Risk of Drug Interactions With St John's Wort

The FDA has asked health care professionals to caution patients about the risk of potentially significant interaction between St John's wort (*Hypericum perforatum*), an herbal product marketed as a dietary supplement, and other drugs, including indinavir, a protease inhibitor (PI) used for HIV infection.

The agency's warning is based on a study conducted by the National Institutes of Health with eight healthy, HIV-negative volunteers. Participants received 800 mg of indinavir administered on an empty stomach every 8 hours for 4 doses, with serial pharmacokinetic sampling before and after the fourth dose. For the next 14 days, volunteers took 300 mg of St John's wort (0.3% hypericin) three times daily with food. On the last day of St John's wort, volunteers again received took 800 mg of indinavir every four hours for a total of 4 doses, with pharmacokinetic sampling before and for 5 hours serially after the fourth dose.

In this study, St John's wort decreased the area under the curve (AUC) of indinavir plasma concentration by a mean (SD) of 57% (19%) and the extrapolated minimum plasma concentration (C_{min}) 8 hours after dose by a mean (SD) of 81% (16%). (For full study results, see *Lancet.* 2000;355;547-548.)

Another report strongly suggests that the herb causes a drop in plasma levels of cyclosporine after heart transplantation (*Lancet.* 2000;355;548-549). St John's wort appears to be an inducer of the metabolic pathway cytochrome P450 and may significantly decrease blood concentrations of all PIs for HIV, including amprenavir, indinavir, nelfinavir, ritonavir, and saquinavir. The herbal product may have a similar effect on the nonnucleoside reverse transcriptase inhibitors (NNRTIs) delavirdine, efavirenz, and nevirapine, which are metabolized via the same pathway. Consequently, concomitant use of St John's wort and PIs or NNRTIs is not recommended, because it may result in suboptimal antiretroviral drug concentrations, leading to loss of virologic response and development of resistance or class cross-resistance.

Because many drugs that are used to treat heart disease (such as digoxin, diltiazem, nifedipine, digitoxin, or β-blockers), depression (such as imipramine, amoxapine, or amitriptyline), seizures (such as carbamazepine, phenytoin, or phenobarbital), certain cancers (such as cyclophosphamide, tamoxifen, taxol, or etoposide) or to prevent transplant rejection (such as cyclosporine, rapamycin, or tacrolimus) or pregnancy (ethinyl estradiol) are metabolized through this pathway, health care providers should alert patients about these potential drug interactions.

Serious adverse events associated with St John's wort–drug interaction should be reported to the FDA MEDWATCH by telephone at (800) FDA-1088, fax (800) FDA-0178, or Internet at http://www.fda.gov/medwatch.

First Drug for Penicillin-Resistant Community-Acquired Pneumonia

The FDA has approved a new indication for levofloxacin (Levaquin; Ortho-McNeil Pharmaceutical Inc, Raritan, NJ), a fluoroquinolone previously approved to treat a wide range of gram-negative and gram-positive microorganisms, including the major pathogens in bacterial community-acquired pneumonia (CAP). The added indication is the first treatment to be approved for adult patients with CAP caused by penicillin-resistant strains of *Streptococcus pneumoniae*.

The supplemental approval is based on eight clinical studies involving more than 3900 patients with CAP. About 3000 of them were treated with 500 mg of levofloxacin once daily, orally or intravenously, for 7 to 14 days, and the rest received one of several comparator regimens. Across these studies, 18 levofloxacin-treated and four nonquinolone comparator–treated patients were identified with CAP due to penicillin-resistant *S pneumoniae*.

Of the 18 levofloxacin-treated patients, 15 were evaluable for clinical efficacy following the therapy. Six of the 15 had bacteremic CAP, and five were classified as having severe disease. All 15 achieved clinical success (cure or improvement). Of the four comparator-treated patients, three were evaluable for clinical efficacy, had bacteremic CAP, and had disease classified as severe. All three achieved clinical success.

The FDA wishes to emphasize the need for prudent use of antimicrobial agents to impede the development of antimicrobial resistance.

Advisory Committee Meeting

The FDA's Urology Subcommittee of the Advisory Committee for Reproductive Health Drugs will hold an open meeting on April 10, 9 AM to 5 PM, at the Holiday Inn, 8120 Wisconsin Ave, Bethesda, Md. The committee will consider the safety and efficacy of new drug application for apomorphine hydrochloride tablets, sublingual (Uprima, TAP Holdings Inc, Deerfield, Ill) proposed for use in the treatment of erectile dysfunction. Oral presentations from the public will be scheduled from 1 PM to 2 PM.

For more information, call Sandra Titus at (301) 827-7001 or e-mail tituss@cder.fda.gov, or call the FDA Advisory Committee Information Line at (800) 741-8138, code 12537. Sponsor's and FDA's briefing material may be reviewed on April 9 at http://wwwfda.gov/ohrms/dockets/ac/acmenu.htm.

—Jane E. Henney, MD
Commissioner of Food and Drugs

Written inquiries may be directed to Jane E. Henney, MD, Commissioner of Food and Drugs, HF-1, Room 14-71, 5600 Fishers Ln, Rockville, MD 20857.