NEW APPROVAL

New Antihistamine
A new non-sedating antihistamine to treat seasonal allergy rhinitis (SAR) is now available by prescription. Desloratadine (Clarinex, Schering-Plough), an H-1 receptor antagonist, comes in a once-daily 5-mg tablet that provides 24-hour relief for people 12 years of age and older. In four double-blind clinical trials, desloratadine was studied on over 2,300 patients between the ages of 12 and 75. The tablets can be taken without regard to food and there have been no drug-drug interactions observed when desloratadine was administered with either erythromycin or ketoconazole. The most common side effects observed were dry mouth, pharyngitis, somnolence, and fatigue.

NEW INDICATION

Paxil for PTSD
The FDA has approved paroxetine HCl (Paxil, GlaxoSmithKline) for the treatment of posttraumatic stress disorder (PTSD). The safety and efficacy of paroxetine HCl were demonstrated in three clinical trials with 1,200 patients (18–78 years of age). The most common side effects in the studies included asthenia, sweating, nausea, dry mouth, decreased appetite, diarrhea, somnolence, and sexual side effects. Paroxetine HCl is a selective serotonin reuptake inhibitor that has already been approved for depression, obsessive-compulsive disorder, panic disorder, social anxiety disorder, and generalized anxiety disorder. It has been on the market in the U.S. for eight years.

DRUG NEWS

Aricept for Vascular Dementia
Treatment with donepezil hydrochloride (Aricept, Eisai Co., Ltd.) tablets significantly improved the cognitive and global (overall) functioning of patients with vascular dementia (VaD), compared with placebo, according to results from a clinical study presented at the Second International Congress on Vascular Dementia in Salzburg, Austria in January.

The 24-week, double-blind, randomized, placebo-controlled study included 616 men and women with VaD, with an average age of 75 years. Patients with Alzheimer’s disease were excluded from the study. The majority of patients had a history of stroke, and virtually all (99.7 percent) participants took one or more other medications, most frequently to prevent cardiovascular risk factors.

Participants received daily doses of either 5 mg of donepezil, 10 mg of donepezil, or placebo. Patients who received donepezil showed significant improvement in their cognitive function compared to those taking placebo (P=0.001, 5 mg; P<0.0001, 10 mg), as measured by the Alzheimer’s Disease Assessment Scale (ADAS-cog), a standard test of cognitive abilities. Evaluation of global function also revealed significant improvements for patients at both doses compared to patients who received placebo (P=0.004 and P=0.047, respectively), as measured by the Clinician’s Interview-Based Impression of Change with caregiver input (CIBIC-plus), a standard global assessment tool.

Gastrointestinal side effects, including diarrhea and nausea, occurred more frequently in donepezil-treated patients than in those taking placebo. Other adverse events associated with donepezil included accidental injury, insomnia, leg cramps, rhinitis, and abnormal dreams. Rates of cardiovascular events were similar among all study participants (19 percent in the 5-mg group; 20 percent in the 10-mg group; and 22 percent in the placebo group).

Overall, 491 patients (79.7 percent) completed the study; of the 20.3 percent who did not continue, 73 patients (11.9 percent) stopped because of an adverse event. No deaths were attributed to donepezil.

VaD, cognitive decline caused by a single, localized stroke or a series of strokes, is second only to Alzheimer’s disease as a cause of dementia. Up to one-third of all diagnosed dementia cases are caused by VaD.

Comparing Schizophrenia Drugs
Over two million Americans suffer from schizophrenia, and, according to the American Psychiatric Association, 20% to 50% of people with schizophrenia who are treated with medication are re-hospitalized every year. In a multicenter, randomized, double-blind study published in the New England Journal of Medicine, patients with schizophrenia showed a reduced risk of returning symptoms when they were treated with risperidone (Risperdal, Janssen Pharmaceutical, Inc.) rather than haloperidol (Haldol, Ortho-McNeil Pharmaceutical). The study followed patients for at least one year; some patients were followed for more than two years. There were 365 patients in the final analysis: 177 were randomly assigned to risperidone (average daily dose of 4.9 mg) and 188 received haloperidol (average daily dose of 11.7 mg).

The estimated risk of relapse by the end of the study was 34% for patients taking risperidone compared to 60% for patients taking haloperidol (P<0.001). Those on risperidone also had a longer time to relapse (P<0.001) and showed greater improvement in their total Positive and Negative Syndrome Scale (PANSS) than those on haloperidol (P<0.001). Risperidone was shown to reduce the relative risk of relapse by 48% compared to haloperidol.

The patients taking risperidone had a lower incidence of extrapyramidal symptoms (uncontrolled tremors and muscle stiffness) versus those on haloperidol (8% vs. 15%, respectively). Those who took risperidone reported a lower incidence of somnolence (14% vs. 25%), agitation (10% vs. 18%) and hyperkinesia (5% vs. 20%). Patients taking risperidone had a mean...
increase in mean body weight of 5 pounds, whereas those on haloperidol had a mean decrease of 1.6 pounds.

This was the first long-term study published that compared the abilities of atypical antipsychotic agents to prevent relapse. Financial support was provided by the Janssen Research Foundation.

**Topical Aspirin for Dermatosis**

Lichen simplex chronicus, also known as localized circumscribed neurodermatitis, is a condition that can often outlast intensive treatment, including potent topical corticosteroids.

Recent research has shown that a topical aspirin solution with dichloromethane can relieve both histamine-related itching and pain, such as that associated with shingles. Based on those findings, researchers from the National Skin Center and the National Medical Research Council in Singapore assessed the effect of topical aspirin on lichen simplex chronicus in 29 patients.

Of the 24 evaluable patients, 11 (46%) reported a greater than 50% reduction in the intensity of itching by week 2, as did three patients receiving placebo. Seven patients receiving aspirin treatment showed significant healing in active lesions, compared with one patient on placebo. The aspirin treatment had no significant adverse effects.

The researchers say that although the mechanisms of antipruritic action are not yet clear, the salicylic acid could have a peripheral nociceptive effect on itch and pain fibers. Recent studies, they note, have shown higher skin levels of acetylsalicylic acid after an aspirin/diethyl ether mixture was applied to patients with acute herpes zoster and postherpetic neuralgia, compared with patients who took the aspirin orally; and patients with excellent pain relief showed a trend toward higher acetylsalicylic concentrations in the skin. In the current study, the researchers used dichloromethane solvent as a vehicle, rather than the volatile and flammable diethyl ether mixture. (J Am Acad Dermatol. 2001 45:910–913).

**Medication Error-Prevention Software**

At the Annual Society of Healthcare System Pharmacists meeting in December, ALARIS Medical, Inc. announced the North American market release of the first modular intravenous infusion platform with proprietary medication error-prevention software. The MEDLEY Medication Safety System, with its proprietary Guardrails Safety Software, was released after a year of clinical experience on patients in four teaching hospitals in North America with over three million hours of use. The MEDLEY System, the first IV-related innovation, is a modular bedside platform that supports four other modules (e.g., a programming module, and a pulse oximetry module).

The Guardrails software will prompt caregivers when programming goes beyond any of the up to 1,000 hospital-determined best-practice guidelines. This software also keeps a detailed event log, which includes all programming. The system itself has the ability to connect to computers to access and assist physician order entry, medication administration records, pharmacy information systems, and automated drug and delivery supply systems.

**Drug Combination Reduces LDL**

The new National Cholesterol Education Program (NCEP) guidelines, issued this past May, specify that patients at high risk for coronary heart disease must be treated more aggressively. They also note that combination therapy is a safe and effective way of lowering LDL cholesterol and reaching goal.

In a new study published in the October 2001 issue of *Atherosclerosis*, 94 men and women with moderate hypercholesterolemia (LDL cholesterol=160 mg/dl, triglycerides=300 mg/dl) were monitored to determine the efficacy and safety of combination therapy with colesevelam HCl (WelChol, Sankyo Pharma) and atorvastatin calcium (Lipitor, Pfizer). This four-week multicenter, double-blind, placebo-controlled study randomly assigned patients to one of five treatment groups: placebo, colesevelam HCl 3.8 g/day, atorvastatin calcium 10 mg/day, colesevelam HCl 3.8 g/day plus atorvastatin calcium 10 mg/day, or atorvastatin calcium 80 mg/day.

At the end of the trial, the combination appeared to cause a 48% reduction in mean LDL cholesterol levels—a reduction statistically superior to either therapy alone. The study demonstrated that patients receiving this combination experienced additive reductions in LDL that were not significantly different from the maximum recommended dose of atorvastatin calcium alone (80 mg).

This is the third such combination study to demonstrate the efficacy of colesevelam HCl with a leading statin. A study published in the April 1, 2001 issue of the *American Journal of Medicine* showed colesevelam HCl, taken in combination with simvastatin (Zocor, Merck & Co.), lowered LDL cholesterol levels by 42% in patients with moderately high cholesterol—a reduction more dramatic than either therapy alone. In the June 2001 issue of *Clinical Cardiology*, another study demonstrated that colesevelam HCl combined with lovastatin (Mevacor, Merck & Co.) was efficacious and well-tolerated, resulting in an additive 34% reduction in LDL cholesterol.

Colesevelam HCl effectively lowers LDL cholesterol and is the only lipid-lowering agent that is FDA-approved for combination use with a statin. It is...
indicated as adjunctive therapy to diet and exercise, either alone or in combination with a statin, for the reduction of elevated cholesterol in patients with primary hypercholesterolemia when diet and exercise alone are not adequate.

Colesevelam HCl is not absorbed into the blood stream. Its common side effects are gas, constipation, infection, upset stomach, and headache. This drug should not be taken by patients who have bowel obstructions. There is no change in the adverse-event profile with the co-administration of atorvastatin calcium (Lipitor), simvastatin (Zocor) or lovastatin (Mevacor). Liver-function monitoring is not required with colesevelam HCl, and in combination with a statin, no additional liver-function monitoring is required beyond that which is required for the prescribed statin alone.

**Robotic Heart Surgery**

On January 15th, Dr. Craig Smith, chief of cardiothoracic surgery, and Dr. Michael Argenziano, director of robotic cardiac surgery, performed a historic heart surgery at Columbia Presbyterian Medical Center in New York. The surgery, part of an FDA-sanctioned clinical trial, was a robotically assisted coronary artery bypass that was performed without opening the patient’s chest. This operation required only three pencil-sized holes made between the ribs—as compared to the eight- to ten-inch incision made in the chest for a regular coronary artery bypass. These little holes allow two robotic arms and an endoscope, a tiny camera, to access the heart. The surgical robot used was Intuitive Surgical’s da Vinci Surgical System, which has been approved by the FDA for clinical trials.

**NHL Drug Combination**

A new study published in the *New England Journal of Medicine* showed that more patients with aggressive non-Hodgkin’s lymphoma (NHL) were alive after two years when they were treated with rituximab (Riuxan/MabThera, Genentech and IDEC) and standard CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy compared to CHOP treatment alone. CHOP is the standard treatment for aggressive NHL; it has a 30% to 40% cure rate.

Two-year follow-up data from a phase III study with 399 patients, ages 60 to 80, showed a 23% relative increase in the number of patients living with the rituximab/CHOP combination. A significant endpoint of event-free survival was seen after a median follow-up of two years with the addition of rituximab to CHOP regimen. Event-free survival was defined as ongoing survival without events including disease progression or relapse, death or initiation of new alternative treatment.