The Pharmacist Activist

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Editorial

Ten Thousand and One Pfizer Employees Lose Jobs – But the *"One"* is Very Different!

"Pfizer to cut 10,000 positions" and similar statements were prominent headlines in news reports in late January. The reports describe the "struggle" that Pfizer faces as some of its most important drugs lose patent protection and face generic competition, and as insurance companies and other large purchasers of drugs expect lower prices. Poor Pfizer!

I read several stories about this situation that were written by different reporters. I was struck by the fact that the stories focused exclusively on Pfizer's concerns. There was not one word about the concerns that will be faced by the 10,000 men and women who will lose their jobs. Perhaps we don't expect to find such observations in "business" stories but most, if not all, of these 10,000 people will experience uncertainty and anxiety that warrant concern and support. Many will find it very difficult to obtain another position.

There have been other recent headlines about the loss of a single position at Pfizer. However, this individual will not experience the uncertainty and anxiety faced by 10,000 of his former colleagues because he is the former Chairman and Chief Executive. The headline of the *Wall Street Journal* story (December 22, 2006) about the financial terms for his departure reads, "Payout for Former Pfizer Chief is Valued at Nearly $200 Million." This amount includes about $82 million in pension benefits, about $78 million in deferred compensation, and severance pay, bonuses, stock options, and "performance shares" that bring the total to almost $200 million. This is in addition to the wealth he already accrued in more than three decades of employment at Pfizer, the last five of which were as the CEO.

The circumstances facing many of the 10,000 and the "one" could not be more different. It is my hope that the former CEO is extremely generous and will commit a large portion of his wealth to assist his former colleagues who will face financial hardship as a result of losing their positions at Pfizer. A generous share of this wealth would also be of great benefit for many patients in the United States and throughout the world who have serious medical problems but cannot afford to obtain medications. Wouldn't it be wonderful if this would be the next Pfizer story we hear about in the news?

Daniel A. Hussar

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News, Information and Career Opportunities
NEWS - Line PUBLISHING

Editor's Note

The birthdays of two great American presidents are celebrated in this month of February. Abraham Lincoln was born on February 12 and George Washington on February 22. Lincoln's Gettysburg Address is a presentation that many consider to be America's greatest speech. Having recently read it again, I find it to be even more meaningful and inspiring now than when I memorized it as a school assignment years ago.

The Gettysburg Address

by Abraham Lincoln – July 4, 1863

Four score and seven years ago our fathers brought forth on this continent, a new nation, conceived in Liberty, and dedicated to the proposition that all men are created equal.

Now we are engaged in a great civil war, testing whether that nation, or any nation so conceived and so dedicated, can long endure. We are met on a great battlefield of that war. We have come to dedicate a portion of that field, as a final resting place for those who here gave their lives that that nation might live. It is altogether fitting and proper that we should do this.

But, in a larger sense, we can not dedicate – we can not consecrate – we can not hallow – this ground. The brave men, living and dead, who struggled here, have consecrated it, far above our poor power to add or detract. The world will little note, nor long remember what we say here, but it can never forget what they did here. It is for us the living, rather, to be dedicated here to the unfinished work which they who fought here have thus far so nobly advanced. It is rather for us to be here dedicated to the great task remaining before us – that from these honored dead we take increased devotion to that cause for which they gave the last full measure of devotion – that we here highly resolve that these dead should not have died in vain – that this nation, under God, shall have a new birth of freedom – and that government of the people, by the people, for the people, shall not perish from the earth.

New Drug Review

Posaconazole (Noxafil – Schering)

Antifungal Agent

New Drug Comparison Rating (NDCR) = 4

(significant advantages)

in a scale of 1 to 5, with 5 being the highest rating

Indications:

Prophylaxis of invasive Aspergillus and Candida infections in patients 13 years of age and older who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies who develop prolonged neutropenia from chemotherapy; treatment of oropharyngeal candidiasis including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.

Most important risks/adverse events:

Hepatic adverse events (liver function tests should be monitored); inhibits the CYP3A4 metabolic pathway and concurrent use with ergot-type products is contraindicated (concurrent use with other CYP3A4 substrates [e.g., cyclosporine (e.g., Neoral), tacrolimus (Prograf)] should be closely monitored); prolongation of the QT interval of the electrocardiogram (concurrent use with other drugs that prolong the QT interval and are metabolized via the CYP3A4 pathway [e.g., quinidine, pimozide (e.g., Orap)] is contraindicated); action may be reduced by cimetidine (e.g., Tagamet), phenytoin (e.g., Dilantin), and rifabutin (e.g., Mycobutin), and concurrent use is best avoided.

Most common adverse events:

Nausea (7%), vomiting (5%), diarrhea (5%).

Usual dosage:

Should be administered with a full meal or with a liquid nutritional supplement if the patient cannot eat a full meal; prophylaxis – 200 mg three times a day; treatment (oropharyngeal candidiasis) – 100 mg twice a day on the first day, then 100 mg once a day for 13 days; oropharyngeal candidiasis that is refractory to itraconazole and/or fluconazole – 400 mg twice a day; in patients taking cyclosporine or tacrolimus, the dosage of the immunosuppressant should be reduced.

Product:

Oral suspension – 40 mg/mL

Comparable drugs:

Fluconazole (e.g., Diflucan), itraconazole (e.g., Sporanox), voriconazole (Vfend).

Advantages:

- First drug approved for prophylaxis against invasive Aspergillus infection;
- More effective in preventing invasive Aspergillus infection;
- May be effective in the treatment of oropharyngeal candidiasis that is refractory to other agents;
- Less likely to cause visual disturbances (compared with voriconazole).

Disadvantages:

- Fewer labeled indications;
- Absorption and activity may be less predictable;
- Not available in a parenterally-administered formulation.

Comments:

Posaconazole is a triazole antifungal agent that is effective in preventing certain invasive fungal infections in patients who are at high risk of serious consequences. It is the first drug to be approved for prophylaxis against invasive Aspergillus infection. When compared with fluconazole and itraconazole, substantially fewer breakthrough infections caused by Aspergillus species occurred in patients receiving prophylaxis with posaconazole. It is also effective in many patients with oropharyngeal candidiasis that is refractory to itraconazole and/or fluconazole.

Although posaconazole is not a substrate for CYP3A4, it does inhibit this metabolic pathway and may increase the action of numerous other medications that are CYP3A4 substrates. Posaconazole is incompletely absorbed following oral administration, but its bioavailability and peak concentrations are three to four times higher when it is administered with a meal, relative to a fasting state. Therefore, it should be administered with a full meal or a liquid nutritional supplement.

Daniel A. Hussar

New Drug Review

Ranibizumab (Lucentis – Genentech)

Agent for Macular Degeneration

New Drug Comparison Rating (NDCR) = 5

(important advance)

in a scale of 1 to 5, with 5 being the highest rating

Indication:

Administered by intravitreal injection for the treatment of patients with neovascular (wet) age-related macular degeneration (AMD).

Most important risks/adverse events:

Stroke; endophthalmitis; retinal detachment; patients should be monitored during the week following each injection; contraindicated in patients with ocular or periocular infections.

Most common adverse events (probably often attributable to the injection procedure rather than to the medication):

Conjunctival hemorrhage (60%); eye pain (27%); vitreous floaters (27%), retinal hemorrhage (21%).

Usual dosage:

0.5 mg (0.05 mL) via intravitreal injection once a month; after the first four monthly injections, frequency of administration may be reduced to once every three months if monthly injections are not feasible (however, this modified regimen is less effective than the monthly regimen).

Product:

Vials – 0.5 mg in 0.05 mL

Comparable drugs:

Pegaptanib (Macugen), verteporfin (Visudyne).

Advantages:

- First drug to provide improvement in vision in AMD;
- Maintains vision after 24 months;
- Indicated for treatment of all subtypes of neovascular AMD (compared with verteporfin).

Disadvantages:

- Administered by intravitreal injection (compared with verteporfin).

Comments:

Ranibizumab is a recombinant humanized immunoglobulin G1 kappa isotype monoclonal antibody fragment that binds to vascular endothelial growth factor-A (VEGF-A) and prevents its interaction with its receptors. In one of the clinical studies, 95% of patients maintained their vision after 12 months, and 90% after 24 months. Approximately one-third of the patients experienced improved vision after 12 and 24 months, and it is the first drug demonstrated to be effective in improving vision in a substantial number of patients. In a comparative study, it was more effective than verteporfin. Although ranibizumab has not been directly compared with pegaptanib, the results of separate studies of the two agents suggest that the latter agent is less effective. The antineoplastic agent, bevacizumab (Avastin), is related to ranibizumab and is also a VEGF inhibitor. It has been used successfully "off-label" in the treatment of AMD, and its use is much less expensive than the use of ranibizumab. A study that will compare the two drugs is being planned. (A first-page story in the February 22, 2007 issue of *The Wall Street Journal* addresses the multiple issues pertaining to the use of these agents in treating AMD).

Daniel A. Hussar