

## Health Matters June 2008; Volume 2, Issue 9

### FDA Proposes New Rules on the Labeling of Prescription Drugs for Pregnancy and Lactation by Amy Harris

By June 2010, pregnant and lactating women, as well as their health care providers, could see a major makeover to the labeling of prescription drugs (including biological agents). The U.S. Food and Drug Administration (FDA) has proposed a change in design of the labeling to provide better information about the effects of medicines used during pregnancy and lactation.<sup>1</sup>

The current labeling, dating back to 1979, utilizes a five-letter system which categorizes the risks of drug use during pregnancy and lactation (i.e. A, B, C, D, or X). It has long been criticized by medical experts as being confusing, overly simplistic, and not reflective of newer studies and medical knowledge.<sup>2</sup> In the 1990s, the FDA held public meetings and focus groups to obtain comment on the current labeling from health care professionals and scientific experts.<sup>3</sup>

On May 28, 2008, the FDA announced a proposal to require major changes to the sections of prescription drug labeling concerning pregnancy and lactation. "With this proposal, the FDA's goal is to help women, their physicians, and their pharmacists have better information about the effects of prescription medicines so that pregnant women, nursing mothers, and breastfeeding infants will benefit," says Rear Adm. Sandra Kweder, M.D., Deputy Director of FDA's Office of New Drugs.<sup>2</sup>

There are approximately six million pregnancies in the United States each year, half of which are unplanned, exposing women to drugs before they know they are pregnant. Additionally, women with pre-existing medical conditions, such as asthma, high blood pressure, depression, or diabetes may need to continue to use prescription drugs to treat those conditions during pregnancy.<sup>2</sup>

Under the proposed rule, the letter categories would be replaced with a newly designed format containing the following three sections: Fetal Risk Summary, Clinical Considerations, and Data.<sup>1</sup>

In **Fetal Risk Summary**, known effects of the drug on the fetus would be addressed. If there is risk, it is noted whether the risk is based on information collected from studies on animals or humans.

In **Clinical Considerations**, information would be provided about the effects of the use of a drug if it is taken before a woman knows she is pregnant. Risks of the untreated disease to the mother and the baby, dosing information, and how to address complications would also be covered in this section.

In **Data**, available data used to develop the fetal risk summary would be described in more detail.

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Following a 90-day comment period, the FDA will consider all comments and prepare a final rule. Electronic comments can be submitted via the Federal Documents Management System/eRulemaking portal at [www.regulations.gov](http://www.regulations.gov).<sup>3</sup>

#### References:

1. US FDA proposes new rules on use of Rx drugs during pregnancy, breast feeding. Pharma Marketletter. June 2, 2008.
2. FDA Consumer Health Information. Food and Drug Administration Web site. Available at: <http://www.fda.gov/consumer/updates/pregnancy052808.html>. Accessed June 5, 2008.
3. FDA News page. Food and Drug Administration Web site. Available at: <http://www.fda.gov/bbs/topics/NEWS/2008/NEW01841.html>. Accessed June 5, 2008.

## FDA Approves New Antidepressant

Pristiq (desvenlafaxine), a serotonin/norepinephrine reuptake inhibitor (SNRI) manufactured by Wyeth, has been approved for the treatment of depression. Desvenlafaxine is the major metabolite of venlafaxine (Effexor), a currently available SNRI.

As with many of the newer medications which are structurally related to existing drugs, no head-to-head studies comparing desvenlafaxine to venlafaxine are available. Short-term placebo-controlled trials have shown some benefit in the treatment of major depressive disorder, although studies longer than 8 weeks in length are not available.

The most commonly reported adverse effects in clinical trials were nausea, headache, dizziness, sweating, insomnia, diarrhea, constipation and dry mouth. Desvenlafaxine is metabolized by CYP3A4, and strong CYP3A4 inhibitors may increase desvenlafaxine concentrations. Desvenlafaxine may also increase the risk of bleeding, especially for patients on concomitant NSAIDs, aspirin or anticoagulants. The standard antidepressant black box warnings apply to desvenlafaxine. Similar to other SNRIs, desvenlafaxine can cause hypertension. Withdrawal symptoms are possible when discontinuing the medication, so tapering via an extended dosing interval is recommended.

Studies with lower doses are currently underway. Preliminary data indicates a flat dose response curve for efficacy, but a clear dose response curve for increasing adverse events as doses increase. The FDA has requested additional studies to identify the lowest effective dose.

Despite the lack of head-to-head comparisons, desvenlafaxine and venlafaxine are considered to be equipotent and similar in efficacy. The current recommended starting dose of desvenlafaxine is 50mg daily, which correlates with venlafaxine 37.5-75mg daily. Pricing for the two products appears to be similar; however, the patent for Effexor XR may be expiring within the next 18 to 24 months. If this occurs, Effexor XR will likely be a less expensive option for patients. Given the need for additional data on desvenlafaxine, the therapeutic use for this drug still needs to be defined.



### References:

1. Food and Drug Administration. Pristiq approval letter. February 29, 2008. Available at <http://www.fda.gov/cder/foi/appletter/2008/021992s000ltr.pdf>. Accessed May 2008.
2. Pharmacists Letter/Prescribers Letter. Pristiq (desvenlafaxine). 2008 May;24:240509.

## Half of All Americans Taking Chronic Medications

According to data released by Medco Health Solutions, Inc., a pharmacy benefit manager (PBM) responsible for managing prescription benefits for approximately 20% of all Americans, more than 50% of insured American are taking prescription drugs on a routine basis. For the first time, a majority of the population is being treated for a chronic medical condition, with one in five taking 3 or more chronic medications.

Findings were based on a review of prescription records spanning 2001 to 2007 from a representative sample of 2.5 millions customers. Although persons aged 65 and older showed the highest prevalence of chronic medication use, surprising results regarding younger Americans were uncovered. 48% of women aged 20-44 were being treated for a chronic condition, an increase of more than 20% between 2001 and 2007. Hypertension and lipid-lowering agents were the top medications in the general population, with cholesterol-lowering drug use increasing by 80% in men aged 20 to 44 in the seven year time period.

### Other findings of interest included:

- Nearly 30% of children 19 years of age or younger take a chronic medication
- Use of hormone replacement therapy (HRT) in women decreased 15% in 2007
- Among those 65 years of age or older, 28% of women and 22% of men take five or more chronic medications

### Reference:

Medco Health Solutions News Alert. Chronic medication nation: research finds chronic health problems now afflict more than half of all Americans. May 14, 2008. Available from [http://www.medcohealth.com/medco/corporate/home.jsp?BV\\_SessionID=@@@1213431063.1213045534-mm548461697452@@@@&BV\\_EngineID=cjjiadeegdgijehcfklcgffdfghdfkg.0&articleID=CorpAlertMedco\\_ChronicMedication](http://www.medcohealth.com/medco/corporate/home.jsp?BV_SessionID=@@@1213431063.1213045534-mm548461697452@@@@&BV_EngineID=cjjiadeegdgijehcfklcgffdfghdfkg.0&articleID=CorpAlertMedco_ChronicMedication). Accessed May 2008.

## Americans Desire Transparency in Physician-Pharmaceutical Industry Relationships

Both patients and physicians are keenly aware of the continuing increase in prescription drug costs. Subsequently, relationships between pharmaceutical companies and physicians are highly scrutinized. A recent survey of Americans assessed these concerns, and showed that consumers are interested in the relationships between physicians and the pharmaceutical industry.

The Prescription Project, a group created with the Pew Charitable Trusts, promoted evidence-based prescribing and is concerned with eliminating potential conflicts of interest which results from pharma industry marketing to physicians. Currently, pharma spends in excess of \$7 billion annually for this marketing, predominantly in the form of free gifts, ranging from pens to lucrative speaking engagements. This spending is reported to be greater than the amount spent by the pharmaceutical industry on research and development.



The telephone survey was conducted over a one-week time period in June 2008, and consisted of 1,009 subjects. The average age of respondents was 45 years old, and the sample was evenly distributed between men and women. The majority were white, employed, married and without college degrees. The average annual household income was \$51,000.

Questions assessed respondents' views on pharma industry influence of physicians, including gifts or payments, and financial ties. Seventy-eight percent of Americans surveyed believe that accepting gifts from the pharmaceutical industry has a moderate to large impact on how physicians make prescribing decisions, and overall disapprove of the practice. Interestingly, even the routine practice of free pens and office lunches was condemned by approximately 75% of those surveyed. However, despite the widespread concern with pharma relationships and physicians, more than half of the sample reported they would be unlikely to directly ask their physician about any industry financial relationship, including the receipt of gifts. Additionally, the majority of those responding would support legislation introducing transparency into the relationship between physicians and the pharma industry.

Researchers conclude that concerns over pharmaceutical marketing may be having an adverse effect on the trust between physicians and patients. Survey results indicate Americans desire a clearer understanding of these relationships and the possible repercussions. For more information on survey results from The Prescription Project, visit [www.prescriptionproject.com](http://www.prescriptionproject.com).

### Reference:

International Communications Research. The Prescription Project, June 2008. Available at [www.prescriptionproject.com](http://www.prescriptionproject.com). Accessed June 24, 2008.

### News Clips



The following medications have recently had generic equivalents become available:

- Wellbutrin XL 150mg (bupropion)
- Paxil CR (paroxetine)
- Requip (ropinirole)

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