

Five Brands of Risk

Now That an FDA Official Has Voiced Concerns About A Group of Popular Medications, Some Patients Who Take Them Are Seeking Safer Options

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It's been a tough couple of weeks for the U.S. Food and Drug Administration (FDA) and pharmaceutical companies. But it's also been difficult for the millions of people who are taking any of five medications cited as potentially dangerous at a Nov. 18 Senate hearing.

That hearing was held to explore the FDA's record on warning people about drug risks. During his testimony, David J. Graham, associate director of the FDA's office of drug safety, said underpublicized safety risks of five drugs -- weight loss medication Meridia; acne drug Accutane; asthma medication Serevent; cholesterol drug Crestor; and painkiller Bextra -- could lead to restrictions or withdrawal of the drugs from the market.

More than 15 million prescriptions were filled for the five drugs during the first nine months of this year, according to IMS Health, a pharmaceutical information and health care consulting company. While the makers rigorously defend the drugs' safety when taken as directed, some people who take them are scared.

Michael Miller, director of the Center for Preventive Cardiology at the University of Maryland Medical Center in Baltimore, said at least 10 patients have called asking what to do. While some research suggests that Crestor carries greater risk of serious side effects than other statins, Miller said current knowledge does not warrant taking most patients off the drug. He will continue to monitor patients carefully and won't prescribe Crestor to those at high risk for the most serious side effects.

If you are taking one of these drugs and want to consider another treatment, experts recommend consulting with your doctor before stopping or changing any regimen. Some drugs interact with others, so you should tell your doctor about any drugs -- prescription or over-the-counter -- you're taking on a regular basis.

For those taking any of the five drugs, risks and options are discussed below.

- **Meridia** Used for weight loss, works by "acting on the appetite control centers in the brain," according to its maker, Abbott Laboratories. The drug works best when combined with a low-calorie diet, the company says.

Risks Elevated risk of cardiovascular side effects, including heart attack and stroke.

Drugmaker Response Illinois-based Abbott says it stands behind the safety of the drug.

Alternatives The best way to drop pounds: Eat less, move more, doctors said. "I very much believe in behavior modification and lifestyle changes," said Tania Heller, medical director of Suburban Hospital's Center for Eating Disorders and Adolescent Obesity. For patients at high risk for complications of obesity -- such as those with type 2 diabetes -- drugs may help speed weight loss, Heller said. "But the key point to get across is not to rely only on medication" to lose weight, she said.

For patients who need medication, obesity drug Xenical, made by Roche Pharmaceuticals, is another option. The drug works by preventing about a third of the fat in the food you eat from being digested. Studies show that patients taking the drug lost twice as much weight as those on the same diet without medication. Side effects -- increased frequency and urgent need to empty the bowels, and gas with an oily discharge -- do not enhance its popularity.

- **Accutane** A synthetic form of Vitamin A, used to treat severe acne.

Risks Can cause severe birth defects when taken by pregnant women.

Drugmaker Response The risk for birth defects when the drug is taken by pregnant women has been known since its 1982 approval, said Carolyn Glynn, spokeswoman for Roche Pharmaceuticals. Roche and the companies that distribute the three generic forms of Accutane require doctors to test women for pregnancy before prescribing the drug, and to sign forms stating they've educated patients about known risks.

Alternatives Oral antibiotics and topical medications should be tried before taking Accutane. But neither type of drug is considered as effective as Accutane in treating the most severe cases of acne, said Paula Bourelly, assistant professor of dermatology at Georgetown University Hospital. Since Accutane is the only medication considered effective for the most severe forms of acne, patients with the very worst cases have limited options. Bourelly said she has had new patients report taking antibiotics for months in an effort to clear up their acne.

- **Serevent** A long-acting inhaled bronchodilator (a drug that widens the airways in the lungs) used for long-term management of asthma and chronic obstructive pulmonary disease.

Risks "Rare but serious asthma episodes and asthma-related fatalities occurred in a study with Serevent," GlaxoSmithKline reports on its Web site. "These risks may be greater in African Americans." Researchers think risks are higher for people with certain types of beta receptors (which exist on cells that line the surface of organs, including the lungs); this type of receptor seems more common in black patients. Some people of other races may have this type of beta receptor, too, doctors said.

Drugmaker Response GlaxoSmithKline says it addressed this concern by adding a "black box" to Serevent's label in August 2003, warning patients and doctors of this risk, according to a written statement the company issued on the day of Graham's testimony.

Patients should not stop taking Serevent without their doctor's approval, the statement says.

Alternatives For those who don't want to take Serevent, there are several options, depending on the severity of the patient's asthma. Those with mild asthma may use a rescue medication like albuterol, which is taken only when the patient feels short of breath or has other asthmatic symptoms, said Martha White, an allergist at the Institute for Asthma and Allergy in Wheaton and Chevy Chase.

People with asthma who have symptoms at least twice a week need more treatment, White said. Options include another long-acting bronchodilator called Foradil, inhaled corticosteroids and Singulair, a leukotriene inhibitor (which is thought to work by blocking a substance that is released by cells in the lungs during asthma attacks).

Inhaled corticosteroids are considered the most effective at managing asthma symptoms, but they carry a heightened risk -- particularly at higher dosages -- of oral thrush (mouth infection), skin thinning and bruising with long-term use. The side effects for Foradil, usually used in combination with inhaled corticosteroids, include tremors, fast or irregular heartbeat, headache, muscle cramps or pain and, in rare cases, bronchospasms (narrowing of the airways). The side effects for Singulair -- which is not as effective as inhaled corticosteroids at controlling asthma symptoms -- include fatigue, fever, stomach pain and upset stomach.

- **Bextra** A COX-2 painkiller often used to treat osteoarthritis.

Risks Bextra may have the same cardiovascular risks as those that caused Merck & Co. to pull Vioxx from the market in September. Some experts say that COX-2 drugs in general may be unsafe for long-term use. Existing research both confirms and refutes this risk, so more studies are needed.

Drugmaker Response Pfizer considers the drug to be "safe and effective," said spokeswoman Mariann Caprino. The drug company looks forward to the FDA's February 2005 meeting on the safety of Bextra and Celebrex, the only other COX-2 drug left on the market, Caprino said.

Alternatives Other choices include NSAIDs (nonsteroidal anti-inflammatory drugs), available by prescription (including Mobic and Daypro) and over-the-counter (including Motrin, Aleve and Advil).

Weight loss, if needed, and regular exercise may also ease pain. To relieve pain temporarily, heat and ice may help. Topical medications such as corticosteroids, Bengay and capsaicin may also ease soreness. Some patients may find relief through corticosteroid or hyaluronic acid injections into sore joints. Injection complications include infection, and repeated corticosteroid shots can increase risks of cataracts and bone weakening. In rare cases, skin whitens and thins at the injection site.

- **Crestor** A statin drug used to treat high cholesterol.

Risks Kidney failure and rhabdomyolysis, a rare but potentially fatal muscle disease. Complications are more likely at higher doses (the highest approved dose in the United States is 20 milligrams; highest dosages elsewhere extend to 40 milligrams).

Drugmaker Response In a written statement issued Nov. 19, AstraZeneca said senior FDA officials reassured the firm that "there is no concern in relation to Crestor's safety and that they [the FDA] have issued a statement explaining that Dr. Graham's testimony does not reflect the views of the agency." The company has also run newspaper advertisements to reassure patients taking Crestor of the drug's safety.

Alternative treatments Other statin drugs include Lipitor, Zocor, Pravachol and Lescol. The decision on which to take should be made in consultation with your doctor, since dose and duration of treatment may vary depending on how high your cholesterol is, how low the target is and other factors. All statin drugs carry some risk for rhabdomyolysis, as well as risk of increasing liver enzymes. Liver function should be monitored regularly.

Diet and exercise are also powerful tools to help keep cholesterol and blood pressure in check, though doctors caution patients not to forego medication for levels deemed dangerously high by their doctors.

But don't stop taking your medication even if your cholesterol levels dip into safer territory. Former president Bill Clinton, who underwent emergency heart bypass surgery in September, had stopped taking his statin medication after losing weight and becoming more fit. His LDL -- or "bad" cholesterol -- level had decreased since his last presidential physical, from 177 to 114 when measured the week before his heart surgery. The recommended LDL level is less than 70.

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