Indication-Specific Drug Pricing – Simple in Theory, Complex in Reality

Varying drug prices by indication could be an important value-based strategy in oncology, where multiple indications are becoming the rule. But will administrative costs offset any benefit? And legal and regulatory obstacles could get in the way.

By Sarah Kwon

Cancer treatment is advancing rapidly but at eye-popping prices. Six-figure oncology drugs are increasingly common, necessitating new approaches that will bring the drugs back into the orbit of affordability.

The notion that drug payment based on value rather than volume could help reduce drug costs has been percolating for years. Up to now, this most often has taken the form of outcomes-based contracts that tie clinical outcomes to payer rebates and discounts. From 2015 through early 2017, commercial payers and pharmaceutical manufacturers announced 16 outcomes-based agreements, according to a tally in March 2017 by PhRMA, the industry's trade association.

But other types of value-based payments have been proposed as a remedy for oncology's affordability woes. A leading candidate is indication-specific pricing, also called indication-based pricing or multi-indication pricing. A 2014 *JAMA* commentary by Peter Bach, MD, put it on the map for many researchers and drug company and payer executives. Bach, who as director of Memorial Sloan Kettering's Center for Health Policy and Outcomes has become an influential voice in the debate about drug pricing, argued that indications for individual drugs can vary widely in their clinical benefit. He proposed pricing indications separately, in line with the benefit conferred for each indication.

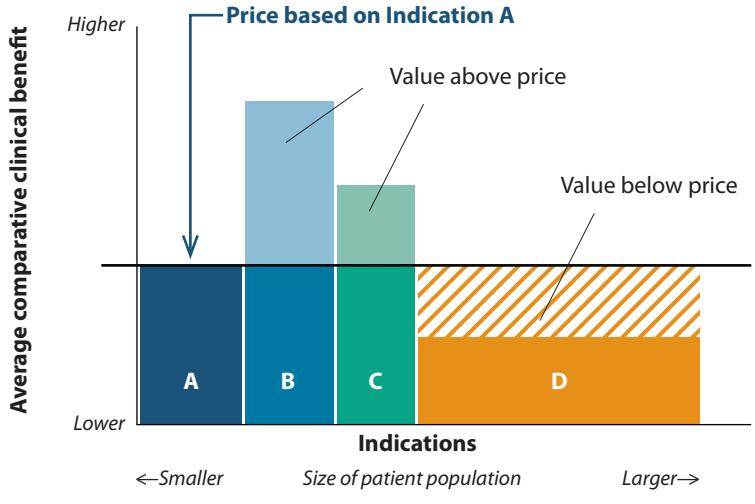
Although outcomes-based pricing has proven to be more popular, some experts say indication-specific pricing deserves more attention, especially in oncology. Getting FDA approval for multiple indications is increasingly common and an important part of most drugmakers' marketing strategies, especially for cancer drugs. A 2015 IMS report predicted that by 2020 most new oncology drugs will have three or more indications.

Weighted-average common variant

Indication-specific pricing is new to oncology, but the basic concept has been around awhile. Manufacturers market different drug indications under different brand names with different prices; for example, sildenafil is marketed as Viagra for erectile dysfunction but as Revatio for pulmonary arterial hypertension. Payers are certainly not blind to indications when it comes to coverage decisions. They may, for example, cover a growth hormone drug for growth hormone deficiency but not short stature. "Taking the indication into consideration is not new," says Bill Dreitlein, director of pharmaceutical policy at the Institute for Clinical and Economic Review (ICER), an independent not-for-profit research group. "But indication-specific pricing takes it a step further and factors [the indication] into the price of the product."

In its purest form, an indication-specific pricing agreement between a drugmaker and a payer applies a separate price, including discounts, to a drug depending on the indication it was used for. This means, of

A single price creates mismatch with value



Adapted from ICER, "Indication-specific Pricing of Pharmaceuticals in the United States Health Care System," March 2016

course, that payers need to know the indication for which a drug was purchased.

The more common variant of indication-specific pricing calculates a single weighted-average price based on estimates of the different indications that a drug is used for. The manufacturer retrospectively reviews actual use and then reconciles the difference through rebates. England, Germany, and Italy use versions of this approach, according to ICER's 2016 primer on indication-specific pricing.

Express Scripts, which announced three years ago that it was starting to pay different prices for different indications, has indication-specific pricing arrangements for drugs that treat multiple myeloma, breast and prostate cancer, renal cell carcinoma, non–small-cell lung cancer, and inflammatory diseases. In an email, Express Scripts said that "in some cases" it calculates a weighted-average price based on estimates of indication use, but did not address whether it receives rebates from manufacturers.

Last year, CVS announced indication-specific pricing arrangements for hepatitis C and autoimmune diseases. They offer preferred formulary placement to more effective indications, then negotiate "better pricing and rebates with manufacturers," according to their website.

Although it has been reported that CVS is negotiating indication-specific prices for cancer drugs, the CVS media office refused to confirm that information.

After the FDA approved Kymriah (tisagenlecleucel), Novartis worked to diffuse some of the shock from the CAR-T drug's $475,000 price tag with assurances that it would enter into value-based contracts for the therapy, which was approved as a treatment for B-cell acute lymphoblastic leukemia in patients younger than 25. Novartis initially took an outcomes-based approach, saying that it would charge for the drug only if patients responded in the first month, but it also announced a collaboration with CMS on value-based approaches for future indications "intended to include indication-based pricing."

Indication has always been watched, but now it could be factored more into the price of the drug, says Bill Dreitlein of ICER.

Neither Express Scripts nor CVS has publicly shared the number of indication-specific pricing contracts or results, but in 2015, Precision for Value, a consultancy, surveyed 29 U.S. payers and found that three had indication-based arrangements. Jeremy Schafer, a senior vice president, says now "there could be dozens of health plans taking advantage of indication-based drug contracting through [CVS and Express Scripts]."

The survey also found that payers were most interested in applying this arrangement to oncology. Schafer thinks autoimmune disease drugs are more likely to have indication-specific pricing arrangements than cancer drugs. Payers have more control over drug utilization for autoimmune diseases than they do for oncology, says Schafer, because cancer is a more sensitive disease area with higher stakes and fewer head-to-head competitors.

Worth the while?

Linking a drug's price to its indication (if outcomes vary with indication) is certainly an appealing notion, and groups representing oncologists, health plans, and manufacturers publicly support exploring indication-specific pricing (and other forms of value-based contracting) for oncology. But they use the word "explore" for a reason, as indication-specific pricing may have some inherent problems.

For one thing, some experts say, indication-specific pricing may have only an incremental impact on drug prices. "It's a good idea, but is the juice worth the squeeze, administratively? Is the administrative cost less than the benefit?" says James Robinson, a University of California–Berkeley health economist. "Even if we solve that, this means we've solved relative price, but not absolute price."

Others think indication-specific pricing could increase overall spending. Health economists Amitabh Chandra and Craig Garthwaite asserted in a *New England Journal of Medicine* commentary that indication-specific pricing, by selling the same product at different prices to different customers, represents price discrimination, a profit-maximizing strategy. By increasing access to drugs currently priced so high that they're unavailable for some indications—while charging the highest price to patients who receive the most value from the drug, all the while with low marginal costs—indication-specific pricing could increase manufacturer profits.

Indication-specific pricing may falter—or fail to catch on in the first place—because of the administrative burden and related costs. Identifying the indication is critical to enabling this pricing model, and some payers will struggle to find these data, notes Dreitlein at ICER. "The indication might be in an electronic medical record, but at the point of sale when the drug is dispensed, [the indication] might not be captured," he says.

Legal and regulatory requirements also loom as obstacles, although this isn't unique to indication-

specific pricing. The Anti-Kickback Statute prohibits exchange of anything of value in return for federal health care program business, and existing safe harbors may not sufficiently protect some activities required to execute value-based agreements, said a 2017 report from the Network for Excellence in Health Innovation (NEHI), a not-for-profit research organization whose members include insurers, drug companies, and health care systems.

Medicaid's "best price" requirement may be another sticking point. Some manufacturers fear that a lower price for one indication could create a lower "best price" for all indications, triggering price cuts that will cut deeply into their revenues and profits. NEHI and ICER have stated that in some cases, weighted-average pricing may help indication-specific contracts avoid affecting the best price requirement.

Drug prices are just one facet of managing cancer costs, says Debra Patt, MD, of ASCO. Think outside of the pharmaceutical box.

At a Federation of American Hospitals meeting in March, the new HHS secretary, Alex Azar, signaled the government's commitment to addressing regulatory barriers to value-based payment, including "certain Medicare and Medicaid price-reporting rules" and "various well-meaning fraud protections." How this plays out remains to be seen, but many are optimistic. "I expect the administration is going to be tackling these impediments much more aggressively over the course of the next year," says Dan Mendelson, president of Avalere, the health care consultancy.

Looking to ICER

Even if indication-specific pricing were to catch on, not every multi-indication cancer drug is a good fit for it. ICER, acknowledging the implementation costs, recommends applying indication-specific pricing to drugs for common conditions and when the value varies significantly by indication. ICER also says it would be wise to focus on drugs with limited off-label use, given that manufacturers can negotiate reimbursement contracts only for FDA-approved indications.

In certain circumstances, Medicare's reimbursement rate for physician-administered drugs could drop to the point where physicians couldn't recoup the cost of acquiring the affected drugs, so ICER also advises limiting indication-specific pricing to orally administered drugs.

Express Scripts said in an email that it decides on a case-by-case basis which cancer drugs it will apply indication-specific pricing, noting that indication-specific pricing "doesn't necessarily need to be limited to oral products" and "this model can be used in small or large population sizes."

Defining each indication's value could, arguably, be one of the most complex and contentious parts of implementing indication-specific pricing. Several groups have developed value frameworks to provide guidance for value-based contracts. ICER's value assessments are intended to help guide pricing and coverage discussions between manufacturers and payers. Bach's DrugAbacus, intended for policymakers, allows the user to factor in toxicity, the population burden of the disease, and other variables. The American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) have created tools to facilitate shared decision making for doctors and patients.

Several surveys suggest that some payers are using at least one framework to guide value-based contract pricing decisions. NCCN topped some 2016 surveys, but some experts think this is changing. Many payers use NCCN guidelines to make coverage decisions, and the NCCN value framework is a convenient and natural extension of those guidelines, notes Schafer at Precision for Value.

But ICER is gaining ground. Schafer pointed to the announcement last year by the Department of Veterans Affairs that it will incorporate ICER's work into price negotiations with manufacturers and the decision by Sanofi, also last year, to use ICER's cost-effectiveness review of Praluent (alirocumab), its PCSK9 inhibitor, in price negotiations with payers. Jason Gomberg, a principal at Milliman, says industry recognition is growing that "ICER numbers are commonly quoted" in drug pricing negotiations.

Regardless of when or how indication-specific pricing and other value-based arrangements play out, Debra Patt, MD, warns against thinking too much inside the pharmaceutical box. Drug prices are just one facet of managing cancer costs, says Patt, a Texas private practice oncology group executive and immediate past chair of ASCO's clinical practice committee. Inappropriate end-of-life care also adds to the country's cancer care bill, as does the shift in cancer care delivery from physician offices to outpatient hospital settings. "Payers and providers need to be more collaborative in solutions," says Patt. "There's a lot of fat to be trimmed." MC

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