Drug Regulation and Pricing — Can Regulators Influence Affordability?

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Public debate in the 1990s over drugs' clinical toxicity has given way to concerns about their financial toxicity. Although drug regulators aren't supposed to be concerned with pricing, they've been drawn into an acrimonious debate over the cost of medicines.

At the European Medicines Agency (EMA), we often hear conflicting arguments: high and inflexible regulatory standards drive up the cost of pharmaceutical research and development (R&D), thereby increasing drug prices; regulators license products even when the data are insufficient for assessing their value and allow drug makers to overcharge; more generics, biosimilars, and me-too drugs are needed to create a dynamic market that will keep prices down; me-too drugs should be discouraged, since they offer no added benefit to patients and lead to overutilization and higher spending; and regulators shouldn't allow drugs on the market that no one can afford.

So are regulators responsible for high drug prices? The short answer is yes and no. Before drug regulatory agencies existed, all sorts of "remedies" were sold on street corners — sometimes for a penny. But even if high prices weren't always an issue, concerns about product quality, safety, and lack of efficacy created a need for regulation. In the ensuing decades, regulatory agencies have developed sophisticated evidence standards to ensure that approved drugs have favorable benefit–risk profiles. Regulators have, for example, developed rigorous standards for the generation and analysis of clinical trial data and for acceptable trial end points and study designs. Regulatory requirements have undoubtedly made pharmaceutical R&D expensive.

At the same time, a regulatory seal of approval is the most important distinguishing factor that allows drug developers to charge high prices for products. Without evidence that has been vetted by regulators, why would anyone pay more for any drug than they would for, say, a dietary supplement? If we eliminated regulation, the current biopharmaceutical business model would collapse — and so would science-based drug development. Without a requirement for regulatory approval, companies would have no incentive to conduct expensive clinical trials of their products. Lowering regulatory standards would be unwise for both patients and organizations that invest in pharmaceutical R&D. Robust regulation improves public health and creates economic value.

But the fact that regulation drives up R&D costs doesn't mean it's the only factor contributing to high prices — or even the most important one. Nor can we conclude the converse — that if only the high cost of R&D (driven by regulations) could be reduced, then prices would automatically drop. Even pharmaceutical executives admit that this assumption is naive; companies tend to charge whatever the market will bear. Any belief in a correlation between R&D costs and market price was dispelled during the recent debate over the price of the new hepatitis C drug Sovaldi.[1]

Regulators should not, for the sake of affordability, yield to pressure to lower standards. But it's also inappropriate for them to be oblivious to the growing budget pains caused by newly authorized products. We believe there are several ways regulators can contribute to keeping drug spending sustainable, at least in the European Union (EU). (We recognize that some of these steps may not be readily implementable in the United States, owing to its legislative framework.)

First, by rapidly approving generics and biosimilars and allowing them to enter the market once patents or exclusivity periods have expired, regulators can facilitate competition, which drives down prices. Regulators could, for example, fast-track additional generic authorizations when companies are taking advantage of monopoly conditions for generic drugs.

Second, regulators can work to ensure that me-too products continue to come on the market at a reasonable speed. Some consumer advocates lament the high proportion of me-too products

that provide limited or no added value over available drugs. But added value is difficult to predict, and some me-too products that were originally criticized have benefited patients and provided additional treatment options. More important, sometimes the availability of these products can drive down prices almost as much as the availability of generics. When hepatitis C medications similar to Sovaldi entered the market, for example, prices were reduced and access to treatment broadened.[2]

Third, regulators can encourage clinical trials that measure value. Payers need data that enable them to assess value in order to determine how much they should pay for a given drug. Health technology assessment (HTA) bodies that advise payers say that the clinical trials supporting marketing authorization often fall short in providing such data. The additional information required may relate to, for example, measures of quality of life or health care resource utilization. To bridge this gap, the EMA, and some EU member states, have been hosting "parallel scientific advice" sessions at which regulators, HTA experts, and drug developers discuss premarketing clinical trial designs. Experience from nearly 70 of these sessions shows that studies can generally be designed to satisfy the needs of regulatory decision makers and support demonstration of value to payers.

Fourth, regulators can facilitate collection of other kinds of data that are important to payers. Increasingly, payers and pharmaceutical companies are considering outcome-focused deals tying a drug's price to the results achieved. Although pay-for-performance schemes are attractive in theory, practical hurdles have prevented widespread adoption. Most important is the difficulty of collecting and interpreting the relevant patient-level data in a given health care system. Regulators, at least in some countries, can facilitate data collection by considering payers' needs when asking companies to conduct post-approval studies. In at least one case, a company was able to piggyback an outcomes-based scheme on processes already in place to monitor a drug's safety.[3] The EMA is now exploring with HTA bodies ways to collaborate on registries or other forms of post-approval evidence generation to achieve these dual goals.

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It's clear that in the future, the market will not bear some of the higher drug prices that are being fetched today. One implication for public health is that potentially useful products may not be developed if companies fear they won't be able to recoup their R&D costs. When prices are squeezed, improving R&D efficiency will become even more important than it is today. How can regulators help achieve this goal?

Clinical drug development is generally an inefficient process. The cost of conducting clinical trials drives R&D spending, and much of the elaborate superstructure involved needs to be reassessed and could be pared down without harming participants. The EMA actively promotes better design and more efficient trial conduct[4] and supports the efforts of the Clinical Trials Transformation Initiative, created by the Food and Drug Administration and Duke University, and other efforts to streamline trials.

Similarly, conventional development and licensing pathways are often economically inefficient. Working with HTA bodies and patient groups, the EMA is exploring whether a more flexible development, licensing, and reimbursement approach called adaptive pathways may help companies stagger clinical development costs, generate revenue earlier, and remove some risk from R&D without relaxing the criteria for determining products' risk–benefit profiles.[5] We expect that this kind of "life span" approach to generating evidence — with more targeted selection of trial participants, managed growth of the treatment-eligible population, and full use of postlicensing Risk Management Plans (EU) or Risk Evaluation and Mitigation Strategies (United States) — will lower the threshold for financing drug development at a time when prices are coming under pressure.

We firmly believe that assessment of quality, safety, and effi-

cacy should remain separate from pricing and reimbursement decisions. Regulators alone cannot solve the growing problem of high drug prices. We understand that new drugs should command prices that reward and provide incentives for R&D investment. However, we fail to comprehend prices that, like Sovaldi's, recoup the entire investment within the first few months after a product's launch but are so unaffordable that patients in need are denied access.[1] We are committed to doing our part to facilitate continued access to effective and safe treatments.

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

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DOI: 10.1056/NEJMp1601294