

Acne-Friendly Oral Contraceptives

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* Note: Progestins marked with an asterisk are not FDA-approved for use in the US.

Combined oral contraceptives (COCs) are thought to improve acne via several mechanisms.¹ In addition to decreasing free testosterone *production* by suppressing luteinizing hormone, COCs are believed to decrease testosterone *bioavailability* by increasing levels of sex hormone-binding globulin. Finally, COCs decrease *conversion* of testosterone to dihydrotestosterone in the skin by inhibiting 5-alpha-reductase activity. It has been suggested that the different progestins contained in COCs exert an anti-acne effect to varying degrees through these mechanisms, and thus may be more or less “acne-friendly.”

Currently, norethindrone acetate–ethinyl estradiol (Estrostep^R) and norgestimate–ethinyl estradiol (Ortho Tri-cyclen^R) are FDA-approved for the treatment of acne.² However, a recent Cochrane review of 23 clinical trials found that all COCs studied improved acne lesion count and acne severity grades.¹ The COCs in the trials that were reviewed contained ethinyl estradiol 30 to 50 mcg in combination with various progestins including desogestrel 0.025-0.125 mg (biphasic), drospirenone 3 mg, levonorgestrel 0.1 mg, norethindrone acetate 1 mg, norgestimate 0.18-0.215-0.25 mg (triphasic), chlormadinone acetate* 2 mg, cyproterone acetate* 2 mg, and gestodene* 0.075 mg. Although all COCs produced improvement in acne compared to placebo or other COCs, the authors of the review concluded that comparative efficacy of COCs remains difficult to assess due to a lack of adequately powered, randomized, controlled, double-blind trials. Specifically, cyproterone acetate and chlormadinone acetate, which have been suggested as particularly effective progestins for the improvement of acne, could not be conclusively proven superior to other progestins.

Other recent trials, including those studying the effects of low-dose oral contraceptives containing ethinyl estradiol 20 mcg, have come to similar conclusions regarding the general benefit that COCs appear to have on the severity of acne.^{3,4} As a result, it can be concluded that most COCs currently marketed (see attached table) will likely result in improvement in acne, although the time to achieve optimal results and side effect profiles of the different COCs varies from patient to patient.

References

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Table I: Common Acne-Friendly Oral Contraceptives Organized by Type and Progestin

(Adapted from: Oral Contraceptives. In: Facts and Comparisons 4.0 On-line. Copyright 2007 Wolters Kluwer Health Inc. Available from www.factsandcomparisons.com/. Last accessed 4/14/07.)

Type	Common Brand Names	Progestin	Estrogen	UW Medicine Drug Formulary Status
Monophasic	Kariva, Mircette	0.15mg desogestrel	20mcg and 10mcg ethinyl estradiol	non-formulary
		Note: 28-day package includes 5 tablets containing 10mcg ethinyl estradiol + 2 inert tablets		
	Apri, Desogen, Ortho-Cept	0.15mg desogestrel	30mcg ethinyl estradiol	non-formulary
	Yasmin	3mg drospirenone	30mcg ethinyl estradiol	non-formulary
	Demulen 1/35, Zovia 1/35E	1mg ethynodiol diacetate	35mcg ethinyl estradiol	non-formulary
	Demulen 1/50, Zovia 1/50E	1mg ethynodiol diacetate	50mcg ethinyl estradiol	non-formulary
	Alesse, Aviane, Lessina, Levlite	0.1mg levonorgestrel	20mcg ethinyl estradiol	uw formulary
	Levlen, Levora, Nordette, Portia	0.15mg levonorgestrel	30mcg ethinyl estradiol	non-formulary
	Ovcon-35, Balziva	0.4mg norethindrone	35mcg ethinyl estradiol	non-formulary
	Brevicon, Modicon, Necon 0.5/35	0.5mg norethindrone	35mcg ethinyl estradiol	non-formulary
	Norinyl 1+35, Ortho-Novum 1/35	1mg norethindrone	35mcg ethinyl estradiol	uw formulary
	Ovcon-50	1mg norethindrone	50mcg ethinyl estradiol	non-formulary
	Norinyl 1+50, Ortho-Novum 1/50	1mg norethindrone	50mcg mestranol	non-formulary
	Loestrin 21 1/20, Loestrin Fe 1/20	1mg norethindrone acetate	20mcg ethinyl estradiol	uw formulary
	Loestrin 21 1.5/30, Loestrin Fe 1.5/30, Microgestin Fe 1.5/30	1.5mg norethindrone acetate	30mcg ethinyl estradiol	non-formulary
	Ortho-Cyclen, Sprintec	0.25mg norgestimate	35mcg ethinyl estradiol	uw formulary
Cryselle, Lo-Ovral, Low-Ogestrel	0.3mg norgestrel	30mcg ethinyl estradiol	non-formulary	
Ovral, Ogestrel	0.5mg norgestrel	50mcg ethinyl estradiol	uw formulary	
Biphasic	Seasonique	0.15/0mg levonorgestrel	30/10mcg ethinyl estradiol	non-formulary
	Ortho-Novum 10/11	0.5/1mg norethindrone	35mcg ethinyl estradiol	non-formulary
Triphasic	Cyclessa	0.1/0.125/0.15mg desogestrel	25/25/25mcg ethinyl estradiol	non-formulary
	Enpresse, Tri-Levlen, Triphasil, Trivora	0.05/0.075/0.125mg levonorgestrel	30/40/30mcg ethinyl estradiol	uw formulary
	Necon 7/7/7, Ortho-Novum 7/7/7	0.5/0.75/1mg norethindrone	35/35/35mcg ethinyl estradiol	uw formulary
	Tri-Norinyl, Aranelle	0.5/1/0.5mg norethindrone	35/35/35mcg ethinyl estradiol	non-formulary
	Estrostep 21, Estrostep Fe (FDA approved for acne)	1/1/1mg norethindrone	20/30/35mcg ethinyl estradiol	non-formulary
	Ortho Tri-Cyclen Lo	0.18/0.215/0.25mg norgestimate	25/25/25/mcg ethinyl estradiol	non-formulary
	Ortho Tri-Cyclen (FDA approved for acne), Trinessa	0.18/0.215/0.25mg norgestimate	35/35/35mcg ethinyl estradiol	uw formulary

Statin Formulary Update: Simvastatin Elevated to Preferred Drug Status 25

Extracted from a monograph prepared by Steve Riddle, R.Ph.

Table 1: Statin Comparisons Based on LDL-Lowering and Cost[#]

LDL Reduction	Lovastatin	Pravastatin	Simvastatin UW-PDF	Atorvastatin	Rosuvastatin	Vytorin ^R
20-30%	20mg - \$7	20mg - \$11	10mg - \$9	-	-	-
31-35%	40mg - \$21	40mg - \$13	-	-	-	-
36-40%	80mg - \$39	80mg - \$22	20mg - \$12	10mg - \$83	-	-
41-45%	-	-	40mg - \$12	20mg - \$128	5mg - \$85	-
46-50%	-	-	80mg - \$12	40mg - \$128	10mg - \$85	10/10 - \$101
50-55%	-	-	-	80mg - \$128	20mg - \$85	10/20 or 10/40 - \$101
56-60%	-	-	-	-	40mg - \$85	10/80 - \$101

[#]Cash price for 30-day supply from UWMC or HMC ambulatory pharmacies

Simvastatin offers solid clinical supporting data and is the lowest cost statin currently available.

Drug Cost Savings from Switching from Atorvastatin (A) to Simvastatin (S) or Rosuvastatin (R)

A 10mg to S 20mg: \$169,000
A 20mg to S 40mg: \$354,000
A 40mg to S 80mg: \$267,000
A 40mg to R 10mg: \$96,000
A 80mg to R 20mg: \$40,000
Total: \$659,000 – \$830,000

Table 2: Evidence Supporting Effects of Statins

Agent	CV Outcomes: Prevention		Surrogate Outcomes (i.e., plaque regression)
	Primary	Secondary	
Atorvastatin	YES	YES	YES
Fluvastatin	NO	YES	
Lovastatin	YES	NO	
Pravastatin	YES	YES	
Rosuvastatin	Underway	Underway	
Simvastatin	YES	YES	
Simvastatin/Ezetimibe	NO	NO	

Generic simvastatin became available in 2006.

This statin offers extensive outcomes data and is associated with LDL-lowering potency in the range of 45–47%, thereby permitting use of a low-cost generic agent in place of the more costly brand-name agents for a number of patients. In addition, the high-potency agents, rosuvastatin (Crestor^R) and ezetimibe/simvastatin (Vytorin^R), also provide cost savings over atorvastatin. Current expenditures for statins at UW Medicine approach \$1.3 million with atorvastatin representing the most widely utilized agent (55% of patients) and the greatest portion of costs (78%).

• **LDL-C Lowering:** The relative effects of statins on LDL are well documented (see Table 1) and can be compared on the basis of cost per

degree of LDL reduction. Simvastatin doses of 20–40mg deliver similar LDL-lowering effects compared to atorvastatin 10–20mg, respectively. Rosuvastatin and ezetimibe/simvastatin are the most potent agents. Therefore, conversion of high-dose atorvastatin to these alternative agents is possible without compromising LDL lowering.

• **HDL-C and Triglycerides:** All statins lower triglycerides in a dose-dependent manner with a range of effect from 14%–40% with the more potent agents providing greater lowering. Statins typically provide modest increases in HDL-C levels with the typical effect range of 3–9%. Atorvastatin is known to provide less HDL benefits at higher doses (i.e., 5.7% with 10mg and 2.1% at 80mg). Conversion from atorvastatin to simvastatin would not appear to result in significant changes in HDL-C or triglyceride benefits.

• **Conversion:** Switching from atorvastatin to simvastatin is supported within the definition of evidence-based therapy. Conversion from high-dose atorvastatin to rosuvastatin or ezetimibe/simvastatin is less supported within the strict bounds of evidence-based medicine. Clinicians supporting the lipid hypothesis will likely be comfortable with the degree of data available for these agents. Conversion from atorvastatin to simvastatin or ezetimibe/simvastatin would necessitate a review of patient medication profiles to assure appropriateness and safety. Populations of patients more likely to be taking medications implicated in serious interactions with simvastatin, such as the HIV population (HAART therapy) and transplant patients (i.e., cyclosporin) are poor candidates for this conversion. It is likely that most patients converted to simvastatin from another agent will require a lipid panel at 6–8 weeks to assure appropriate response. The cost for a lipid panel at UW Medicine is approximately \$58. While recent literature does not necessarily recommend liver function tests for all patients treated with statins, the majority of UW Medicine experts surveyed indicated that they would obtain this data for most patients converting to another statin. The cost for a liver function panel is approximately \$44. Thus, each patient converted to simvastatin will likely incur \$102 for additional laboratory tests. This extra cost would be offset within the first 1–2 months for patients converted from any brand statin agent (\$83–128) to generic simvastatin (\$12). Patients converted from atorvastatin (\$128) to rosuvastatin (\$85) or Vytorin (\$101) would take 2.5 and 5 months respectively to recoup these costs.

• **P&T Action:** Simvastatin was elevated to “preferred” formulary status (uw-PDF) and prescribers are encouraged to prescribe this agent unless there is a medically compelling rationale for doing otherwise. Atorvastatin was retained on formulary, but stripped of “preferred” formulary status.

Pharmacy & Therapeutics Committee Actions

Formulary Additions	Dosage Form(s), Strength(s), & Cost [‡]	Therapeutic Classification	Use	Usual Adult Starting Dose*
Azacitidine (Vidaza[®])	IV: 100mg	Methyltransferase Inhibitor	Myelodysplastic syndromes	75mg/m ² IV
Quinine sulfate (Qualaquin[®])	Capsule: 324mg	Antiinfective	Malaria	325mg PO
	The P&T Committee approved automatic substitution of the 324mg quinine product for prescriptions that call for 300mg. Prescriber clarification is required for prescriptions calling for 200mg of quinine.			
Other Actions				
HMG CoA Reductase Inhibitors	The P&T Committee voted to replace atorvastatin (Lipitor [®]) and lovastatin (generic for Mevacor [®]) on the UW preferred drug formulary (uw-PDF) with simvastatin (generic for Zocor [®]).			
IVIG	<p>The P&T Committee voted to require the use of the existing IV Immune Globulin (IVIG) Orders form (UH2262) for all IVIG orders and to make completion of the form, INCLUDING PATIENT WEIGHT, mandatory prior to dispensing by pharmacy. Other UW Medicine restrictions regarding IVIG administration follow:</p> <ul style="list-style-type: none"> • Product with low IgA content (Gammagard[®] or equivalent): Restricted to patients with IgA deficiency without antibodies to IgA . • Sucrose-free product (Gamunex[®] or equivalent): Restricted to patients with creatinine clearance <50mL/minute or patients with creatinine clearance <60mL/minute + risk factor for renal insufficiency (e.g., diabetes, NYHA Class III/IV heart failure, kidney transplant, liver failure). 			

[‡] Contact pharmacy for information on drug costs.

* Refer to product labeling for full prescribing information.

Benzocaine Reminder

The P&T Committee voted to remove all topical benzocaine products (e.g., Cetacaine[®]) from the UW Medicine Drug Formulary in June 2006 and to authorize automatic substitution by pharmacy of lidocaine 4% solution or phenol spray based on the indication for use. This action followed an FDA Public Health Advisory reminding prescribers that benzocaine is associated with methemoglobinemia and that cases of methemoglobinemia have also resulted from medication errors due to incorrect use of benzocaine sprays (e.g., longer duration or more frequent sprays than recommended). Prescribers are urged to remain vigilant regarding the safe use of topical anesthetics.

Vol. 36, No. 5

Acne-Friendly Oral Contraceptives, 23-24

Statin Formulary Update: Simvastatin Elevated to UW-PDF, 25

Benzocaine Reminder: Methemoglobinemia, 26

April P&T Committee Actions, 26



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