

## Health Matters January 2008; Volume 2, Issue 6

### FDA approves 49 new drugs and biologicals in 2007

The Food and Drug Administration (FDA) approved 49 new drugs or biologicals during 2007, with 22 of them being considered “new molecular entities” or “significant new biologicals”. A listing of these medications is included in the table below:

Brand	Generic	Indication/Use
	Influenza vaccine, H5N1	Vaccine against H5N1 influenza vaccine (avian or bird flu). Not commercially available.
ACAM 2000	Smallpox (vaccinia)	Live vaccine against smallpox.
Afluria	Influenza vaccine	Inactivated influenza virus vaccine.
Altabax	Retapamulin	Topical antibiotic for impetigo.
Bystolic	Nebivolol	Beta-blocker for hypertension.
Ceptroin	Protein C	Prevention/treatment of blood clots in patients with congenital deficiency.
Doribax	Doripenem	Antibiotic for intra-abdominal infections and UTIs.
Evithrom	Thrombin, topical (human)	Protein to help control surgical bleeding.
Isentress	Raltegravir	Integrase inhibitor for HIV-1.
Ixempra	Ixabepilone	Metastatic/advanced breast cancer.
Kuvan	Sapropterin	Enzyme enhancer for phenylketonuria (PKU).
Letairis	Ambrisentan	Endothelin receptor antagonist for pulmonary arterial hypertension.
Mircera	Methoxy-polyethylene glycol-epoetin beta	Anemia associated with chronic renal failure.
Neupro	Rotigotine	Transdermal patch for Parkinson’s Disease.
Selzentry	Maraviroc	Antiretroviral for HIV-1.
Soliris	Eculizumab	Anemia in patients with paroxysmal nocturnal hemoglobinuria.
Somatuline	Lanreotide	Depot injection for acromegaly.
Tasigna	Nilotinib	Kinase inhibitor for chronic myelogenous leukemia.
Tekturna	Aliskiren	Direct renin inhibitor for hypertension.
Torisel	Temsirolimus	Kinase inhibitor for advanced renal cell carcinoma.
Tykerb	Lapatinib	Kinase inhibitor used with capecitabine for advanced breast cancer.
Vyvanse	Lisdexamfetamine	Prodrug of dextroamphetamine for ADHD.

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In addition, 28 significant new dosage forms were approved in 2007. New dosage forms are unique formulations of previously approved products. Included in this group were combination products, transdermal preparations and novel administration routes.

For more information on the drugs and biologicals approved in 2007, please contact the Center for Drug Information & Evidence-Based Practice at 280-5100 or [druginfo@creighton.edu](mailto:druginfo@creighton.edu).

#### References:

1. U.S. Food and Drug Administration Center for Drug Evaluation and Research. Accessed at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/> January 3, 2008.
2. New drugs approved by the FDA in 2007. Pharmacist’s Letter/Prescriber’s Letter 2007.

## **Short-term nitrofurantoin effective for uncomplicated cystitis**

Currently, trimethoprim-sulfamethoxazole (TMP-SMX) is widely accepted as the treatment of choice for uncomplicated acute cystitis. The Infectious Diseases Society of America (IDSA) recommends three days of TMP-SMX therapy for uncomplicated cystitis in non-pregnant women. Fluoroquinolone therapy offers an alternative to TMP-SMX, and also offers the advantage of a three-day regimen. However, the development of resistance to these therapies is becoming a greater concern.

Nitrofurantoin also provides an alternative therapy. Although traditional treatment for acute uncomplicated cystitis has been at least seven days of therapy, a recent study published in the Archives of Internal Medicine investigated a five-day course of nitrofurantoin for treatment of acute uncomplicated cystitis in women.

An open-label study of 315 women (ages 18-45 with confirmed bladder infections and acute cystitis symptoms) randomized participants to either TMP-SMX one double-strength (DS) tablet twice daily for three days or to nitrofurantoin (Macrobid™) 100mg orally twice daily for five days. The primary outcome was clinical cure rate 30 days post-treatment. Participants with persistent or new urinary tract infection symptoms, or pyelonephritis symptoms, were considered clinical treatment failures. Secondary outcomes assessed clinical and microbiological cures at 5-9 days post-treatment. There was no significant difference shown in clinical cure rate for the TMP-SMX group (79%) compared to the nitrofurantoin group (84%). Clinical and microbiological rates measured were also not found to be significantly different between the two treatment arms.



The authors concluded that a five-day course of nitrofurantoin is as effective as a three-day course of TMP-SMX, and offers an alternative for treatment of acute uncomplicated cystitis in women if allergy or resistance to TMP-SMX is a concern. Limitations to the study include the open-label design, and concerns of external validity to the general population. The study population was composed primarily of students who were highly compliant to therapy, which could limit the applicability to the population at large. Also of note is the fact the twice daily preparation of nitrofurantoin (Macrobid™) was used in the study. Extrapolation to the four-time daily preparation (Macrochantin) may not yield comparable results.

### References:

1. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE for the Infectious Diseases Society of America. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Clin Inf Dis 1999;29:745-58.
2. Gupta K, Hooton TM, Roberts PL, Stamm WE. Short course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. Arch Int Med 2007;167:2207-12.
3. Tom WC. Nitrofurantoin (Macrobid) shortened treatment duration for acute uncomplicated cystitis. Pharmacist's Letter/Prescriber's Letter 2008;24(1):240107.

## **FDA finds no evidence of PPI-related cardiac events**

Based on data submitted to the Food and Drug Administration (FDA) in May 2007 from long-term studies of omeprazole (Prilosec™) and esomeprazole (Nexium™), a comprehensive scientific review was undertaken to determine any relationship between long-term use of proton pump inhibitors and the risk of developing cardiovascular events.

The FDA reviewed a 14 year European study of severe gastroesophageal reflux disease (GERD) patients. 298 patients were randomly assigned to either omeprazole or anti-reflux surgery. More than 50% of patients dropped out of the study prior to completion of the protocol. Each patient enrolled in the study, including those failing to complete, were reviewed for potential safety issues. Although a review of the raw data showed a larger number of the cardiac-related adverse effects in the omeprazole group than the surgery group, further analysis revealed different baseline characteristics between the groups that could have contributed to these outcomes. Surgery patients were more likely to be young and healthy, some patients randomized to the surgery arm did not actually undergo a procedure, and some patients actually received both treatments. These limitations make it difficult to conclude any association between omeprazole treatment and cardiovascular effects.



A second European study comparing esomeprazole to surgery randomized 554 severe GERD patients to either esomeprazole or laparoscopic surgery. They were followed for 5 years, and although initial data suggested an increase in cardiovascular risk with proton pump inhibitor treatment, further analysis showed similar numbers of cardiovascular events in both treatment groups.

Additional analyses were performed on 14 comparative studies of omeprazole. Although patient follow up data was incomplete, these studies did not suggest an increased risk of heart problems with proton pump inhibitor use.

Based on this comprehensive review, the FDA has concluded that no true cardiovascular effect can be related to long-term proton pump inhibitor use. No labeling changes are being recommended at this time.

### References:

1. U.S. Food and Drug Administration. FDA's safety reviews of prilosec and nexium find no evidence of increased rates of cardiac events. December 10, 2007. Available from <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01754.html>, accessed 1/3/08.
2. U.S. Food and Drug Administration. Follow-up to the August 9, 2007, communication about the ongoing safety review of omeprazole and esomeprazole. December 10, 2007. Available from [http://www.fda.gov/cder/drug/early\\_comm/omeprazole\\_esomeprazole\\_update.htm](http://www.fda.gov/cder/drug/early_comm/omeprazole_esomeprazole_update.htm), accessed 1/3/08.



### News Clips

- The FDA has granted approval to Dexcel Pharma Technologies Ltd for sale of over-the-counter omeprazole tablets. Currently, Prilosec OTC is the only approved OTC proton pump inhibitor. Shipments to pharmacies are expected to begin in the first quarter of 2008.
- The FDA reports that Bayer has recalled diabetes test strips used with its Contour TS Blood Glucose Meter because they may result in inaccurate blood glucose readings of 5 to 17% higher than actual levels. More than 200,000 strips are included in the recall. The recall does not include strips for other Bayer-manufactured blood glucose monitors. Detailed information regarding lot numbers and product codes can be accessed at [www.fda.gov/medwatch/safety/2007/contourTS\\_recall.htm](http://www.fda.gov/medwatch/safety/2007/contourTS_recall.htm)
- The FDA has approved tablet, chewable tablet and syrup formulations of Zyrtec (cetirizine) for non-prescription use. The OTC product is indicated for the temporary relief of symptoms due to hay fever or other respiratory allergies. It is also approved for treatment of itching related to hives in adults and children over the age of 6. Zyrtec-D, containing the antihistamine pseudoephedrine, is also available without a prescription. Zyrtec-D is subject to restrictions in the Combat Methamphetamine Epidemic Act.

## **Effectiveness of antibiotics and nasal steroids for acute maxillary sinusitis**

A recent trial published in the Journal of the American Medical Association investigated the effectiveness of antibiotics and topical steroids in the treatment of acute maxillary sinusitis. The double-blind, randomized, placebo-controlled trial enrolled 240 adults (ages 16 and older) with acute non-recurrent sinusitis. To be included in the study, patients had to have at least two of four clinical features consistent with acute bacterial sinusitis: purulent nasal discharge with unilateral predominance, local pain with unilateral predominance, purulent nasal discharge bilaterally, and pus inside the nose upon inspection. Patients were randomized to one of four groups: *antibiotic + nasal steroid*; *placebo antibiotic + nasal steroid*; *antibiotic + placebo nasal steroid*; or *placebo antibiotic + placebo nasal steroid*.



Active treatment interventions were amoxicillin 500 mg three times daily for 7 days and budesonide 200 mcg in each nostril once daily for 10 days. The primary outcome was the proportion of clinically cured patients at day 10. Clinical cure was measured by self-reported patient diary, and included variables for assessment such as nasal blockage, discharge, face pain, unpleasant taste or smell and headache. Patients were asked to rank each variable with a 7-point Likert scale. Results showed the proportions of patients with symptoms lasting 10 or more days were 29/100 (29%) for amoxicillin and 36/107 (33.6%) for no amoxicillin. (Adj OR 0.99; 95% CI, 0.57-1.73). The proportions of patients with symptoms lasting 10 or more days were 32/102 (31.4%) for topical budesonide versus 33/105 (31.4%) for no budesonide. (Adj OR 0.93; 95% CI, 0.54-1.62).

Based on the results of this study, researchers concluded that among typical acute sinusitis cases, neither antibiotics nor nasal steroids, alone or in combination, were found to be effective in altering the symptom severity, duration or natural history of the condition. However, data do suggest that nasal steroids were significantly more effective in patients presenting with less severe symptoms initially.

### Reference:

1. Williamson IG, Rumbsy K, Bengt S, Moore M, Smith PW, Cross M, et al. Antibiotics and topical nasal steroid for treatment of acute maxillary sinusitis: a randomized controlled trial.



*Best wishes for a successful 2008! Thank you for using the Creighton University Center for Drug Information & Evidence-Based Practice.*

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