New Plavix Warning: Lack of Effect in Many People

The FDA has put a new "black box" warning on the anti-clotting drug Plavix, the second best-selling drug in the world. The new label warns that normal doses of Plavix have a potentially deadly lack of effect in 2% to 14% of patients. Such patients are so-called "poor metabolizers" who carry a variant CYP2C19 gene affecting the enzyme that converts Plavix into its active form. A less strident warning about poor metabolizers first appeared on the Plavix labels in May 2009. Based on new information from a drugmaker-funded study and other research, the FDA has now strengthened the warning. A genetic test can tell whether a person is a poor metabolizer. The test costs about $500, according to Courtney Harper, PhD, director of the FDA's division of chemistry and toxicology devices. But cost isn't the only issue. "The time to get a test result varies. It may be a few hours to a day or two, or other labs may take a few weeks," Harper said at a news conference held to discuss the FDA action. For many patients at risk of a second heart attack or stroke, time is of the essence, noted Robert Temple, MD, director of the FDA's office of medical policy. "Unfortunately, waiting to see if Plavix will work isn't easy. This drug is to keep you from having a heart attack or stroke or dying, so waiting is not a good idea," he said at the news conference. "And this drug is used acutely, when a person is having angioplasty. So you really can't wait for the test results in that case. But for people who had a heart attack some time ago, they might want to wait for the test."

Antithrombotic Polypharmacy Increases Bleeding Complications after First Myocardial Infarction

According to a study recently published in Lancet, patients who have suffered a first-time myocardial infarction are more likely to be readmitted to the hospital with a bleeding complication when they are prescribed triple therapy (aspirin, clopidogrel, and vitamin K antagonist) or dual therapy with clopidogrel plus vitamin K antagonist than when they received monotherapy with either aspirin, clopidogrel, or a vitamin K antagonist. The investigators used a Danish nationwide registry to identify patients aged 30 years or older who had been hospitalized because of a first-time myocardial infarction between 2000 and 2005. Patients had been started on various combinations of aspirin, clopidogrel, and vitamin K antagonists. The investigators assessed the risks of nonfatal and fatal bleeding events in the patients in order to identify the safest combinations of antithrombotic drugs. A total of 40,812 patients were included in the study. According to a comment published in the same issue of Lancet, dual therapy with clopidogrel plus vitamin K antagonist was associated with an almost four times increased risk of bleeding. The writers explained that this risk was similar to that of triple therapy, noting, "These drug combinations lead to high rates of bleeding with an apparent loss of protection against death, possibly because the reduction in ischemic events is offset by an increased risk of death associated with bleeding." The editorials commented that new stent technologies, medications, and equipment capable of assessing platelet reactivity may assist in developing antiplatelet therapies that are both efficacious and safe. Antithrombotic pharmacotherapy decreases the incidence of future ischemic events in people who have had a myocardial infarction. Bleeding complications increase with the number of antithrombotics prescribed, and patients who experience bleeding complications are more likely to have a recurrent myocardial infarction or die. Patients who are prescribed more than one antithrombotic agent should speak with their prescribers about the risks and benefits.

Source: APHealth.com
Results of a meta-analyzed data from six randomized, placebo-controlled trials concluded that the effects of tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are non-existent to negligible in patients with mild to moderate baseline symptoms; however, these agents are significantly more effective than placebo for patients with very severe symptoms.

Jay Fournier and colleagues from the University of Pennsylvania conducted a meta-analysis of data published from January 1980 to March 2009 to determine the differences in the effects of antidepressants and placebo for patients with varying baseline depressive symptoms. A total of 718 adult patients with baseline Hamilton Depression Rating Scale (HDRS) scores ranging from 10 to 39 were assessed; 434 patients were given an active drug and 284 patients were in the placebo group.

The investigators noted that the magnitude of the effect of antidepressants versus placebo increased as baseline depression severity increased. A clinically significant difference between the two treatments was only noted for patients with very severe depression, defined as those with a baseline HDRS score of 2 or greater. The treatment effect for patients with mild to moderate depression (HDRS scores of 18 or less) or those with severe depression (HDRS scores between 19 and 22) was nonexistent to negligible.

The effectiveness of these agents for patients with milder depression can be attributed to the placebo effect. Given the potential risks associated with these agents, such as increased risks of suicidal thinking and behavior in youths and young adults and the association of increased risk of developing type 2 diabetes after long-term use, it seems reasonable to recommend an evidence-based psychotherapy for patients with mild to moderate depression.

Patients who are prescribed antidepressants should know that a recent study suggests that these agents have a clear benefit for patients with more severe symptoms but the effects of these agents are unclear for patients with less severe depressive symptoms. Patients who are currently taking antidepressants should not stop their treatment and to discuss the findings of this trial with their prescriber.

Source: APha DrugInfoLine

Aspirin and Heart Disease

Some experts are backpedaling on aspirin to prevent heart disease. Aspirin is beneficial for SECONDARY prevention...to prevent a SECOND heart attack or stroke in patients who've already had one. For these patients, aspirin's benefit significantly outweighs its major downside...the risk of major bleeding. But it's a different story for PRIMARY prevention...to prevent a FIRST heart attack or stroke. Aspirin prevents only about one initial serious CV event for every 1000 patients/yr, but causes a similar number of major bleeds. Many men and women are routinely started on aspirin when they reach a certain age. But some experts are skeptical about the benefits of using aspirin for PRIMARY prevention at any age.

In general, recommend aspirin in men at age 45 and women at 55 IF they have additional cardiovascular risk factors such as hypertension, dyslipidemia, etc. AND they aren't at high risk for bleeding. Diabetes patients used to get aspirin for primary prevention after age 40 OR sooner if they have cardiovascular risk factors. We've all been taught that having diabetes is just as big a risk for a heart attack or stroke as actually having heart disease.

Many experts now say this just isn't true. Now the American Diabetes Association recommends aspirin for most diabetic men over 50 and women over 60 IF they have other risks...hypertension, smoking, dyslipidemia, family history of heart disease, or albuminuria. Aspirin shouldn't be encouraged for primary prevention except for people who meet the criteria. For patients on aspirin who don't need it, they should speak with their prescriber...and not to stop it on their own. Just 81 mg/day of aspirin for primary prevention is suggested. There's no proof that higher doses work better, plus it may increase bleeding. It's recommended getting BP under 150/90 mmHg before starting aspirin...uncontrolled hypertension increases the risk of hemorrhagic stroke.

Source: pharmacistsletter.com
Losartan will be the first GENERIC angiotensin receptor blocker. This is a big deal. More money is spent on ARBs than any other antihypertensive class because there are no generic ARBs. But that will soon change. Losartan should be available by mid-April. The generics will cost about 70% less than Cozaar's current price once MULTIPLE generics are out...either in April or later this year. Expect to see formularies force switching other ARBs to losartan. To determine the equivalent dose, consider the indication.

**Hypertension.** Losartan 50 mg/day for Avapro 150 mg or Diovan 80 mg. Go to losartan 100 mg/day for Atacand 16 mg...Avapro 300 mg...Benicar 20 mg...Diovan 160 mg...or Micardis 40 mg. It's suggested giving losartan 50 mg BID instead of 100 mg ONCE a day if needed...dividing the dose may boost its blood pressure-lowering effects.

**Heart failure.** Losartan isn't approved for heart failure...but there's evidence of improved outcomes with higher than usual doses. If you need to switch, a target dose of losartan 150 mg once a day for Atacand 32 mg/day or Diovan 160 mg BID for heart failure is suggested.

When switching between ARBs it's recommended that blood pressure is monitored...and serum creatinine and potassium is checked. ACE inhibitors still have the most evidence showing they're effective...especially for heart failure. Generics for Atacand, Avapro, and Diovan should be available in 2012.

Source: Pharmacist's Letter

Liraglutide (Victoza-Novoo Nordisk) - Treatment of adults with type 2 diabetes as an adjunct to diet and exercise. Liraglutide is a glucagon-like peptid-1 (GLP-1) receptor agonist that exerts its mechanism of action by increasing insulin release in the presence of elevated glucose concentrations, decreasing glucagon secretion in a glucose-dependent manner, and delaying gastric emptying. Liraglutide is administered subcutaneously once daily at a starting dose of 0.6 mg/d and is increased to 1.2 mg/d after 1 week to a maximum dose of 1.8 mg/day. Liraglutide has a boxed warning for risk of thyroid C-cell tumors because tumors were seen in animal models.

Source: AphA DrugInfoLine

**Rumor vs. Truth**

**RUMOR:** Glymetrol can help maintain healthy blood glucose.

**TRUTH:** It's just a rumor. Don't rely on Glymetrol to help anyone. You may have heard about Glymetrol from infomercials or internet ads claiming that it maintains healthy blood glucose, glucose metabolism, and insulin sensitivity. Glymetrol is a supplement containing a variety of natural ingredients that may affect glucose metabolism and insulin sensitivity...alpha-lipoic acid, Gymnema sylvestre, cinnamon extract, fenugreek, bitter melon extract, nopal cactus, American ginseng, Salacia oblonga extract, banana leaf extract, chromium, zinc, and biotin. While it makes some sense that a manufacturer would combine these...many have been studied for their effects on glucose. Some are even possibly helpful for glucose control...alpha-lipoic acid, nopal cactus, American ginseng, and chromium. But there is no proof that this specific combination works...or that it's safe. It combines all the side effects and drug interactions of its ingredients. Nausea, diarrhea, and flatulence are problems with many of the ingredients taken individually. Discourage its use with antiplatelet and anticoagulant drugs like aspirin and warfarin...it may enhance their effects. Avoid Glymetrol in pregnancy and children. There is another reason not to use Glymetrol...the manufacturer won't disclose the amount of each ingredient in the product and recommends that one-size-fits-all dosing...3 tablets a day. If the product worked, it would require careful glucose monitoring and titration. Seek medical advice if there's a concern about developing diabetes. Patients with diabetes should seek medical advice before starting any supplements, especially those claiming to help glucose control.

Source: Pharmacist's Letter
Drinking two or more soft drinks a week increases the risk of developing pancreatic cancer by two-fold compared to people who do not drink soft drinks, says a report in Cancer Epidemiology, Biomarkers & Prevention, a journal of the American Association for Cancer Research.

People who drink soft drinks on a regular basis tend to have poor behavior patterns overall, but the effects of soft drinks on pancreatic cancer may be unique, Mark Pereira, Ph.D., senior author of the study and associate professor in the School of Public Health at the University of Minnesota, said in a statement.

“The high levels of sugar in soft drinks may be increasing the level of insulin in the body, which we think contributes to pancreatic cancer cell growth,” said Pereira.

Pereira and colleagues followed 60,524 men and women in the Singapore Chinese Health Study for 14 years. During that time, there were 140 pancreatic cancer cases. Those who consumed two or more soft drinks per week (averaging five per week) had an 87 percent increased risk compared with individuals who did not.

The researchers found no link between fruit juice consumption and pancreatic cancer.

Pereira said that these results from Singapore probably apply to the United States.

Singapore is a wealthy country with excellent health care. Favorite pastimes are eating and shopping, so the findings should apply to other western countries,” said Pereira.

According to the American Cancer Society, risk factors for pancreatic cancer include:

- Age. Nearly 90 percent of people with pancreatic cancer are older than 55, and the average age at the time of diagnosis is 72.
- Gender. Men are slightly more at risk.
- Race. More African-Americans develop pancreatic cancer than whites.
- Smoking. Smoking increases the risk as much as 300 percent.
- Chronic diseases. Diabetes, pancreatitis, and cirrhosis of the liver all raise risk.
- Obesity and physical activity. Obese people and couch potatoes have a higher risk.
- Family history. Pancreatic cancer seems to run in some families, perhaps due to inherited genes.

Each year, more than 42,000 Americans are diagnosed with pancreatic cancer. Fewer than 5 percent are alive five years after diagnosis, making it one of the deadliest forms of cancer.