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Modern industrial pharmaceutical forms used in dermatological practice in the Republic of Moldova

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Abstract

Background: Fighting skin diseases is a strict medical, as well as socio-economic issue for the Republic of Moldova, since they may have an aesthetic and psychological impact. The author of this scientific article presented an analysis of the pharmaceutical preparations and their forms used in the treatment of dermatological diseases based on those recorded in the State Nomenclature of the Republic of Moldova according to Anatomical Therapeutic Chemical classification, dose, division, manufacturing country and industrial pharmaceutical company, producer price, and terms of validity.

Material and methods: This research paper is based on the literature and 400 clinical documents, State Nomenclature of the Republic of Moldova, the result analysis of dermatological drug manufacturers and producers, the shelf life declared by the manufacturer, etc.

Results: From a total of 10924 preparations registered in the Republic of Moldova on 14.04.2017 – 526 were preparations used in dermatological practice. The top of pharmaceutical forms used in dermatological practice and registered in the Republic of Moldova were the ointments – 274 (52.09%) and solutions for external use – 162 (30.80%). Of the 27 producing countries, the most pharmaceutical preparations, registered in the Republic of Moldova, 212 preparations (40.30%) were of domestic origin, which also had the lowest price. The leader was *Farmaprim SRL* with 46 registered preparations. The shelf life of most dermatological preparations – 505 (96%), registered in the Republic of Moldova was at least 24 months – a parameter-guarantor of quality.

Conclusions: The share of preparations used in dermatological practice in the Republic of Moldova was 4.82%, of which pharmaceutical external forms accounted for over 80%. Most preparations registered and used in the dermatological practice in the Republic of Moldova were of local origin, which are qualitative, as well as the most accessible.

Key words: pharmaceutical forms, dermatology diseases, preparations, dose, accessibility.

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Introduction

Statistical data show that skin pathology is quite common in the world, with an estimated incidence of 250 million cases per year. Skin diseases and infections in this segment can severely affect both the vital prognosis, as, for example, in the case of autoimmune pemphigus, and the functional prognosis, by affecting the quality of life reported in many dermatoses [1, 2]. The idea that “common things happen frequently” is a true finding in dermatology – a huge chapter, embracing more than 2000 different conditions. It is estimated that approximately 70% of a dermatologist's work is caused by only nine types of skin disorders: malignant skin tumours, acne, atopic dermatitis, psoriasis, viral warts, infectious skin diseases, benign tumours and vascular lesions, leg ulcers, contact dermatitis and other eczemas. In the United States, almost half of all dermatologist visits are for one of these three diagnoses: acne, warts, and skin tumours. Whatever the cause, skin diseases should not be ignored, as they can worsen and have a negative impact on the quality of life [3, 4].

In general, the literature reveals that skin diseases include

a wide range of causal factors, among which we can notice fungal, viral, bacterial, parasitic infections, etc. Likewise, quite frequently in the etiopathogenesis of skin diseases are involved practically all types of immuno-allergic reactions, which lead to the appearance of allergic dermatoses, autoimmune dermatoses or immune-mediated dermatoses. Finally yet importantly, skin disorders are caused by other extracutaneous pathological diseases, being often attested as complications [3].

Most of them, skin diseases are diagnosed by a careful examination of the skin to which is added information related to the patient's medical history. Some skin conditions are more difficult to diagnose, as they resemble other skin diseases, but not only. For example, rosacea requires further investigation and clinical examination by a dermatologist, so as not to be confused with acne in adolescents [5]. Even skin biopsy or tissue culture may be required to accurately diagnose and differentiate skin diseases [6].

Among the most serious skin diseases, some authors note toxic bullous necrolysis, Stevens-Johnson syndrome, pemphigus vulgaris, acne, malignant tumours, skin lym-

phomas, etc., a multitude of diseases and pathological conditions, which involve the use an equally varied arsenal of active substances and pharmaceutical forms in their treatment, according to the ATC classification in the D – code Dermatological preparations.

The purpose of this study is to assess the pharmaceutical forms and preparations used in the specific treatment of skin diseases based on bibliographic analysis and practice of those registered in the State Nomenclature of the Republic of Moldova, according to ATC classification, dose, division, country and industrial enterprise, shelf life, cost, etc.

Material and methods

The data materials were collected from specialized literature, clinics (400 documents) and the State Nomenclature of the Republic of Moldova, as well as based on the results of a systemic analysis of producers and production in this segment of drugs, prices for manufactured drugs, the shelf life declared by the manufacturer, etc. The methodology of scientific research was developed based on the publications of local authors [7, 8], using the methods of analytics, descriptive statistics, comparison, price analysis, etc.

Results

In the Republic of Moldova, 526 preparations are used in the treatment of dermatological diseases according to the ATC classification [9], with code – D Dermatological preparations, which also includes 11 subcodes, namely:

Table 1

Dermatological preparations registered in the Republic of Moldova, according to the ATC classification

Sub-code	The destination of the preparations	Quantity of preparations registered in the Republic of Moldova
D01	Antifungals for dermatological use	98
D02	Emollients and protectors	10
D03	Preparations for the treatment of wounds and ulcers	31
D04	Antipruritic, includes antihistamines and local anesthesia	7
D05	Antipsoriatic	6
D06	Antibiotics and chemotherapeutics for dermatological usage	66
D07	Corticosteroids, dermatological preparations	93
D08	Antiseptics and disinfectants	160
D09	Medicinal dressings	0
D10	Acne preparations	27
D11	Other dermatological preparations	28

Note. These 11 ATC subcodes include another 40 subcodes.

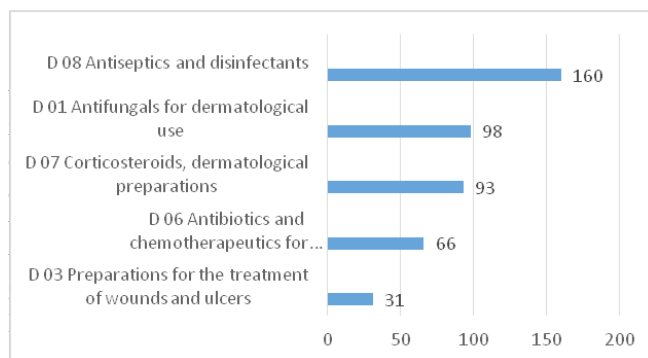


Fig. 1. Preparation used in dermatological practice, registered in the Republic of Moldova, according to ATC

On 14.04.2017, 18 pharmaceutical registered preparations used in dermatological practice were exhibited on the pharmaceutical market of the Republic of Moldova, among which: ointments – 274 (incl. nasal ointment – 1, ophthalmic ointment – 1, creams – 104, vaginal creams – 2, gels – 31, liniments – 8, pastes – 3); cutaneous solutions – 162 (incl. solutions – 7, alcoholic solutions – 5, cutaneous alcoholic solutions – 8, oropharyngeal solutions – 3, cutaneous solutions – 141, oily solutions – 5, shampoos – 10); tablets – 16; sprays – 19 (incl. skin spray, sol. – 16, skin spray, susp. – 2, buccopharyngeal / cutaneous / vaginal spray, sol. – 1); powders – 11 (incl. powder + solvent / skin solution – 1, skin powder – 7, powder / cutaneous sol.– 3, powder / injectable sol. – 2), etc. [10, 11].

The distribution of preparations and their pharmaceutical forms used in dermatological practice accounts for 4.82%, of which ointments – 52.09%, skin solutions – 30.80%, tablets – 3.04%, spray – 3.61%, powders – 2.09%, capsules – 1.52%, herbal products – 0.57%, injectable solutions – 0.38%, suppositories – 0.19% and others (fig. 2).

It is necessary to mention the specific group of herbal products used in the treatment of dermatological diseases, registered in the Republic of Moldova:

1. Elecasol, herbal combination, vegetable product / tea, 1.5 g N20, Ukraine;
2. Elecasol, vegetable product / tea, 75g N1, Ukraine;
3. Aerial parts of dentition, Bidens tripartite, fragmented plant product, 50g N1, Ukraine.

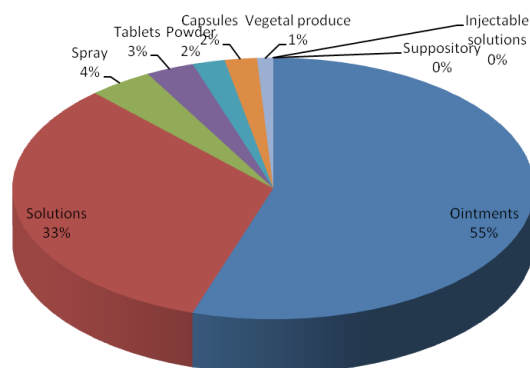


Fig. 2. The distribution of pharmaceutical forms, used in dermatological practice in the Republic of Moldova

As it is shown in figure 2 the ointments and skin solutions are among the top pharmaceutical forms used in dermatological practice and registered in the Republic of Moldova. [11].

Dermatological preparations were assessed according to the manufacturing country, shown in figure 3. Of the 27 drug-producing countries, registered in the Republic of Moldova regarding preparations and pharmaceutical forms used in dermatological practice, the Republic of Moldova is on the first place with 212 registered pharmaceutical forms (40.30%), followed by the Ukraine – 45 preparations (8.55%) and Switzerland – 33 preparations (6.27%). Other countries (in alphabetical order): Austria – 12 (2.28%), Belgium – 7 (1.33%), Bosnia and Herzegovina – 4 (0.76%), Bulgaria – 6 (1.14%), Czech Republic – 3, Croatia – 1, Egypt – 1, Estonia – 1, France – 2, Georgia – 1, Germany – 24 preparations (4.56%), India – 16 (3.04%), Italy – 2, Latvia – 3, Great Britain – 20 preparations (3.80%), Netherlands – 15, Poland – 14, the Republic of Belarus – 13, Romania – 26 preparations (4.94%), Russia – 32 (6.08%), Serbia – 1, Slovenia – 6 (1.14%), Turkey – 14, Hungary – 12 preparations (2.28%) [10, 11].

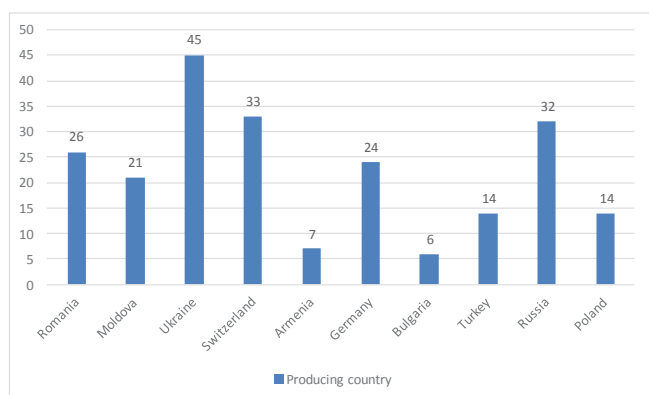


Fig. 3. Top 10 producing countries with the largest number of dermatological preparations and their pharmaceutical forms, registered in the Republic of Moldova

The list of drug manufacturing companies used in dermatological practice and registered in the Republic of Moldova, is as following: *Farmaprim SRL*, the Republic of Moldova ranks first with 46 preparations, followed by *Beta SRL*, Moldova – 33 preparations, *I.M. RNP Pharmaceuticals SRL*, Moldova – 24, *Universal-Farm SRL*, Moldova – 21, *Bayer Consumer Care AG*, Germany – 20, *Farmacia Cojusna SRL*, Moldova – 20, *I.M. Farmaco SA*, Moldova – 20, *Niffarm SA*, Russia – 19, *Astellas Pharma Europe B.V.*, Netherlands – 15 (fig. 4) [10, 11].

One of the decisive factors in ensuring the competitiveness of medicines is their quality. An important parameter of the quality of pharmaceutical forms is considered the “shelf life”, determined by experimental methods, such as the «accelerated aging» method or other methods [12].

As it is shown in figure 5, 237 preparations and their pharmaceutical forms were declared by the manufacturers

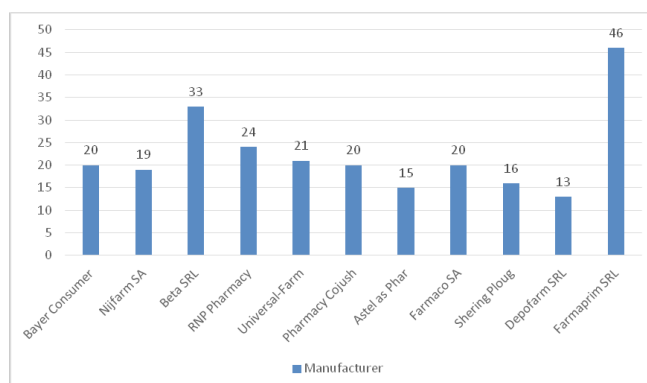


Fig. 4. Top 10 dermatological drug manufacturers with the highest number of drug preparations, registered in the Republic of Moldova

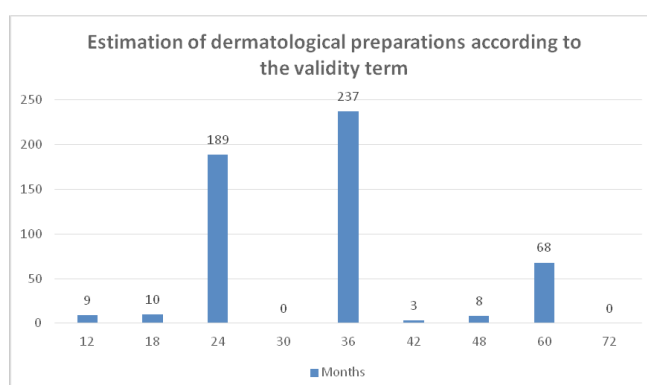


Fig. 5. Shelf life as a parameter of the quality of preparations used in dermatological practice, registered in the Republic of Moldova

as having a 36-month shelf life of (e.g. *Triderm®* ointment, 0.5 mg + 10 mg + 1 mg/g, 15 g N1, D07CC01, *Betamethasonum + Clotrimazolum + Gentamicinum*, *Schering-Plow Central East AG* (prod.: *Schering-Plough Farma Lda*, Portugal; *Schering-Plow Labo NV*, Belgium); 189 preparations and their pharmaceutical forms were declared to have a 24-month shelf life (e.g. skin spray, *Mycofin®* sol., 10 mg g, 30 ml N1, D01AE15, *Terbinafinum*, *Nobel Ilac Sanayii ve Ticaret A.S.* (prod.: *Nobel Ilac Sanayii and Ticaret AŞ*, Turkey); 68 preparations and their pharmaceutical forms – 60-month shelf life (e.g. skin spray, *Acerbine* sol. 2.15 g + 0.15 g + 0.04 g / 100 g, 80 ml N1, D03AX, *Acidum malicum + Acidum benzoicum + Acidum salicylicum*, *Pharmazeutische Fabrik Montavit Ges.mbH*, Austria); 2 preparations and their pharmaceutical forms do not have a declared shelf life (e.g. *Polividon-iodine* skin alcohol solution, 10%, 100ml No1, D08AG02, *Povidoni iodidum*, *Beta SRL*, the Republic of Moldova) [10, 11].

A particularly important index that describes the accessibility of the population to an adequate and effective treatment (and the “cost-effectiveness” index) is the price of medicines declared by the manufacturer. Thus, in the chapter of “price declared by the manufacturer”, dated on 14.04.2017, the highest declared prices for preparations and their pharmaceutical forms, used in dermatological practice

and registered in the Republic of Moldova (fig. 6) were as follows:

1. Gelatin capsules Roaccutane® 20mg, N10x3, D10BA01, Isotretinoinum, *F. Hoffmann-La Roche Ltd* (prod.: *Catalent Germany Eberbach GmbH*, Germany), Switzerland. Shelf life – 36 months, Manufacturer's price (ex works) MDL – 310.38, EUR – 14.06.
2. Skin solution Betadine®, 10%, 1000 ml, N1, D08AG02, Povidoni iodidum, *Egis Pharmaceuticals PLC*, Hungary. Shelf life – 36 months, Manufacturer's price (ex works) MDL – 258.83, USD – 12.84.
3. Lyophilized / injectable sol., Chymotrypsin 10 mg, N10, D03BA, Chymotrypsinum, *Samson-Med SRL*, Russia. Shelf life – 36 months. Manufacturer price (ex works) MDL – 222.24, USD – 11.20.
4. Tablets Terbibil®, 250 mg, N14x2, D01BA02, Terbinafinum, *Gedeon Richter PLC*, Hungary. Shelf life – 60 months, Manufacturer's price (ex works) MDL – 208.58, EUR – 9.50, etc.

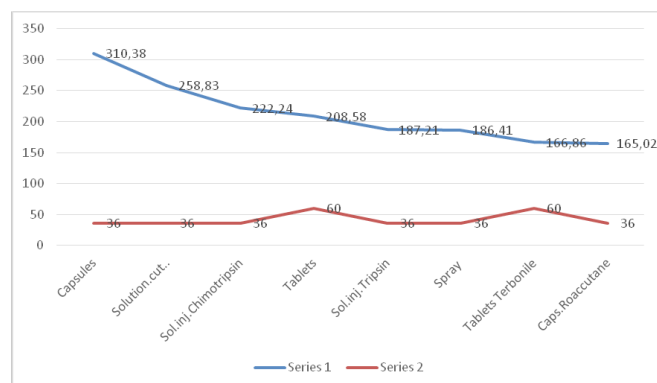


Fig. 6. The assessment of the manufacturer's price on preparations used in dermatological practice, registered in the Republic of Moldova

5. Lyophilized / crystalline sol., Tripsin injection, 10mg, N10, D03BA01, Trypsinum, *Samson-Med SRL*, Russia. Shelf life – 36 months, Manufacturer's price (ex works) MDL – 187.21, USD – 9.50.
6. Skin spray, sol., Pifud®, 50 mg / ml, 60 ml N1, D11AX01, Minoxidilum, *Bosnalijek*, Pharmaceutical and Chemical Industry JSC, Bosnia and Herzegovina. Shelf life – 36 months, Manufacturer's price (ex works) MDL – 186.41, EUR – 8.35.
7. Tablets Terbonile, 250 mg, N14x2, D01BA02, Terbinafinum, *Bilim Pharmaceuticals AS*, Turkey. Shelf life – 60 months, Manufacturer's price (ex works) MDL – 166.86, USD – 8.44.
8. Caps., Roaccutane® 10mg, N10x3, D10BA01, Isotretinoinum, *F.Hoffmann-La Roche Ltd* (prod.: *Catalent Germany Eberbach GmbH*, Germany); Switzerland, Shelf life – 36 months, Manufacturer's price (ex works) MDL – 165.02, EUR – 7.76.
9. Skin spray, sol., Pifud® 2%, 60ml N1, D11AX01, Minoxidilum, *Bosnalijek*, Pharmaceutical and Che-

mical Industry JSC, Bosnia and Herzegovina. Shelf life – 36 months. Manufacturer's price (ex works) MDL – 164.84, EUR – 7.50.

10. Gel Skinoren® 150 mg / g, 50 g N1, D10AX03, Acidum azelaicum, *Bayer AG* (prod.: *Bayer Health Care Manufacturing S.R.L.*, Italy), Germany. Shelf life – 36 months, Manufacturer's price (ex works) MDL – 157.14, EUR – 7.15.

The lowest price was attested at 3% Boric acid-RNP sol., 10 ml N1, D08AD, Acid boric, *RNP Pharmaceuticals SRL*, the Republic of Moldova. Shelf life – 24 months, Manufacturer's price (ex works) MDL – 3.68, USD – 0.18 [10, 11].

Discussion

1. The fight against skin diseases is a persistent medical and socio-economical problem for the Republic of Moldova, as these can have a strong psychological and aesthetic impact on people who constantly struggle for improving self-image. Untreated dermatological skin diseases might leave deep marks, which are often difficult to reverse, thus causing emotional and physical discomfort among population.

2. According to the ATC classification, out of the total of 10924 preparations registered in the Republic of Moldova on 14.04.2017, 526 are used in dermatological practice. The most registered preparations refer to the subcode D08 Antiseptics and disinfectants – 160 preparations, the least ones refer to subcode – D05 Antipsoriasis – 6 preparations. Among the subcodes, most of the registered preparations belong to the subcode D08AX – 68 preparations, D08A – 21 et al. The subcode D09 Drug dressings do not contain any preparations.

3. According to the data from the State Nomenclature of the Republic of Moldova, the distribution of preparations used in dermatological practice makes up 4.82%, which are present in various pharmaceutical forms: ointments – 52.09% (274), solutions for external use – 30.80% (162), sprays – 3.61% (19), tablets – 3.04% (16), powders – 2.09% (11), capsules – 1.52% (8), plant products – 0.57% (3), injections – 0.38% (2), and suppositories – 0.19% (1).

4. Of the 27 dermatological drug manufacturing countries, most preparations were registered in the Republic of Moldova including: the *Republic of Moldova* – 212 preparations (40.30%), the *Ukraine* – 45 preparations (8.55%), *Switzerland* – 33 preparations (6.27%), *Russia* – 32 (6.08%), *Romania* – 26 preparations (4.94%) etc.

5. The list of dermatological drug manufacturing companies, registered in the Republic of Moldova includes: *Farmaprim SRL*, Republic of Moldova – 46 preparations, *Beta SRL*, Republic of Moldova – 33 preparations, *RNP Pharmaceuticals SRL*, IM, Republic of Moldova – 24, *Universal-Farm SRL*, Republic of Moldova – 21, *Bayer Consumer Care AG*, Germany – 20, etc.

6. The maximum shelf life of 60 months is stated for 68 pharmaceutical preparations and forms. The shortest shelf life – 12 months is stated for 9 pharmaceutical forms.

7. A particularly important index of the accessibility of

the population to adequate and effective treatment is the price of the medicine declared by the manufacturer. Thus, as regarding to the “manufacturer’s price” for the pharmaceutical forms used in dermatological practice, the lowest price was registered for 3% Boric acid – RNP, 10 ml N1, D08AD, Acidum Boricum, *RNP Pharmaceuticals SRL*, the Republic of Moldova – (ex works) MDL – 3.68, USD – 0.18. Shelf life – 24 months. The highest price declared for preparations in this group is Roaccutane® 20mg, N10x3, D10BA01, Isotretinoinum, *F. Hoffmann-La Roche Ltd* (producer: *Catalent Germany Eberbach GmbH*, Germany), Switzerland. Shelf life – 36 months, Manufacturer’s price (ex – works) MDL 310.38, EUR – 14.06.

Conclusions

The dermatological drug distribution across the Republic of Moldova was 4.82%, of which over 80% accounted for pharmaceutical forms for external use. The most registered and used dermatological drugs from the Republic of Moldova were of local origin, which are both qualitative and the most accessible ones.

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Authors’ contribution

MF, AZ designed the study and performed its logistic part, drafted the first manuscript; MF, TC collected and processed the material, performed the work; AZ, VG interpreted the data, revised the manuscript. All the authors revised and approved the final version of the manuscript.

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Ethics approval and consent to participate

No approval was required for this study.

Conflict of Interests

No competing interests were disclosed.