The Pharmacist Activist

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Editorial

Patients Held Hostage!

Exorbitant Drug Prices Will Result in Rationing of Treatment and Price Controls!

I am an advocate for entrepreneurism and opportunities for companies to be highly profitable. I have been tolerant of the common perception that pharmaceutical companies will set prices for their drugs based on what the market will bear. However, there are an increasing number of situations in which companies have established prices for their drugs that must be challenged.

The marketing of sofosbuvir (Sovaldi) in December 2013 for the treatment of chronic hepatitis C virus (HCV) infection has sparked an avalanche of praise for its breakthrough benefits but strong criticism of its price ($1,000 a tablet). Sovaldi's unique mechanism of action, high rate of effectiveness, safety, and convenient once-a-day dosage regimen establish it as a remarkably important advance in the treatment of a potentially devastating infection with consequences such as cirrhosis, liver cancer, liver transplants, and death. In my ratings for new drugs I have given it the highest rating of 5, in a scale of 1 to 5. It is used in a treatment regimen that, for many patients, will be continued for 12 weeks and require the use of 84 Sovaldi tablets (representing a cost of $84,000). This amount does not include the cost of the one or two other medications with which it must be used in combination, or other related costs incurred in treating the infection. Some patients experience types and severities of HCV infection that will require treatment for 24 weeks or longer at a correspondingly increased cost.

When I discuss Sovaldi in my continuing education presentations on new drugs I identify its high price but also note that concerns about drug prices is a much larger issue that should not be focused on one condition and one drug. Indeed, the availability of Sovaldi offers the hope of a *cure* of HCV infection and additional, productive decades of life. For many patients, it will enable prevention of the health consequences and costs associated with liver cancer and the need for a liver transplant. The experience with many new anticancer drugs exists in sharp contrast to the anticipated outcome with the use of Sovaldi. There are more than a dozen new anticancer drugs for which the cost of treatment will often exceed $100,000. Not only do these drugs *not* offer the hope of a cure for the cancer, but they often do

Contents

not prolong the patient's survival. Nevertheless, Sovaldi is a lightning rod that increases the urgency to address the concerns about drug prices.

HCV infection affects more than 3 million Americans and well over 100 million individuals worldwide. A large percentage of these individuals could be candidates for treatment with a regimen that includes Sovaldi. This very large size of the patient population that could be treated with Sovaldi is the factor that distinguishes the cost of its use from that with most other very expensive medications and has prompted some to conclude that patients and society can't afford its cost. In the first 6 months of 2014, the revenue from sales of Sovaldi is approximately $6,000,000,000.

There is another factor that distinguishes the treatment of HCV infection from most other medical problems and that is the pace at which important advances in treatment have occurred in the last 3 years and will continue to occur in the near future. As recently as four years ago the standard treatment for chronic HCV infection was peginterferon alfa and ribavirin for a period of 48 weeks. The cure rate with this regimen was less than 50%, peginterferon alfa must be administered by injection, and many patients experienced adverse events. In 2011, boceprevir (Victrelis) and telaprevir (Incivek) were approved. These agents significantly increased the cure rate of the regimens in which they were included, permitted a reduction in the duration of treatment, and were considered important advances in the treatment of HCV infection. However, the approval of Sovaldi and simeprevir (Olysio) in late 2013 has permitted the use of regimens with even higher cure rates (e.g., 90% or greater in some studies), a duration of treatment as short as 12 weeks for many patients, and other advantages. The availability of these agents has for practical purposes rendered the use of Victrelis and Incivek obsolete in less than 3 years in the context of the most current treatment guidelines for HCV infection. Although Sovaldi should escape a similar fate, it is likely to experience very strong competition even before the end of this year with the anticipated FDA approval of additional agents that may be equally effective in interferon-free and ribavirin-free regimens for shorter periods of treatment and in combination formulations.

Some anticipate that the increased competition for Sovaldi will result in opportunities to substantially reduce the cost of treatment for HCV infection. However, the possibility also exists that the newer treatments could be equally or even more expensive. Very few, if any, individuals anticipated that the cost of Sovaldi would be $1,000 per tablet. In the meantime, patients are being held hostage!

Patients in the middle

Caught in the middle between the determination of the company (Gilead Sciences) to quickly obtain large revenues from Sovaldi sales and the efforts of insurance companies, pharmacy benefit managers, and government agencies to avoid or delay the use of Sovaldi are the PATIENTS with HCV infection. Many of these patients have been eagerly awaiting the completion of the clinical studies and FDA approval of Sovaldi and other medications for which there have been such high expectations. The clinical benefits are very encouraging and, as the better drugs have become available, it was anticipated that therapy would be quickly initiated in patients who need treatment. However, the celebration of the success of the research and treatment is being obscured by the battle regarding the cost and coverage of the drugs. Some of the organizations that pay for and administer prescription benefit programs have developed strategies to restrict the use of Sovaldi to only the sickest patients with HCV infection, and some have implemented tactics to delay treatment until additional medications are approved and create competition that will make treatment more affordable. Although many patients with HCV infection do not require immediate or prompt initiation of treatment, it is reasonable to anticipate that optimum results will be obtained when treatment is started sooner rather than later, and when there is not an extended delay in treatment. Patients are being held hostage and treatment is being rationed while the battle between the pharmaceutical company and those who are responsible for covering most of the costs of the therapy continue.

Rationing and price controls

There is only one thing that is completely clear about the cost of Sovaldi and the underlying pricing strategy.

(Continued on Page 4)

New Drug Review

Umeclidinium bromide/vilanterol trifenatate

(Anoro Ellipta – GlaxoSmithKline)

Bronchodilator

New Drug Comparison Rating (NDCR) = 4
(significant advantages)
in a scale of 1 to 5 with 5 being the highest rating

Indication:

For oral inhalation for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

Comparable drugs:

Other long-acting muscarinic antagonists (LAMA) that are used as bronchodilators via oral inhalation: Aclidinium (Tudorza Pressair); tiotropium (Spiriva HandiHaler).

Advantages:

- Is the first combination formulation for oral inhalation that includes a LAMA and a long-acting beta2-adrenergic agonist (LABA);
- More convenient administration and lesser likelihood of problems associated with administration (compared with tiotropium that is supplied in capsules that are placed in a device for oral inhalation);
- Is administered less frequently (compared with aclidinium that is administered twice a day).

Disadvantages:

- Indication does not include use to reduce exacerbations of COPD (whereas the labeled indication for tiotropium includes use to reduce exacerbations);
- Umeclidinium is not available as a single agent (has been subsequently approved in a formulation as a single agent [Incruse Ellipta]).

Most important risks/adverse events:

Contraindicated in patients with severe hypersensitivity to milk proteins or hypersensitivity to any of the components of the formulation; paradoxical bronchospasm (treatment should be discontinued); worsening narrow-angle glaucoma; worsening urinary retention; must not be used for the relief of acute bronchospasm (i.e., rescue therapy); action may be increased by other agents with anticholinergic activity and concurrent use should be avoided; increased risk of asthma-related death (attributable to vilanterol; boxed warning; not indicated for the treatment of asthma); other risks and adverse events attributable to vilanterol are included in the labeling.

Most common adverse events:

Pharyngitis (2%), diarrhea (2%), pain in extremity (2%).

Usual dosage:

One inhalation (umeclidinium/vilanterol: 62.5 mcg/25 mcg) once a day via oral inhalation; should be administered at the same time every day, and should not be used more than 1 time every 24 hours.

Product:

Inhaler containing 2 blister strips of powder for oral inhalation, each with 30 blisters; one strip contains 62.5 mcg of umeclidinium in each blister and the other contains 25 mcg of vilanterol in each blister; inhaler unit is supplied in a moisture-protective foil tray and removed immediately before initial use—should be discarded when the dose counter reads "0" after all blisters have been used, or 6 weeks after opening the foil tray, whichever comes first.

Comments:

Umeclidinium is the third long-acting anticholinergic agent, also designated as long-acting muscarinic antagonists (LAMA), to be approved for use via oral inhalation as bronchodilators in the treatment of patients with COPD, joining tiotropium and aclidinium. It was initially approved in a formulation with the LABA vilanterol, and is the first combination formulation to include both a LAMA and LABA. Therefore, patients who do not experience adequate benefit with the use of one inhaled bronchodilator can be treated with two bronchodilators with one dose from the same delivery device. Although a combination formulation (Combivent Respimat) of ipratropium and albuterol is also available, these agents have a shorter duration of action and must be administered more frequently.

The effectiveness of umeclidinium/vilanterol was demonstrated in studies in which the new combination formulation provided a larger increase in FEV1 (forced expiratory volume in the first second of expiration) at 24 weeks than either of the individual components or placebo.

Daniel A. Hussar

It has absolutely no relationship to the cost of the active ingredient and the cost of formulating tablets. Some would say that it is also very clear that the cost of $1,000 a tablet shouts a message of greed!

A consequence of this situation is that many patients who could benefit from treatment with Sovaldi will not be able to receive treatment solely because of its cost. Individuals in specialty pharmacies inform me that it is extremely difficult for patients who need assistance to obtain it through the program the company provides. In a word, the drug is being *rationed*, and is available only to those who can afford it or otherwise have the necessary prescription benefit coverage. It is unconscionable for this situation to exist while the company is well on its way to receiving unprecedented income approximating $12,000,000,000 in the first year following its arrival on the market.

The greatest fear of the pharmaceutical companies is that price controls for drugs will be established in the United States as they have been in most other countries. I have not been an advocate for price controls. However, there is probably no better justification for price controls than the experience with the cost of Sovaldi. This situation could be the call for action for those who consider price controls to be necessary. If this matter is not equitably resolved, and if additional companies use similar pricing strategies, price controls will be established. The implementation of price controls will have been self-inflicted and the companies will have only themselves to blame.

Other examples

There are numerous other drugs about which concerns regarding cost have been raised and the anticancer drugs have been mentioned earlier. However, most of these medications have been approved for conditions experienced by a small number of patients, or are used for chronic conditions in which the cost is incurred over a much longer period of time than is the situation with Sovaldi. As a result, there is a more limited awareness of these situations and less publicity.

The treatment of cystic fibrosis is an example of a situation in which drug cost issues must be addressed. Cystic fibrosis affects approximately 30,000 individuals in the United States. The average life expectancy of people with the disease is about 40 years. In 2012, ivacaftor (Kalydeco) was marketed as the first treatment for cystic fibrosis that targets the underlying genetic defect that causes the disease, whereas other therapies are of benefit only for managing the symptoms of the disease. The benefit of Kalydeco has been demonstrated only in patients with certain gene mutations that are identified in approximately 5% of patients, and its effectiveness has not been demonstrated in patients with cystic fibrosis with the most common gene mutation. Kalydeco is administered orally and the cost of treatment is more than $300,000 a year. In a recent lawsuit several patients have alleged that they have been denied access to the drug in a Medicaid program because of its cost (*Wall Street Journal*; July 17, 2014; p.A1).

Studies of Kalydeco in combination with a second drug that may be effective in patients with the most common gene mutation are currently being conducted. The potential exists for the combined use of two specialty drugs for a much larger number of patients over a period of many years. I hope that this treatment is highly effective, and that an equitable strategy pertaining to its price and availability will enable all patients with cystic fibrosis who can benefit from the treatment to receive it.

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