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Editorial

Bigger Won't Be Better If Pfizer Acquires AstraZeneca!

And Tens of Thousands Will Lose Their Jobs

Pfizer's acquisition of other pharmaceutical companies has been a recurring story in recent years. In 2000, it paid $112 billion to acquire Warner-Lambert (including Parke-Davis and Lipitor), in 2003 it paid $60 billion to acquire Pharmacia (including Upjohn that had already acquired Searle, as well as Celebrex), and in 2009 it paid $68 billion to acquire Wyeth (my editorial in the February 2009 issue of *The Pharmacist Activist* is titled, "Pfizer Should Not be Permitted to Acquire Wyeth").

Most recently, Pfizer has made a determined effort to acquire AstraZeneca with an initial offer of approximately $100 billion that was subsequently increased to $106 billion and, eventually, to a "final offer" of approximately $119 billion. The board of directors of AstraZeneca rejected each of these offers with the explanation that the offers undervalued the company, most notably with respect to the anticipated value of investigational drugs in its research pipeline. The attempted acquisition has the expected and important implications such as loss of jobs, value of shares, and integration of the programs and facilities of the companies, and has been a dominant news story over the last month. However, there are also other important considerations. Pfizer's corporate headquarters are in the United States and AstraZeneca's corporate headquarters are in England. Although Pfizer's reason for wanting to acquire AstraZeneca has been described as a strategy to strengthen its new product pipeline, some contend that the primary motivation for the acquisition is to permit the proposed new company to have its legal headquarters in England while maintaining its operational headquarters in the US. Because the tax rates for corporations are higher in the US than in England, this would permit the company

to pay an estimated $1 billion less taxes per year. The possible exploitation of a tax "loophole" in the US, as well as the potential loss of thousands of jobs in each country, has resulted in the involvement of government officials and legislators in both countries addressing this potential acquisition.

Because AstraZeneca has rejected Pfizer's "final" offer and Pfizer has indicated it will not pursue a hostile takeover, it could seem that this potential acquisition will not be considered further. However, some are of the opinion that Pfizer will persist in its efforts with a combination of strategies including increasing its offer again and encouraging activism of AstraZeneca shareholders who are supportive of further negotiations between the companies. Therefore, a further review of potential benefits and problems of such an acquisition is warranted.

Who benefits?

If the proposed acquisition was to occur, the following would be expected to benefit:

The *CEOs* and other top *executives* of both companies who are involved in negotiating the acquisition would receive the largest benefit. In a recent example of a merger/acquisition of large companies, the CEO of the former American Airlines and the CEO of the new company representing the combination of American Airlines and US Airways each received cash and/or stock valued at more than $15 million.

Shareholders could benefit, at least on a short-term basis, because of the increased value of their shares when the acquisition occurs. The justification always provided by the executives of the company being acquired is that they took the action that was in the best interests of their shareholders. However, Pfizer's stock price has declined in recent years, even with its earlier acquisitions, and greater value over the longer term for Pfizer shares received in exchange for AstraZeneca shares is hardly assured.

Pfizer would be expected to benefit as a consequence of becoming even bigger and strengthening its new product pipeline. However, this was also the anticipated benefit when Pfizer acquired Warner-Lambert, Pharmacia, and Wyeth. Even after these huge acquisitions, Pfizer does not have a strong pipeline, and blockbusters like Lipitor have lost patent protection and most of their market share.

Who is at risk?

The employees! Tens of thousands of them from both companies will lose their jobs. "In Drug Mergers, There's One Sure Bet: The Layoffs," is the title of a *Wall Street Journal* article (April 30, 2014, B1, Loftus, Falconi, and Plumridge) on Pfizer's proposed acquisition of AstraZeneca. The article begins, "Since 2005, Pfizer Inc. has eliminated more than 56,000 jobs worldwide . . . " Many of these individuals are long-term employees whose abilities, productivity, and loyalty have contributed more than any other factor to the success of their companies. However, when a proposal appears to have financial benefits, it is the executives and investors who receive priority consideration, and there is often little or no consideration of the employees. Indeed, the anticipated success of an acquisition/merger is often predicated on the number of jobs that can be eliminated in the name of efficiency. Even the terminology typically used is lacking in consideration—"jobs" are being eliminated rather than "employees," "people," or "individuals" are losing their positions.

The public is at risk of a delay and reduction in the development of new beneficial drugs when innovation and research programs are reduced in number and/or scope when pharmaceutical companies are acquired or merge and consolidate these programs. Following

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New Drug Review

Avanafil
(Stendra – Auxilium; Vivus)

Agent for Erectile Dysfunction

New Drug Comparison Rating (NDCR) = 3
(no or minor advantages/ disadvantages) in a scale of 1 to 5 with 5 being the highest rating

Indication:
Treatment of erectile dysfunction.

Comparable drugs:
Sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra, Staxyn).

Advantages:
- May have a faster onset of action (is administered approximately 30 minutes before sexual activity whereas sildenafil and vardenafil are usually taken approximately 60 minutes before sexual activity);
- Less risk of problems associated with QT interval prolongation (compared with vardenafil);
- Dosage adjustment is not needed in patients with mild to moderate hepatic impairment (compared with sildenafil and tadalafil with which dosage adjustment may be needed).

Disadvantages:
- Labeled indications are more limited (compared with tadalafil that is also indicated for use once a day in a lower dosage for erectile dysfunction, and for the treatment of benign prostatic hyperplasia);
- Has a shorter duration of action (compared with tadalafil);
- Use is not recommended in patients with severe renal impairment (whereas comparable drugs can be used with dosage adjustments and/or appropriate precautions).

Most important risks/adverse events:
May potentiate the hypotensive effects of nitrates (e.g., nitroglycerin) and concurrent use with any form of an organic nitrate is contraindicated (if a nitrate is considered necessary in a life-threatening situation, at least 12 hours should elapse after a dose of avanafil before a nitrate is administered); may increase the blood pressure-lowering action of alpha-adrenergic blocking agents (e.g., tamsulosin) and antihypertensive agents; consumption of alcoholic beverages may increase the risk of orthostatic signs and symptoms (e.g., decrease in standing blood pressure, dizziness); use should be avoided in patients in whom sexual activity is inadvisable due to their cardiovascular status/risk; prolonged erection (greater than 4 hours)/priapism (emergency treatment should be obtained); sudden loss of vision (may be related to non-arteritic ischemic optic neuropathy (NAION); sudden decrease or loss of hearing; is a CYP3A4 substrate and concurrent use with a strong CYP3A4 inhibitor (e.g., clarithromycin, ritonavir) should be avoided; use is not recommended in patients with severe hepatic impairment or severe renal impairment.

Most common adverse events:
Headache (7%), flushing (4%), nasal congestion (3%), nasopharyngitis (3%), back pain (2%).

Usual dosage:
Initially, 100 mg, taken as needed approximately 30 minutes before sexual activity; based on individual efficacy and tolerability, the dose may be increased to a maximum dose of 200 mg or reduced to 50 mg; maximum recommended dosing frequency is once a day; in patients who are stabilized on therapy with an alpha-blocker, initial dose should be 50 mg; in patients treated with a moderate CYP3A4 inhibitor (e.g., diltiazem), the maximum recommended dose is 50 mg.

Products:
Tablets – 50 mg, 100 mg, 200 mg.

Comments:
Avanafil is the fourth phosphodiesterase type 5 (PDE5) inhibitor to be approved for the treatment of erectile dysfunction, joining sildenafil, tadalafil, and vardenafil. Erection of the penis involves the release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation. Inhibition of PDE5 enhances the effect of NO. Avanafil and the other PDE5 inhibitors have been demonstrated to be significantly more effective than placebo in the treatment of erectile dysfunction in clinical trials. The drugs have not been compared with each other in clinical studies but avanafil appears to have a faster onset of action than the other agents and most patients can take it approximately 30 minutes before sexual activity. Tadalafil has the slowest onset of action of the four agents but also the longest duration of action. It is also used in a lower dosage once a day for the treatment of erectile dysfunction. Tadalafil is also indicated for the treatment of benign prostatic hyperplasia, and formulations of both sildenafil (Revatio) and tadalafil (Adcirca) are also approved for the treatment of pulmonary arterial hypertension.

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Pfizer's acquisition of Wyeth in 2009, it closed 6 of 20 research centers worldwide. I can't believe that Pfizer's scientific and research operations are more productive now than if Pfizer, Warner-Lambert, Pharmacia, and Wyeth each continued to have its own scientific and research operations. Indeed, Pfizer's effort to acquire AstraZeneca to strengthen its new product pipeline gives reason to conclude that its current programs are less productive than what would have resulted from the combined productivity of the companies it previously acquired. I find no reason to think that the results would be any different if it acquired AstraZeneca.

Communities may be at risk when a large company is closed or experiences a substantial reduction in the number of employees. In addition to the increased number of individuals who are unemployed, the tax revenues on which the community is dependent may be significantly reduced.

Pfizer's effort to acquire AstraZeneca also has international implications. In England there is great concern about the potential loss of jobs and the reduction of strength of scientific and research programs. The CEO of Pfizer has responded with several specific commitments for a five-year period including basing 20% of the company's research group in the United Kingdom. However, in response to concerns raised by the governors of Delaware and Maryland regarding the almost 6,000 AstraZeneca employees in their states, the Pfizer CEO indicated that it is too soon to determine the effect that the proposed acquisition would have on these positions. Also in the US there is concern that Pfizer's plan to change its corporate address to England will permit it to substantially reduce its US taxes. Several legislators are planning to introduce a bill that would close the loophole that enables this whereas others contend that this is only one of many serious flaws in the tax laws/regulations and are advocates for more comprehensive tax reform.

For Pfizer, bigger won't be better

Some will contend that the issues and differences of opinion identified above are to be expected in a free enterprise system, and that this system has greatly facilitated the economic success of most individuals, corporations, and the country. I recognize that there are acquisitions and mergers in which synergies can be achieved and in which advantages far exceed disadvantages. The *Wall Street Journal* editorial ("Pfizer and the Protectionists," May 14, 2014, A12) includes the statement, "Merger decisions ought to be made on the business merits, which means they are best left to shareholders and directors, who know their own business and products far better than politicians and pundits." Although I can agree that this observation will often be valid, I also believe that there must be safeguards against decisions that place many at risk for the benefit of a few who are not at risk. In my opinion, Pfizer's plan to acquire AstraZeneca is such a decision and should be opposed. AstraZeneca does not need Pfizer to continue to be a successful company, and previous acquisitions strongly suggest that Pfizer will not be better by becoming bigger.

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