

Wyoming Drug Utilization Review

The Use of Fibrates and Statins Together For Dyslipidemia

Jamie Johnson, PharmD Candidate

The recent marketing of Trilipix (fenofibric acid) as approved for use in combination with a statin for the treatment of dyslipidemia has caused many health care providers and pharmacists to question the implications newer drugs have on the treatment of dyslipidemias, as well as the potential for serious adverse effects in the patient population when combinations of medications are used.

Recent research into this topic provides some clarification but leaves many questions unanswered.

The rationale for the combined use of a statin and a fibrate is relatively straightforward. The link between elevated LDL-C and cardiovascular events has been long established.¹ It is well known that the use of statins can cause marked decreases in LDL-C, and providers of patients with mixed disorders (elevated triglycerides and/or lower than optimal HDL-C) have long been recommending concurrent use of a fibrate, which has been shown to increase HDL-C and decrease triglyceride levels.¹ However, concerns were raised with using one particular fibrate, gemfibrozil, in combination with statins after increased adverse events such as rhabdomyolysis and myopathy were reported.^{2,3} The method by which gemfibrozil affects the metabolism of statins is thought to increase their blood levels, leading to worsened

side effect profiles.⁴ Other fibrates available, including fenofibrate and fenofibric acid, have a different metabolism that does not appear to increase the blood level of statins in the same manner as gemfibrozil, making them potentially safer for use in combination therapy.^{1,5-7} Despite the clear rationale for trying a newer fibrate in patients who have continued mixed dyslipidemia while on a statin alone, it is important to mention that there is currently no evidence of a decrease in cardiovascular morbidity or mortality with the combination compared to statin monotherapy.¹ The ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial, the results of which are expected in 2010, has followed approximately 10,000 patients over 4-8 years to determine, among other outcomes, whether the use of a fibrate plus a statin will reduce the rate of cardiovascular events compared to a statin alone.⁸

Three recent clinical trials compared the use of fibrate or statin monotherapy with the combination of fenofibric acid and either atorvastatin, simvastatin, and rosuvastatin. Results showed that fenofibric acid in combination with both low- and medium-dose statin therapy resulted in greater HDL-C increases and triglyceride decreases than that seen with statin monotherapy. The decrease in LDL-C was greater with a combination regimen than with fibrate therapy alone.⁵⁻⁷ Similar results were seen in trials using fluvastatin and pravastatin.⁹ No cases of rhabdomyolysis or clinical myopathy were seen in any of the treatment groups, a result which assisted in gaining FDA approval for Trilipix (fenofibric acid) being used concurrently with a statin. Although Tricor (fenofibrate) has not specifically received this indication, it has not been shown to have the problems associated with gemfibrozil and has been used for many years to supplement a statin regimen in patients with stubborn triglyceride and HDL-C levels.¹

The conclusion is that both fenofibrate and fenofibric acid appear to be relatively safe for use in combination with a statin for patients with mixed dyslipidemia. Some patients should avoid the combination or be carefully monitored, including patients with renal dysfunction, liver disease, gallbladder disease, untreated hypothyroidism, low muscle mass, diabetes, and advanced age.⁵⁻⁷ Dispensing

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Board Meeting Update

The DUR Board met for its bimonthly business meeting on July 30, 2009. Highlights of this meeting include the following.

1. The Board proposed adding Lyrica to the fibromyalgia criteria previously approved for Cymbalta and Savella. The addition of Lyrica will be sent out for public comment prior to implementation. The criteria for Cymbalta and Savella have been implemented.
2. Prior authorization criteria for Nucynta (trial of a short-acting C-II agent) and Nuvigil (trial of Provigil) were proposed. Multaq was discussed. Additional information regarding the clinical impact of this new medication will be requested from current prescribers of amiodarone.
3. Niravam will require a prior authorization. Patients using the medication currently will be asked to switch to another form of alprazolam.
4. Lexapro will be allowed first-line for adolescents aged 12 – 17. It will remain a step 3 agent for all other age groups.
5. A large increase in pharmacy claims for Synagis occurred between the 2007 and 2008 RSV seasons. The Board proposed limiting use to the RSV season (approximately November through March) and to a total of five doses per recipient per season.
6. Propoxyphene products will be limited to the maximum dose of propoxyphene or acetaminophen, whichever is lower.

All proposed prior authorization criteria will be posted for public comment. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to August 28th.

The next DUR Board meeting will be held September 24, 2009 in Laramie. Topics for discussion will include Provigil, tablet splitting and a proposed PDL for 2010. An agenda will be posted approximately two weeks prior to the meeting at www.uwyo.edu/DUR.

The Use of Fibrates and Statins

Trilipix requires a medication guide, and common side effects of fibrates such as nausea, vomiting, and abdominal pain should be discussed with the patient regardless of whether a statin is part of the patient's regimen.⁹

Of interest to pharmacists, Trilipix and Tricor are both manufactured by Abbott and are priced very similarly. Tricor's patent will run out in 2011, so a generic version of fenofibrate will most likely be marketed sometime that year. Abbott and AstraZeneca are expected to file a new drug application for a Trilipix/Crestor (fenofibric acid/rosuvastatin) combination in 2009, which if approved will be the first combination medication of its kind.¹⁰ While lifestyle changes and statins continue to be the mainstays of treatment, pharmaceutical companies and physicians continue to look at new ways to treat cholesterol disorders in hopes of designing a regimen which will optimize all lipid levels.

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Wyoming Department of Health

Cost Containment

Antoinette Brown R.Ph., Pharmacy Program Manager, Wyoming Department of Health

Many of you are aware of the recent budget cuts announced by Governor Freudenthal in June 2009. The Department of Health in projecting for future years has taken the initiative to look at what can be done now and in the near future to further reduce the Department's budget. Because Medicaid comprises the largest percentage of the Department's budget, the Office of Pharmacy Services (OPS) has taken and will continue to take several steps to contain both Medicaid and State general fund pharmacy expenditures.

The most recent action taken by the OPS is to expand the Preferred Drug List (PDL). The OPS is aware of the impact this has had on both medical and pharmacy providers. The OPS is empathetic to the extra effort this has placed on providers to handle prior authorization (PA) requests, however, necessary steps must be taken in order for the OPS to operate within its budget. There are steps that both medical and pharmacy providers can take to ease their burden when working within the confines of the Medicaid PDL.

1. Familiarize yourself with the Medicaid PDL. Post it in your pharmacy, offices, and share it with key staff. The PDL is posted on the GHS Website at: <http://www.wyequalitycare.org/>. It is also available for *free* on your hand held device through Epocrates. You will be notified of updates to the PDL by either a faxed or mailed EqualityCare Pharmacy newsletter.
2. **Prescribers**, prescribe preferred medications when possible. By prescribing preferred medications, you will not have to spend additional time filling out PA forms.
3. **Pharmacies**, inform prescribers of the preferred medications when calling them to let them know a pharmacy claim has rejected due to a non-preferred medication being prescribed.
4. **Prescribers**, when prescribing non-preferred medications and submitting PA requests, be sure to include *diagnosis, past trials of medications, the dates of those trials, and the details as to why the preferred medications do not work for your patient*. This will alleviate the additional amount of time it takes the PA Help Desk pharmacists in processing your requests and the amount of time YOU have to spend providing additional information.

The OPS will continue to expand the PDL, as well as implement further limits on many medications. Though it would be more desirable for all concerned for Medicaid to operate with an open formulary, it is not possible within the overall Medicaid budget. Increased expenditures on the Medicaid Pharmacy side equal reductions in other areas, such as physician reimbursement. Your assistance in containing medication expenditures allows more flexibility for other funding priorities. Reductions in medication expenditures must be taken where they can be reasonably obtained.

The pharmacy benefit for Medicaid is an *optional* service that the State of Wyoming has elected to provide. The OPS asks for your cooperation now and going forward with adhering to the PDL and medication limits and prior authorization. If we cannot achieve appropriate cost containment with these measures, more drastic options have been considered and may be implemented. These include limiting the number of prescriptions an EqualityCare client can receive in a month, requiring the use of mail-order pharmacies, reducing pharmacy provider reimbursement, or drastically limiting the formulary.

Also, please keep in mind that Goold Health Systems (GHS), who is our new pharmacy benefits manager, is not the entity who created the PDL or sets pharmacy benefits policy. Policy and PDL decisions are made by the OPS with the assistance of the DUR Board, Wyoming psychiatrists, the Department of Health Medical Director, and other specialists practicing medicine in Wyoming. Great care, time and effort is spent in creating the PDL and coverage decisions, and input from prescribers is always appreciated and solicited before, during and after implementation of limits. In addition, the OPS made the decision that verbal PAs can no longer be accepted. In order to effectively manage the PDL and maintain best business practices, all PA requests must be submitted on paper and documented by GHS. The OPS asks that both you and your staff be polite and professional when working with GHS staff. This will make the process much faster and easier for all involved.

Thank you for your assistance in caring for WY Medicaid/ Equality Care clients, and for helping to maintain access to our pharmacy benefit by supporting our PDL.

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