Novartis Pharmaceutical Canada has introduced an extension to their product line of transdermal delivery systems in the treatment of hormone-replacement therapy for menopausal women. Current available products are Estraderm™, Estracomb™, and Vivelle™. Estalis™ is a new matrix patch system that contains estradiol-17β as the estrogen and norethindrone acetate as the progestin. Estalis™ is unique in that both estradiol-17β and norethindrone acetate are delivered through a one patch system given in a continuous combined regimen. Estalis™ is an adhesive-based matrix transdermal drug delivery system, comprising of 3 layers, a backing layer, an adhesive layer and a protective layer. Inside the adhesive layer contains the 2 active ingredients, estradiol-17β and norethindrone acetate mixed together.

Estalis™ is indicated for the relief of menopausal and post-menopausal symptoms, which appears due to naturally or surgically induced estrogen deficiency such as hot flushes, sleep disturbances and vulvar and vaginal atrophy. Estalis™ is only recommended in women with an intact uterus since the patch includes a progestin whose role in to prevent endometrial hyperplasia.

In a clinical trial it was demonstrated that with a continuous transdermal regimen of estradiol-17β and norethindrone, there were significantly less cases of endometrial hyperplasia and uterine bleeding as compared to woman using single-entity estradiol transdermal systems. This clinical trial also revealed that continuous combined transdermal delivery systems provide increased dosing flexibility and improved convenience and compliance in HRT. Another clinical trial demonstrated that the combined transdermal delivery system reduces uterine artery resistance and induces a self-limiting growth of the uterus and endometrium.

Drug interactions are the same with estrogens. These include diminishing the effects of anticoagulants, hypoglycemics, and antihypertensives. Certain drugs that induce liver enzymes such as phenytoin, carbamazepine, and barbiturates can interfere with estrogens. The extent of this interference is not clear for transdermal delivered estrogens.

Dosing of Estalis™ can be initiated immediately for women who are not currently taking oral estrogens. In women who are currently taking oral estrogens, dosing can begin on reappearance of menopausal symptoms, following the discontinuation of oral therapy. Estalis™ is available in two strengths: 250/50 µg per day (16cm²) which delivers 250 µg norethindrone acetate and 50 µg estradiol-17β and 140/50 µg per day (9cm²) which delivers 140 µg norethindrone acetate and 50 µg estradiol-17β. Usually starting dose is 250/50, however the 140/50 maybe be used only when considered more appropriate. A new patch should be applied twice weekly during a 28-day cycle. Pharmacists should counsel women that irregular uterine bleeding may occur particularly in the first six months, but generally decreases with time, and often to an amenorrheic state.
The dose of Estalis™ may be decreased to 140/50 if adverse effects related to the progestin dose occur. For any HRT regimen, whether oral or transdermal, the requirement for HRT for menopausal symptoms should be monitored periodically. Any attempts to taper or discontinued therapy should be made in 3- to 6-month intervals.

Appropriate sites for patch application should be one at which less skin wrinkling occurs during bodily movements and these sites include the buttocks and abdomen. It is important that pharmacists suggest to patients to rotate the site of application and the patches should not be applied to the same skin site for at least one week.

Novartis distributes Estalis™ in the 2 strengths, 140/50 and 250/50. Both strengths are available in cartons of 8 transdermal patches and the wholesale cost for each is $23.21/carton. I am not sure of this cost. Our ex-factory sales is $21.80 for 8 patches. Estalis™ should be stored in the refrigerator (2-8° C) until the time of dispensing. During use, the patient should store the patches at room temperatures (20-25° C) and the patch should be used within 6 months.

REFERENCES:


