

Seasonale® (levonorgestrel 0.15 mg/ethinyl estradiol 0.03 mg)

Corrine Sloan - 4th year Pharmacy Intern

January 2008

Historically, all regimens of oral contraceptives were designed to mimic a woman's natural menstrual cycle; however, there seems to be no inherent medical need for the 28-day cycle regimen.¹ The concept of extending the hormone free interval by taking oral contraceptives continuously for 3 months is not new, as many have been using their monophasic pills in this fashion; however, Seasonale® is the first extended-use oral contraceptive approved for use in Canada.²

Seasonale® is a good option for women who do not want the inconvenience of having a monthly period, and for women who suffer from period-related symptoms such as cramping, heavy bleeding and headaches.

Indications²

Seasonale® is a monophasic extended-use combined oral contraceptive (COC) used for the prevention of pregnancy.

Contraindications³

(Similar to other ethinyl estradiol and levonorgestrel COC's)

- Hypersensitivity to ethinyl estradiol, levonorgestrel, or any component of the formulation
- History of or current thrombophlebitis or venous thromboembolic disorders (including DVT, PE)
- Active or recent (within 1 year) arterial thromboembolic disease (e.g. stroke, MI)
- Cerebral vascular disease, coronary artery disease, valvular heart disease with complications, severe hypertension
- Diabetes mellitus with vascular involvement
- Severe headache with focal neurological symptoms
- Known or suspected breast carcinoma, endometrial cancer, estrogen-dependent neoplasms, undiagnosed abnormal genital bleeding
- Hepatic dysfunction or tumor, cholestatic jaundice of pregnancy, jaundice with prior combination hormonal contraceptive use
- Major surgery with prolonged immobilization
- Heavy smoking (≥ 15 cigarettes/day) in patients >35 years of age
- Pregnancy
- Ocular lesions due to ophthalmic vascular disease including partial or complete loss of vision or defect in visual fields
- Severe dyslipoproteinemia
- Hereditary or acquired predisposition for venous or arterial thrombosis

Warnings and Precautions⁴

- Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels. This risk increases with age, and becomes significant in oral contraceptive users older than 35 years of age.

- Oral contraceptives do not protect against sexually transmitted diseases including HIV/AIDS.
- An increased risk of the following serious adverse reactions has been associated with the use of oral contraceptives:
 - Thrombophlebitis
 - Arterial thromboembolism
 - Pulmonary embolism
 - Myocardial infarction
 - Cerebral hemorrhage
 - Cerebral thrombosis
 - Hypertension
 - Gallbladder disease
 - Hepatic adenomas or benign liver tumors

Adverse Effects⁴

Associated with oral contraceptive use:

- Nausea/Vomiting
- Gastrointestinal symptoms (such as abdominal cramps and bloating)
- Breakthrough bleeding
- Spotting
- Change in menstrual flow
- Amenorrhea
- Temporary infertility after discontinuation of treatment
- Edema/fluid retention
- Melasma/chloasma which may persist
- Breast changes: tenderness, enlargement, and secretion
- Change in weight or appetite (increase or decrease)
- Change in cervical ectropion and secretion
- Possible diminution in lactation when given immediately postpartum
- Cholestatic jaundice
- Migraine headache
- Mood changes, including depression
- Vaginitis, including candidiasis
- Change in corneal curvature (steepening)
- Intolerance to contact lenses

Supplied⁴

Ethinyl estradiol (EE) 0.03 mg and levonorgestrol 0.15 mg per tablet for 84 consecutive days followed by seven days of placebo tablets (91-day regimen).

Administration⁴

The dosage of Seasonale® is one pink (active) tablet daily for 84 consecutive days, followed by 7 days of white placebo tablets. Seasonale™ tablets should be taken exactly as directed at intervals not exceeding 24 hours. Ideally, the tablets should be taken at the same time of the day on each day of active treatment to achieve maximum efficacy.

Potential Benefits over 28-day regimen^{1,2,5}

The extended COC regimen has been shown to be as effective in preventing pregnancy compared to the 28-day regimen. Some clinicians also believe the extended regimen has increased contraceptive efficacy over the 28-day regimen since there is a decrease in hormone free intervals, so it may suppress ovulation more effectively.

Seasonale® allows women to reduce the number of menstrual periods to only four per year. The same thing can be accomplished with other monophasic pills if they take their active pills for 12 weeks straight and then skip a week before starting another cycle. Any oral, vaginal, or transdermal contraceptive with less than 50 mcg of estrogen (monophasic or multiphasic) can be used for continuous or extended-cycles; however, there has not been a lot of research done with triphasic COC's being used in an extended regimen, so currently the evidence is limited in that area.

A potential benefit of using the Seasonale® product over using monophasic pills in the same extended regimen, is that the number of transitions between packs is decreased to four per year, which may contribute to improved compliance. If adherence is not an issue, it is less expensive to use their monophasic pills in an extended 12 week regimen, compared to Seasonale® (Refer to cost section).

Women using an extended regimen can expect their fertility to return to their previous level immediately once they discontinue taking the contraceptive.

Potential Risks over 28-day regimen^{2,4}

Women using Seasonale® will have 9 additional weeks of hormonal exposure per year compared to a 28-day regimen. This could pose an additional risk of thrombotic and thromboembolic diseases; however, studies done with Seasonale® have neither shown nor excluded this additional risk. Further studies need to be completed to obtain long term safety data on the use of extended-use oral contraceptives for longer periods of time beyond two years.

Table1. Summary of Advantages and Disadvantages of Seasonale®²

Advantages	Disadvantages
Decreased incidence of menstrual symptoms (e.g. dysmenorrhea, menorrhagia, menstrual migraines, PMS)	Adverse effect profile (similar to or better than the 28-day regimen)
Fewer symptoms present that are seen in the hormone free interval associated with the 28-day regimen	Unscheduled bleeding and spotting may occur (mostly confined to the earlier cycles) ³
More convenient for some women	Possible delay in recognition of pregnancy (although not teratogenic if taken during pregnancy)
Potential improvement in compliance and an increase in contraceptive efficacy	Although short-term safety is documented (up to two years), evidence for long term safety is not available
Fewer bleeding days resulting in a lower cost of menstrual-hygiene supplies	Cost of medications

Cost (Prices from McKesson + Professional Fees)

Comparison with other COC's (EE/levonorgestrel)

- Seasonale® (0.03mg/0.15mg) - \$70.68/pack
- Min-Ovral® (0.03mg/0.15mg) - \$57.39/ 3 packs
- Portia™ (0.03mg/0.15mg) - \$40.71/ 3 packs
- Alesse® (0.02mg/0.1mg) - \$57.40/ 3 packs

Drug Status

- Approved by Health Canada in July 2007
- Not currently on the Saskatchewan Drug Formulary

References

- 1) Anderson FD, Hait H. A multicenter, randomized study of an extended cycle oral contraceptive. *Contraception*, August 2003; 68(2): 89-96.
- 2) Canadian consensus guideline on continuous and extended hormonal contraception, 2007. Pharmacist's Letter/Prescriber's Letter 2007; 23(8):230815.
- 3) Seasonale™ (Ethinyl Estradiol and Levonorgestrel). *Lexi-Drugs Online*. 1978-2008 Lexi-Comp Inc. Retrieved 15JAN2008; cited <http://online.lexi.com.cyber.usask.ca/crlonline?siteid=293>
- 4) Product monograph for *Seasonale*. Paladin Labs Inc, Montreal, QC, 2007. Retrieved 11JAN2008; cited <http://www.seasonale.com/>
- 5) Hormonal contraception. Pharmacist's Letter/Prescriber's Letter 2003; 19(10):191010.