

## Pharmaceutical forms used in the gynecology practice

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### Abstract

**Background:** One of the main indicators of the welfare of a nation is the index of women's health status. Women's health (or health care) is the key factor, on which depends the happiness and wellbeing of each family. During her life cycle, a woman passes through several stages that affect the health of the genital organs: menstruation, fertility, pregnancy, childbirth, and menopause. When ladies are facing these situations, most of them remember that they followed some drug treatments for long period of time. This scientific study represents an analysis of the pharmaceutical preparations and their forms used in gynecology practice. According to records from the State Nomenclature of the Republic of Moldova, research methodology was developed (using the following criteria: anatomical therapeutic chemical classification, dose, division, country and industrial pharmaceutical company producer, producer's price, terms of validity), based on local authors publications. The research study was conducted and reveals the information gathered before (until) 31st of March, 2016.

**Conclusion:** Taking into consideration all pharmaceutical forms registered in the State Register of the Republic of Moldova, used in gynecological practice can be divided into: a) pills, b) pessaries, c) injection solutions. The Republic of Moldova is located at the top of the list of the 21-producing countries, which have registered pharmaceutical forms, used in gynecological practice. Domestic producers of medicines are covering approximately 10.98% of pharmaceutical products segment.

**Key words:** pharmaceutical forms, formulations, gynecology, dose, preparations, price, accessibility.

### Introduction

One of the main indicators of well-being of a country is the health of women who live in it. And on this factor depends the happiness of every family. The statistic information attests the fact that women's health in the Republic of Moldova is alarming. The number of women of childbearing age suffering from various diseases is growing. At present stage, every second woman reaches reproductive age with seriously modified maternal land [3, 6, 12]. Only in the last 10 years, in the Republic of Moldova, sterile couples increased approximately twice and reached the number of 16.0% [1], one of the main causes of infertility being consequences or complications of gynecological pathologies [5, 7].

During her life cycle, a woman passes through several stages that affect her genital health: menstruation, fertili-

ty, pregnancy, childbirth, menopause, and then we should not forget that some of them followed some drug treatments for long period of time.

Some authors state that, in general, gynecological diseases can be divided into three groups: a) inflammatory diseases of the female genitals, b) diseases caused by endocrine disorders, c) hyper-plastic, degenerative and neoplastic diseases in sexual field [4, 13].

Taking into consideration this fact, the multitude of diseases and pathological gynecological conditions, assumes using in their treatment various types of formulations and active ingredients, and not only from the G-code Genitourinary Unit and sex hormones, but some other codes as well, for example – J Anti-infective systemic use, – L Antineoplastics and immunomodulators, etc.

**Material and methods**

As materials served the information regarding registration of medicinal preparations and their pharmaceutical forms taken from State Nomenclature of the Republic of Moldova (producers analysis results and results of production in this specific segment of medicines, prices of manufactured products and validity period, stated by the producer).

The research methodology was developed based on local author’s publications [2, 12] using the following methods: analytical, descriptive statistics, comparison, price analysis, etc. The research study was conducted and reveals the information gathered until 31st of March, 2016.

**Results and discussions**

According to ATC List with a total of 528 preparations, G-code class Genitourinary Unit and sex hormones, includes 4 sub-codes:

- G01 Gynecological antiinfectives and antiseptics,
- G02 Other gynecological preparations, -G03 Sex hormones and modulators of the genital system,
- G04 medication of urinary system (urological) [8].

The pharmaceutical forms used in gynecological practice, according to the ATC, are shown in figure 1.

As shown in figure 1, according to ATC classification, sub-code -G03 Sex hormones and modulators of the genital system accumulate the highest number of registered preparations.

Preparations used in gynecological practice, registered in Moldova, are present in the following pharmaceutical forms: vaginal spray-1-topical solution, oral solution-3, cutaneous solution-2, vaginal solution-1, implants-2, effervescent granules-1, vaginal gel-5, oral gel-1, gel-8, drinkable drops-1, oral paste-1, fragmented vegetal product-3, oral drops, solution-11, syrups-3, dragees-18, ovules -63, pessaries-19, capsules-71 (including, gastro-resistant soft capsule-1, soft capsules-9, capsules with long drug expiration-3capsules with modified release-15, vaginal capsules-14) vaginal cream-5, cream-3, trans-dermal patch-2, tablets-218 (incl. chewable tablets-3, extended release tablets-8, tablets-108, extended release tablets-2, effervescent tablets-1, lozenges-3, orodispersible tablets-6, vaginal tablets-23, homeopath tablets-3), injectable solutions-45 (including injectable solution in a cartridge-6, solution for injection in pre-filled syringe-5, solution for injection in pre-filled pen-5, oil injection-4) lyophilized + solvent / solution for injection-11, powder + solvent / solution for injection-17, suspension for injection-4, solution for infusion-14, powder / vaginal solution-2, lyophilized powder / injection-1, releasing intrauterine system-2, releasing vaginal system-1 [8,10].

According to the records from the State Nomenclature of the Republic of Moldova of March 31st, 2016, from the total share of authorized medicinal products, preparations used in gynecological practice were 5.54%. From these preparations, pharmaceutical forms can be divided into: soluti-

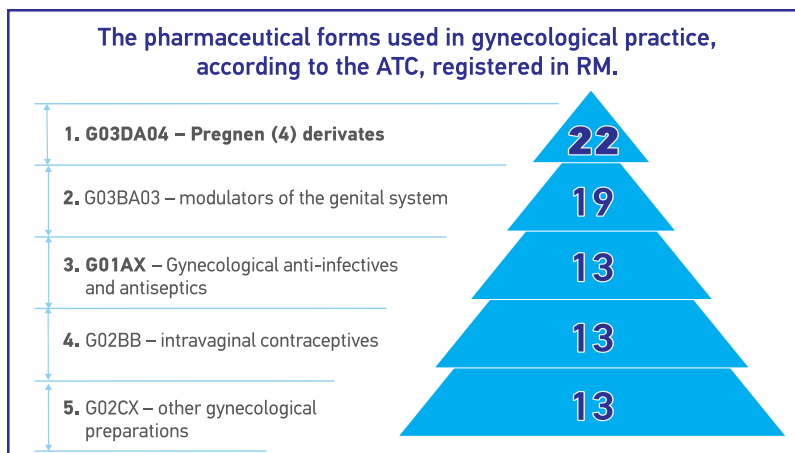


Fig. 1. Presentation of ATC code - G Unit preparations Genitourinary system and sex hormones.

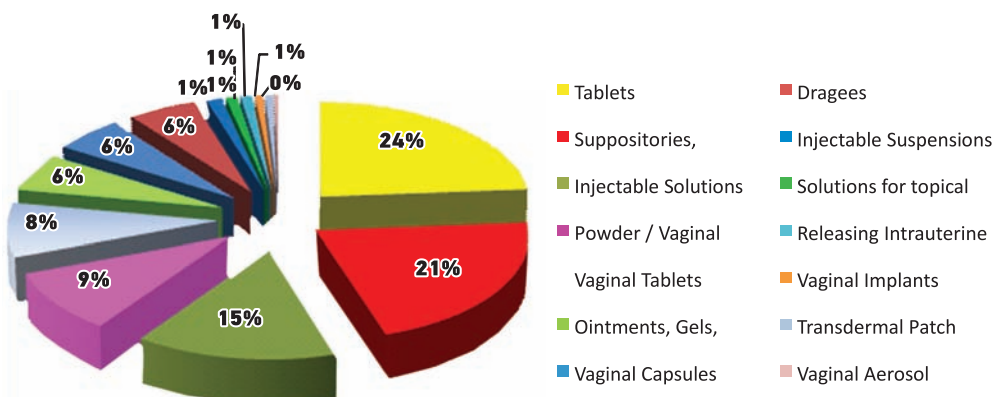


Fig. 2. Pharmaceutical forms used in gynecological practice, according to the State Nomenclature of the Republic of Moldova.

ons for topical use, irrigation - 0.95%, vaginal tablets - 7.62%, ointments, gels, vaginal creams - 6.03%, vaginal implants - 0.63%, suppositories, pessaries - 15.53%, releasing intrauterine systems - 0.95%, transdermal patch - 0.63%, vaginal aerosol - 0.32%, vaginal capsules - 5.71%, tablets - 24%, injectable solutions - 15% , injectable suspensions - 1.27%, powder / vaginal solution - 9.21%, dragees - 5.08% [8,10].

Formulations (pharmaceutical forms) used in gynecological practice, according to the State Nomenclature of the Republic of Moldova are presented in figure 2.

The data shown in figure 2 proves that ovules, tablets and injectable solutions are in the top of pharmaceutical forms, used in the treatment of gynecological diseases, recorded in the Republic of Moldova [8, 10].

**Medicine producers (Drug makers)**

**A. Countries (figure 3)**

From the number of medicines used in gynecological practice, in Moldova were registered preparations from 21 countries, in the top 10 - the first position is held by the Republic of Moldova - with 18.53% (58 medicines - produced and registered), Switzerland holds the second position with 12,78% (40 medicines), on the third place is Hungary and Germany with 11.50% each (36 medicines) [8,10].

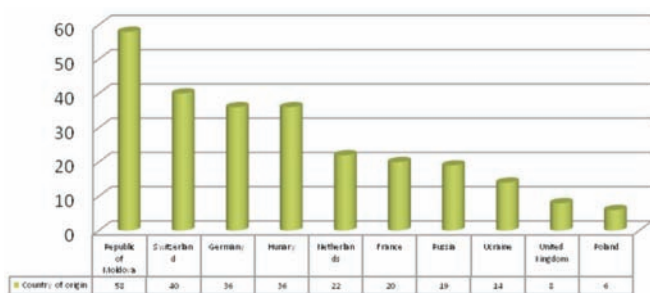


Fig. 3. Top 10 countries producing pharmaceutical forms, used in gynecological practice registered in the Republic of Moldova.

As to information reflected in figure 3, local producers cover production of pharmaceutical forms, used in gynecological practice by 10.98%.

**B. Pharmaceutical industry, producing enterprise**



Fig. 4. Top 10 Pharmaceutical industrial producing enterprises, used in gynecological practice, registered in the Republic of Moldova.

The leading pharmaceutical company producing industrial products used in gynecological practice registered in the

Republic of Moldova, is Gedeon Richter PLC, Hungary; followed by industrial enterprises: FARMAPRIMSRL, Moldova and Bayer Pharma AG, Germany (fig. 4) [8,10].

**Terms of validity (Expiration date)**

One of the decisive factors ensuring competitiveness of medicines is their quality. Many pharmaceutical forms are in native equilibrium, but degrade as disposal of free energy, being in a phase when their therapeutic value decreases. Therefore, an important parameter of the quality of the pharmaceutical forms is the term of expiry, determined through different experimental methods, e.g. "Method of accelerated aging" or through other degrading methods [9].



Fig. 5. The expiration date as a parameter of the pharmaceutical forms quality used in gynecological practice, registered in the Republic of Moldova.

As shown in figure 5 the longest expiration date stated by the manufacturer - 60 months, 74 pharmaceutical forms have this validity terms (e.g. suspension for injection - Depo-Provera, 150 mg / mL, 1 mL N1, G03AC06, Medroxyprogesteronum, Pharmacia NV / SA, Belgium); - 12 pharmaceutical forms declared the expiration date of 48 months (e.g., Logest® tablets, 0.02 mg + 0.075 mg, N21, G03AA10, Ethinylestradiolum + Gestodenum, Bayer Schering Pharma AG (Bayer Schering Pharma AG prod.: Germany; Delpharm SAS Lille, France), Germany); - 1 pharmaceutical form announced the expiration date of 40 months (releasing vaginal system - NuvaRing®, 11.7 mg + 2.7 mg, N1, G02BB01, Etonogestrelum + Ethinylestradiolum, Schering-Plough Central East AG (prod.: Organon (Ireland) Ltd., Ireland Organon NV, Netherlands), Switzerland); - 272 pharmaceutical forms stated expiration date - 36 months (e. g. transdermic patch (STT) - Climara®, 3,8 mg (50 mcg / 24 h), N4, G03CA03, Estradiolum, Bayer Schering Pharma AG (prod.: 3M Drug Delivery System, USA), Germany); - 2 pharmaceutical forms stated terms of validity - 30 months; - 163 pharmaceutical forms announced expiration date - 24 months (e.g. Pessaries - Dalacin vaginal pessaries, 100 mg, N3, G01AA10, Clindamycinum, Pharmacia & Upjohn Company, USA); - 2 pharmaceutical forms declared expiration date - 18 months (e.g. Vaginal soft capsules - Polygynax® Virgo, 35000 + 35000 UI UI UI + 100000, N3x2, G01A, Polymyxinum Neomycinum + B + Nystatinum, Laboratoire Innotech International (prod.: Innothera Chouzy, France), France) [8].

**Producer's prices**

A very important index that describes the accessibility of a proper and efficient treatment (and correlation "cost-effectiveness"), is the price of medicines input by the manufactu-



Fig. 6. Estimation of the preparations used in gynecological practice, registered in the Republic of Moldova, according to price of the producer.

rer. This way, the price declared by the producer in decreasing for some pharmaceutical forms used in gynecological practice (fig. 6):

1. Solution for injection in pre-filled syringe - Elonva<sup>®</sup>, 150 mcg / 0.5 ml, 0.5 ml, N1, G03GA09, Corifollitropin alpha, Schering-Plough Central East AG (prod.: Organon (Ireland) Ltd., Ireland; VetterPharma-FERTIGUNG GmbH & Co.KG, Germany), Switzerland, term of validity - 36 months, producer's price (ex works) - € 455.19 or 8835.60 MDL.

2. Solution for injection in pre-filled syringe - Elonva<sup>®</sup>, 100 mcg / 0.5 ml, 0.5 ml, N1, G03GA09, Corifollitropin alpha, Schering-Plough Central East AG (prod.: Organon (Ireland) Ltd., Ireland; VetterPharma-FERTIGUNG GmbH & Co.KG, Germany), Switzerland, term of validity - 36 months, producer's price (ex works) - € 412.03 or 7997,83MDL.

3. Solution for injection in pre-filled pen - Gonal-f<sup>®</sup> 900 IU (66 mcg), 1.5 ml, N1 G03 GA05, Follitropin alpha, Merck Serono S.A. (Prod.: Merck Serono S.P.A., Italy), Switzerland, term of validity - 24 months, producer's price (ex works) or -310.15 USD 6176.11 MDL.

4. Powder + solvent / solution for injection - Bravelle 75 IU N5x2 + 1ml, N5x2, G03GA04, Urofollitropin, Ferring GmbH, Germany, term of validity - 24 months, producer's price (ex works) - € 159.03 and 3420.23 MDL.

5. Solution for injection in cartridge - Puregon<sup>®</sup>, 600 IU / 0.72 ml, 0.780 ml, N1, G03GA06, Follitropi beta-num, Schering-Plough Central East AG (prod.: Organon (Ireland) Ltd., Ireland Vetter FERTIGUNG-Pharma GmbH & Co.KG, Germany), Switzerland, term of validity - 36 months, producer's price (ex works) - € 162.75 or 3159.11 MDL.

6. Tablets - Esmya<sup>®</sup>, 5 mg, N14x2, G03AD02, Ulipristalum, Gedeon Richter PLC, Hungary, term of validity - 24 months, producer's price (ex works) - € 115.69 or 2591.33 MDL.

7. Releasing intrauterine system - Jaydess<sup>®</sup>, 13.5 mg, N1, G02BA03, Levonorgestrelum, Bayer Pharma AG (prod.: Bayer Oy, Finland), Germany, term of validity - 24 months, producer's price (ex works) - € 121.30 or 2354.53 MDL.

8. Solution for injection in pre-filled pen - Gonal-

f<sup>®</sup> 300 IU (22 mcg), 0.5 ml, N1 G03 GA05, Follitropin alpha, Ares Trading S.A. (Prod.: Merck Serono S.P.A., Italy), Switzerland, term of validity - 24 months, producer's price (ex works) - \$ 103.35 or 2058.04 MDL.

9. Releasing intrauterine system - Mirena<sup>®</sup>, 52 mg (20 mcg / 24 hours), N1, G03AC03, Levon-gestrelum, Bayer Oy, Finland, term of validity - 36 months, producer's price (ex works) - 86.5 EUR or 1679.03 MDL.

10. Films - Clostilbegyt, 50 mg, N10, G03GB02, Clomifenum, Egis Pharmaceuticals PLC, Hungary, term of validity - 60 months, producer's price (ex works) - \$ 2.76 or 55.18 MDL.

The lowest price can be seen at pharmaceutical form - vaginal tablets - Clotrimazol MCC 100 mg, N6x2, G01AF02, Clotrimazolium, Magistra C & C SRL, SC, Romania, term of validity - 24 months, producer's price (ex works) MDL - 8.35, EUR - 0.43 [8,10].

The number and prices of products manufactured and registered in the Republic of Moldova varies depending on producing enterprises: lower price <50.00 MDL - 37 medicines >50.00 <100.00 MDL - 66 medicines >100 <200 MDL - 76 medicines, > 200 <400 MDL - 35 medicines, > 400 <1000 MDL - 6 medicines, over > 1000 MDL - 16 medicines.

## Conclusions

1. In the Republic of Moldova, according to ATC classification code G-Unit genitourinary system and sex hormones, includes 4 sub-codes that represent the following sub-code -G03 Sex hormones and modulators of the genital system and accumulates the highest number of registered medicines, the lowest is sub-code - G 02 Other gynecological medicines.
2. From pharmaceutical forms registered in the State Nomenclature of the Republic of Moldova used in gynecological practice, the largest number goes to: a) tablets, b) ovules and c) injectable solutions.
3. Moldova is located at the head of the 21 producing countries, which have registered pharmaceutical forms used in gynecological practice. Domestic producers of medicines are covering 10.98 % from this segment of pharmaceutical market.

4. The biggest amount of medicines used in gynecological practice and registered in Moldova lies with the company manufacturing industrial medicines Gedeon Richter PLC, Hungary.
5. The term of validity (expiration date) of the pharmaceutical forms used in gynecological practice declared by the manufacturer vary depending on the nature of the active substance and pharmaceutical form from 60 months till 18 months.
6. Producer's price for pharmaceutical forms used in gynecological practice varies between 8.35 MDL and 8835.60 MDL. Prices of the medicines used in gynecological practice produced by domestic medicine manufacturing enterprises have medium range of competitiveness and vary from - 13.22 MDL to - 1800.00 MDL.

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