



Family Medicine Clinical Pharmacy Forum Vol. 5, Issue 1 (January/February 2009)

Family Medicine Clinical Pharmacy Forum is a brief bi-monthly publication from the Family Medicine clinical pharmacists distributed to faculty and residents of the Department of Family Medicine. Our intent is to provide timely information on broad-based issues of pharmacotherapy, as well as regulatory and practiced-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.

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New Drug for Hyperlipidemia: (fenofibric acid) Trilipix™

Fenofibric acid (Trilipix™) was recently approved by the FDA for treatment of hyperlipidemia. Fenofibric acid is the active metabolite of fenofibrate (Tricor®), which is used primarily to target high triglycerides and low high density lipoprotein (HDL). Fenofibric acid is currently the only approved fibrate to be used in combination with a statin.

The combination of a statin and a fibrate can increase the risk for both myopathy and rhabdomyolysis. However, the overall incidence of these events is rare, and they most often occur when a statin is used in combination with gemfibrozil (Lopid). Very few post-marketing reports of these events have been reported with the combination of a statin and fenofibrate. These data indicate that combination therapy with statins and fenofibrate remains a safe and effective therapeutic option for most patients.

Fenofibric acid is available in 45 and 135 mg capsules and is dosed once daily. The cash price is comparable to brand name Tricor®. However, fenofibrate will go off patent in 2011. While it may prove beneficial in patients who do not tolerate combination statin and fenofibrate, its overall therapeutic use will likely be limited due to the limited advantage it offers over fenofibrate.

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New drug for gout: Febuxostat (Uloric®)

Febuxostat (Uloric®), a xanthine oxidase inhibitor, is the first agent approved by the FDA for chronic management of gout in over 40 years. The approval of febuxostat was initially delayed when clinical trials showed an increased incidence of death and cardiac problems in patients on febuxostat compared to allopurinol. However, later trials did not show an increased risk for these events.

Although its mechanism of action is the same as that of allopurinol, febuxostat does offer the advantage of minimal renal excretion. In clinical trials, febuxostat 80 mg was superior to allopurinol 300 mg daily in the percent of patients with serum uric acid levels of <6 mg/dL after 6 months of treatment (67% vs. 42%, $p < 0.001$).

The recommended dose of febuxostat is 40 mg daily. If serum uric acid levels remain above 6 mg/dL after 2-4 weeks of treatment, the dose may be increased to 80 mg daily. Concurrent treatment with a prophylactic agent (i.e. colchicine) should be considered for a minimum of 6 months to prevent acute gout exacerbations from occurring. While no dose adjustments are necessary based on renal or hepatic function, it is recommended that this agent be used cautiously in patients with CrCl <30 mL/min or severe hepatic impairment. The most common side effects reported were diarrhea, headache, arthralgia, and liver enzyme elevation. It is recommended that liver function tests are monitored periodically.

For more information on febuxostat, please refer to the [press release](#)

Will all propoxyphene-containing products soon be off the market?

Recently, an FDA advisory panel voted in favor of banning all propoxyphene-containing products, including Darvon and Darvocet. The decision was made based on a lack of efficacy data and possible safety concerns. In clinical trials, the combination of propoxyphene and acetaminophen has minimal added analgesic benefit when compared with acetaminophen alone.

Despite the lack of efficacy data, Darvocet remains widely used in the U.S., with over 20 million prescriptions written in 2007. In addition to efficacy concerns, the safety of Darvocet remains in question. Over 3000 adverse events, including suicide, drug dependence, and overdose, have been reported to the FDA. In addition, 503 deaths related to Darvon were reported in 2007. No immediate action on product removal has been taken.

Potential variation in the efficacy of clopidogrel (Plavix®) among patients

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The FDA is currently investigating whether a possible variation in efficacy of clopidogrel (Plavix[®]) exists in certain individuals. This decrease in efficacy may be secondary to either genetic factors or concomitant medications as a result of changes in the metabolism of clopidogrel. A main class of medications currently being evaluated is the proton pump inhibitors (PPIs). It is thought that PPIs inhibit the conversion of clopidogrel to its active form, thereby decreasing its effectiveness. Since PPIs are often prescribed with clopidogrel to decrease gastric irritation, the impact of any negative findings could be significant.

Until further data are available, the FDA recommends that providers:

- Continue to prescribe clopidogrel because of its documented benefit
- Re-evaluate the need for concurrent PPI therapy in patients on clopidogrel

For more information on this topic, please refer to [FDA press release](#).

Updated guidelines: American Diabetes Association Standards of Care 2009

Recent changes to the “Standards of Medical Care in Diabetes” issued by the American Diabetes Association were published in January 2009. Some key revisions are listed below:

- Immunizations
 - Administer pneumococcal polysaccharide vaccine to **all diabetic patients ≥ 2 years of age**. A one-time revaccination is recommended for individuals >64 years of age previously immunized when they were <65 years of age if the vaccine was administered >5 years ago. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and other immunocompromised states, such as after transplantation. (C)
- Metformin use in patients with heart failure (CHF)
 - Metformin may be used in patients with stable CHF if renal function is normal. It should be avoided in unstable or hospitalized patients with CHF. (C)

To read the full report, visit [Diabetes Care](#) and click on executive summary pages S6-S12.

FDA Advisory statement: New warnings issued for varenicline (Chantix[™])

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Since its approval in 2006, varenicline (Chantix™) has been used by millions of Americans as a smoking cessation aid. However, concerns regarding the safety of this agent continue to surface. Previously, the FDA issued a public health advisory statement on possible neuropsychiatric side effects in patients taking this medication.

Recently, the FDA reported that more serious adverse events were reported for varenicline than for any other prescription medication for the second straight quarter. Overall, over 3300 serious injuries, including 112 deaths, have been attributed to varenicline. Several types of events have been reported, including cardiac arrhythmias, acute myocardial infarctions, seizures, and skin reactions.

Current recommendations for appropriate use of varenicline include the following:

- Varenicline should be avoided in pilots, air traffic controllers, truckers, and bus drivers.
- Patients taking varenicline should contact their doctors if they experience behavior or mood changes, and healthcare professionals should monitor patients for these changes.
- Patients should use caution when driving or operating machinery until they know how varenicline may affect them.

For more information, please refer to the [FDA advisory](#) for health care professionals.

Clinical Pearl: Monitoring INR when initiating antibiotics in patients on warfarin

Case: TS is a 65 year old female with on warfarin for atrial fibrillation. She is diagnosed with a urinary tract infection and is prescribed Bactrim DS x 7 days. Her INR today is 2.5 (goal 2.0-3.0). Are any special considerations warranted regarding this patient's anticoagulation therapy?

Numerous antibiotic classes can affect the INR by a variety of mechanisms (see table below). In general, it is prudent to check the INR level when starting an antibiotic that may potentially interact with warfarin, particularly if one was not checked within the past week. In addition, the INR should be rechecked 3 days after starting an antibiotic and the dose of warfarin should be adjusted accordingly. A prophylactic decrease in the warfarin dose may be appropriate for certain patients, especially those who are elderly or who take other interacting medications.

Increase INR	Decrease INR
Bactrim	Dicloxacillin
Macrolides	Nafcillin
Metronidazole	Rifampin
Quinolones	
Tetracyclines	

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