**Noxafil® (posaconazole) Approved to Prevent Invasive Fungal Infections**

On September 18, 2006, the Food and Drug Administration (FDA) approved Noxafil® (posaconazole) for prevention of fungal infections caused by *Aspergillus* and *Candida*. Noxafil®, manufactured by Schering Corporation, is approved for treatment of patients who have weakened immune systems following bone marrow transplants and for patients with decreased white blood cell counts which makes it difficult to fight infections following chemotherapy for cancer. Although most healthy individuals would not develop fungal infections for which Noxafil® is indicated, patients with severely weakened or abnormal immune systems may develop serious and even fatal fungal infections which Noxafil® might prevent.

Noxafil® is approved as a new molecular entity (NME) since it contains an active substance never before approved in the United States for marketing. It is a triazole antifungal which blocks the synthesis of ergosterol, a key component of the fungal cell membrane, by inhibition of lanosterol 14-alpha-demethylase and accumulation of methylated sterol precursors. It has demonstrated in vitro activity specifically for *Candida albicans* and *Aspergillus fumigatus*. Its safety and efficacy were evaluated in clinical trials including 1844 patients between thirteen and eighty-two years of age. In two, randomized, controlled studies of patients with compromised immunity and at high risk for invasive fungal infections, those patients who were administered Noxafil® had comparable or lower rates of invasive *Aspergillus* and *Candida* infections than those patients who were administered other antifungal medications.

The most common adverse reactions to treatment with Noxafil® were nausea, vomiting, diarrhea, rash, a decrease in potassium blood levels and platelet counts, and abnormalities in liver function tests. Prolongation of the QTc interval as well as liver function impairment are rare adverse effects that may be related to Noxafil®. Due to the possibility that Noxafil® may prolong the QTc interval, it is contraindicated for use with terfenadine, astemizole, cisapride, pimozide, halofantrine and quinidine as these drugs may have similar effects. Noxafil® is also contraindicated in combination with ergot alkaloids. Noxafil® should be used cautiously in patients with potentially proarrhythmic conditions, pre-existing hepatic impairment or hematologic malignancies.

Noxafil® must be administered with a full meal or nutritional supplement to allow adequate absorption of the drug into the body so that it can be effective. Noxafil® has been shown to interact with several medications, including drugs that suppress the immune system, and these reactions may be serious. Cyclosporine, vinblastine, vincristine and vinorelbine are examples of these medications.
Exubera®: Risk of Dosing Errors

This month, September, 2006, Exubera® has become available to patients, as a new option in insulin therapy. Exubera®, insulin human (rDNA origin), is an insulin for inhalation. Its onset of action is similar to rapid-acting insulin analogs and must be inhaled about ten minutes before a meal. Its duration of action is comparable to subcutaneously administered regular human insulin. Exubera® is available as a powder in 1 mg and 3 mg blisters, to be administered using an Exubera® Inhaler. Pharmacists and other healthcare professionals advising prescribers and patients on dosage for this medication need to be aware of some critical details. Exubera® is dosed in mg, with a weight-based dosing chart for initial mg doses, and a conversion chart for equivalent doses in units. Confusion is likely to result between doses ordered in mg and those ordered in units, especially since it will be used in conjunction with injectable insulin, ordered in units. Also, the 1 mg blister is equivalent to 3 units of insulin and the equivalency of mg to units is not exactly incremental. Note that 1 mg of Exubera® is equal to 3 units of insulin but a 3 mg dose is equal to 8 units, not 9 units of insulin. Also, consecutive inhalation of 1 mg blisters results in significantly greater insulin exposure than inhalation of one 3 mg blister due to retention of blister contents. Thus, three 1 mg Exubera® doses should NOT be substituted for one 3 mg dose.

Sources:
www.fda.gov
www.thomson.com
Institutes for Safe Medication Practices (ISPN) DocAlert

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Drug Information Highlights

- **Avastin® (bevacizumab) Intravenous Solution**: Genentech and the FDA have announced revisions to the Warnings and Adverse Reactions sections of the prescribing information for Avastin®, a recombinant humanized monoclonal IgG1 antibody, which binds to vascular endothelial growth factor (VEGF) and inhibits the interaction of VEGF to Flt1 and KDR receptors on the surface of endothelial cells. In the process, it prevents the proliferation of endothelial cells and formation of new blood vessels. It is indicated for treatment of metastatic colorectal cancer, to be used in combination with 5-fluorouracil-based chemotherapy as first-line or second-line therapy. Non-FDA labeled indications include metastatic breast cancer, HER2-negative disease, as first-line therapy in combination with paclitaxel, as well as non-small cell lung cancer, as first-line therapy in combination with paclitaxel and carboplatin for advanced/metastatic non-squamous cell disease. The prescribing information revisions for Avastin® relate to cases of a rare brain-capillary leak syndrome, reversible posterior leukoencephalopathy syndrome (RPLS), as well as postmarketing reports of nasal septum perforation. RPLS is a neurological disorder associated with hypertension, fluid retention and cytotoxic effects of immunosuppressive drugs on the vascular endothelium. It can present with headache, seizure, lethargy, confusion, blindness and other visual and neurological disturbances. Although mild to severe hypertension may be present, diagnosis does not require it. Onset of symptoms has been reported as early as sixteen hours after initiation of Avastin® therapy or as long as one year after therapy initiation. Magnetic Resonance Imaging (MRI) is necessary for confirmation of diagnosis of RPLS.

- **Ortho Evra® (norelgestromin/ethinyl estradiol) Transdermal Patch, Extended-Release**: Prescribing information for Ortho Evra® continues to recommend that women with concerns or risk factors for thromboembolic disease talk with their healthcare professionals about using Ortho Evra® versus other contraceptive options. Concern is related to exposure to higher levels of estrogen than most oral contraceptives. Ortho Evra® is a weekly patch. Revision to the prescribing information is related to the results of two separate epidemiology studies, whose results differ, which evaluate the risk of developing a serious blood clot in women using Ortho Evra® as compared to women using a different oral contraceptive. One study found similar risk and the other found an approximate two-fold increase in risk for users of Ortho Evra®. The new warning in the prescribing information states that women using Ortho Evra® are exposed to about 60 percent more estrogen in the blood than if taking a typical oral contraceptive formulated with 35 micrograms of estrogen. However, the peak blood level of estrogen with Ortho Evra® is about 25 percent lower than with the typical oral contraceptive. Estrogen levels with the patch remain constant for one week while peak blood levels with a daily oral contraceptive rapidly decline to levels lower than those for Ortho Evra®.

- **Videx® (didanosine) Chewable/Dispersible Buffered Tablets**: Bristol-Myers Squibb has voluntarily discontinued sale and distribution in the United States of all strengths of this formulation of Videx®. This action is not due to any safety or efficacy issues. Options for continuing didanosine therapy include Videx® EC Delayed-Release Capsules Enteric-Coated Beadlets or Videx® Pediatric Powder for Oral Solution. Bioavailability of didanosine from Videx® tablets is equivalent to that of both Videx® EC capsules and Videx® Pediatric Powder for Oral Solution which can also be used by adults. Adequate gastric buffering is necessary for administration of the Pediatric Powder; therefore, the reconstituted powder is immediately mixed with antacid. Videx® EC capsules are to be swallowed whole and should not be opened. Videx® EC contains no buffer due to possible stomach upset and/or bitter or chalky taste in some patients; therefore, some buffer-related drug interactions are avoided.