



## Family Medicine Clinical Pharmacy Forum Vol. 3, Issue 4 (July/August 2007)

*Family Medicine Clinical Pharmacy Forum is a brief bi-monthly publication from the Family Medicine clinical pharmacists distributed to faculty and residents of the Department of Family Medicine. Our intent is to provide timely information on broad-based issues of pharmacotherapy, as well as regulatory and practiced-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.*

### Contents

- Generic drugs – see what is coming!
- Simvastatin – does it help prevent dementia and Parkinson’s Disease?
- Elestrin – a new estradiol gel for menopausal vasomotor symptoms
- Vitamin E – an update
- Expecta – a DHA dietary supplement during pregnancy/breastfeeding
- Zelnorm – it’s back....(but with restricted use)
- Smoking cessation clinic

### Generic Drugs

Generic drugs – saving money is a good thing!

Currently, over 50% of prescriptions are filled with generic drugs that average \$50-\$60 less than brand name drugs and save the public and their insurance companies over \$20 billion per year. Most patients and insurance companies, however, would like those numbers to be even higher.

Here are a few of the newest generics to come to market along with the price comparison to their brand name counterparts. Keep in mind that one generic company will have exclusive rights to the generic patent for 6 months, therefore, the prices for the generics will be higher at first until other generic companies are allowed to compete and drive the prices down.

Qty	Brand Name	Price	Generic Name	Price
30	Lotrel 2.5/10mg	\$74.40	Amlodipine/ Benazapril	\$73.99
30	Lotrel 5/20mg	\$87.38	Amlodipine/ Benazapril	\$78.99
30	Lotrel 5/10mg	\$83.51	Amlodipine/ Benazapril	\$74.99
30	Lotrel 10/20mg	\$101.11	Amlodipine/ Benazapril	\$92.99
<b>30</b>	<b>Norvasc 2.5mg</b>	<b>\$53.74</b>	<b>Amlodipine</b>	<b>\$45.99</b>
<b>30</b>	<b>Norvasc 5mg</b>	<b>\$53.74</b>	<b>Amlodipine</b>	<b>\$46.99</b>

This issue authored by:

Jim Hoehns, Pharm.D., BCPS, Northeast Iowa Family Medicine Residency, Waterloo, Iowa. Fellow contributors are: Kristi Kavanaugh, Pharm.D., Jennifer Goings, and Jessica Eveleth



<b>30</b>	<b>Norvasc 10mg</b>	<b>\$73.67</b>	<b>Amlodipine</b>	<b>\$64.00</b>
30	Toprol XL 25mg	\$30.00	Metoprolol succinate	\$22.80
<b>30</b>	<b>Ambien 5mg</b>	<b>\$134.12</b>	<b>Zolpidem</b>	<b>\$15.39</b>
<b>30</b>	<b>Ambien 10mg</b>	<b>\$134.12</b>	<b>Zolpidem</b>	<b>\$19.39</b>

What's next? Here is the anticipated availability of first-time generics and/or patent expiration dates for the rest of 2007. Don't forget, however, that patent expiration and generic availability are complicated by legal maneuvers on both sides and the ultimate release date on all of these products is TBD.

<b>Brand Name</b>	<b>Generic Name</b>	<b>Manufacturer</b>	<b>Anticipated Availability</b>
Imitrex	Sumatriptan	GlaxoSmithKline	June
Lamisil	Terbinafine	Novartis	June
Cerebyx	Fosphenytoin	Parke-Davis	August
Exelon	Rivastigmine	Novartis	August
Geodon	Ziprasidone	Pfizer	September
Coreg	Carvedilol	GlaxoSmithKline	September
Toprol XL	Metoprolol succinate	AstraZeneca	November
Meridia	Sibutramine	Abbott	December
Mavik	Trandolapril	Abbott	December
Kytril	Granisetron	Roche	December
Risperdal	Risperidone	Janssen	December
Tequin	Gatifloxacin	GlaxoSmithKline	December
Zyrtec	Cetirizine	Pfizer	December

Anticipated Availability of First-Time Generics. Pharmacist's Letter/Prescriber's Letter 2006; 22(1): 220101.

FDA Center for Drug Evaluation and Research. First-Time Generics-May 2007.  
<http://www.fda.gov/cder/ogd/approvals/1stgen0507.htm> (Accessed July 25, 2007).

<http://www.drugstore.com> (Accessed July 27, 2007).

### **Simvastatin use associated with lower risk of dementia and Parkinson's Disease?**

According to a recent study headed by Dr. Benjamin Wolozin at the Boston University School of Medicine, simvastatin use was associated with a 50% lower incidence of dementia and

This issue authored by:

Jim Hoehns, Pharm.D., BCPS, Northeast Iowa Family Medicine Residency, Waterloo, Iowa. Fellow contributors are: Kristi Kavanaugh, Pharm.D., Jennifer Goings, and Jessica Eveleth



Parkinson's Disease. Published in the July 19, 2007 online addition of BMC Medicine, Wolozin stated "we were very surprised by the size of the effect associated with simvastatin and that it worked for both Parkinson's disease and dementia." As for how this works, several theories abate. "The most likely answer is that statins protect the brain through an anti-inflammatory mechanism," he said. However, apparently not all statins are created equally. Atorvastatin showed a subtle but insignificant reduction in the incidence, while lovastatin had no impact. Fluvastatin and pravastatin were also included in the study, but the number of people on pravastatin was too small to produce reliable data and subjects were not on fluvastatin long enough to include it in the data. Subjects had to be on a statin for at least 7 months before they could be included in the study. The study looked at 727,128 patients taking simvastatin, 53,869 patients taking atorvastatin and 54,052 patients taking lovastatin. All patients were obtained through the VA system database and prescription utilization was tracked for every subject between 2003 and 2005. Wolozin aptly noted that "these findings need to be prospectively confirmed on other population-based studies."

Wolozin B, Wang SW, Li NC, et al. Simvastatin is associated with a reduced incidence of dementia and Parkinson's disease. BMC Med 2007; DOI:10.1186/1741-7015-5-20. Available at: <http://www.biomedcentral.com/1741-7015/5/20> .

## **Elestrin – a new estradiol gel for menopausal vasomotor symptoms**

Elestrin is an estradiol gel indicated for treatment of moderate to severe vasomotor symptoms associated with menopause. Elestrin is a hydroalcoholic gel for transdermal application supplied in a pump formulation. The recommended dose is one pump, which is equivalent to 0.52mg estradiol. The recommended application site is the upper arm and shoulder, but it may also be applied to the thighs or abdomen. With one or two pumps, Elestrin gel systemically delivers 0.0125mg and 0.0375mg of estradiol, respectively. In comparison, estradiol patches like Climara release between 0.025 and 0.1mg estradiol per patch. In clinical trials, two pumps of Elestrin daily produced statistically significant reductions in number and severity of hot flashes compared to placebo by the fourth week. One pump daily produced similar results by week 5. [Simon JA, Bouchard C, Waldbaum A, Utian W, et al. *Low dose of transdermal estradiol gel for the treatment of symptomatic postmenopausal women*. Obstet Gynecol. 2007; (109)3:588-96.]

Common side effects include breast tenderness (9%), metrorrhagia (6%), nasopharyngitis (14%), and URI (8%). Other side effects include nausea, increased blood pressure, hypothyroidism, photosensitivity, and fluid retention. As Elestrin is an estrogen product, similar contraindications exist that are present with other estrogen formulations, including increased risks of endometrial cancer, cardiovascular disease, and blood clots. Sunscreen should not be applied before use or until 30 minutes after Elestrin application, as it increases the absorption of Elestrin. Retail cost for Elestrin runs \$134.99 for one tube, while EstroGel, a similar product approved in 2004, runs \$99.37 for a 93 gram tube. A one month supply (15ml) of an estradiol cream similar in strength to both products costs \$33.73 through a local compounding pharmacy (NuCara), so you may save money if you check with your local pharmacist first.

This issue authored by:

Jim Hoehns, Pharm.D., BCPS, Northeast Iowa Family Medicine Residency, Waterloo, Iowa. Fellow contributors are: Kristi Kavanaugh, Pharm.D., Jennifer Goings, and Jessica Eveleth



## **Vitamin E – An Update**

Many people continue to take Vitamin E supplements in the belief that it will prevent various chronic diseases. Vitamin E is the most widely used vitamin in the U.S., with 22% of adults greater than 55 years of age reporting daily use. However, recent studies have reported no benefit, and the possibility for harm with “high” dose ( $\geq 400$  IU/day) Vitamin E use.

A 2005 meta-analysis (Ann Intern Med 2005;142:37-46) of Vitamin E use reported a significant dose-dependent relationship between vitamin E use and all-cause mortality (RR 1.04 (1.01-1.07) for dosages  $\geq 400$  IU daily). Mortality increased for dosages  $>150$  IU/day. The authors felt that use of Vitamin E supplements should be discouraged pending proof of efficacy.

The 2005 report from the Women’s Health Study (JAMA 2005;294:56-65) reported no effect of Vitamin E 600 IU every other day on preventing major cardiovascular events or total mortality in women. However, they did note a significant 22% reduction in cardiovascular mortality, largely attributable to fewer sudden deaths. The researchers felt their data do not support recommending Vitamin E supplementation for cardiovascular disease or cancer prevention.

Most recently, another meta-analysis of primary and secondary prevention trials (JAMA 2007;297:842-57) observed a small, but significant, 4% increase in total mortality with Vitamin E supplement use.

Considering these recent studies, it seems the message to patients should be that Vitamin E won’t help for cardiovascular disease prevention, and may even be associated with some increased risks.

## **New Dietary Supplement Promoted to Pregnant and Nursing Moms**

Expecta Lipil DHA, by Mead Johnson, is a new 200mg capsule dietary supplement for pregnant and nursing moms. Expecta Lipil DHA is a docosahexaenoic acid (DHA) supplement to be taken once daily throughout pregnancy and nursing. DHA is an omega-3 fatty acid found primarily in seafood that has been associated with improved brain, nervous system, and retinal fetal development and function. Animal studies have shown that DHA promotes the development of hippocampal neurons in vitro by increasing neurite extension and branching<sup>2</sup>. As it has been long recommended for pregnant women to avoid seafood products due to a higher risk of mercury toxicity, the advent of a safer alternative to obtain DHA is appealing. One long-term observational study in England showed that maternal consumption of 340mg per week of DHA-containing seafood actually provided beneficial effects on child development via measurement of intelligence quotient tests.<sup>1</sup> Expecta is made from a non-fish source derived from

This issue authored by:

Jim Hoehns, Pharm.D., BCPS, Northeast Iowa Family Medicine Residency, Waterloo, Iowa. Fellow contributors are: Kristi Kavanaugh, Pharm.D., Jennifer Goings, and Jessica Eveleth



Crypthecodinium cohnii oil, which contains the only DHA source that is accepted as Generally Recognized as Safe (GRAS) for use in infant formula. (Food and Drug Administration. Agency Response Letter. GRAS Notice Nos. GRN000041. 05-27-2001 and GRN000080. 12-11-2001.)

There is little primary literature available to support the use of this product in the pregnant and nursing population. There are no guidelines set by the FDA or the American College of Obstetrics and Gynecology regarding daily intake of DHA. However, a panel of experts on lipid nutrition (ISSFAL) has recommended DHA intake of 300mg per day for pregnant and nursing mothers. The manufacturer does not recommend a specific start time for Expecta, but they do point to studies that show DHA is most important to baby's growth in the third trimester through 18 months.

A randomized trial (N=291) of pregnant women taking 33-133 grams of DHA (through egg intake) during the 3<sup>rd</sup> trimester showed increased gestational duration (6 days  $\pm$  2.3 days) which may improve fetal growth<sup>3</sup>. No safety concerns were noted from this study.

<sup>1</sup>Hibbeln JR, Davis JM, Steer C, et al. *Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study*. Lancet. 2007;369; 578-85.

<sup>2</sup>Calderon F, Kim HY. *Docosahexaenoic acid promotes neurite growth in hippocampal neurons*. J Neurochem. 2004;(90); 979-88.

<sup>3</sup>Smuts CM, Huang M, Mundy D. *A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy*. American Journal of Obstetrics and Gynecology. 2003; (101); 469-79.

## Zelnorm – it's back...but via restricted use

Novartis removed Zelnorm (tegaserod maleate) from the market in March 2007 when a new safety analysis (involving over 18,000 patients) identified it was associated with a higher risk of MI, stroke, and unstable angina compared to placebo. Zelnorm is a prescription drug approved for short term treatment of women with irritable bowel syndrome with constipation and for patients younger than 65 years with chronic constipation.

Just recently, the FDA announced it is allowing the restricted use of Zelnorm under a treatment IND protocol to treat women with irritable bowel syndrome with constipation and chronic idiopathic constipation in women younger than 55 who meet specific guidelines. Patients must have no known or pre-existing heart problems. Patients will have to sign an informed consent form prior to receiving the drug.

Physicians who have patients that may be interested should contact Novartis at 888-669-6682 or 866-248-1348.

This issue authored by:

Jim Hoehns, Pharm.D., BCPS, Northeast Iowa Family Medicine Residency, Waterloo, Iowa. Fellow contributors are: Kristi Kavanaugh, Pharm.D., Jennifer Goings, and Jessica Eveleth



## SMOKING CESSATION GROUP CLINIC

The Smoking Cessation Group Clinic continues to be available to assist patients in smoking cessation. A clinical pharmacist leads the clinic to provide a well-rounded approach to help people stop smoking. The next two clinics start on September 11<sup>th</sup> and November 6<sup>th</sup>.

- Each group consists of six sessions held over the period of eight weeks.
- Each session will meet over the noon hour on Tuesdays.
- There is currently no charge to participate.
- Sessions are held in Counseling and Health Promotion Services in the Family Care Center.
- To participate in this clinic, the patient must be older than 18, smoke daily, and be willing to quit smoking within the first 30 days of the clinic.

To request this service, an electronic consult form is available in IPR as an e-Order. The order is titled: Smoking Cessation Group Clinic Consult and can be found in the FCC Family Practice and Master folders.

Questions may be directed to Ann Philbrick at 6-4712 or 5527.

This issue authored by:

Jim Hoehns, Pharm.D., BCPS, Northeast Iowa Family Medicine Residency, Waterloo, Iowa. Fellow contributors are: Kristi Kavanaugh, Pharm.D., Jennifer Goings, and Jessica Eveleth