FDA approves boceprevir (Victrelis) and telaprevir (Incivek) for hepatitis C

FDA approves boceprevir (Victrelis) and telaprevir (Incivek) for hepatitis C

The U.S. Food and Drug Administration approved boceprevir (Victrelis) on May 13, 2011 and telaprevir (Incivek) on May 23, 2011 for the treatment of hepatitis C in combination with peginterferon alfa and ribavirin in adult patients.

Boceprevir and telaprevir are hepatitis C virus (HCV) NS3/4A protease inhibitors. They inhibit HCV NS3/4A serine protease needed for proteolytic cleavage of the HCV encoded polyprotein into mature forms. Both are indicated for treatment of chronic hepatitis C (CHC) genotype 1 infection in combination with peginterferon alfa and ribavirin, specifically for adults with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy.

Compared with the control group patients who received the standard of care (ribavirin plus pegylated interferon), the patients received boceprevir additionally had a significantly higher rate of sustained virologic response (SVR). The new treatment effectively doubled the SVR rate, from approximately 20% to 40% with the standard of care to more than 60% with added boceprevir in some cases. Compared with the control group patients who received ribavirin and pegylated interferon, patients received telaprevir additionally had a significantly higher rate of SVR of about 80%

or more. The SVR rate for patients treated with telaprevir across all studies, and across all patient groups, was 20% to 45% higher than the current standard of care.

The dosage of telaprevir is 750 mg taken 3 times a day (7-9 hours apart) with food (not low fat), while boceprevir is administered 800 mg orally three times daily (every 7 - 9 hours) with food (a meal or light snack). They must be administered with both peginterferon alfa and ribavirin.

The most common adverse drug reactions to telaprevir (incidence at least 5% higher with telaprevir than in controls) were rash, pruritus, anemia, nausea, hemorrhoids, diarrhea, anorectal discomfort, dysgeusia, fatigue, vomiting, and anal pruritus. The most commonly reported adverse reactions (greater than 35% of subjects) in clinical trials in adult subjects receiving the combination of boceprevir with peginterferon alfa-2b and ribavirin were fatigue, anemia, nausea, headache and dysgeusia.

Prostate cancer risk with 5-alpha reductase inhibitors

The US FDA alerted healthcare professionals on June 9, 2011 about changes in the labeling for 5-alpha reductase inhibitors (5-ARI), which include dutasteride and finasteride, of an increased risk of being diagnosed with a high-grade prostate cancer while taking these drugs.

Both drugs are licensed for use in benign prostate hypertrophy and have also been investigated for, but not approved for, prostate cancer prevention in men at high risk. However, it was in these studies looking at prostate cancer prevention that there was a finding of an increased incidence of high-grade prostate cancer.

The Prostate Cancer Prevention Trial (PCPT) and the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trials both showed a reduction in the cumulative incidence of prostate cancer with the use of finasteride and dutasteride. This overall risk reduction was limited to a decrease in prostate cancers with a GS of 6 or lower. In contrast, there was an increased incidence of cancers with a GS of 8 to 10 with finasteride vs placebo (1.8% vs 1.1%, respectively) and dutasteride vs placebo (1% vs 0.5%, respectively).

FDA restricts use of simvastatin 80 mg

The FDA recommended on 8th June 2011 that physicians to restrict the prescribing of high-dose simvastatin to patients, given an increased risk of muscle damage particularly in the first 12th months of use.

The changes to the label are based on the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH). The risk of muscle injury is highest during the first year of treatment with the 80 mg dose of simvastatin, which is often the result of interactions with certain other medicines, and is frequently associated with a genetic predisposition for simvastatin-related muscle injury.

The FDA notes that the risks of myopathy and rhabdomyolysis were the highest in the first year and that older age and female sex increased the risks.

Simvastatin 80-mg dose lowers the LDL cholesterol by an additional 6% over simvastatin 40 mg. Simvastatin 80 mg should be used only in patients who have been taking this dose for 12 months or more and have not experienced any muscle toxicity. It should not be prescribed to new patients. The FDA is requesting additional changes should be made to the drug's label, including the new dosing recommendations:

Contraindicated with simvastatin:	Itraconazole, Ketoconazole, Posaconazole, Erythromycin, Clarithromycin, Telithromycin, HIV protease inhibitors, Nefazodone, Gemfibrozil, Cyclosporine, Danazol
Do not exceed 10 mg simvastatin daily with:	Amiodarone, Verapamil, Diltiazem
Do not exceed 20 mg simvastatin daily with:	Amlodipine, Ranolazine
Others	Avoid large quantities of grapefruit juice (>1 quart daily, or >~946ml daily)

Fidaxomicin (Dificid) approved for the treatment of *Clostridium difficile*-associated diarrhea (CDAD)

The U.S. Food and Drug Administration approved fidaxomicin (Dificid) tablets for the treatment of Clostridium difficile-associated diarrhea (CDAD) on May 27, 2011.

Fidaxomicin was granted an orphan drug designation by the FDA for the treatment of Clostridium difficile infection (CDI) in pediatric patients aged 16 years and younger on 10th January, 2011. The safety and efficacy of fidaxomicin were demonstrated in two trials that included 564 patients with CDAD that compared fidaxomicin with vancomycin, and the clinical response was similar in the fidaxomicin group compared with the vancomycin group in both studies. In the fidaxomicin trials, a greater number of patients treated with fidaxomicin had a sustained cure three weeks after treatment ended versus those patients treated with vancomycin.

Fidaxomicin is a macrolide antibacterial drug indicated in adults (≥18 years of age) for treatment of Clostridium difficile-associated diarrhea. The dosage is one 200 mg tablet orally twice daily for 10 days with or without food. The most common adverse reactions are nausea (11%), vomiting (7%), abdominal pain (6%), gastrointestinal hemorrhage (4%), anemia (2%), and neutropenia (2%).

Ellen LAI is a pharmacist working at the Queen Mary Hospital