Family Medicine Clinical Pharmacy Forum
Vol. 4, Issue 1 (January/February 2008)

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

New Drug for Hypertension: Nebivolol (Bystolic™)

Nebivolol hydrochloride (Bystolic™) was recently approved by the FDA for treatment of hypertension. Nebivolol is a beta-1 selective blocker at doses of ≤10 mg per day. Potential advantages of nebivolol over other beta-blockers are decreased vascular peripheral resistance, improved left ventricular performance, and a lack of an acute decrease in cardiac output upon initiation.

In randomized clinical trials, the safety and efficacy of nebivolol for patients with mild to moderate hypertension when used alone and in combination therapy appears to be similar to that of other FDA approved beta-blockers. Although not yet approved for this indication, nebivolol has also been studied in patients with heart failure.

The recommended starting dose of nebivolol is 5 mg daily and may be increased every 2 weeks to a maximum of 40 mg daily. The most common adverse effects reported were headache, dizziness and diarrhea. Average cost for a thirty-day supply of nebivolol is $55.99 and $56.99 for the 5 and 10 mg tablets, respectively.

For more information on nebivolol, please refer to www.fda.gov/bbs/topics/NEWS/2007/NEW01757.html.

Authored by:
Kristin Horning, Pharm.D., BCPS, East Des Moines Family Care Center, Des Moines, IA.
(Special thanks this edition also to contributors: Ellen Sievers and Michelle Wannemuehler Pharm.D. candidates at The University of Iowa College of Pharmacy.)

New drug for allergy symptoms: Levocetirizine (Xyzal®)

Levocetirizine (Xyzal®), a new second generation oral antihistamine, has been FDA-approved for idiopathic urticaria, perennial allergic rhinitis with seasonal variation, and seasonal allergic rhinitis. Levocetirizine is the R-enantiomer of cetirizine (Zyrtec®).

Although levocetirizine is promoted as having a faster onset and longer duration of action than cetirizine, these differences are not clinically significant (see Table 1). In addition, current head to head studies show similar control of most allergy symptoms with these two agents.

The recommended dose of levocetirizine is 5 mg daily for patients ages 12 and older and 2.5 mg daily for children ages 6-11. The side effect profiles of levocetirizine and cetirizine are similar and include somnolence, fatigue, muscle weakness and dry mouth.

Overall, levocetirizine should be reserved for those patients who have failed other less expensive antihistamines. Also keep in mind that cetirizine is expected to be available **over-the-counter** by the end of January 2008.

Table 1. Comparison of levocetirizine and cetirizine.

	Levocetirizine (Xyzal®)	Cetirizine (Zyrtec®))
Onset of action	0.5-1 hr	1-1.5 hrs
Duration of action	24 hrs	24 hrs
Age approved	>6 **years**	>6 **months**
Formulations	Tablet	Liquid, tablet

New Drug: Xyzal (levocetirizine). *Pharmacist's Letter/Prescriber's Letter* 2007;9:230910.
Micromedex. Xyzal. http://www.thomsonhc.com. Accessed January 2008.
Product information for Xyzal. Sanofi-Aventis. Bridgewater, NJ 08807. January 2008.

New drug: Doripenem (Doribax™) for complicated infections

Doripenem is a new member of the antipseudomonal carbapenem antibiotic class. While its pathogen coverage is comparable to imipenem (Primaxin) and meropenem (Merrem), Doripenem has slightly greater activity against *Pseudomonas aeruginosa* and has been shown to be effective against pathogens resistant to these 2 agents.

Doripenem is FDA-approved for treatment of **complicated urinary tract infections** including pyelonephritis caused by *E. coli*, *Klebsiella pneumoniae*, *Proteus mirabilis, Pseudomonas aeruginosa, or Acinetobactor baumannii*; **complicated intra-abdominal infections** caused by *E.coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides spp., Streptococcus intermedius, S. constellatus, or Peptostreptococcus micros*. FDA-approval for treatment of nosocomial pneumonia is being pursued.

The recommended dose of doripenem is 500 mg every 8 hours. The most common side effects reported are headache, nausea, diarrhea, rash, and phlebitis. Drug

Authored by:
Kristin Horning, Pharm.D., BCPS, East Des Moines Family Care Center, Des Moines, IA.
(Special thanks this edition also to contributors: Ellen Sievers and Michelle Wannemuehler Pharm.D. candidates at The University of Iowa College of Pharmacy.)

interactions include probenecid (decreases doripenem excretion) and valproic acid (doripenem decreases plasma levels). Although seizures have been reported with other carbapenems, doripenem has not shown convulsive activity in animal models. However, obtaining plasma levels of anticonvulsants is still recommended until further studies confirm these results. The average wholesale price is $138 per day.

Comparison of carbapenem antibiotics. *Pharmacist's Letter/Prescriber's Letter* 2007;23(12):231205.
Product information for Doribax. Ortho-McNeil Pharmaceutical, Inc. Raritan, NJ 08869. January 2008.
Horiuchi M., Kimura M., Tokumura M., et. al. Absence of convulsive liability of doripenem, a new carbopenem antibiotic, in comparison with beta-lactam antibiotics. *Toxicology*. 2006; 222: 114-124.

Updated guidelines: American Diabetes Association Standards of Care 2008

Recent changes to the "Standards of Medical Care in Diabetes" issued by the American Diabetes Association were recently published January 2008. Some key revisions are listed below:

- Testing for pre-diabetes in asymptomatic patients (previously screening for diabetes):
  - Consider testing adults of **any age** who are either overweight or obese and have additional risk factors for diabetes

- For prevention or delay of type 2 diabetes
  - In addition to lifestyle counseling, **metformin** may be considered in those who have combined impaired fasting glucose and impaired glucose tolerance plus other risk factors (high risk) as well as being obese and under 60 years of age

- Diabetes care in special populations
  - Hypothyroidism
    - Patients with type 1 diabetes should be screened for thyroid peroxidase and thyroglobulin antibodies at diagnosis
    - Thyroid-stimulating hormone (TSH) concentrations should be measured after metabolic rate control has been established and, if normal, they should be rechecked every 1 to 2 years or if the patient develops symptoms of thyroid dysfunction, thyromegaly, or an abnormal growth rate. If TSH levels are abnormal, free T4 levels should then be checked.

To read the full report, visit: http://care.diabetesjournals.org/content/vol31/Supplement_1/
and click on summary of revisions pages S3-S4.

Preliminary results of the ENHANCE trial question medication efficacy

The recently released preliminary results of the ENHANCE study have questioned the efficacy of simvastatin/ezetimbe (Vytorin) and ezetimibe (Zetia®) for preventing

Authored by:
Kristin Horning, Pharm.D., BCPS, East Des Moines Family Care Center, Des Moines, IA.
(Special thanks this edition also to contributors: Ellen Sievers and Michelle Wannemuehler Pharm.D. candidates at The University of Iowa College of Pharmacy.)

atherosclerosis. The ENHANCE study was conducted in patients with heterozygous familial hyperlipidemia, a rare genetic form that affects 0.2% of population. Patients were randomized to receive ezetimibe/simvastatin (Vytorin) 10/80 mg or simvastatin (Zocor) 80 mg, and had **baseline LDL cholesterol levels were 318 and 319 mg/dL, respectively.** After two years, there was no significant difference in the primary end point, mean change in the intima-media thickness (IMT) measured at three sites in the carotid arteries. While this **surrogate marker** for atherosclerosis was not different between the two groups, there was a difference in the LDL-lowering effect between patients receiving ezetimibe/simvastatin and simvastatin alone (58% vs. 41%, $p<0.01$). The LDL-lowering benefit of adding ezetimibe to simvastatin is similar to that observed in previous trials.

Since other studies have shown that high-dose statins may delay the progression of atherosclerosis, the role of Vytorin and Zetia® is now being questioned. However, it is important to note that the results of this study cannot be compared to those evaluating high-dose statins due to the high baseline LDL levels among the patients in the ENHANCE trial. Also, this study's findings are limited by the fact that it is not an outcomes based trial. At this point, it is appropriate to encourage patients to continue Vytorin and Zetia®, as the results of the ENHANCE trial likely do not warrant a change in current clinical practice.

For more information, refer to the ACC Statement on ENHANCE.

FDA Advisory statement: New warnings issued for varenicline (Chantix™)

The FDA recently issued a public health advisory statement on possible neuropsychiatric side effects in patients taking varenicline (Chantix™). Concerns regarding these effects first surfaced in November 2007 after reports of behavior changes, depressed mood, and suicidal ideations. Although these symptoms may occur as a result of nicotine withdrawal, some patients who had not yet completely discontinued smoking also experienced these symptoms. The product information for varenicline has been updated to include these warnings.

Based on these reports, the FDA now recommends the following:

- Healthcare professionals should monitor patients taking varenicline for behavior and mood changes.
- Patients taking varenicline should contact their doctors if they experience behavior or mood changes.
- Patients should use caution when driving or operating machinery until they know how quitting smoking with varenicline may affect them.

For more information, please refer to the FDA advisory for health care professionals.

Authored by:
Kristin Horning, Pharm.D., BCPS, East Des Moines Family Care Center, Des Moines, IA.
(Special thanks this edition also to contributors: Ellen Sievers and Michelle Wannemuehler Pharm.D. candidates at The University of Iowa College of Pharmacy.)

Clinical Pearl: Nitrofurantoin duration for uncomplicated UTI

JW is a 22 year old female who presents to the clinic with complaints of dysuria, urgency, and increased frequency for the past 3 days. She is allergic to sulfa. You are hesitant to prescribe nitrofurantoin (Macrobid) because of the 7 day length of treatment. Is a shorten regimen beneficial?

Recent studies have determined that nitrofurantoin 100 mg BID for **5 days** is as effective as 3 days of trimethoprim/sulfamethoxazole (TMP/SMX) for uncomplicated UTI. Cure rates were 84% vs. 79% for nitrofurantoin and TMP/SMX, respectively. Therefore, the shorter course of nitrofurantoin is a reasonable second-line treatment option for uncomplicated UTI in patients allergic to sulfa or in areas with high resistance to TMP/SMX.

Authored by:
Kristin Horning, Pharm.D., BCPS, East Des Moines Family Care Center, Des Moines, IA.
(Special thanks this edition also to contributors: Ellen Sievers and Michelle Wannemuehler Pharm.D. candidates at The University of Iowa College of Pharmacy.)