pain, and fever without steroid components.
2. Analgesics (24%) – drugs that are prescribed to reduce pain without affecting inflammation.
3. Glucocorticoids (9%) are drugs that have an anti-inflammatory effect and are often used to treat inflammatory diseases of the musculoskeletal system.
4. Hyaluronates (6%) – drugs that contain hyaluronic acid and are used to lubricate and protect joints.
5. Muscle relaxants (6%) – drugs used to reduce muscle tension and spasms.
6. Glucosamine and chondroitin (5%) are components of cartilage tissue, so they are often used to treat joint diseases.
7. Opioids (7%) are strong analgesics used to treat severe pain.

Other medicines (4%), herbal preparations (3%) are used less often, but can also have their place in therapy depending on the specific situation and individual characteristics of the patient.

Further research into the pharmaceutical development of new drugs to ensure musculoskeletal health may be promising precisely in the range of the indicated groups.

Conclusions. During the research the author studied musculoskeletal health. An objective review of disorders of the musculoskeletal system was conducted in the areas of administration, clinical and pharmacological, organizational and legal, pharmaceutical management. The results of the systematic review show a limited number of diagnoses presented on the platform of the state expert center of the Ministry of Health of Ukraine in the section "Orthopedics and traumatology". There is a need for greater validity and a wider range of scientific information for practitioners in this area. The use of new clinical protocols in medical and pharmaceutical practice is defined as an important stage in the implementation of evidence-based medicine and evidence-based pharmacy in Ukraine. Gradual improvement of medical and pharmaceutical practice allows to increase the quality,

efficiency, safety, availability of pharmacotherapy for patients with disorders of the musculoskeletal system. The author's study of health evidence-based guidelines shows the availability of a wide range of treatment methods and helps determine optimal therapy strategies in the field of orthopedics. It was found that non-steroidal anti-inflammatory drugs and analgesics are more often prescribed for the pharmacotherapy of disorders of the musculoskeletal system, which emphasizes the perspective of further clinical and pharmacological, organizational and legal research in the pharmaceutical development and management of new drugs.

Conflict of interest. The author confirms the authorship of this work and have approved it for publication. The author also certify that the obtained data and research were conducted in compliance with the requirements of moral and ethical principles based on the medical and pharmaceutical law, and in the absence of any commercial or financial relationships that could be interpreted as a conflict or potential conflict of interest.

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