The Drug Scene

FDA Warns Against Taking Antidepressants, Migraine Drugs Together

The Food and Drug Administration (FDA) has important new safety information about taking triptans (drugs used to treat migraine headaches) together with certain types of antidepressants. The antidepressant medicines of concern are selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs); brand names are provided below. **A life-threatening condition called serotonin syndrome may occur when triptans are used together with an SSRI or an SNRI**.

Serotonin syndrome occurs when the body has too much serotonin, a chemical found in the nervous system. Symptoms may include restlessness, hallucinations, loss of coordination, fast heartbeat, rapid changes in blood pressure, increased body temperature, overactive reflexes, nausea, vomiting, and diarrhea. Serotonin syndrome may be more likely to occur when starting or increasing the dose of a triptan, SSRI, or SNRI.

The FDA has determined that serotonin syndrome occurs with combined use of triptans and an SSRI or SNRI through patient reports. Each of these types of medicine increases serotonin levels on its own, as well. *Patients who are taking a triptan along with an SSRI or SNRI should talk to their doctor before stopping their medications.*

Physicians prescribing a triptan, SSRI, or SNRI should:

- Keep in mind that triptans are often used intermittently and that either the triptan, SSRI, or SNRI may be prescribed by a different physician
- Weigh the potential risk of serotonin syndrome with the expected benefit of using a triptan with an SSRI or SNRI
- Discuss the possibility of serotonin syndrome with patients if a triptan and an SSRI or SNRI will be used together
- Follow patients closely if a triptan and an SSRI or SNRI are used together, particularly during treatment initiation, with dose increases, or with the addition of another serotonergic medication
- Instruct patients who take a triptan and an SSRI or SNRI together to seek medical attention immediately if they experience the symptoms of serotonin syndrome (described above).

Patients should know which medicines they take and tell all their health-care providers (physicians, nurses, and pharmacists) what these medicines are. In short, triptans treat migraine headaches, and SSRIs and SNRIs treat depression and other mood disorders.

The FDA has requested that all manufacturers of triptans, SSRIs, and SNRIs update their prescribing information to warn of the possibility of serotonin syndrome when triptans and SSRIs or SNRIs are taken together.

Drug Names

SSRIs and a Combination Drug Containing an SSRI	SNRIs	Triptans
Celexa (citalopram)	Cymbalta (duloxetine)	Amerge (naratriptan)
Fluvoxamine	Effexor (venlafaxine)	Axert (almotriptan)
Lexapro (escitalopram)		Frova (frovatriptan)
Paxil (paroxetine)		Imitrex (sumatriptan)
Prozac (fluoxetine)		Maxalt and Maxalt-MLT (rizatriptan)
Symbyax (olanzapine/fluoxetine)		Relpax (eletriptan)
Zoloft (sertraline)		Zomig and Zomig ZMT(zolmitriptan)

New HIV Treatment Approved for Patients Who Don't Respond to Existing Drugs

The FDA has approved Prezista (darunavir), a new drug for adults whose infection with the human immunodeficiency virus (HIV) has not responded to treatment with other antiretroviral drugs. Prezista, a new protease inhibitor, is approved to be coadministered with a low dose of ritonavir and other active anti-HIV agents. Ritonavir, a protease inhibitor approved in 1996, slows the breakdown of Prezista in the body, thereby increasing its concentration in the patient's system.

The most common side effects reported by patients on the Prezista-ritonavir regimen included diarrhea, nausea, and headache. About 7% of patients on this combination therapy experienced skin rashes ranging from mild to serious. The risks and benefits of Prezista have not been established for adults who have not been previously treated for HIV or for children.

As a condition of the accelerated approval, the manufacturer is required to conduct postmarketing trials to verify and describe the clinical benefits of Prezista. Other postmarketing studies that the manufacturer has committed to conduct include studies in pediatric populations, studies to better define certain drug interactions, and studies to evaluate the drug in patients with varying degrees of liver impairment to identify appropriate dosing for this patient population.

Patients are advised to take the combination with food and not to use the combination therapy together with St. John's wort or various other drugs, including certain anticonvulsants, antihistamines, sedatives, and a few protease inhibitors.

FDA Approves New Treatment for Parkinson Disease

The FDA cleared Azilect (rasagiline), a new molecular entity, for the treat-

ment of Parkinson disease. The drug is a monoamine oxidase type B (MAO-B) inhibitor that blocks the breakdown of dopamine, a chemical that sends information to the parts of the brain that control movement and coordination.

Parkinson disease is a chronic, progressive neurodegenerative condition caused by the destruction of the brain cells that produce dopamine. As the level of this chemical declines, messages from the brain telling the body how and when to move are delivered more slowly, leaving a person incapable of initiating and controlling movements in a normal way.

Azilect, manufactured by Teva, was approved for use as an initial single-drug therapy in early Parkinson disease and as an addition to levodopa in more advanced patients. The safety and effectiveness of Azilect was demonstrated in three 18- to 26-week controlled clinical trials.

Azilect may be associated with hypertensive crisis if patients also consume tyramine-rich foods and beverages (such as cheese and red wine) or dietary supplements or amines contained in many cough/cold medications. Therefore, patients will need to avoid these sources of tyramine and amines when taking the drug. As with most other medications for Parkinson, Azilect has the potential to cause involuntary movements (dyskinesias), hallucinations, and lowered blood pressure. These side effects are described in the product labeling.

FDA Rapidly Approves New Treatment for Rare Leukemia

The FDA granted accelerated approval for Sprycel (dasatinib), a new oral treatment for patients with chronic myeloid leukemia (CML), a rare cancer characterized by the uncontrolled growth of white blood cells. In the United States, CML affects about 4600 people annually. In addition, the FDA gave regular approval to Sprycel for use in adults who have Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph^+ ALL), a more serious form of leukemia.

Manufactured by Bristol-Myers Squibb, Sprycel is intended for patients with CML who are no longer responding to or can no longer tolerate therapy with Gleevec (imatinib), a drug approved in 2001 for this life-threatening disease. This new option works by reducing the activity of one or more proteins responsible for the uncontrolled growth of the leukemia cells. Sprycel treatment has been shown to reduce, and in some cases eliminate, detectable leukemia cells in the blood and bone marrow of patients with CML. As provided for under FDA-accelerated approval regulations, studies are underway to demonstrate that these improved white blood cell counts also result in clinical benefit, such as improved survival or improvement in related symptoms.

The approval of Sprycel is based on evidence from four single-arm studies in more than 400 patients who were no longer responsive to or tolerant of treatment with Gleevec. Efficacy was determined by the response rate, defined as the percentage of patients in whom treatment resulted in the elimination of or significant reduction in leukemia cells. Responses were measured primarily in the bone marrow for those patients with the earliest stage of disease and in the blood for patients with later stage disease. Forty-five percent of patients with the earliest stage of CML (chronic phase) responded to the drug. Response rates for patients with advanced phases and Ph^+ ALL ranged from 31% to 59%.

Side effects reported in clinical trials included fluid retention, bleeding, diarrhea, skin rash, infections, headache, fatigue, and nausea. Sprycel also frequently causes low red blood cell counts (anemia), low white blood cell counts (neutropenia) and low platelet counts (thrombocytopenia).

First Treatment for Dementia of Parkinson Disease Gets FDA Nod

The FDA has approved Exelon (rivastigmine tartrate) for the treatment of mild to moderate dementia (chronic loss or impairment of intellectual capacity) associated with Parkinson disease, a disorder of the central nervous system. Exelon, manufactured by Novartis, was previously approved for the treatment of mild to moderate dementia of Alzheimer type.

"It's been recognized for almost a decade that the dementia of patients with Parkinson's disease differs from the dementia of patients with Alzheimer," said Dr. Steven Galson, Director of FDA's Center for Drug Evaluation and Research, "but until now, there has been no treatment that has been shown to be effective specifically for the dementia associated with Parkinson disease. Approval of Exelon helps to fill this medical need."

An estimated 0.2% to 0.5% of people over 65 are affected by Parkinson dementia and experience symptoms such as impairments in executive function, memory, and attention. The approval of Exelon for this dementia is given on the basis of results of a randomized, placebo-controlled clinical study with 541 patients who showed symptoms of mild to moderate dementia 2 years or more after their diagnosis. At the end of the 24-week trial, the condition of the Exelon-treated patients, as shown on a scale that measures mental processes, was significantly better than the condition of the patients on placebo.

The use of this drug, however, has been associated with significant gastrointestinal adverse reactions. In clinical trials, 47% of the patients developed nausea, and 26% of women and 18% of men on high doses experienced significant weight loss. Other common adverse events reported include vomiting, anorexia, dyspepsia, and asthenia (loss of strength). In some patients with