Pharmaceutical Horizons

Engineering Efficient and Effective Drug Therapy

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Our summary of news concerning medications and prescription drug benefit programs

Clinical Literature Digest

Complications Associated with Lotronex Under Investigation by FDA

At our first client roundtable the new drug Lotronex was presented and discussed. This drug is the first new therapy in the management of irritable bowel syndrome in over a decade. The FDA is reviewing this drug because practitioners have issued 49 reports of ischemic colitis among Lotronex users, including three women who died. It has also received 21 reports of severe constipation including 2 deaths. Glaxo is currently negotiating with the FDA over whether it can launch a major consumer advertising campaign, including TV ads for Lotronex. Glaxo contends that Lotronex is safe and effective and that some of the severe adverse events occurred in women that should have never received the drug in the first place due to a history of ischemic colitis.

Reduced GI Adverse Events with Vioxx?

The new COX-2 Inhibitors (Celebrex and Vioxx) have been extremely popular alternatives to the traditional NSAIDs ibuprofen, naproxen, Daypro and Relafen. Physicians and patients have found them to be as effective with fewer gastrointestinal side effects. To confirm these observations, a comparative trial of rofecoxib (Vioxx) versus ibuprofen (Motrin), diclofenac (Voltaren) or nabumetone (Relafen) was conducted. This study sought to evaluate how often treatment with one of these medicines was stopped due to GI adverse events among patients with osteoarthritis. Rofecoxib (Vioxx) was associated with a lower incidence of treatment discontinuations due to GI adverse events over a 12-month time period and a lower incidence of dyspeptic-type GI adverse events over 6 months of treatment compared to the other medicines. However, for patients on any one of these medicines for six months, there were no discernable differences in the frequency of dyspeptic-type GI adverse events. *Comment: This study may help to explain the lack of discontinuation of PPI's in patients initiated on COX selective inhibitors.* (*Arch Intern Med. 2000;160:2998-3003)*

Hormone replacement therapy (HRT) in women with coronary artery disease

A long-standing debate concerning the benefits of estrogen replacement therapy will be re-ignited due to the results of a recent study published in the *Archives of Internal Medicine*. The primary conclusion of this research is that women with or at risk for coronary artery disease should not start HRT. The investigators further stated that women without coronary heart disease might also be at increased risk of harm from HRT. *Comment: Because the number of women at risk for or who have coronary artery disease continues to grow, the results of this study will likely cause reevaluation of long term HRT. It may also alter the use of hormone replacement therapy for the treatment of osteoporosis. This could increase the use of the more expensive drugs Evista, Fosamax and Actonel for osteoporosis.* (*Arch Intern Med. 2000;160:2897-2900)*

Inhaled Zanamivir for the Prevention of Influenza in Families

The November 2, 2000 issue of the *New England Journal of Medicine* reports that inhaled zanamivir is effective in the treatment and prevention of influenza in families. In this study, a qualifying family had two to five members and at least one child five years of age or older during the 1998-1999 influenza season. The study demonstrated a 79% reduction in the proportion of families with at least one affected influenza contact. When combined with the treatment of index cases, prophylactic treatment of family members with once-daily inhaled zanamivir was demonstrated to be well tolerated and p revented the development of influenza. In this study there was no evidence of the emergence of resistant influenza variants. *Comment: This study could result in an increased use of Relanza and Tamiflu to prevent or reduce the severity of influenza infection in other family members once one member of the family exhibits signs of infection. The issue of appropriate use will remain though as Relenza and Tamiflu currently does not have a place in the treatment of the common cold. (N Engl J Med 2000;343:1282-9.)*

FDA Updates

Once-Weekly Fosamax Approved for Treatment and Prevention of Postmenopausal Osteoporosis

The FDA has approved two new dosage strengths of Merck's alendronate sodium (Fosamax) – once-weekly tablets: 70 mg for the treatment of postmenopausal osteoporosis, and 35 mg for the prevention of postmenopausal osteoporosis. In a clinical trial, the safety, tolerability and effectiveness of Fosamax 70 mg once weekly and the 10 mg once daily regimen were similar. The medication continues to be available in once-daily dosages for the treatment (10 mg) and prevention (5 mg) of postmenopausal osteoporosis. *Comment: Merck has restricted the distribution of the Fosamax 40mg tablet (with labeling for Paget's Disease) through a specialty pharmacy and only for patient's with a documented diagnosis of Paget's Disease. This is noteworthy because the monthly cost of 2 – 40mg tablets was approximately one-half that of the new 70mg tablet.*

Novantrone (Mitoxantrone Hydrochloride) – Immunex Corp

For reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (i.e., patients whose neurologic status is significantly abnormal between relapses).

Lescol XL (Fluvastatin Sodium) – Novartis

For the use as an adjunct to diet to reduce elevated total cholesterol (total-C), LDL-C, TG, and Apo B levels and to increase HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia (Frederickson Type IIa and IIb) whose response to dietary restriction of saturated fat and cholesterol and other nonpharmacological measures has not been adequate; to slow the progression of coronary atherosclerosis in patients with coronary heart disease as part of a treatment strategy to lower total and LDL cholesterol to target levels.

Lunelle

(Estradiol Cypionate and Medroxyprogsterone Acetate) was approved for the prevention of pregnancy

Generic Drug Approvals

Doxazosin Mesylate (Cardura)
KV Pharmaceutical Co.
Invamed Inc.

Bupropion HCL (Wellbutrin)
Eon laboratories