

Norelgestromin/Ethinyl Estradiol Transdermal System

Surasak Taneepanichskul MD*

* Department of Obstetrics and Gynecology Faculty of Medicine Chulalongkorn University

The transdermal contraceptive patch is an innovative contraceptive technology. The failure rate is quite low and has high continuation rate. The side effects and complications are not different from other hormonal contraceptives. This contraceptive method should be an alternative birth control technique for women.

Keywords : Norelgestromin, Ethinyl estradiol, Transdermal system

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Norelgestromin / ethinyl estradiol transdermal system (ORTHO EVRA®) is a combination transdermal contraceptive patch with a contact surface area of 20 cm². It contains 6.00 mg norelgestromin and 0.75 mg ethinyl estradiol (EE), and releases 150 micrograms of norelgestromin and 20 micrograms of EE to the bloodstream per 24 hours. It is a thin, matrix-type transdermal contraceptive patch consisting of three layers. The backing layer is composed of a beige flexible film consisting of a low-density pigmented polyethylene outer layer and a polyester inner layer. It provides structural support and protects the middle adhesive layer from the environment. The middle layer contains polyisobutylene / polybutene adhesive, crospovidone, non-woven polyester fabric and lauryl lactate as inactive components. The active components in this layer are the hormones, norelgestromin and ethinyl estradiol. The third layer is the release liner, which protects the adhesive layer during storage and is removed just prior to application. It is a transparent polyethylene terephthalate (PET) film with a polydimethylsiloxane coating on the side that is in contact with the middle adhesive layer.

Pharmacodynamics and pharmacokinetic

Norelgestromin is the active progestin largely responsible for the progestational activity that occurs in women following application. Norelgestromin is also the primary active metabolite produced following oral administration of norgestimate (NGM). Although the

primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus and the endometrium. Receptor and human sex hormone-binding globulin (SHBG) binding studies, as well as studies in animals and humans, have shown that both norgestimate and norelgestromin exhibit high progestational activity with minimal intrinsic androgenicity. Transdermally-administered norelgestromin, in combination with ethinyl estradiol, does not counteract the estrogen-induced increases in SHBG, resulting in lower levels of free testosterone in serum compared to baseline. ORTHO EVRA® demonstrated consistent elimination kinetics for norelgestromin and EE with half-life values of approximately 28 hours and 17 hours, respectively. The return of hypothalamic-pituitary-ovarian axis function post-therapy was found that FSH, LH, and estradiol mean values, though suppressed during therapy, returned to near baseline values during the 6 weeks post therapy. Both norelgestromin and EE rapidly appear in the serum, reach a plateau by approximately 48 hours, and are maintained at an approximate steady-state throughout the wear period.

Daily absorption of norelgestromin and EE from ORTHO EVRA® was determined by comparison to an intravenous infusion of norelgestromin and EE. The results indicated that the average dose of norelgestromin and EE absorbed into the systemic circulation is 150 mcg/day and 20 mcg/day, respectively. The absorption of norelgestromin and EE following application of ORTHO EVRA® to the abdomen, buttock, upper outer arm and upper torso (excluding breast) was considered therapeutically equivalent. The absorp-

Correspondence to : Taneepanichskul S, Department of Obstetrics and Gynecology Faculty of Medicine Chulalongkorn University, Bangkok 10330, Thailand.

tion of norelgestromin and EE following application of ORTHO EVRA® was studied under conditions encountered in a health club (sauna, whirlpool and treadmill) and in a cold water bath. The results indicated that for norelgestromin there were no significant treatment effects on serum concentration of EE and NGM when compared to normal wear.

Indication and use

Clinical trials demonstrated that pregnancy rates were approximately 1 per 100 women-years of ORTHO EVRA® use. The greater proportion of pregnancies among women at or above 198 lbs. was statistically significant and suggests that ORTHO EVRA® may be less effective in these women.

Dosage and administration

This system uses a 28-day (four-week) cycle. A new patch is applied each week for three weeks (21 total days). Week Four is patch-free. Withdrawal bleeding is expected during this time. Every new patch should be applied on the same day of the week. This day is known as the "Patch Change Day." For example, if the first patch is applied on a Monday, all subsequent patches should be applied on a Monday. Only one patch should be worn at a time. On the day after Week Four ends a new four-week cycle is started by applying a new patch. Under no circumstances should there be more than a seven-day patch free interval between dosing cycles. If the woman is starting ORTHO EVRA® for the first time, she should wait until the day she begins her menstrual period. Either a First Day start or Sunday start may be chosen. The day she applies her first patch will be Day 1. Her "Patch Change Day" will be on this day every week. The patch should be applied to clean, dry, intact healthy skin on the buttock, abdomen, upper outer arm or upper torso, in a place where it won't be rubbed by tight clothing. ORTHO EVRA® should not be placed on skin that is red, irritated or cut, nor should it be placed on the breasts. To prevent interference with the adhesive properties of ORTHO EVRA®, no makeup, creams, lotions, powders or other topical products should be applied to the skin area where the ORTHO EVRA® patch is or will be placed. If the ORTHO EVRA® patch becomes partially or completely detached and remains detached, insufficient drug delivery occurs. If a patch is partially or completely detached for less than one day (up to 24 hours), the woman should try to reapply it to the same place or replace it with a new patch immediately. No back-up contraception is needed. The woman's "Patch

Change Day" will remain the same. If a patch is partially or completely detached for more than one day (24 hours or more) or if the woman is not sure how long the patch has been detached, she should stop the current contraceptive cycle and start a new cycle immediately by applying a new patch. There is now a new "Day 1" and a new "Patch Change Day." Back-up contraception, such as condoms, spermicide, or diaphragm, must be used for the first week of the new cycle. A patch should not be re-applied if it is no longer sticky, if it has become stuck to itself or another surface, if it has other material stuck to it or if it has previously become loose or fallen off. If a patch cannot be re-applied, a new patch should be applied immediately. Supplemental adhesives or wraps should not be used to hold the ORTHO EVRA® patch in place.

Switching from an oral contraceptive

Treatment with ORTHO EVRA® should begin on the first day of withdrawal bleeding. If there is no withdrawal bleeding within 5 days of the last active (hormone-containing) tablet, pregnancy must be ruled out. If therapy starts later than the first day of withdrawal bleeding, a non-hormonal contraceptive should be used concurrently for 7 days. If more than 7 days elapse after taking the last active oral contraceptive tablet, the possibility of ovulation and conception should be considered.

Use after Childbirth

Women who elect not to breast-feed should start contraceptive therapy with ORTHO EVRA® no sooner than 4 weeks after childbirth. If a woman begins using ORTHO EVRA® postpartum, and has not yet had a period, the possibility of ovulation and conception occurring prior to use of ORTHO EVRA® should be considered, and she should be instructed to use an additional method of contraception, such as condoms, spermicide, or diaphragm, for the first seven days.

Use after Abortion or Miscarriage

After an abortion or miscarriage that occurs in the first trimester, ORTHO EVRA® may be started immediately. An additional method of contraception is not needed if ORTHO EVRA® is started immediately. If use of ORTHO EVRA® is not started within 5 days following a first trimester abortion, she should be advised to use a non-hormonal contraceptive method. Ovulation may occur within 10 days of an abortion or miscarriage. ORTHO EVRA® should be started no earlier than 4 weeks after a second trimester abortion or

miscarriage. When ORTHO EVRA® is used postpartum or postabortion, the increased risk of thromboembolic disease should be considered.

Breakthrough Bleeding or Spotting and Skin Reaction

In the event of breakthrough bleeding or spotting (bleeding that occurs on the days that ORTHO EVRA® is worn), treatment should be continued. If breakthrough bleeding persists longer than a few cycles, a cause other than ORTHO EVRA® should be considered. In the event of no withdrawal bleeding (bleeding that should occur during the patch-free week), treatment should be resumed on the next scheduled Change Day. If ORTHO EVRA® has been used correctly, the absence of withdrawal bleeding is not necessarily an indication of pregnancy. Nevertheless, the possibility of pregnancy should be considered, especially if absence of withdrawal bleeding occurs in 2 consecutive cycles. ORTHO EVRA® should be discontinued if pregnancy is confirmed. If patch use results in uncomfortable irritation, the patch may be removed and a new patch may be applied to a different location until the next Change Day. Only one patch should be worn at a time.

Drug Interactions

The metabolism of hormonal contraceptives may be influenced by various drugs. Of potential clinical importance are drugs that cause the induction of enzymes that are responsible for the degradation of estrogens and progestins, and drugs that interrupt entero-hepatic recirculation of estrogen (e.g. certain antibiotics). The proposed mechanism of interaction of antibiotics is different from that of liver enzyme-inducing drugs. However, in a pharmacokinetic drug

interaction study, oral administration of tetracycline HCl, 500 mg q.i.d. for 3 days prior to and 7 days during wear of ORTHO EVRA® did not significantly affect the pharmaco-kinetics of norelgestromin or EE.

Patch Adhesion

In the clinical trials with ORTHO EVRA®, approximately 2% of the cumulative number of patches completely detached. The proportion of subjects with at least 1 patch that completely detached ranged from 2% to 6%, with a reduction from Cycle 1 (6%) to Cycle 13 (2%).

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ยาคุมกำเนิดชนิดแผ่นแปะผิวหนัง

สรุปคดีฐานนิพานิชสกุล

ยาคุมกำเนิดชนิดแผ่นแปะผิวหนัง (Ortho Evra) เป็นแผ่นแปะผิวหนังเพื่อการคุมกำเนิดโดยมีขนาด 20 ตารางเซนติเมตร ประกอบด้วย norelgestromin 6 มิลลิกรัม และ ethinylestradiol 0.75 มิลลิกรัม โดยจะมีระดับฮอร์โมนในกระแสโลหิตเป็น ethinylestradiol 20 ไมโครกรัม และ norelgestromin 150 ไมโครกรัม ยาคุมกำเนิดชนิดแผ่นแปะผิวหนังนับว่าเป็นนวัตกรรมใหม่ในการคุมกำเนิด จากการศึกษาทางคลินิกพบว่า มีประสิทธิภาพสูง ผลข้างเคียงต่ำ มีอัตราการใช้สูง นับว่าเป็นวิธีการคุมกำเนิดชนิดใหม่ที่สามารถนำมาใช้เป็นอีกทางเลือกหนึ่งในการคุมกำเนิดของสตรีไทย