

# INSIGHT

FEBRUARY 2008

The Vytorin Controversy	1
New Brand Drugs	2
New Generic Drugs	3
Zyrtec and Zyrtec-D	3
Public Health Advisory	4

## The Vytorin<sup>®</sup> Controversy — Are Two Drugs Really Better Than One?

Cholesterol disorders are a common medical condition that are increasing in prevalence in the United States. Currently, an estimated 106.7 million adults have total blood cholesterol levels greater than 200mg/dl, putting them at risk for coronary heart disease.<sup>1</sup> Medications are commonly used to help decrease cholesterol levels.

Recently, there has been some controversy surrounding the cholesterol drug Vytorin<sup>®</sup>, which is a combination of ezetimibe and simvastatin. Ezetimibe, which is also available as brand name Zetia<sup>®</sup>, helps to decrease blood cholesterol by inhibiting the absorption of dietary cholesterol in the small intestine.<sup>2</sup> Simvastatin is available generically and as the brand-name version Zocor<sup>®</sup>. Simvastatin belongs to the class of cholesterol medications referred to as statins and works by interfering with the production of cholesterol in the body.<sup>3</sup>

The Vytorin controversy stems from the recent release of a summary of results from the ENHANCE trial. The ENHANCE trial involved 720 patients with a rare cholesterol disorder (known as heterozygous familial hypercholesterolemia) and tested Vytorin (the combination of ezetimibe/simvastatin) versus simvastatin alone for a period of two years. The primary goal of the study was to measure the size of the blood vessels at several sites in the carotid arteries to see if there was a difference in progression of carotid atherosclerosis between the ezetimibe/simvastatin group and the simvastatin group. The results showed there was no statistical difference in the size of the blood vessels between the two groups.<sup>4</sup> Another point of controversy involved the delay in releasing the results from the ENHANCE trial. The trial was completed in April 2006 and the summary of results has only recently been released.<sup>5</sup>

It is important to keep in mind that these are results from just one study. Several studies already exist

involving Vytorin and there are a few studies currently in progress. Previous studies have shown Vytorin to be more effective than simvastatin alone in reducing LDL cholesterol. One study reported an average decrease in LDL cholesterol of 53 percent with Vytorin.<sup>6</sup>

It is important for patients not to discontinue treatment with Vytorin without first speaking with their doctor. Patients are encouraged to speak with their doctor regarding any questions or concerns. There are currently several medications available on the FutureScripts<sup>®</sup> formulary to treat cholesterol disorders. These include generic medications such as simvastatin, pravastatin, and lovastatin, which are available at the lowest copay to members.

### References:

<sup>1</sup> American Heart Association website [Cholesterol statistics]. Available at [www.americanheart.org](http://www.americanheart.org). Accessed January 16, 2008.

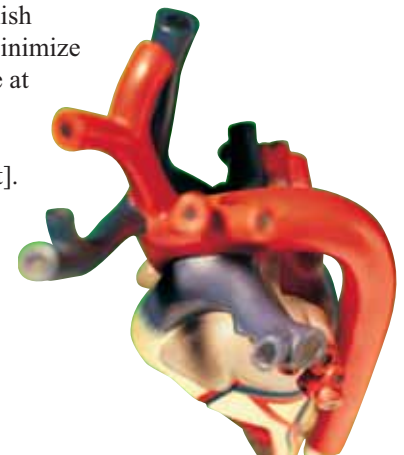
<sup>2</sup> Micromedex website [Zetia and Vytorin]. Available at [www.micromedex.com](http://www.micromedex.com). Accessed January 16, 2008.

<sup>3</sup> Facts and Comparisons website [Zetia and Vytorin]. Available at [www.factsandcomparisons.com](http://www.factsandcomparisons.com). Accessed January 16, 2008.

<sup>4</sup> Merck website. Available at [www.merck.com](http://www.merck.com). Accessed January 16, 2008.

<sup>5</sup> Can ENHANCE diminish Vytorin? Schering, Merck Minimize Trial's importance. Available at [www.thepinksheet.com](http://www.thepinksheet.com). Accessed January 17, 2008.

<sup>6</sup> Vytorin [package insert]. North Wales, PA: Merck/Schering-Plough; 2007.



## New Brand Drugs

The FDA has approved **CaloMist™ (cyanocobalamin 25mcg/0.1ml) Nasal Spray** for maintenance of vitamin B12 concentrations after normalization with intramuscular vitamin B12 therapy. It is approved specifically for vitamin B12-deficient patients with no nervous system involvement. CaloMist is the product of Fleming & Co., St. Louis, MO.

Daiichi Sankyo in Parsippany, NJ, has received FDA approval for the combination agent **Azor™ (amlodipine besylate and olmesartan medoxomil)** as a once-daily oral tablet containing both a calcium-channel blocker and an angiotensin-receptor blocker. Azor can be used alone or in combination with other drugs for the treatment of hypertension, but is not indicated for initial blood hypertension treatment. Tablets are available in four strengths (amlodipine/olmesartan medoxomil): 5/20mg, 10/20mg, 5/40mg, and 10/40mg.

**Isentress™ (raltegravir)** received accelerated approval from the FDA as the first in a new class of antiretrovirals called integrase inhibitors. Isentress is indicated for use in combination with other antiretrovirals for the treatment of HIV in treatment-experienced patients with evidence of resistance to multiple agents. Isentress (available as 400mg tablets) is produced by Merck, Whitehouse, NJ.

The FDA has approved **Ixempra™ (ixabepilone)** as a monotherapy and in combination with capecitabine (Xeloda®) for patients with metastatic or locally advanced breast cancer. Ixabepilone is the first in a new class of chemotherapy agents called epothilones and is produced by Bristol Myers Squibb, Princeton, NJ. Ixempra is available in 15mg

and 45 mg vials to be used as an intravenous product.

**Doribax™ (doripenem for injection)**, a broad-spectrum antibiotic, was approved by the FDA for the treatment of complicated intra-abdominal and complicated urinary tract infections. Doripenem is a member of the carbapenem family of antibiotics. Doribax will be available in 500mg vials of sterile doripenem powder and is being marketed by Ortho-McNeil, Titusville, NJ.

**Tasigna® (nilotinib capsules)** has been granted an accelerated approval for the treatment of Philadelphia chromosome-positive chronic myelogenous leukemia (CML) in adult patients resistant or intolerant to prior therapy that included imatinib (Gleevec®). Tasigna is produced by Novartis, East Hanover, NJ, and is available as 200mg capsules.

**Flector® (diclofenac transdermal 1.3% patches)** was approved and indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions. Flector is produced by Alpharma, Baltimore, MD.

The FDA has approved the combination product **Combigan™ (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%**. It is an alpha adrenergic receptor agonist/beta adrenergic receptor inhibitor combination and is indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension who require adjunctive or replacement therapy due to inadequately controlled IOP. Combigan is produced by Allergan Inc., Irvine, CA.

**Kuvan™ (sapropterin dihydrochloride)**, a synthetic form of tetrahydrobiopterin, was approved

by the FDA and is indicated to reduce blood phenylalanine levels in patients with hyperphenylalaninemia caused by tetrahydrobiopterin-(BH4-) responsive phenylketonuria. Kuvan is produced by BioMarin Pharmaceuticals Inc., Novato, CA and is to be used in conjunction with a phenylalanine-restricted diet.

Beta-blocker **Bystolic™ (nebivolol)**, from both Forest Laboratories, New York, NY, and Mylan, Inc., Morgantown, WV, has been approved by the FDA for the treatment of hypertension. The new molecular entity is orally available as **2.5mg, 5mg, and 10mg** tablets and can be used alone or in combination with other antihypertensive agents.

The FDA has approved Nycomed's **Alvesco® (ciclesonide)** inhalation aerosol for the maintenance treatment of asthma and as prophylactic therapy in patients 12 years of age and older. The medication is an inhaled corticosteroid with novel release and distribution properties. Nycomed, which is part of GE Healthcare, is located in Waukesha, WI.

### DRUGS MENTIONED IN ARTICLE

Alvesco®  
Azor™  
Bystolic™  
CaloMist™  
Combigan™  
Doribax™  
Flector®  
Isentress™  
Ixempra™  
Kuvan™  
Tasigna®

## New Generic Drugs

Two generic manufacturers — Roxane Laboratories, Columbus, Ohio, and Caraco Pharmaceutical Laboratories, Detroit, MI — have been granted FDA approval for **oxcarbazepine tablets in 150mg, 300mg, and 600mg** strengths. As a generic alternative to Novartis' antiepileptic drug Trileptal®, oxcarbazepine is indicated as monotherapy or adjunctive therapy in the treatment of partial seizures in adults and in children four years of age and older.

Two generic manufacturers — Barr Laboratories, Inc., Woodcliff, NJ, and Watson Laboratories, Inc., Corona, CA — have been granted FDA approval for **Tilia Fe** and **Tri-Legest Fe**. They are generic alternatives to a triphasic oral contraceptive, Warner Chilcott's Estrostep® FE, and are indicated for prevention of pregnancy and treatment of acne vulgaris in females of at least 15 years of age.

Both Watson and Barr Pharmaceutical have received FDA approval for generic formulations of Forest Laboratories Inc.'s Combunox®. The **oxycodone hydrochloride 5mg and ibuprofen 400mg**

combination product is indicated for the short-term (not more than seven days) management of acute, moderate to severe pain.

Cobalt Pharmaceuticals, Bonita Springs, FL, launched **ramipril capsules 2.5mg, 5mg, and 10mg**, the generic formulations of Altace after having received the FDA approval. Altace®, manufactured by King Pharmaceuticals, belongs to class of drugs known as the ace inhibitors. It has the indication to treat hypertension, for reduction in risk of myocardial infarction, stroke, and death from cardiovascular causes, and for decrease of mortality in patients with heart failure post myocardial infarction.

Barr Laboratories, Inc., Woodcliff, NJ, has received approval

from the FDA for the generic version of Roche Laboratories Inc.'s Kytril® tablets, 1mg. **Granisetron hydrochloride tablets, 1mg** are indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin and nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

The FDA has approved Mylan Pharmaceuticals, Roxane Laboratories, and Watson Pharma's ANDAs for **balsalazide disodium 750mg capsules**, indicated for the treatment of mildly to moderately active ulcerative colitis. The medication is the generic equivalent of Colazal® by Salix Pharmaceuticals.



## Zyrtec® and Zyrtec-D 12 Hour® Available Over-the-Counter

Allergies affect as many as 40 to 50 million people in the United States.<sup>1</sup> One of the commonly prescribed allergy medications, Zyrtec® (cetirizine HCl) has recently been approved for nonprescription use.<sup>2</sup> Zyrtec is an antihistamine that relieves symptoms caused by allergy triggers such as dust, mold, pet dander, and tree pollen. Zyrtec also relieves itching due to hives. Zyrtec is a once-a-day medication, while Zyrtec-D 12 Hour® (cetirizine HCl/pseudoephedrine HCl) pro-

vides the added benefit of relieving nasal congestion. Some of the most common side effects include drowsiness, fatigue, and dry mouth. Zyrtec is approved in 5mg and 10mg tablets, 5mg and 10mg chewable tablets, and 1mg/mL syrup. Zyrtec-D 12 Hour is approved as a tablet<sup>3</sup>. As with all over-the-counter medications, consumers should carefully follow all directions on the label.

### References:

<sup>1</sup> American Academy of Allergy,

Asthma and Immunology (AAAAI). The Allergy Report: Science Based Findings on the Diagnosis & Treatment of Allergic Disorders, 1996-2001.

<sup>2</sup> FDA News: FDA Approves Zyrtec for Nonprescription Use in Adults and Children. 11/21/07. Available at: [www.fda.gov/bbs/topics/NEWS/2007/NEW01750.html](http://www.fda.gov/bbs/topics/NEWS/2007/NEW01750.html). Accessed January 18, 2008.

<sup>3</sup> Zyrtec Press Release. Available at: [www.zyrtecotc.com/econsumer/zyrtec/images/pdf/zyrtec\\_fda.pdf](http://www.zyrtecotc.com/econsumer/zyrtec/images/pdf/zyrtec_fda.pdf). Accessed January 18, 2008.

# FDA Public Health Advisory

## Recommendations Regarding Use of Over-the-Counter Cough and Cold Products

The U.S. Food and Drug Administration (FDA) issued a Public Health Advisory on January 17, 2008, after completing its review regarding the safety of over-the-counter (OTC) cough and cold medications in infants and children 2 years of age and younger. The FDA recommended these medicines not be used in infants and children 2 years of age and younger due to the potential for serious and life-threatening side effects. The advisory does not contain a



recommendation for the use of these medicines in children ages 2 through 11. The review of information concerning OTC cough and cold products in children ages 2 through 11 years is ongoing and will be communicated to the public once completed.<sup>1</sup>

Until the review is concluded, the FDA has provided guidance for the use of OTC cough and cold medicines in children 2 through 11 years of age. First, the FDA

reminds everyone that OTC cough and cold medicines only relieve symptoms to make children feel more comfortable while sick.

### **The FDA recommends that OTC medications should not be used in children 2 years of age and younger due for potential serious and life-threatening side effects.**

These medicines do not treat the cause of the symptoms or shorten the length of time that children are sick. When using these medicines in children 2 through 11 years of age, check the “Drug Facts” label to learn what active ingredients are in the medicine and the correct dosing directions.

OTC cough and cold medicines often contain more than one active ingredient (for example, an antihistamine, a cough suppressant, a decongestant, an expectorant, or a pain reliever). If a child receives two medicines that have the same or similar “active ingredients,” the child may get too much of an ingredient, which may harm the child. In conjunction with following the dosing directions, be sure

to use measuring spoons or cups accompanying the particular medicine or those made specifically for measuring drugs. Never

use common household spoons to measure these products. Finally, contact a physician, pharmacist, or other health care professional if you have any questions about using cough and cold medicines in children 2 years of age and older.<sup>2</sup>

#### *References:*

<sup>1</sup> FDA Releases Recommendations Regarding Use of Over-the-Counter Cough and Cold Products. FDA News. January 17, 2008. Found at: [www.fda.gov/bbs/topics/NEWS/2008/NEW01778.html](http://www.fda.gov/bbs/topics/NEWS/2008/NEW01778.html). Accessed January 17, 2008.

<sup>2</sup> U.S. Food and Drug Administration. Public Health Advisory Nonprescription Cough and Cold Medicine Use in Children. January 17, 2008. Found at: [www.fda.gov/cder/drug/advisory/cough\\_cold\\_2008.htm](http://www.fda.gov/cder/drug/advisory/cough_cold_2008.htm). Accessed January 17, 2008.

## INSIGHT STAFF

MANAGING EDITOR - CIBBEY ABRAHAM, PHARMD

CONTRIBUTING EDITOR - CHARLES THOMAS

CONTRIBUTING WRITERS - PATRICK DEHORATIUS, PHARMD  
JOMY JOSEPH, PHARMD  
DIANE KARPETIS, PHARMD  
JOCELYN SCOUT, PHARMD