

Pharmacokinetic Profile of AG200-15, a Transdermal Contraceptive Delivery System, in Healthy Women

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Objective: Evaluate the ethinyl estradiol (EE) and levonorgestrel (LNG) pharmacokinetic (PK) profile of AG200-15, a transdermal contraceptive delivery system, and determine EE exposure of AG200-15 versus the oral contraceptive Ortho-Cyclen[®], in healthy women.

Methods: Phase 1, open-label, single-center study conducted over 3 cycles. Subjects were randomized to a crossover design following a run-in cycle with AG200-15 administered to all 36 women. The sequence in the crossover cycles 2 and 3 was a 21-7 day cycle of AG200-15 either followed by or preceded by 1 cycle of Ortho-Cyclen.

Results: For EE, C_{max} was approximately 60% lower and steady-state concentrations (C_{ss}) were 15%-20% lower than C_{avg} for the AG200-15 patch versus Ortho-Cyclen. Calculated daily dose of AG200-15 was equivalent to approximately 30 µg EE. LNG PK parameters are shown (Table).

Week 3 Cycles 2/3 PK Parameters	AG200-15	Ortho- Cyclen	P Value
EE	(N=32)	(N=32)	
C_{max} (pg/mL)	51.3 ± 17.3	131 ± 45.4	<0.0001
AUC _{0-168h} (ng.h/mL)	6.26 ± 2.46	6.97 ± 2.25	0.0532
C_{ss} (1) ^a (pg/mL)	35.7 ± 14.5	-	0.0167 ^c
C_{ss} (3) ^b (pg/mL)	37.3 ± 14.7	-	0.0532 ^d
C_{avg} (pg/mL)	-	41.5 ± 13.4	-
LNG	(N=34)		
C_{max} (pg/mL)	2400 ± 1140		
AUC _{0-168h} (ng.h/mL)	317 ± 159		
C_{ss} (1) ^a (pg/mL)	1847 ± 930		

^a48-168 h time interval.
^bCalculated from trapezoidal AUC 0-168h (AUC/time interval)
^c C_{ss} (1) vs C_{avg} (Ortho-Cyclen)
^d C_{ss} (3) vs C_{avg} (Ortho-Cyclen)

Conclusion: Overall, lower EE exposure was evident for AG200-15 versus Ortho-Cyclen. LNG exposure after treatment with AG200-15 was similar to low-dose LNG/EE oral contraceptives. AG200-15 was generally safe and well tolerated.