



## INNOVATIVE TECHNOLOGY FOR THE MENOPAUSE

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Transdermal patch drug delivery systems utilize a drug/adhesive mix, which is administered through the skin and into the bloodstream over an extended period of time. The absorption of molecules following transdermal administration follows zero order pharmacokinetics, and the skin acts as the rate-limiting step in absorption.

Such systems may offer significant advantages over conventional oral and parenteral dosage forms, including non-invasive administration, controlled, steady state delivery, avoidance of first-pass metabolism, improved patient compliance and avoidance of certain adverse side effects. This makes transdermal systems an ideal delivery modality for estrogen replacement following decline of ovarian function at the menopause.

The first administration of estradiol across the skin was a hydroalcoholic gel for direct application to the skin over a large area. Subsequently transdermal patch delivery systems were developed. Early reservoir systems contained estradiol dissolved in an alcoholic gel separated from the skin by a rate-limiting membrane and attached to the skin by a surrounding adhesive border. The drawbacks to this system are cosmetic (relatively bulky) and irritation in some patients caused by the alcohol. In more recent matrix systems the estradiol is dissolved directly in the adhesive matrix and the rate of release is controlled by the matrix composition. The first generation matrix system, Menorest® (Vivelle®) has been demonstrated clinically to be an effective

and acceptable therapy for climacteric symptoms and prevention of postmenopausal osteoporosis.

The development of the DOT (Delivery Optimized Thermodynamics) technology and formulation techniques ensure the delivery of a safe and effective dose and adherence for the intended wear period. The patches are formulated to deliver the estradiol without enhancers, the stability of the drug delivery maintained by ethyl-cellulose.

This has resulted in the new generation transdermal 17 $\beta$ -estradiol delivery system, Estradot® (VivelleDot™). This innovative system is even more flexible and comfortable to wear than the first generation patches. The dissolution of the drug in the adhesive matrix allows a greater reduction in size (66% smaller than Menorest®). This has added benefits in both cosmetic appeal and reduction of skin irritation. The adhesive properties are also higher, resulting in lower loss of the patch during the wear period. Estradot® is formulated in four strengths for dose flexibility.

Pharmacokinetic studies have substantiated the efficiency of the estradiol delivery, and demonstrated the ability to sustain delivery of estradiol to mimic the hormonal milieu of the premenopausal state.

The technology could be used to further enhance the range of DOT therapies available for effective treatment of menopausal symptoms.