

## Levonorgestrel / ethinyl estradiol

### Product:

LEVONORGESTREL / ETHINYL  
ESTRADIOL (Seasonale®)

### Class of drugs:

Oral contraceptive

### Indication:

Prevention of pregnancy

### Manufacturer:

Paladin Labs Inc.

### CED Recommendation

The CED recommended that levonorgestrel/ethinyl estradiol (Seasonale) not be funded through the Ontario Public Drug Programs. The CED noted that many oral contraceptives are already available on the Formulary and that levonorgestrel/ethinyl estradiol (Seasonale) does not offer any additional clinical or quality of life benefits. Furthermore, the CED had concerns regarding the long-term safety of this product.

### Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided not to fund levonorgestrel/ethinyl estradiol (Seasonale).

### Status

Funding not available through Ontario Public Drug Programs.

### Highlights of Recommendation:

- ◆ Levonorgestrel/ethinyl estradiol (Seasonale) is an oral contraceptive (birth control pill) that combines two synthetic hormones, estrogen and progesterone, used to prevent pregnancy. It is a new regimen made up of 84 consecutive days of active tablets followed by seven days of placebo (inactive) tablets. Using this regimen reduces menses to four times per year, compared to 13 times per year with monthly oral contraceptive regimens.
- ◆ Only one study directly compared the efficacy and safety of levonorgestrel/ethinyl estradiol (Seasonale) to another oral contraceptive. In this study, levonorgestrel/ethinyl estradiol (Seasonale) provided similar efficacy in preventing pregnancy as Nordette, a monthly oral contraceptive that also combines levonorgestrel and ethinyl estradiol.
- ◆ Direct comparisons studies between levonorgestrel/ethinyl estradiol (Seasonale) and other commonly prescribed oral contraceptives on the Formulary are not available. There is no evidence that levonorgestrel/ethinyl estradiol (Seasonale) improves treatment adherence or provides any added clinical benefits compared with alternative products.
- ◆ Side effects reported with levonorgestrel/ethinyl estradiol (Seasonale) are similar to those of other oral contraceptives and include nausea, vomiting, stomach cramps, bloating, headache, changes in weight, breakthrough bleeding or spotting, swelling of ankles and feet, breast tenderness or enlargement, and yeast infections.
- ◆ Because levonorgestrel/ethinyl estradiol (Seasonale) is administered in 91-day cycles, there is more exposure to estrogen and progesterone to women on a yearly basis as compared to most monthly regimens. Only two small studies of short duration (up to two years) evaluating the safety of levonorgestrel/ethinyl estradiol (Seasonale) are available. The Committee is of the opinion that the studies are insufficient to assess long-term risks, such as excessive endometrial hyperplasia (excessive growth of the uterine lining).
- ◆ Furthermore, with only four menses per year, it is possible that women who become pregnant unknowingly may continue to use the product, thereby potentially exposing the fetus to additional estrogen.
- ◆ Levonorgestrel/ethinyl estradiol (Seasonale) costs \$52 per package (3 months) or \$16-17 per month. Monthly oral contraceptives listed on the Formulary costs \$10-13 per month. More than 20 oral contraceptives are currently available on the Formulary.
- ◆ **Overall, the Committee acknowledged that levonorgestrel/ethinyl estradiol (Seasonale) is effective in preventing pregnancies. However, many oral contraceptives are already available on the Formulary; and levonorgestrel/ethinyl estradiol (Seasonale) does not offer any additional clinical or quality of life benefits. Furthermore, the Committee had concerns regarding the long-term safety of this product. As such, it was recommended that levonorgestrel/ethinyl estradiol (Seasonale) not be funded.**

### Background:

Oral contraceptives (birth-control pills) are used to prevent pregnancy. Estrogen and progesterone are two female sex hormones. Combinations of estrogen and progesterone work by preventing ovulation (the release of eggs from the ovaries). They also change the lining of the uterus (womb) to prevent pregnancy from developing and change the mucus at the cervix (opening of the uterus) to prevent sperm from entering.

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**Detailed Discussion:**

No additional details. The full CED discussion is as outlined in the *Highlights of Recommendation* section.

**CEDAC Recommendation:**

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) did not review levonorgestrel/ethinyl estradiol (Seasonale).



Ministry of  
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