

Overig	Stof	Effect
SPC Incivo	EE/norethisteron + telaprevir	<i>afname ethinylestradiol AUC 0.72, Cmax 0.74 en Cmin 0.67. Voor norethisteron is de afname veel kleiner.</i>
Garg V. J Clin Pharmacol 2011 Oct 30. [Epub ahead of print]	EE/norethisteron + telaprevir	<p>Telaprevir is a hepatitis C virus protease inhibitor that is both a substrate and an inhibitor of CYP3A. Study Design: The effect of steady-state telaprevir (750 mg every 8 hours) on the steady-state pharmacokinetics of ethinyl estradiol (EE) and norethindrone (NE) was evaluated in 24 healthy women receiving oral contraceptives (OC) containing 0.5 mg NE and 0.035 mg EE for at least 3 months at the time of screening. This was a phase 1, open-label, single-center, non-randomized study that included a cycle 1 (OC only for 21 days, followed by no OC for 7 days), cycle 2 (OC plus telaprevir for 21 days, followed by telaprevir alone for 7 days), and a follow-up period. Results: When administration with or without telaprevir was compared, the least-squares mean ratios (90% confidence limits) for EE were 0.74 (0.68; 0.80) for C(max), 0.67 (0.63; 0.71) for C(min), and 0.72 (0.69; 0.75) for AUC; neither NE nor telaprevir exposure was affected.</p> <p>Conclusions: The efficacy of the OC may be compromised by the 26% to 33% reduction in EE exposure. Therefore, alternative methods of nonhormonal contraception should be used when hormonal contraceptives are coadministered with telaprevir and for up to 2 weeks following cessation of telaprevir.</p>
SPC Victrelis  EPAR	EE/drospirenon + boceprevir	<p>- drospirenon: <i>toename Cmax met 57% en AUC met 99%;</i>  - EE: <i>afname AUC 24%, Cmax onveranderd</i>  Regime: drospirenon 3 mg/dag en EE 0.02 mg/dag + boceprevir 800 mg 3dd.  Overweeg alternatieve anticonceptiva; voorzichtig bij patiënten met risico op hyperkaliëmie of die kaliumsparende diuretica gebruiken.  Fabrikant: van drospirenon is bekend dat het hyperkaliëmie kan veroorzaken in hoog-risicopatiënten, vandaar dat de SPC waarschuwt.</p> <p>p.36 The effect of boceprevir on oral contraceptive drugs is complex. Boceprevir increased drospirenone exposure substantially. Drospirenone metabolism only involves CYP3A4 to a minor extent. Therefore, the observed interaction with boceprevir is <u>unexpected</u>. Boceprevir may affect other metabolic pathways, however it remains unclear which ones. A study is being conducted with boceprevir and a combination oral contraceptive containing norethindrone and ethinylestradiol, to identify if the effect on drospirenone is relevant also for norethindrone. The results of the study will be provided to the CHMP. Attention of physicians will be alerted on the need for alternative contraceptives.</p>
Loughlin J. Contraception 2008;78:377-83.	drospirenon	<p>drospirenon heeft K-sparende eigenschappen, vergelijkbaar met spironolacton. Matched cohort studie, start pil juli 2001 en juni 2004; match drospirenonpil (n= 22,429) met andere pillen in ratio 1:2 (n= 44,858).</p> <p>'Composite clinical surrogate hyperkalemia end point' kwam met dezelfde frequentie voor, 118 vs 260 cases (rate ratio (RR) 0.9, 95% confidence interval (CI) 0.7-1.1].</p> <p>Conclusie: drospirenonstarters lopen niet meer risico op hyperK dan andere pilstarters.</p>

**Opmerkingen**

WFG 27-3-2012: beoordeling interacties HCV-middelen gedelegeerd naar de tabel die is opgesteld door prof. dr. D.M. Burger, Apotheek/Klinische Farmacie, UMC St Radboud Nijmegen. Er wordt dus ook geen alfanumerieke code (voor bewijs en potentiëel effect) meer aan toegekend.

PubMed, Stockley, Hansten etc: --

Informatorium - drospirenon: wordt vrijwel volledig gemetaboliseerd, in geringe mate door CYP3A4.