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Knowns and unknowns of US drug pricing

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In the U.S. spending on drugs represents 10% of overall health care costs.(1) Together, hospital and physician expenditures account for 6 times the spending on drugs.(2) Despite a recent uptick in the rate of drug cost growth, over the past 10 years the pace of hospital and physician expenditures has exceeded prescription drugs.(2) Apparently, these facts do not make for eye-catching headlines. By contrast, the recent surge in the price of drugs targeting hepatitis C, HIV, and various cancer and orphan diseases, is salient and the focal point of media attention. For example, last month's reported 50-fold price increase of

Daraprim drew the ire of politicians, policymakers, and patient advocates. Here, we unravel several mysteries surrounding drug pricing and alignment of price and value.

Why is pricing in the U.S. different?

Lack of price controls distinguishes the U.S. from other countries. Moreover, the U.S. does not have a government authority that serves as a single purchaser of drugs and manager of a national formulary. Consequently, the leverage each U.S. purchaser has to exert downward pressure on prices is limited compared to a single-payer system, or multi-payer arrangements in which the government oversees drug procurement. The prices of single-source drugs are on average approximately 30% higher in the U.S. than other comparable industrialized nations.(3)(4)

Higher prices are a driver of higher healthcare costs. However, the impact of higher prices on patient access cuts two ways: They establish incentives for drug manufacturers to launch more drugs earlier (than in markets where there are price controls), which can imply greater access. At the same time, they lead to increases in patient cost-sharing, which can be a barrier to access.

Higher branded drug prices induce a relatively competitive generics market once patents expire, with generics representing over 80% of prescriptions. As such, the U.S. has a higher rate of generic prescriptions than most other industrialized nations.(5) Generics therefore generally serve as a countervailing force to increases in branded prices, as generics are less prone to suboptimal market conditions. Nevertheless, there have been examples of market failure – Daraprim being Exhibit A – when the supply of generics is handled by only one or a few manufacturers.

Although price controls may help reduce the level of spending on drugs

and patient cost-sharing they do not resolve the price-value conundrum. This is because of the arbitrary nature of price controls. To illustrate, if policymakers were to impose an arbitrarily chosen $100,000 ceiling on cancer drug prices without reference to the benefits conferred by each individual drug, then there would be no connection between the price ceiling and value. In other words, the price ceiling fails to distinguish between drugs which provide benefits that justify prices at or above $100,000, from those that do not. The use of cost-effectiveness thresholds to exert control over price does incorporate measurement of benefits, and as such constitutes an improvement. However, the numeric ratios that comprise cost-effectiveness thresholds (e.g., £20,000/QALY used by NICE) are set in a similarly arbitrary way and often do not change over time.

How are drugs priced in the US?

The American public is generally not privy to the pricing of drugs – the process by which drugs are priced – or even the negotiated prices at which drugs are bought and sold. This lack of transparency does not, however, preclude researchers from being able to gather evidence (some anecdotal, some revealed in publicly available documents) on the general contours of pricing.

Here's what we do know about how drugs are priced by pharmaceutical companies:

- How high can we go? When deciding upon a new drug's list price, companies perform a pre-approval assessment prior to regulatory approval, positioning the drug relative to comparators, which includes an evaluation of the anticipated price sensitivity of payers, patients, and healthcare providers.
- What added benefits does it provide? If companies believe the drug provides additional benefits compared to existing treatment,

this will be incorporated in the price point offered at launch. Furthermore, if companies anticipate a high willingness to pay on the part of payers because of a certain property the drug has – targets a rare disease, has a novel mechanism of action, addresses an unmet medical need – this will be reflected in the list price.

- What does it cost to make? When pricing a new drug, companies take marginal cost of production into account, i.e., the cost of producing each additional unit, such as a pill or vial. The marginal cost of production is significantly higher for large-molecule biologics than small-molecule pharmaceuticals, because the manufacturing process is more complex. Marginal cost of production is distinct from the cost of drug development. The former is a function of production once a drug is approved, while cost of development refers to resources allocated to developing a new drug prior to its approval.

What about R&D and its relation to price?

The rationale that we intentionally omit from the list above is cost of development. Some in industry have justified high prices of branded drugs as a way of recouping investment in drug development. This is a flawed argument, however. While a company's revenue from its portfolio of marketed products will have to exceed its operating costs in order to remain a going concern, the level of investment in a product should bear little or no relation to its market price. It is a sunk cost. In a competitive market setting, purchasers do not pay for a product's cost of research. They pay for a product's perceived value relative to other products. Hence, asserting that the reason a product is x dollars is because so much effort was put into it is inconsistent with market principles. Critics of the current system of pricing where price and value may not be optimally aligned suggest therefore that drug prices should be value- and not cost-based. This implies the need to establish measures of a drug's value.

Then what?

Once a manufacturer sets a price payers express a willingness to pay at that price or not. A negotiation will likely ensue resulting in a transaction price lower than the list price. Mutually agreed upon transaction prices are value-based to the extent that they reflect how much purchasers are willing to pay for a drug, provided several key assumptions underlying a competitive market hold.

But does price = value?

Notably, by design the pharmaceutical market lacks certain features of a competitive market. First, drugs are patented as single-source (branded) monopoly products for a period of marketing exclusivity. It is during this period without generic competition that companies can charge a price that is higher than the marginal cost of production. Second, third-party insurance shields patients from the actual cost of prescription drugs, which may encourage higher prices. Third, the existence of asymmetries in information between suppliers and purchasers of drugs, as well as prescribers and users, drives a wedge between price and value. Buyers cannot readily ascertain the value of the drugs offered.

What are the alternatives?

The Drug Abacus developed by Peter Bach of the Memorial Sloane Kettering Cancer Center is one proposed solution to establish the value of newly approved drugs.(6) Based on data drug manufacturers submit to FDA for approval, the Drug Abacus enables a patient or healthcare provider to decide a drug's value, based on a number of factors which include a willingness to pay amount for added life years conferred by the drug, perceived toxicity, convenience, rarity of disease targeted, and novelty of mechanism of action. As a gauge to align price and value the

Drug Abacus is a useful first step. However, it suffers from an overly optimistic view of what is known about a drug's real-world effectiveness at launch.

Summary

Drug pricing is complex, and its impact on healthcare systems varied. Absent a competitive market, a drug's price and value may differ.While the Drug Abacus is a good first step as a gauge to align price and value, it will rely on the generation of significantly more safety and effectiveness evidence than currently exists, not only at launch but also post-launch. Moreover, the evaluation of evidence will have to take place in a dynamic setting, i.e., over time, in order to better align price and value. In this respect, pay-for-performance arrangements may be an option in cases in which there is great uncertainty at launch. Here, payers collect real-world data on a drug's safety and effectiveness post-launch and price is linked to outcomes.

More information: S. P. Keehan et al. National Health Expenditure Projections, 2014-24: Spending Growth Faster Than Recent Trends, *Health Affairs* (2015). DOI: 10.1377/hlthaff.2015.0600

J. Cohen et al. Compared To US Practice, Evidence-Based Reviews In Europe Appear To Lead To Lower Prices For Some Drugs, *Health Affairs* (2013). DOI: 10.1377/hlthaff.2012.0707