

## COMPLETE AND ROBUST OVULATION INHIBITION WITH NUVARING

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One advantage of vaginal hormone administration is that controlled-release formulations achieve more uniform systemic exposure than pills. NuvaRing, a novel contraceptive vaginal ring, releases only 15 µg of ethinylestradiol (EE) and 120 µg etonogestrel (ENG) per day. A randomized pharmacokinetic study compared NuvaRing with a combined oral contraceptive (COC) containing desogestrel 150 µg and EE 30 µg. Maximum hormone levels were reached approximately one week after NuvaRing insertion.  $C_{max}$  levels with NuvaRing for ENG and EE were 40% and 30%, respectively, of those with the COC. Because ENG bioavailability was higher following vaginal compared with oral administration (103% versus 79%), systemic progestogen exposure was comparable with the two contraceptives. However, EE bioavailability was similar via both administration routes. So EE exposure with NuvaRing was only half that with the 30 µg EE COC.

Two pharmacodynamic studies examined ovarian function during recommended and altered NuvaRing use. Ovarian suppression was assessed at least every or every other day by vaginal ultrasound and serum concentrations of FSH, LH, estradiol and progesterone. Using NuvaRing for the recommended 3-week period completely inhibited ovulation. During an additional 2 weeks of NuvaRing use with the same ring, ovulation continued to be inhibited. The effect of early NuvaRing removal on ovarian function was also addressed. After 2 cycles of recommended use the median time to ovulation was 19 days (first ovulation day 13). However, the time to ovulation was similar if the second ring was removed after only 3 days (median 17 days; first ovulation day 12). Thus, 3 days of NuvaRing use suppressed ovarian activity in such a way that a new cohort of follicles needed to be recruited. The inhibition of ovulation after delayed ring insertion was also examined. When the ring-free period was extended until follicles developed to 13 mm (median 11 days; range 8–21 days), subsequent NuvaRing insertion inhibited ovulation in all women.

In summary, NuvaRing effectively inhibits ovulation during recommended and altered use, showing it is a robust contraceptive method.