



Saskatchewan Drug Information Services  
College of Pharmacy and Nutrition, U of S  
T: (306)966-6340 F:(306)966-2286

[www.usask.ca/druginfo](http://www.usask.ca/druginfo)



---

Volume 20, Issue No. 3

October 2003

---

Evra®, soon to be marketed by Janssen-Ortho™, is the first transdermal contraceptive delivery system approved for use in Canada. Health Canada approved the use of Evra® for the prevention of pregnancy in August 2002. The company anticipates this product will be available in Canadian pharmacies during the first half of 2004. Janssen-Ortho™ has delayed marketing the product due to difficulties in acquiring a sufficient supply of raw materials. The initial demand in the United States has been overwhelming; Janssen-Ortho™ would like to ensure supply meets demand upon hitting the Canadian market. (1)

**What is it?**<sup>2</sup> Evra® is a combination contraceptive patch (norelgestromin 6mg/ethinyl estradiol 0.75mg) which is applied once weekly for three consecutive weeks followed by a patch free week. Evra® is a 20cm<sup>2</sup> beige coloured patch with three layers. The outer layer provides stability, the middle layer holds the active drug, and the inner layer is a liner that protects the adhesive material of the patch. The liner is removed prior to application.

**Place in therapy**<sup>2</sup>: Evra® is used by women as a form of contraception.

**Mechanism of Action**<sup>2,3</sup>: The MOA of Evra® is similar to currently available combination oral contraceptive pills (COC). Estrogens suppress follicle-stimulating hormone (FSH) thus preventing the development of the dominant follicle. Estrogens also potentiate the action of the progestin component that suppresses the luteinizing hormone surge thereby blocking ovulation. Changes in the endometrial lining by estrogen and thickening of the cervical mucosa by progestin also hamper implantation.

The hormones are absorbed through the skin within hours of application. Steady state is reached within 48 hours of application and is maintained throughout the 7-day patch wearing period. Withdrawal bleed is expected on the fourth day of the patch free week as opposed to the second day during the pill free week for women on oral contraceptives.

**Application**<sup>2,3</sup>: Evra® is applied to clean, dry, intact skin on the buttock, abdomen, upper outer arm or upper torso where it will not be rubbed by tight clothing. The patch should not be placed on the breast or on any irritated, red or cut skin. The patch has been shown to provide efficacious hormone concentrations under conditions of heat, humidity, exercise and cool water immersion. In one study, 4.6% of all patches were replaced for either complete (1.8%) or partial (2.8%) detachment.

**What if the patch falls off?**<sup>2,3,4</sup> If less than 24 hours has elapsed since the patch has become detached, the same patch can be reapplied to the same place immediately. If the same patch no longer adheres to the skin, a new patch should be applied. Under no circumstances should supplemental adhesives (ex. tape) or wraps be used to hold the patch in place. In this case, a back-up method is not required.

If greater than 24 hours has elapsed, a new patch is applied. This is now a new Day 1, the beginning of a new cycle. The same instructions would apply if the patient is uncertain when the patch detached or fell off. A back-up contraceptive method is required for 7 days.

**When can I apply the first patch?**<sup>2,3,4</sup> A woman can choose the “first day start” (i.e. apply within 24 hours of day 1 of menstrual cycle) or the “Sunday start” (i.e. first Sunday after her period starts). When using Evra® for the first time a back-up method is required for 7 days only if the patch is applied after the first day of her menstrual cycle. If her period falls on a Sunday and the patch is applied on this day, a back-up method is not necessary.

When switching from oral contraceptives, Evra® is applied on the first day of withdrawal bleed. Pregnancy should be ruled out if there is no active bleed within 5 days of the last active tablet.

Pharmacists are likely to encounter individuals who have trouble remembering their patch change day. Solutions to this problem have been identified. (Table 1) Note that under no circumstances should the patch free interval be longer than 7 consecutive days.

**Table 1: Patient Instructions for Missed Patch Change**

I forgot to change the patch on...	Should I apply a new patch?	Will the “patch change day” change?	Should I use a back-up method???
Week 1/day 1	As soon as possible (ASAP)	Yes – This is now day 1 of a new cycle	Yes – 7 days
Week 2/day 8 or week 3 /day 15			
◆ < 48 hrs elapsed	ASAP	No – carry on as usual	No
◆ > 48 hrs elapsed	ASAP – begin new 4 week cycle	Yes – this is now day 1 of a new cycle	Yes – 7 days
Week 4/day 22	No – remove patch immediately. This is her patch free week.	No – carry on as usual	No

Adapted in part from Pharmacist’s Letter, Detail document 180609: New Drug: Ortho Evra (Norelgestromin/ethinyl estradiol) Transdermal System

**Clinical Trials**<sup>4,5</sup>: Evra® has been evaluated in several trials including a dose ranging study, two comparative trials and one non-comparative trial. The first comparative trial measured the efficacy of Evra® against a European oral contraceptive, Mercilon® (17-deacetyl norgestimate 150ug/ ethinyl estradiol 20ug). Over 13 cycles, the rate of contraceptive failure was low and not significantly different between the two agents (Evra®:0.5% vs. Mercilon®:0.3%) The second trial compared Evra®

and Triphasil® (levonorgestrel 50ug/ethinyl estradiol 30ug: days 1-6; 75ug/40ug: days 7-11; 125ug/30ug: days 12-21). This study suggested improved contraceptive efficacy in the patch group; however, the investigators deemed this difference clinically insignificant due to a small sample size. Study results have suggested decreased efficacy in women over 90kg. This association has also been shown in oral contraceptive users. Further research in this area is required to adequately explain this relationship.

**Adverse Effects<sup>2,3,4</sup>:** The most common adverse effects were breast symptoms, headache, application-site reactions, nausea, upper respiratory infections, menstrual cramps and abdominal pain. The incidence of adverse effects was generally similar between the patch group and COC group with the exception of increased breast discomfort (18.7% vs 5.8%, respectively;  $p < 0.001$ ), headache (1.5% vs 0.3%;  $p = 0.03$ ) and dysmenorrhea (1.5% vs 0.2%,  $p = 0.01$ ). Breast symptoms tended to subside after the first two cycles. Application-site irritation was reported in 20.2% of the patch users.

**Cost<sup>6</sup>:** The average wholesale price for a one month supply of Evra® (three patches) is 33.72 USD. This is equivalent to approximately 50.00 CDN, roughly twice the average monthly price for COC's. Evra® will be available as a box of three patches for one cycle or as single replacement patches.

**Precautions and Contraindications<sup>2,3,4</sup>:** These are the same as for COC's; however formal studies have not been conducted.

**Drug Interactions<sup>2,3,4</sup>:** Drugs known or suspected to interact with COC's are thought to also interact with Evra®.

**And the big deal is<sup>4</sup>....** Compliance appears to be improved in the patch users. Whether this will reduce the number of unwanted pregnancies is yet to be determined. Certain side effects appeared to be more prominent in the Evra® group. If cost is an issue to your patient, a COC might still be the way to go.

*Prepared by Carlee Thorsen, Hospital Resident and  
Zahra Hirji, Drug Information Consultant  
References available upon request*

**References:** 1)Manzer Judy. SOGC: Birth-control patch on its way. [http://www.medicalpost.com/mpcontent/article.jsp?content=20030811\\_114117\\_2620](http://www.medicalpost.com/mpcontent/article.jsp?content=20030811_114117_2620) Last access 13/08/03. 2)Ortho Evra Prescribing Information 3) O'Mara NB. New Drug: Ortho Evra (Norelgestromin/ethinyl estradiol) Transdermal System. Pharmacist's Letter Detail Document 180609 2002; 18. 4) Sicat BL. Ortho Evra, a New Contraceptive Patch. Pharmacotherapy 2003; 23(4): 472-480.. 5)Zieman M, Guillebaud J, Weisberg E et al. Contraceptive efficacy and cycle control with the Ortho Evra™/Evra™ transdermal system: the analysis of pooled data. Fertil Steril 2002; 77 (Suppl 2): S13-18. 6) Personal communication Medical Information, Ortho-McNeil United States