

NEW DRUG EVALUATION

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EVRA®

Evra® is the first combination transdermal contraceptive patch to be launched in the UK. There are limited data to suggest improved compliance with Evra® compared with oral contraceptives however this was not associated with increased efficacy. In clinical trials, Evra® had similar adverse effects to combined oral contraceptives (COCs) but was associated with application site reactions and an increased frequency of breast discomfort. The patch has no long-term safety data and it is significantly more expensive than COCs. Evra® offers no clear advantages over COCs therefore it cannot be recommended as a first line contraceptive for most women.

What is it?

Evra® (Janssen-Cilag Ltd) is the first combination transdermal contraceptive patch to be launched in the UK. Each 20 cm² patch releases 150 mcg norelgestromin and 20 mcg ethinylestradiol per 24 hours for 7 days.^{1,2} Norelgestromin is the primary active metabolite of norgestimate, the progestogen in the combined oral contraceptive (COC), Cilest®.² The patch is applied on the first day of menses for the first cycle and is changed every 7 days for 3 consecutive weeks followed by one patch free week during which the withdrawal bleed occurs. Consecutive patches should be applied to a different place on the buttock, abdomen, upper outer arm or upper torso. Evra® should not be applied to the breast or to red, irritated or broken skin.¹

How effective is it?

The efficacy of Evra® has been evaluated in a non-comparative study involving 1672 women who received either 6 (n=1171) or 13 (n=501) cycles of treatment.³ The primary endpoint was the pregnancy rate, reported as the Pearl Index (PI, number of pregnancies per 100 woman-years of use). There were 5 method failure pregnancies and 1 user failure pregnancy. The overall PI was 0.71 and the method failure PI was 0.59 (PIs for COCs range from 0.1 to 3.0⁴).³

In an open label comparative study, 300 women were randomised to either Evra® or to the COC, Cilest® for up to 4 cycles.⁵ Presumed ovulation (determined by a serum progesterone of ≥ 3 ng/ml) occurred in 6.2% of patients on Evra® compared with 7.2% on Cilest® (p=ns).⁵

There are 2 open label studies that have compared pregnancy rates with Evra® or a COC.^{6,7} In the first study (published as an abstract only), patients were

randomised to Evra® (n=861) or Mercilon® (n=656) for 6 or 13 cycles.⁶ The overall and method failure PIs were higher for Evra® (0.88 and 0.66, respectively) than for Mercilon® (0.56 and 0.28 respectively), although the difference was not statistically significant. In the second study, patients were randomised to Evra® (n=812) or Triphasil® (n=605), a triphasic COC (UK equivalents are Logynon® and Trinordiol®) for 6 or 13 cycles.⁷ Here, the overall and method failure PIs were lower for Evra® (1.24 and 0.99, respectively) than for Triphasil® (2.18 and 1.25 respectively), although again the difference was not statistically significant. However, the sample size of these 2 studies may have been insufficient to detect a clinically relevant difference in efficacy between the different treatment groups.⁶⁻⁸

Two of these comparative studies reported that Evra® was associated with a statistically significant improvement in compliance compared with COCs.^{5,7} However compliance was assessed solely by patients' diary card recordings and patients knew which preparation they were using therefore bias cannot be excluded.^{5,7,8}

In the 3 studies that looked at pregnancy rate, five of the 15 pregnancies in the Evra® treatment groups occurred in women weighing ≥ 90 kg, a group who constituted <3% of the total study population.⁹ Therefore, the contraceptive efficacy of Evra® may be reduced in patients weighing ≥ 90 kg.¹ It has been suggested that the efficacy of low dose COCs may also be reduced in overweight women.¹⁰

How safe is it?

In a pooled analysis of the results from the non-comparative trial, and the comparative trials with Mercilon® or Triphasil®, the most common adverse events in Evra® treated patients were breast symptoms

(22%), headache (21.1%), application site reactions (17.4%), nausea (16.8%), upper respiratory tract infection (10.1%), and dysmenorrhoea (10.1%).¹¹ More patients treated with Evra[®] withdrew due to adverse events compared with Triphasil[®] (12.6% vs 5.5%) or Cilest[®] (4.0% vs 1.3%), although the difference was statistically significant only with Triphasil[®].^{5,7,8} The incidence of most adverse events was similar between Evra[®] and the COCs.⁵⁻⁷ However, Evra[®] was associated with a greater frequency of breast discomfort compared with Triphasil[®] (18.7% vs 5.8%, $p < 0.001$) or Mercilon[®] (19% vs 6%, statistical significance not given).^{6,7}

From the current safety data, it is not possible to establish the relative risk of venous thromboembolism with Evra[®] compared with COCs.²

What other options are there?

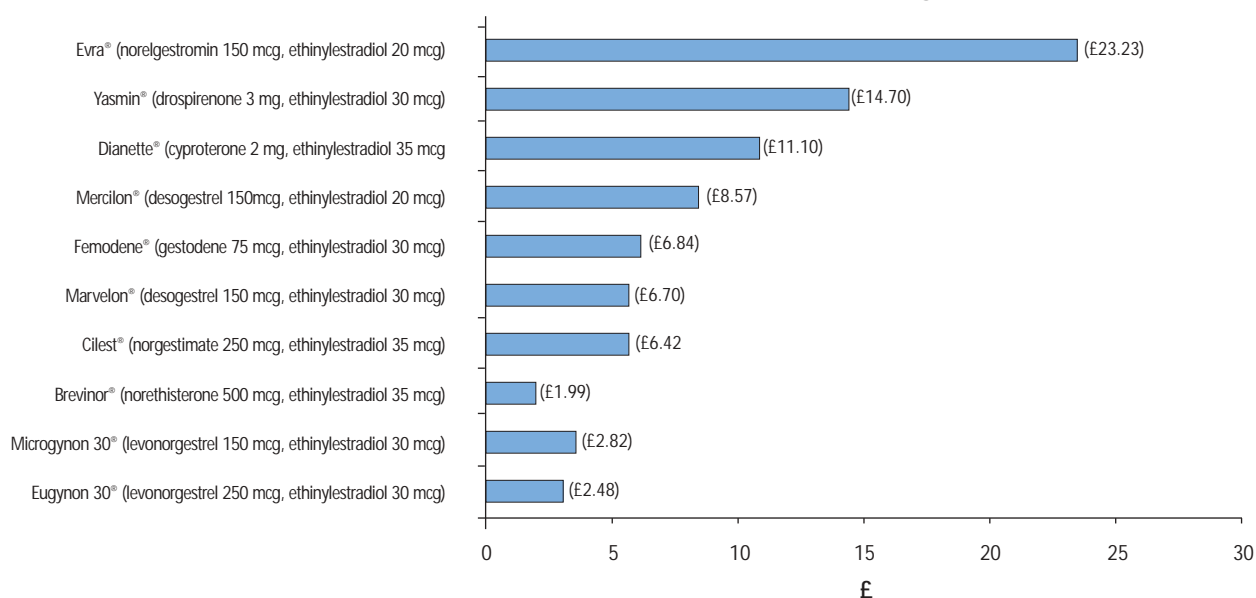
The choice of contraceptive method will depend on several factors including efficacy, safety, plans for future pregnancies and patient preference.¹²

When should it be used?

Evra[®] has similar efficacy to COCs, and it is not better tolerated. Although self-reported compliance was higher with Evra[®] compared with oral contraceptives, this was not associated with increased efficacy. The patch has no long-term safety data and it is considerably more expensive than COCs. Evra[®] does not offer any clear advantages over COCs therefore it cannot be recommended as a first line contraceptive for most women.

How much does it cost?

Cost for 3 months treatment (prices from MIMS August 2003)



NB Doses shown are for general comparison only and do not imply therapeutic equivalence.

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KEY RCT - randomised controlled trial, CT-controlled trial, O-open study, MA-meta analysis, R-review, U-unpublished, A- abstract, E-editorial