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Specialty Pharmaceuticals for Hyperlipidemia — Impact on Insurance Premiums

Kevin A. Schulman, M.D., Suresh Balu, M.B.A., and Shelby D. Reed, Ph.D.

The Food and Drug Administration (FDA) recently approved alirocumab and evolocumab, PCSK9 inhibitors, for the treatment of hyperlipidemia. These novel biologic agents offer the promise of reductions in blood cholesterol levels. Specifically, the FDA approved alirocumab as an "adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL [low-density lipoprotein]-cholesterol."[1] This broad indication sets the practice of cardiology on a collision course with specialty pharmaceutical pricing models that were previously reserved for drugs that benefited relatively limited patient populations.

Alirocumab was launched at a list price of $14,600 per patient per year. Of course, as other products in this class are introduced, there may be price competition, in the form of either differences in list prices or exclusive commercial arrangements between manufacturers and pharmaceutical benefits managers. These therapies may also lead to savings down the road, by reducing rates of cardiovascular events, though the FDA label clearly states that "the effect of alirocumab on cardiovascular morbidity and mortality has not been determined." According to post hoc analyses, clinical trials of alirocumab and evolocumab revealed a relative reduction of approximately 50% in the risk of cardiovascular events, but the study populations had low absolute event rates of only 2 to 3%. Even if these findings are substantiated, our preliminary analysis suggests that the average cost offsets that stem from lower rates of cardiovascular events are likely to be nominal. Even if there were a 100% reduction in cardiovascular events (i.e., a 3% absolute risk reduction) at an average of $20,000 for each event, the annual cost reduction would be at most $600 — a small offset relative to alirocumab's list price.

There will surely be formal economic evaluations of these data, and there are long-term outcome studies under way to elucidate the potential effect of these therapies on cardiovascular event rates and survival. But it is apparent that the prices for these drugs will result in net costs to the health care system, even if they may eventually be found to offer good value for the money.

With expected total annual costs in the billions, it's important to ask who will bear these costs. In the current market, these products will most likely be considered as part of the drug benefits of insurance plans because they are self-administered. Patients will probably face some degree of cost sharing for the products, possibly including coinsurance, a variable payment amounting to 20 to 25% of the cost, subject to a maximum out-of-pocket cost threshold (although manufacturers are likely to reduce this financial burden with coupon programs to spur adoption and continuation of the therapy for non-Medicare patients). The balance of the cost will be supported through health insurance premiums.

We estimated the magnitude of additional costs per beneficiary in a typical insurance pool by applying a 25% reduction (negotiated discount, cost sharing, or both) to the list price of alirocumab, accounting for the estimated $600 in savings due to fewer cardiovascular events, and varying clinical criteria for use of these therapies. If 5% of the estimated 27% of U.S. adults 40 to 64 years of age who have high LDL cholesterol levels[2] were eli-

gible for a PCSK9 inhibitor, annual insurance premiums would increase by $124 for every person in the insurance pool. This cost would, of course, increase proportionately with broader eligibility for therapy. Beyond these increases in health insurance premiums, taxpayers will have the additional burden of paying for similar increases in the cost of the Medicare Part D program that result from the use of these self-administered agents by Americans over 65 years of age, since 86% of the program's costs are funded through federal and state tax revenues.

Given the enormous prices of specialty pharmaceuticals — from $84,000 for hepatitis C therapy to more than $100,000 for some cancer therapies (often used in combination and sequentially) to $300,000 per year for cystic fibrosis therapy — the health care market seems to have limited tools for restraining the pricing power of suppliers. This market is nearly unique in fostering demand that is seemingly impervious to price escalation ("price-inelastic demand") — a phenomenon with many contributing causes, including consumer behavior shaped by aversion to loss and other responses to life-threatening conditions, providers' outsized profit incentives, market power shaped by limited markets for drugs used to treat rare diseases or specific genetic mutations, and insurers' limited tools for responding to pharmaceutical companies' monopoly pricing power.[3] Overall, there seems to be little natural tension within the market regarding the prices of specialty pharmaceutical products. Although greater attention is being paid to managing the use of these products, there is, as Lotvin et al. have argued, "no one 'magic bullet' that can slow the rising costs of specialty medications."[4]

An audio interview with Dr. Schulman is available at NEJM.org

This price inelasticity is also a result of an industry that relies on third parties (e.g., insurance companies and governments) to finance the purchase of its products. In industries that sell directly to consumers, affordability is a critical consideration in suppliers' marketing strategies. In the pharmaceutical market, the industry assumes that financing will be provided through public and private third-party insurance and that the public will eagerly share in these costs. Clearly, the entry of alirocumab and evolocumab is going to raise questions about whether (primary or secondary) prevention of cardiovascular disease remains an insurable benefit. For example, we could see the rise of high-deductible health plans with deductibles designed to effectively exclude these products. Would paying the first $10,000 annually in drug costs be worth it to you if you are a patient for whom these products are indicated?

More broadly, the question we must face is whether there is a remedy for the pricing power of suppliers. Options include direct government negotiations with pharmaceutical firms, with or without an economic-analysis requirement; restricting indications to patients who receive the greatest value from therapies (although implementing that approach would be challenging both methodologically and administratively); providing an alternative financing scheme for drug development, such as a "grant and access" program[5]; international reference pricing (e.g., in Germany sofosbuvir for hepatitis C virus is priced at €41,000 [$46,000] for a 12-week course); or reimportation. New approaches could include providing a safe harbor for benefit determinations to prevent litigation over access to therapies that are determined not to be covered because of cost and more aggressively restricting use of new products until market competition drives down prices (although this strategy is difficult to pursue in the face of life-threatening and progressive diseases).

At its core, the current pricing model for these products is driven by a transformation in the pharmaceutical industry, whereby 84% of prescriptions are filled with generic products and follow-on biologics have the potential to disrupt many established markets and firms. Thus, for most firms, future revenue expectations hinge on novel therapies. Moreover, without the potential for outsized returns, capital might not be available for early innovation in biotechnology. Pricing pressure on innovative products would drive a fundamental restructuring of the industry and further increase the financial challenges of bringing scientific innovations to the market. It is important that we manage these downside risks carefully as we work toward a more sustainable pricing model in this market.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Duke Clinical Research Institute (K.A.S., S.D.R.) and the Duke Institute for Health Innovation (S.B.), Duke Translational Medicine Institute, and the Department of Medicine (K.A.S., S.D.R.), Duke University School of Medicine, Durham, NC.

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Caring for the Wave of Refugees in Munich

Thomas Nicolai, M.D., Oliver Fuchs, M.D. and Erika von Mutius, M.D.

Another train carrying about a thousand refugees has arrived at Munich's main station, and the passengers are quickly escorted to the medical reception tent. A pediatrician from the volunteer group examines his share of the arrivals, using a few words in hastily learned Arabic or broken English to take histories: a 14-year-old boy who has been tortured with 40 cigarette burns because he wanted to keep going to school in a region of Syria controlled by the Islamic State, a girl with an untreated jaw fracture from a car accident during her family's trek across the Balkans, patients with old shrapnel wounds and burns from bomb detonations, many people with sore feet from unimaginably long walks, and children who are dehydrated and hypothermic after long trips on crowded trains. Grown men are in tears, for fear of being sent to a hospital. A whole segment of society in the Middle East seems to have fled war and destruction.

The doctors and nurses in this tent are moved by the dignity that most arriving refugees have managed to maintain under these circumstances. The great flow of people that politicians and the media tend to describe only in numbers — or in terms such as swarm, threat, or problem to be somehow ignored or removed — has arrived at this medical facility and turns out to consist of individuals, many of whom have horrific personal histories.

The current so-called refugee crisis in Europe has drawn considerable media interest worldwide. According to the United Nations High Commissioner for Refugees (UNHCR), European countries received 714,000 asylum applications in 2014, an increase of 45% over 2013, and 2015 has seen an even steeper increase; the United States had 134,600 applications in 2014. Whereas in 2014 refugees and migrants came from diverse countries in the Middle East and Africa, in 2015 the intensifying civil war in Syria has caused a large number of people from that country and neighboring areas to flee across the Mediterranean or land borders to the European Union (EU). Germany alone has received asylum applications from 413,000 people in 2015, and 25% of those people arrived in August, according to the German interior ministry.

In theory, the new arrivals should be registered and medically screened at the point of entry into the EU, but owing to their sheer numbers, local facilities have been unable to cope with the task. So hundreds of thousands of people have made their way over land, with very limited resources, toward central and northern EU countries. This migration has led to the unexpected arrival of large numbers of people at points throughout Europe. Germany has waived Europe's previous political decision that asylum seekers should be hosted in the country in which they first arrive. In Germany, the southern Bavarian city of Munich (which has 1.5 million inhabitants) has seen the largest influx of refugees, most of whom arrive at its central station — as many as 20,000 people over a single weekend (see graph). The way in which the medical needs of such a large number of arrivals have been handled may shed some light on the main difficulties that arise in such situations and possible solutions to them.

Aside from the administrative problems of registering and housing large numbers of arrivals, every refugee was offered a rapid medical screening procedure so that health care workers could identify patients with urgent medical needs or potentially contagious conditions that could pose a problem during further transport and housing. (A mandatory full medical exam was performed later, as part of the asylum application, to check for infectious diseases such as tuberculosis and to administer immunizations to