

**Materials and methods.** To achieve this goal, we analyzed organizational structure and approaches to the design of 8 corrective and preventive action plans (CAPA-plans). During the analysis methods of generalization, abstraction, and system analysis were used.

**Results and discussion.** Out of the 8 analyzed CAPA-plans, 62.5% were foreign, 25% were designed on the basis of international audits in Ukraine and 12.5%, as a result of the audit of the CT sponsor. Among the analyzed plans, two organizational structures were used: in the form of a table (62.5%) and in the form of a description of certain non-conformances (37.5 %). Both organizational structures have the following common information: non-conformances, corrective or prevention action, and effective date. In addition to these items, the plans organized in the form of tables divide identified non-conformances to critical, major and minor; contain recommendations for the elimination of the revealed non-conformances, the identity of the person responsible for the effective and timely corrective or preventive action, and the place for the comments. As the advantages of this structure convenience of use, structuring, indicating the items of regulatory requirements, which regulates the process, etc. can be considered. Regarding the organizational form of CAPA-plans in the form of describing individual non-conformances, in addition to common points, as in the form of tables, the reason of occurrence of the identified non-conformance, the description of staff training, the effectiveness of the implementation of corrective or preventive action are additionally indicated. Significant disadvantages of this type of CAPA-plans organizational structure are the lack of indication of the severity of the identified non-conformance, as well as the inconvenience of their use.

**Conclusions.** The approaches to the design of CAPA-plans in CT of new drugs quality management were analyzed, which showed the advantage of such plans organizational structure in the form of tables. It is advisable to further analyze the methodological approaches to CAPA-plans design and development of standard operating procedures for organizing work on this process.

## OFF-LABEL USE OF DRUGS IN TREATMENT OF ENDOMETRIOSIS

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**Introduction.** Expanding of indications to the use of already registered medicines allows manufacturers to save money and time as these drugs have already been tested for toxicity and safety and have no risk of recall at the initial stage of the test. FDA definition of off-label use of drugs is the use of a drug in accordance with indications, administration regimens, in dosages, in the contingent of patients or in other parameters that did not mentioned in the approved instruction. According to the statistics, about 91% of gynecologists use drugs off-label: the incidence of such appointments in pregnant women is 54%. At the same time, only 34% of specialists believe that this kind of treatment can be associated with significant risks. Among gynecological diseases, endometriosis is the presence of an outside tissue that is similar to the endometrium and causes a chronic inflammatory reaction - ranks the third place in the incidence rate. The disease occurs most often in women of reproductive and working age (frequency of occurrence and prevalence is 5-10%), accompanied by pain and occasionally leading to infertility. Drug treatment represents by different groups of drugs, none of which provides for the elimination of symptoms, persistent therapeutic effect and reliable prevention of relapse, which is associated with a fragmentary understanding of the pathogenesis of endometriosis.

**Aim.** The purpose of our work is to expand the indications for the use of combined oral contraceptives (COCs) for endometriosis due to off-label drugs. In Ukraine, patients remain unprotected if doctors prescribe drugs outside the approved indications of use indicated in the instructions. According to the order of the Ministry of Healthcare of Ukraine No. 1422 from 2017, the Ukrainian doctor has the opportunity to work according to international guidelines for treatment and diagnosis.

**Materials and methods.** Analysis of the normative basis for the use of off-label COCs in women suffering from endometriosis in Ukraine and in the world.

**Results and discussion.** One of the widely used off-label drug groups for the treatment of endometriosis-associated symptoms and the prevention of post-operative healing recurrence worldwide is combined hormonal contraceptives that are presented as oral dosage forms. The use of this group of drugs is recommended by the American Association for Reproductive Medicine. Among the combinations of ethinylestradiol, the most proven efficacy in the use of endometriosis COCs with dienogest. The results of the study of the effects of dienogest in the COC can assume that COCs which contain dienogest is different from other drugs of this group precisely due to the individual "specialized" effects of dienogest on endometriosis heterotopy, and the effect of 30 µg ethinylestradiol can be considered as a factor ensuring qualitative control of the menstrual cycle, which creates conditions for long-term administration. COC is approved by the FDA for the treatment of menstrual disorders, but these conditions are not presented in the instructions for the use of most COCs.

In the world, the use of COCs for endometriosis pain is based on the Cochrane Review, which examined the results of four different studies using COCs and compared the use for the treatment of pain associated with endometriosis: 1) COCs and placebo; 2) COC and lack of treatment; 3) COCs and other medicines (danazol, analogues of gonadotropin-releasing hormone (GnRH), progestogens, antiprogestogens, intrauterine systems with release of levonorgestrel); 4) COC and methods of conservative surgical treatment. Only one study compared the use of GnRH analogue goserelin with low dose COCs - 20 µg ethinylestradiol, 150 µg desogestrel. Against the background of both therapies at the end of the 6-month treatment period, a decrease in non-menstrual pains, dyspareunia and dysmenorrhea were observed, compared with baseline. Another study has shown that COCs were effective in preventing recurrence of postoperative treatment only in the case of long-term appointment for a long period of time - not less than 2 years, preferably up to 5 years, or in a mode with a reduced nonhormonal interval of up to 3-4 days. Thus, the noncontraceptive benefits of COCs are considered as an important aspect of their application.

**Conclusions.** It was found that the transfer of women with severe form of dysmenorrhea from cyclic to continuous mode of administration of drugs contributed to a decrease in the intensity of pain in 6 months by 58%, and in 2 years - by 75% ( $p < 0,001$ ). The given data is testified to the necessity of expanding the indications for the use of COCs in endometriosis and their inclusion in the national normative base of prescriptions of drugs off-label, the creation of which is an urgent task in modern conditions.

## **THE COMPARATIVE ANALYSIS OF PREVENTION AND TREATMENT METHODS OF HEPATITIS B IN DOMESTIC AND INTERNATIONAL GUIDELINES**

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**Introduction.** As the degree of negative impact on human health and the extent of the incidence in our country viral hepatitis dominate in the structure of infectious diseases with influenza and acute infectious diseases of the upper respiratory tract. Hepatitis B virus (HBV) is one of the most dangerous infectious diseases affecting the hepatobiliary system. According to the WHO, approximately 257 million people have a chronic HBV infection; about 650,000 people die every year from the complications of chronic HBV. Globally, HBV accounts for about 45% of cases of hepatocellular carcinoma and 30% of liver cirrhosis. So, the questions of both treatment and, in particular, prevention of this dangerous infection are very relevant for our state and the world as a whole.

**Aim.** The aim of our study was to conduct a comparative analysis of treatment and prevention methods of HBV prescribed in the national Unified clinical protocols of primary, secondary (specialized), tertiary (highly specialized) care (UCPC) «Viral hepatitis B in adults» and global international strategies of the Health Care sector about the treatment and prevention of HBV, which are relevant at present.

**Materials and methods.** To achieve this goal, the following documents were analyzed for the subject of coincidences and differences in the field of treatment and prevention of HBV: UCPC «Viral Hepatitis B in Adults» (Ukraine, 2016), «Global hepatitis report» (WHO, 2017) «Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection» (WHO 2015), «2017 interim