

רוקח/ת נכבד/ה,

הנדון: עדכון עלון לרופא

Ovestin Vaginal Cream / אובסטין קרם וגינלי

ההתוויה המאושרת לתכשיר הנדון:

For the treatment of vulvo-vaginal complaints related to estrogen deficiency

הרכב: Each gram of cream contains 1 mg estriol

לאחרונה עודכן העלון לרופא של התכשיר Ovestin בהחמרות בסעיפים הבאים (טקסט שנמחק מסומן בקו חוצה, תוספות - טקסט בולט, מצויינים רק החלקים הרלבנטים לשינויים בכל סעיף):

סעיף (4.4) Special warnings and precautions for use

Breast cancer

■ HRT may increase mammographic density. This may complicate the radiological detection of breast cancer. Clinical studies reported that the likelihood of developing increased mammographic density was lower in subjects treated with estriol than in subjects treated with other estrogens

■ A randomized placebo-controlled trial, the Women's Health Initiative study (WHI), and epidemiological studies, including the Million Women Study (MWS), have reported an increased relative risk of breast cancer in women taking estrogens, estrogen-progestagen combinations or tibolone for HRT for several years (see section 4.8). For all HRT, an excess risk becomes apparent within a few years of use and increases with the duration of intake. The risk returns to baseline within a few (at most five) years after stopping treatment.

■ In the MWS, the relative risk of breast cancer in women treated with conjugated equine estrogens (CEE) or estradiol (E2) was higher when a progestogen was added. The risk increased regardless of the dosing scheme (sequential or continuous administration of progestogen) and the type of progestogen. There was no evidence of a difference in risk between the different routes of administration.

■ In the WHI study, breast tumors diagnosed in women using continuous combined conjugated equine estrogens and medroxyprogesterone acetate (CEE + MPA) were slightly larger in size and more frequently had local lymph node metastases compared to placebo.

■ ~~The limited available data do not contain indications that the use of Ovestin vaginal cream increases the risk of breast cancer.~~

■ It is unknown whether Ovestin carries the same risk. In a recent population-based case-control study in 3,345 women with invasive breast cancer and 3,454 controls, estriol was found not to be associated with an increased risk of breast cancer, in contrast to other estrogens. However, the clinical implications of these findings are as yet unknown. Therefore, it is important that the risk of being diagnosed with breast cancer is discussed with the patient and weighed against the known benefits of HRT.

Other conditions

Ovestin cream contains cetyl alcohol and stearyl alcohol. This may cause local skin reactions (e.g. contact dermatitis).

סעיף (4.5) Interaction with other medicinal products and other forms of interaction

No examples of interactions between Ovestin and other medicines have been reported in clinical practice. Although data are limited, interactions between Ovestin and other medicinal products may occur. The following interactions have been described with use of combined oral contraceptives which may also be relevant for Ovestin.

Effects of other medicines on Ovestin:

The metabolism of estrogens (and progestogens) may be increased by concomitant use of substances known to induce drug-metabolizing enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants (e.g. **hydantoins, barbiturates, phenobarbital, phenytoin, carbamazepin**) and anti-infectives/**antivirals** (e.g. **griseofulvin, rifamycins rifampicin, rifabutin, the antiretroviral agents nevirapine and**



efavirenz) and herbal preparations containing St John's wort (Hypericum Perforatum). Ritonavir and nelfinavir, although known as strong inhibitors of the metabolism, by contrast exhibit inducing properties when used concomitantly with steroid hormones. **Fytotherapeutic preparations containing St John's wort (Hypericum perforatum) may induce the metabolism of estrogens and progestogens.** Clinically, an increased metabolism of estrogens and progestogens may lead to decreased **effectiveness of Ovestin efficacy** and changes in uterine bleeding profile. Estriol may possibly increase the pharmacological effects of corticosteroids, succinylcholine, theophyllines and troleandomycin.

No examples of interactions between Ovestin and other drugs have been reported in clinical practice.

סעיף (4.8) Undesirable effects

From literature and safety surveillance monitoring, the following adverse reactions have been reported:

System organ class	Adverse reactions*
General disorders and administration site conditions	Application site irritation and pruritus
Reproductive system and breast disorders	Breast discomfort and pain

*MedDRA version 9.1

These adverse reactions are usually transient, but may also be indicative of too high a dosage. **As with any product that is to be applied to mucosal surfaces, Ovestin may cause local irritation or itching. Breast tension or pain may occasionally occur, and this may be indicative of too high a dosage. These adverse reactions usually disappear after the first weeks of treatment.**

כמו כן עודכנו הסעיפים הבאים:

סעיף (4.2) Posology and method of administration

למטרת הקלה על השימוש הורחב הסעיף והוספו איורים.

סעיף (6.4) Special precautions for storage

אחסון ב-2-25°C

סעיפים (4.9) Pharmacodynamic properties, Overdose

העלון לרופא מפורסם במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום בטלפון: 073-2731000

בכבוד רב,
אילנה וייל
רוקחת ממונה