MINISTRY OF PUBLIC HEALTH OF REPUBLIC OF UZBEKISTAN

Republican Specialized Scientific and Practical Medical Centre of Obstetrics & Gynaecology of Ministry of Public Health of Republic of Uzbekistan

"APPROVED by"
Director of Republican
Specialized Scientific and
Practical Medical Center of
Obstetrics & Gynaecology of
Ministry of Public Health of
Republic of Uzbekistan
Prof.Sultanov S.N.

REPORT ON THE CLINICAL TRIAL

Research of antibacterial efficiency and tolerance of "**VAGIMILT®**" brand of MILTONIA HEALTH SCIENCE LIMITED [UK] produced by SOFTGEL HEALTHCARE PRIVATE LTD, India

According to the limited program

Executive in charge — As. Prof.Nishanova F.P.
Performed by: — junior scientific specialist Atadzhanova N.P.

TASHKENT - 2010

CONTENTS

1. PREFACE

Inflammation diseases of the organs of small pelvis occupy the leading place among the diseases of the female organs. By their aetiology they may be of bacterial, fungi, parasitic origin.
Vaginitis and vulvovaginitis of bacterial, fungi and combined origin are very often met in medical practice. To treat them, the antibacterial preparations (synthetic antibacterial preparations), antifungal agents, antiseptics and combined preparations are used.

VAGIMILT® is the combined preparation consisting of the antibacterial agent – clindamycin 100 mg and antifungal agent – clotrimazole 100 mg. It manifests the activities of the both components of the preparation:

Clindamycin inhibits the synthesis of protein in the bacterial cell, joining 50S-subunits of ribosomes. Preparation is active against main causative agents of the bacterial Vaginitis.

Clotrimazole is the anti-mycotic preparation of wide spectrum of activity from the group of derivatives of imidazole for the local application. Antifungal effect occurs due to the troubles in synthesis of ergosterin and cell wall of the fungi. Preparation is efficient against yeast-like fungi, all types of dermatophytes and mold fungi, is acts also on gram-positive and gram-negative bacteria.

VAGIMILT® is the soft gelatine ovule containing white greasy mass. In case of intravaginal introduction preparation is active only locally, only about 3% of the introduced dose is absorbed through the mucous tissue of vagina.

2. OBJECTIVE OF THE RESEARCH

Research of antibacterial efficiency and tolerance of "VAGIMILT®" brand of MILTONIA HEALTH SCIENCE LIMITED [UK] produced by SOFTGEL HEALTCARE PRIVATE Ltd, India, to reveal the possibility to prepare recommendations on the preparation for clinical application in Republic of Uzbekistan.

To achieve this objective, the following tasks were formulated:

- research of antibacterial efficiency;
- research of tolerance and safety.

3. JUSTIFICATION TO PERFORM THE RESEARCH

Resolution of Presidium of Pharmacological committee (the minutes № 4 dd. 25.02. 2010)

4. TYPE (DESIGN) OF THE RESEARCH

Limited.
Open, controlled, with two parallel groups.

5. SELECTION OF PATIENTS

5.1. Criteria of inclusion in the research: patients staying at stationary treatment, of female gender, of age over 18 years, who gave the written consent to participate in the research, with

- Vulvovaginitis of bacterial and fungi aetiology,
- Bacterialvaginosis.

To select the patients with various manifestations of inflammation process of genitalia of bacterial or fungal aetiology were consulted and examined in the scientific and consulting polyclinics of Republican Specialized Scientific and Practical Medical Center of Obstetrics and Gynaecology of Ministry of Public Health of Republic of Uzbekistan.

After primary examination the patients conforming to the criteria of inclusion and planned to be included in the principal group received the information on the researched VAGIMILT® preparation, information on the dosage, schemes, ways of introduction and period in order to receive their written informed consent for participation in the research.

As a result, 20 patients with vulvovaginitis or bacterial vaginitis of bacterial or fungal origin as one of the principal diseases, who gave the written informed consent for participation in the research, were included in the principal group receiving the researched VAGIMILT® preparation. Other 20 patients comparable in gender, age and diagnosis with the women of the principal group were included in the control group, and received the traditional therapy, for that Clomezole, the well-known preparation produced by “Farmaprim SRL”, Moldova, was selected (metronidazole 500mg, clotrimazole 150 mg, neomycin sulphate 200 mg).

According to the minutes the following women were not included in the research:

- Younger than 18;
- Pregnant,
- Lactating;
- With extra sensitivity to the components of the preparation;
- During the period of menstrual bleeding,
- Of reproductive age, not using contraception;
- Participating in other clinical researches during the last 30 days;
- Who did not give the informed consent for participation in this clinical trial.

The list of the patients included in the research is given in the Tables 1 and 2.

Table 1

List of the patients receiving VAGIMILT®

	First and last name	№ of case/hospital card	Year of birth	Principal diagnosis	Additional diagnosis
1.	AripovaGulimoi	4419	1985	Vaginitis. NMF. Anovulation. Galactorrhea of the I degree. CMVI	Goiter of 1 degree. Euthyroidism. ZDA of the I degree
2.	BakhriddinovaHuljahon	253	1983	Bacterial vaginitis. NMF. Anovulation. Opsomenorrhea, galactorrhea of the 0-1 degree. Chronic cervicitis.	Goiter of the 1 degree. Euthyroidism
3.	Valieva Aziza	4542	1988	Bacterial vaginitis. NMF. Galactorrhea of the II degree. PMS. Chronic 2-side adnexitis. Cervicitis. ZPPP CVM. VPG	
4.	ZiamukhamedovaHulnoza	4779	1976	Chronic candidosis, vulvovaginitis	Obesity of the 1st degree.
5.	Kaldarova Aziza	4453	1989	Vaginitis. Chronic andexitis from the left. Anovulation	Chronic anemia
6.	KarimovaMadina	4582	1989	Cervicitis. Colpitis. Chronic 2-side salpingoophoritis. Ureaplasmose.	OSA (resection of stomach because of stomach ulcer)
7.	KarimovaNozima	5013	1986	Bacterial vaginitis	Chronic anemia. Chronic Hbs. Ag bearer
8.	KenjaevaHulchkhera	931	1982	NMF. Anovulation. Chronic candidosis. Old ruptures of cervix uteri.	Goiter of the 1 degree. Euthyroidism. Obesity of I degree
9.	LatipovaDildora	4259	1988	Bacterial vaginitis. Chronic cervicitis, ZPPP (CMV, VPG)	
10.	MadrakhimovaSitora	4191	1988	Gardnerellosis, NMF. Anovulation. ПМС	ZDA
11.	MirzaakhmatovaHulnora	1781	1971	Cervicitis. Colpitis. FKM	Fatty hepatosis
12.	NishanovaMukarram	4975	1965	Bacterial vaginitis. Bearer of intrauterine device. Pre-menopause	Chronic anemia
13.	NurievaRaila	4101	1985	Gardnerellosis NMF. Anovulation. PMS.	Goiter of the 1-2 degree. Euthyroidism
14.	SultanovaDilobar	4732	1985	Bacterial vaginitis. Amenorrhea. Galactorrhea of the II degree	Goiter of the 1 degree. Euthyroidism
15.	UralovaBakhor	3094	1984	Chronic candidosis NMF. Anovulation. PMS.	Goiter of the 1-2 degree. Euthyroidism
16.	KhamraevaNigora	71	1985	Chronic 2-side adnexitis. Chronic cervicitis, colpitis ZPPP, Chlamydia	Sells in kidneys
17.	ShodievaFeruza	4730	1984	Gardnerrellosis. Chronic 2-side adnexitis. Cervicitis NMF. Anovulation	Goiter of the 1-2 degree. Euthyroidism
18.	IuldashevaDilafruz	4078	1979	Chronic candidosis. Candida colpitis. Anovulation ZPPP (Chlamydia, CMV, VPG).	ST II
19.	IusmetovaMashkhura	2197	1985	Candida colpitis NMF. Hyperpolymenorrhea PMS. CMVI	Chronic ZDA of the 1st degree. Hemorrhoids

List of patients receiving Clomezole

Table 2

	First and last name	№ of case/hospital card	Year of birth	Principal diagnosis	Additional diagnosis
21.	AskarovaAkmaral	4494	1973	Cervicitis. Colpitis. Bacterial vaginitis	
22.	BebitovaShakhnoza	2006	1985	Colpitis. Chronic cervicitis, ZPPP (toxoplasmosis, CMVI)	Chronic anemia. Urine acid diathesis
23.	BekmuratovaNodira	4781	1977	Colpitis. Endocervicitis. Bearer of intrauterine device	Chronic bronchitis in remission stage
24.	BolatevaAnaposhsha	4829	1990	Candida vulvovaginitis	
25.	IbragimovaMokhira	4776	1974	Bacterial vaginitis. Cervicitis. Coagulated uterine cervix syndrome. PMS	Goiter of the 1-2 degree. Euthyroidism Chronic anemia
26.	IsroilovaMunisa	11592	1986	Cervicitis. Ectopia of uterine cervix. Anti-phospholipid syndrome	Chronic anemia
27.	KamolovaShakhzoda	49055	1972	Gardnerellosis. Bearer of intrauterine device.	Chronic anemia
28.	KurbanovaDilafruz	3466	1980	Gardnerellosis. Colpitis.	Anemia of 1 degree
29.	KurbanovaShakhnoza	3982	1981	Colpitis. Chronic 2-side adnexitis	Chronic anemia
30.	MamarakhirovaDilnoza	4071	1983	Vaginitis of mixed aetiology. Bacterial vaginosis. Chronic cervicitis. Bearer of CVM, VPG	
31.	MirziatovaDilfuza	4825	1980	Cervicitis. Colpitis NMF. Adenomyosis	Anemia of I - II degree
32.	RakhimovaKamola	3454	1987	Chronic Candida. Cervicitis. Colpitis	Chronic pyelonephritis. Nephroptosis of 1 degree. Hydrocalycosis of the right kidney. MKD.
33.	RakhimovaSaierakhon	4242_	1979	Vaginitis. Sactosalpinx on the right. OGA (extra uterine pregnancy, tubectomia on the left. Caesarean section).	Anemia of 1 degree
34.	RakhmonovaOisara	3517	1983	Chronic cervicitis. Colpitis NMF. Secondary amenorrhea. Hirsutism. Adrenal hyperplasia of the I degree	Chronic pyelonephritis
35.	SaparovaBakhtigul	4965	1984	Colpitis. Endocervicitis. Anovulation	Chronic anemia
36.	SaparovaHavhar	4898	1985	Colpitis of mixed aetiology. Lactorrhea 1 -2	Goiter of the 1 degree. Euthyroidism. Chronic anemia
37.	Khegai Elena	11527	1985	Colpitis, anovulation	
38.	KhozhamuratovaHulimhan	4631	1968	Bacterial vaginitis. Hypethrophia of uterine cervix. Endocervicitis. O.naboti. PMS. Fibrosis mastopathy	Chronic colitis OSA (cholecystectomia)
39.	Chufistova Nina	4767	1947	Chronic senile colpitis. Candidosis – bearer. Menopause syndrome. Uterine myoma. FKM	Dislipidemia. Arterial hypertension
40.	EgamovaManzura	4679	1975	Bacterial vaginitis. Colpitis of mixed aetiology	

6. SCHEME OF PRESCRIPTION OF THE PREPARATIONS

"VAGIMILT®" brand of MILTONIA HEALTH SCIENCE LIMITED [UK] produced by SOFTGEL HEALTCARE PRIVATE Ltd, India,wasprescribed to the patients of the principal group as 1 capsule 1 time a day intravaginally, before going to bed, during 7 days.

The patients of the control group received traditional treatment with Clomezole prescribed as 1 ovule 2 times a day, during 5 days.

6.1. Additional types of treatment: the patients with present somatic and/or endocrine diseases were consulted by relevant specialists and received the preparations required for treatment. Treatment, compatible with VAGIMILT® and Clomezole preparations, of other principal diseases was also held (table 3), as well as necessary physiotherapeutic method of treatment. Preparations for local treatment of action similar to VAGIMILT® and Clomezole were not prescribed. In group which received Clomezole, 5 patients also received the systemic antibacterial preparations, which was not necessary in VAGIMILT® group.

Table 3

Preparations prescribed to treat the other principal and adjacent diseases

Medical preparation	Regularity of use	Ways of introduction
ZGT	Cyclic regimen, 5 - 26 days of menstrual cycle, uninterrupted regimen	per os, transdermally, intravaginally
Gestagenes	Uninterruptedly, 5-25 of the cycle or 11- 25, 16 - 25 days of menstruation.	per os, i/m
Phytoestrogens	Uninterruptedly	per os
Prostaglandin inhibitors, NPVS	5-10 days before and during menstruation	per os, i/m, rectally
Systemic antibacterial preparations	Course of 1-14 days	per os, i/m, i/v
Vitamins, microelements	Course of 10 -30 days	per os, i/m
Preparations of iron	Course of up to 30 days	per os, i/m
Antioxidants	Course of 10 -30 days	per os, i/m, i/v
Synthetic prolactin inhibitors	Uninterruptedly or 14 days during 2 phase of menstrual cycle	per os
Iodine preparations	Once, uninterruptedly	per os
Hormonal oral contraception KOK	In cycles, 5 - 26 days of menstruation	per os
Mini-pili	Once, uninterruptedly	per os

7. GENERAL SCHEDULE OF THE RESEARCH

- After primary examination the patients conforming to the criteria of inclusion, in order to receive their written informed consent for participation in the research received information on the researched preparation VAGIMILT®, information about dosage, schemes, ways of introduction and period of treatment.
- In case of receipt from the patient of written consent for participation in the research, the researched preparation or control preparation was prescribed to her.
- The starting point of the beginning of participation of patient in the research: the day of first intake of the researched preparation or control preparation.
- The treatment performed was described in details for all patients included in the trial.
- Any therapy related to the concomitant diseases was registered in the case or in hospital card and in the individual registration form.

The treatment performed is described in details in the hospital card and in the individual registration form of all patients included in the trial.

Other types of therapy related to the concomitant diseases are also registered in the hospital card and in the individual registration form.

8. REGISTRATION OF RECEIPT, CONSUMPTION, STORAGE OF THE RESEARCHED PREPARATIONS AND PROCEDURE TO CONTROL OF PERFORMANCE OF THE DOCTOR'S INDICATIONS BY THE RESEARCHED PATIENTS.

Preparations were transferred with signing of the Statement of transfer-acceptance by the Client to the executive in charge and were stored separately from other preparations prescribed.
The doctor executing the trial was nominated to be the person in charge for delivery of preparations to the patients. To register delivery of the researched preparation to the patients, the special accounting register of the researched preparation and control preparation was formed, including signatures of the patients certifying each receipt of preparation.

The beginning of trial (the first intake of the researched preparations) and the fact of voluntary consent of patient to take the researched substance were registered in cases of patients and hospital cards.

Procedure of verification of respect by the patient of the doctor's indications was regulated by the internal regulations of the clinics of Republican Specialized Scientific and Practical Medical Center of Obstetrics and Gynaecology of Ministry of Public Health of Republic of Uzbekistan.
Executive in charge prevented from use of the researched preparation and control preparation with any other purpose except the purpose stated in protocol of clinical trial.
After termination of the research the report was composed about use of the researched preparation and control preparation corresponding to the form 2 of the Annex №2 to the order of Ministry of public health of Republic of Uzbekistan №334 dd. 25.07.2001.

The researched preparation was stored in closed premises, and only the executive had access to it.

9. EXAMINATION

Gynaecological anamnesis was researched in detail in process of clinical examination of patients: age of menarche appearance, particularities of development, features of menstrual cycle and its troubles during all period of life and at present time, the parities, contraception methods, presence of gynaecological diseases and of the diseases of breasts at the moment of examination and in anamnesis. The special attention was given in process of inquiry to the allergic anamnesis of a woman, to the presence of sensibility stimulating situation in process of intake of the preparations.

In process of objective research the gynaecological examination, palpation of breast, thyroid gland were performed, the state of internal organs, psychic and emotional sphere was evaluated.

In process of the work done the following methods of research were used:

- Survey ofsymptoms: pain, itching, burning in area of genitalia, in process of examination: hyperaemia and oedema, the secretions (intensity of symptoms was stated in points).

- To evaluate the condition of micro flora of vagina and cervical canal bacterioscopic and bacteriological research of smears with determination of bacteria titre was performed. Evaluation of character of leucorrhoea and aminotest were also used.

- Laboratory researches: general blood test, determination of content of aminotransferases in blood (ALT, AST) of bilirubin level in serum.

- Clinical examination: measurement of level of systolic and diastolic arterial tension, of frequency of the heartbeat, temperature of the body.

According to the schedule the patients underwent examination before and after application of VAGIMILT® and Clomezole.

After treatment the efficiency and tolerance of the researched preparation VAGIMILT® and Clomezole preparation (in points) were evaluated according to the criteria prescribed in the protocol.

10. CRITERIA OF EVALUATION OF EFFICIENCY OF THE RESEARCHED PREPARATION

10.1. List of parameters of efficiency:

- Bacteria eradication
- Elimination of inflammatory process and symptoms of the disease.

Evaluation of efficiency of the researched preparation was performed by the researcher basing on the abovementioned criteria, in points, according to the following scale:

4 points	High efficiency	Complete eradication of bacteria in form of elimination of symptoms, the sum of points 0-3. Normalization of laboratory parameters
3 points	Moderate efficiency	Moderate decrease of number of bacteria, considerable elimination of symptoms, the sum of points 4-8. Considerable improvement of laboratory parameters
2 points	Low efficiency	Small decrease of number of bacteria, small decrease of intensity of symptoms, the sum of points 9-12. Light improvement of laboratory parameters
1 point	Absence of efficiency	Absence of changes or aggravation of clinical and laboratory parameters at the end of course of treatment

11. CRITERIA OF EVALUATION OF TOLERANCE OF THE RESEARCHED PREPARATION.

Tolerance of preparation was described basing on the subjective symptoms and feelings declared by patient, and objective data received by the researcher in process of treatment. Dynamics of laboratory parameters as well as the frequency of occurrence and character of side effects were taken into account. Integrative evaluation of tolerance of preparations in points was estimated in points according to the following criteria:

4 points	Very good (no side effects found)
3 points	Good (small side effects are observed, they do not cause the serious problems for the patient and do not require to stop the use of preparation)
2 points	Satisfactory (the side effects are observed, influencing on the condition of patient, but they do not require to stop the use of preparation)
1 point	Unsatisfactory (the undesirable side effect is fixed, it has the important negative impact on the patient's condition and requires to stop the use of preparation)
0 points	Very unsatisfactory (side effect requiring to stop the use of preparation and to perform additional medical procedures)

12. SIDE EFFECTS

In general the preparations were well tolerated and did not cause complaints of patients. Nevertheless, during this research, use of VAGIMILT® preparation caused few small side effects registered at few patients. These side effects did not cause the important problems and did not require to stop the use of preparation: short-term (1 – 2 days) burning in vagina which disappeared itself in process of continuation of use of preparation; one-time falling of ovule in case of its insufficiently deep introduction; increase of number of secretions at the first day.

Use of Clomezole caused the following small side effects which were similar in frequency to those in principal group. They did not cause the important problems and did not require to stop the use of preparation. There were: increase of amount of secretions during the first day which disappeared itself; increase of amount of mucous during the first days of treatment; small itching or burning inside the vagina which disappeared itself in process of continuation of use of preparation; short-term heavy feeling in stomach at the end of course of treatment which disappeared itself after termination of use of the preparation.

13. STATISTICS

Data of the research were PC - processed with use of the system of statistical analysis and calculation of level of importance and credibility of the parameters.

13.1. Number of the researched patients: 20 persons in principal group and 20 person in control group.

13.2. Applied level of importance.

To compare the results received for all researched population which received VAGIMILT® to compare with the primary parameters and with the control group, the level of importance (p) was fixed as equal to 0,05 and 0,01. The value p=0,01 is used in this case as the additional evaluation of level of manifestation of effect of preparation or difference in effect of preparation. Presence of real differences for two values of level of importance evidences the important effect of use of preparation or its difference from the compared preparation.

14. TERMINATION OF THE RESEARCH

No one patient terminated the treatment with VAGIMILT® or Clomezole preparations prescribed.

15. EVALUATION OF THE RESULTS RECEIVED

Clinical and laboratory research of 40 patients with various complaints evidencing the inflammatory processes of genitalia was performed. Average age for all population was 34,5± 3,4 years.

Main part of the women (68,2%) visited gynaecologist because of secretions from genitalia. Almost one of five patients was usual patient for gynaecologist and urologist, depending on prevalence of symptoms of this or that pathology for them.

Examination of premorbid background attracted attention by complication of anamnesis of patients with various diseases (tonsillitis, bronchitis, cholecystitis, pyelonephritis, etc.). Among the women of considerable age each one of four patients at the moment of examination suffered from the chronic diseases of gastrointestinal tract.

All patients researched had typical female phenotype. The index of weight and height (BMI = 20-26) was normal for 14 patients. Excessive weight was observed at 5 women (BMI 26 - 30).

Menarche is in time at all patients researched. For the main part of patients the period of cycle after last delivery was within the limits of 17 - 48 days, duration of menstruation was 1 - 12 days. At 2 patients there were dysfunctional uterine bleedings in anamnesis.

At the moment of examination decrease of the second phase, pains before and during menstruations were observed at the main part of patients.

At each visit to the doctor manifestation of symptoms of inflammation, number and type of secretions from the genital tracts were evaluated.

Dynamics of symptoms is given in Table 4.

At the end of treatment the subjective symptoms (pain, itching, burning), as well as objective signs of inflammation (hyperaemia, oedema) terminated completely at the main part of the patients as in principal group so as in control group.

Before treatment the leucorrhoea was mainly abundant, grayish-puriform, with acute unpleasant smell. Aminotest was positive, pH - alkaline. At the end of treatment in both groups leucorrhoea was mainly white and mucous, without smell, aminotest was negative, pH - acid, that corresponded to the norm.

Table 4

Influence of VAGIMILT® and Clomezole on manifestation of the principal symptoms of colpitis, cervicitis and bacterial vaginosis

Symptoms	VAGIMILT®		P≤	Clomezole		P≤
	Before treatment	After treatment		Before treatment	After treatment	
Pain	1,7±0,11	0,1±0,05	0,001	1,4±0,15	0,2+0,08	0,001
Itching	1,1±0,13	0,00	0,001	1,0±0,14	0,1±0,07	0,001
Burning	1,1±0,09	0,1±0,05	0,001	1,1±0,10	0,2±0,08	0,001
Hyperaemia	1,35±0,11	0,05±0,05	0,001	1,30±0,10	0,2±0,09	0,001
Oedema	1,2±0,09	0,1±0,05	0,001	1,1±0,05	0,2±0,09	0,005
Secretions	2,9±0,08	1,1±0,12	0,001	2,6±0,15	1,5±0,14	0,001

Secretions completely terminated in 3 -5 days at 12 patients after application of VAGIMILT® preparation. At 7 women the vaginal secretions decreased during 6 - 7 days and terminated after 10 days. Only one patient had the secretions which continued till 14 days.

Similar data were received in group which received Clomezole.

During the bacterioscopic and bacteriological research of secretions of cervical canal E. coli, the fungi of Candida family, Gardnerellavaginalis, various cocci flora was found at a lot of women. Growth of micro flora was not observed at the other women, in complex with the character of secretions and positive aminotest that evidenced the presence of anaerobic pathogenic micro flora. Large number of leucocytes (40-50) was found in smear of all women before the treatment, approving infectious and inflammatory character of the disease.

Micro flora did not disseminate in all women of the principal group who received VAGIMILT®, and in all women of the control group who received the traditional antifungal therapy in form of Clomezole, the number of leucocytes decreased to 10-15, evidencing the removal of signs of genitalia inflammation, the parameters of rate of purity of secretions ameliorated.

According to the abovementioned criteria of evaluation of efficiency in points, taking into account the insufficient treatment which had place for few patients during the researched period of treatment, the following average points were calculated: in group of VAGIMILT® treatment: 3,7±0,15 points, in group of Clomezole treatment: 3,6 ± 0,13 points.

Concentration of aminotransferazes, bilirubin of patients before and after treatment with VAGIMILT® preparation was within the normal limits. VAGIMILT® preparation in no case caused negative influence on the liver enzymes and bilirubin (see Tables 5 and 6).

Table 5.

Level of ALT, AST, bilirubin in process of VAGIMILT® treatment

Blood parameters	Before treatment	After treatment
AST (u/l)	24,1±0,68	20,4±1,37
ALT (u/l)	19,8±2,87	17,2±2,07
Bilirubin (mg/l)	13,0±0,79	10,8±0,71

The similar results were received for patients who received Clomezole

Table 6.

Level of ALT, AST, bilirubin in process of Clomezole treatment

Blood parameters	Before treatment	After treatment
AST (u/l)	23,6±1,68	19,6±1,08
ALT (u/l)	17,5+0,68	15,6±1,2
Bilirubin (mg/l)	11,7±0,98	11,4±0,53

VAGIMILT® therapy, as well as Clomezole therapy was not the obstacle for effect of anti-anaemic preparations (prescribed because haemoglobin rates below (102 + 0,3 g/l) below

the reference values. At the end of treatment the level of haemoglobin was close to normal (112 + 0,2 g/l).

Any influence of the researched preparations on the level of AT, heartbeat frequency and temperature of the body was also absent (Table 7).

Table 7

Level of AT, heartbeat frequency and temperature of the body during VAGIMILT® and Clomezole therapy

Indexes	VAGIMILT®		Clomezole	
	Before treatment	After treatment	Before treatment	After treatment
AT systol.	110±1,35	110±1,35	107±2,42	106±2,20
AT diastol.	69,5±0,88	69,5±0,88	68,5±1,31	68,0±1,38
Heartbeat frequency	80,2±0,70	80,5±0,50	81,5±0,84	81,0±0,63
Temperature of the body	36,4±0,04	36,3±0,02	36,4±0,03	36,5±0,03

According to the criteria of tolerance stated above, taking into account the irrelevant side effects which occurred to some of patients, the following average rating was calculated: in group which received VAGIMILT®: 3,8+0,09 points, in group which received Clomezole: 3,7±0,10 points.

16. MONITORING, AUDIT AND INSPECTION.

During the research, monitoring from the part of the Client was held, at the end of the research the inspection audit was held by Pharmacological committee of GUKKLS and Ministry of Public Health of Republic of Uzbekistan, which approved that the research was held without any violations.

17. INFORMATION ON THE PREPARATION.

17.1 Preparation contains as the active agents clindamycin phosphate 100 mg and clotrimazole 100 mg. Dosage form: soft gelatine vaginal ovules.

Storage conditions: at temperature not exceeding 25^0 C, out of reach of children.

Shelf life: 2 years.

CONCLUSIONS

1. VAGIMILT® and Clomesol showed a high efficiency in treatment of bacterial vaginosis and inflammatory diseases of female genitals.
2. Both products caused insignificant side-effects which did not require the drug cancellation or modification of the treatment modes.
3. However, the efficiency of VAGIMILT® vaginal capsules for normalization of lab values of the vaginal microbiocentosis proved to be higher than that of Clomesol.
4. Both drugs had no systemic side effect, as evidenced by the lack of changes of lab values (ALT, AST, billirubin), and somatic data (body temperature, blood pressure values).

OPINION

VAGIMILT® vaginal capsules can be recommended for use in the practice of obstetrician-gynaecologist as an effective and safe topical drug for treatment of bacterial vaginosis and infectious inflammatory diseases of female genitals for women of various age groups, regardless of the concomitant pathology and current systemic therapy.