Plavix’s losses could be Effient’s gains

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Last week’s surprise black box warning for blood thinning drug, Plavix, cautioning about poor responders, is certainly a blow to the multibillion dollar selling product that was already struggling with concerns about its effectiveness when used in combination with other drugs, particularly proton pump inhibitors.

But what could be Plavix’s loss might provide a much needed boost for rival product Effient, which has so far generated much slower than expected sales since its launch in August 2009 (Can evidence be found for slowing drug launches?, February 18, 2010). At the moment consensus sales forecasts for Effient stand at $979m in 2014 for both Eli Lilly and Daiichi Sankyo, according to consensus forecasts from EvaluatePharma. But this figure is expected to come down as some analysts have yet to adjust their sales predictions for the drug following Lilly’s disappointing fourth quarter results for the drug.

A look at archived forecasts for 2012 sales of the drug by Lilly also show that expectations have been falling dramatically; in December 2007 analysts were predicting sales would reach $1.06bn, by February 2010 these estimates had more than halved to $494m.

Poor response

But the travails that Plavix is currently going through could reinvigorate sales in Effient. What is causing Plavix's problems is the fact the drug does not prevent blood clotting until it is metabolised into an active form by the liver enzyme CYP2C19.

As such, people with reduced levels of CYP2C19 cannot convert Plavix into its active form, and are therefore at an increased risk of clotting.

As Plavix is normally used after patients suffer heart attacks, strokes or just before surgery to open blocked arteries in the heart, if efficacy is lowered then patients have an increased risk of suffering all of these complaints. It is thought that between 2-14% of people are in this “poor responders” category.

The FDA has been concerned about this subgroup of patients for a while and in May 2009 requested that information about poor responders be put on the label for Plavix, but this has now been upgraded to the much stronger black box warning.

Risk/reward

As Effient is less reliant on CYP2C19 doctors might now reconsider using the drug despite its high bleeding side effects and the restrictions in its use in certain patient population groups. At the moment the lack of reimbursement for the drug and doctors’ discomfort with the bleeding profile are what some analysts believe is holding back sales.

It is because of this bleeding risk that Effient is currently used in a much narrower patient population. If a sizeable proportion of patients currently using Plavix are found to be at increased risk of serious cardiac events because of their CYP2C19 status, regulators might consider widening out Effient’s use to cover them despite the bleeding concerns surrounding the drug.

What also might help sales of Effient, which could suffer further when Plavix loses patent protection in November 2011, is the study launched by Medco Health Solutions last year, pitching the two drugs against each other to determine their effectiveness in patients who respond normally to Plavix. If Effient is found to be superior in this so-called “normal” population then it could claw back some market share from Plavix, but the data from this 14,000 patient study is not expected until 2012.

Testing, testing, testing

Another knock on effect of the reduced efficacy of Plavix in certain patients could be increased testing when using the anticoagulant. But even this may be problematic. There is currently only one approved genetic test for CYP2C19 levels, Roche’s AmpliChip, and the conundrum facing doctors is while this looks for the variation in liver enzyme levels it does not specifically indicate who might or might not benefit from taking Plavix.
Additionally, as getting test results can vary from one or two days to a week, depending on lab facilities available, doctors may at this point be reluctant to wait for results and start patients on the drug anyway.

But given that the test only costs $500 and an average month’s supply of Plavix costs $155, but will be used for many years, if the pressure does not come from doctors to start testing it will almost certainly come from insurance companies. Also, diagnostic companies who offer similar but unapproved tests will not be slow in trying to increase testing rates so they can benefit from prescriptions of the drug, which is second biggest selling product in the world after Lipitor and last year had revenues of $9.8bn.