No doubt many have seen frequent television advertising touting the benefits of ezetimibe—a drug that inhibits the intestinal absorption of cholesterol. Its use confers an approximate 20% lowering of LDL cholesterol with an acceptable side effect profile.\(^1\) Although ezetimibe does lower LDL cholesterol, when it was marketed and initially prescribed (alone or in combination with a “statin”) there were no clinical studies addressing its efficacy in regard to “hard” endpoints related to atherosclerosis (protection against ischemic events, risk of death, or progression of disease). In 2007, $200 million were spent on direct to consumer marketing of ezetimibe and total sales of the drug hit $5 billion.\(^2\) In early 2008, however, a prospective study was published demonstrating that the addition of ezetimibe to the “gold standard,” a statin, did not slow the progression of atherosclerosis despite a predicted reduction in LDL cholesterol.\(^3\) It was clear before that statins have pleiotropic effects, that is, they do other things than lower cholesterol (e.g., decrease inflammation) that add to their therapeutic effects. This, however, is not the whole story. The hype and marketing of ezetimibe, as well as its prescribing patterns, prior to the ultimately negative data on atherosclerosis end points are what warrant “further review.”

Canada, unlike the U.S., does not permit direct to consumer advertising. From 2002 through 2006, the proportion of prescriptions for ezetimibe rose in Canada from 0.2% to 3.4%, compared to the growth from 0.1% to 15.2% in the U.S.\(^1\) Furthermore the ratio of prescription statins (again, the “gold standard” for not only lowering cholesterol, but also preventing the critical morbidity/mortality outcomes) to ezetimibe in Canada was 26:1 versus 5:1 in the U.S.\(^2\) Even though it was demonstrated that ezetimibe may not yield optimum “bang for its buck,” expenditures for its use in the U.S. exceeded those in Canada by a ratio of approximately 4:1.\(^2\) It appears that prescribing practices changed inappropriately before the critical data was in, and most likely, as a result of advertising. Patients and doctors seemed to respond to the call of the commercials. The bottom line is that ezetimibe cost consumers and insurance companies (including the U.S. government through Medicare and ultimately taxpayers) a lot of money and the important therapeutic outcome was not achieved. So is there a moral to this story?

Healthcare reform is complicated. It is not just merely about the sum total of healthcare financing. Reform does, however, have a certain “reducible complexity.” The ezetimibe story highlights one costly aspect of financing that includes patients as consumers, physicians as prescribers and the pharmaceutical industry as the marketer. These complex relationships inhabiting the marketplace have to be addressed in policy. Recently, the American Medical Student Association (AMSA) published a “Scorecard” grading medical schools for their policies concerning potential conflicts of interest.\(^4\) It focused on the “cozy relationship” of medicine with an industry that entices through many guises: gifts, monetary relationships, consulting and speaking fees, appropriate disclosure, “free” drug samples (totaling $18 billion per year), formulary composition, access to prescribers, and impact on continuing medical education as examples. No one component of the cost generating triad—patients, physicians, and industry—is inherently evil, but it is time to take stock about reasonable efforts to regulate conflicts of interest that may impact efficacy, safety, and costs. The admonition applies not only to academic medical centers, but is a call that should echo throughout the entire medical enterprise. There are portions of the healthcare reform debate that can be placed squarely in our lap, that is, healthcare professionals and patients. The ezetimibe story is one example that carries broader ethical implications.


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