How Drug Cos. Can Adapt To New Reference Pricing Rules

By **Meenakshi Datta** (March 5, 2021)

Meenakshi Datta

The final days of the Trump administration were marked by the publication of a flurry of drug pricing regulations, among the most controversial of which was a regulation that would have purported to test a new most-favored-nations reimbursement mechanism for the top 50 physician-administered prescription medicines paid for under Medicare Part B.

While the regulation is now on hold, it is the most significant attempt to date to use reference pricing to control drug spending. Unfortunately, the attempted implementation of this most-favored-nations regulation may normalize policy discussions in the U.S. around aggressive price control measures for prescription drugs, making such policies a more real and present danger than ever before and undermining policies for fair reimbursement.

Investors and C-suites in the drug and biotech industry should pay close attention for new potential reference pricing regulation in the U.S. and globally, as the U.S. looks to other markets for exemplars on drug cost controls. Companies should:

- Consider monitoring U.S. and other countries that are aggressively pursuing reference pricing and other unfair price-control measures and reimbursement cuts;

- Advocate to protect policies that support fair pricing and reimbursement; and

- Make contingency plans in markets where reference pricing or other price control or unfair reimbursement measures may be a distinct possibility, including by formulating market access strategies that focus on therapeutic value, outcomes and cost savings.

This article provides an overview of the current reference pricing landscape for prescription drugs, and provides executives and investors key takeaways to consider with respect to potential prescription drug price policy changes.

Most-Favored-Nations Reference Pricing Regulation Enjoined

The most-favored-nations regulation was published after the election, on Nov. 27, 2020, as an interim final rule with comment period. The new regulation took effect on the same day with the reimbursement cut on certain Part B drugs scheduled to begin on Jan. 1, 2021, despite the comment period on the rule closing approximately two months later.

In announcing the regulation, the administration predicted litigation would ensue. Four legal challenges followed in early December 2020, filed across the country.

A temporary restraining order was granted on Dec. 23 in one of the cases, Association of

Community Cancer Centers v. Azar, in the U.S. District Court for the District of Maryland.

In a second case in the U.S. District Court for the Northern District of California, a preliminary injunction was granted in California Life Sciences Association v. Centers for Medicare and Medicaid Services on Dec. 28, nationwide.

Also, on Dec. 30, the U.S. District Court for the Southern District of New York granted an injunction specific to the plaintiff's affected drug in Regeneron Pharmaceuticals Inc. v. U.S. Department of Health and Human Services.

In sum, three of the four courts concluded that the government's most-favored-nations rulemaking process violated various requirements under the Administrative Procedure Act, and the fourth case, Community Oncology Alliance v. HHS in the U.S. District Court for the District of Columbia, was stayed as a result of the orders entered in the other three.[1] The government chose not to appeal the rulings.

Had it taken effect, the most-favored-nations regulation would have resulted in a radical change to Medicare Part B reimbursement for a select group of physician-administered drugs and biologicals, beginning on Jan. 1, 2021 and scheduled to last for a seven-year model performance period.

Specifically, if the regulation had taken effect, the impact in year one of implementation would have been on the 50 single source drugs and biologicals — including biosimilar products — that encompass a high percentage of annual Medicare Part B spending in 2019, based on dates of service and subject to certain excluded drug categories.

The regulation would have phased in reductions in Medicare Part B reimbursement for the top 50 to an amount based on the lowest price paid for the same medicine among a group of 22 other nations, with some additional adjustments and a flat add-on payment for administration.

These countries were identified by the Centers for Medicare and Medicaid Services as the member countries of the Organization for Economic Cooperation and Development with the highest GDP per capita worldwide. Under the regulation, new physician-administered drugs and biologicals could have been added to the top 50 in subsequent years, subject to the same exclusions.

CMS estimated that spending on the drugs included in the most-favored-nations model would account for approximately 73% of Medicare Part B drug spending in each year of the model performance period.

Patient access and provider reimbursement would have suffered significant disruption.

What's Next for the Most-Favored-Nations Drug Pricing Regulation

As an initial matter, the comment period to the regulation only recently closed on Jan. 26, 2021. It was issued as an interim final rule with comment period.

CMS received nearly 1,200 comments on the most-favored-nations regulation.[2] Physician groups, disease state groups, pharmaceutical manufacturers and other constituencies vigorously objected to the procedural violations of the rulemaking process and the substantive aspects of the rule.

Looking forward, it is at least conceivable that CMS could try to cure its procedural missteps, though significant litigation would likely follow if it attempts to do so. Or CMS could rescind its regulation and attempt to restart the process by reissuing a proposed regulation that would purport to implement most-favored-nation pricing. Litigation would likely follow in that scenario as well.

It's also possible that CMS will withdraw the regulation altogether. Or CMS might do nothing, leaving drug companies and their investors in a guessing game as to whether the policy door on most-favored-nations drug pricing is open or shut.

No signals were given on this question at the recent U.S. Senate confirmation hearing of HHS secretary nominee, Xavier Becerra, though Becerra has expressed support of other policies that unfairly undermine pricing for innovative products.

Reference Pricing as a Potential Priority for the Biden Administration

President Joe Biden campaigned on two key reference pricing concepts: (1) external reference pricing for new specialty drugs that face no competition, and (2) a drug pricing policy modeled after Germany's approach.

External Reference Pricing for New Specialty Drugs

During his campaign, Biden proposed an independent review board to assess the value of new specialty drugs that lack competition.[3] Some have predicted the board, if it were established, would function much like the nongovernmental Institute for Clinical and Economic Review, although under the proposal it would be housed within HHS.

Under the proposal, if a specialty drug is already on the market in other countries, the board would recommend a ceiling U.S. market price based on the average price of the drug in other countries. If a drug is entering the U.S. market first, the board would independently evaluate the product and determine a reasonable price point.

Under the proposal, Medicare would pay the price determined by the board; private plans participating in the individual marketplace would have the opportunity to access a similar rate.

The German Approach: Internal Reference Pricing for Most Drugs and Collective Negotiations for Innovative Drugs

Without offering many specifics, Biden has also suggested he will look to Germany's reference pricing system as a potential starting point for his administration's consideration of drug pricing policy.

Germany allows pharmaceutical manufacturers to set their own prices during the first year on the market following approval by the European Medicines Agency, but employs a benefits assessment and internal reference pricing framework to determine the reimbursement limits for drugs under the country's statutory health insurance system, which covers 90% of the population.[4]

Notably, if a drug is shown to offer an additional clinical benefit over its alternatives, its price will be determined through collective negotiations as opposed to internal reference pricing.[5]

An umbrella organization represents all insurers as a single buyer in negotiations with the drug manufacturer.[6] If the parties cannot reach an agreement, the drug price is established by an arbitration panel.[7] If the manufacturer is dissatisfied with the arbitration result, it may withdraw its product from the German market, which has happened on occasion.[8]

It remains to be seen exactly what parts of Germany's pricing policy the Biden administration would adopt, if any. Since taking office, Biden has not made any public statements regarding drug pricing as a priority.

Other U.S. Reference Pricing Proposals

Previously proposed reference pricing bills in the U.S. House of Representatives and Senate may also gain new traction now that both are under Democratic control.

The House passed the Elijah E. Cummings Lower Drug Costs Now Act[9] by a 230-192 margin on Dec. 12, 2019. The bill proposed an international price index from which HHS would negotiate drug prices for Medicare and Medicaid, with the option for private insurers to use those government-negotiated prices.

Specifically, under the bill, the reference price would be set at an upper limit of 1.2 times the volume-weighted average of a drug's price in Australia, Canada, France, Germany, Japan and the U.K.[10] The act would apply to up to 250 costly, brand-name drugs with no generic or biosimilar competitors and newly launched brand-name drugs with launch prices in excess of the median U.S. household income.

If a manufacturer fails to reach a price agreement with HHS, the act would impose an excise tax of 65% of the total sales of the drug in question, which would increase 10% each quarter to a maximum of 95% of total sales over the applicable period.[11]

The act did not receive a vote in the previously Republican-controlled Senate, but now that the Senate is under Democratic control, there is at least some possibility that the act may be revived.

Reference pricing is not only of interest at the federal level; a number of states are creating their own reference pricing policies. Effective Jan. 1, 2021, the California Medicaid program has adopted an expanded definition of "best price" that includes "the manufacturer's lowest price available to any foreign or domestic class of trade."[12]

By broadening the "best price" definition, the California Department of Health Care Services may seek to negotiate greater supplemental rebates on California Medicaid drug utilization than the state currently receives from drug manufacturers.

Notably, the statute further provides that the revised "best price" definition and other provisions "shall be implemented only to the extent that any necessary federal approvals are obtained and federal financial participation is available."

Moreover, in the 2021 legislative session, lawmakers in several states have already introduced legislation to establish Canadian reference pricing for the 250 costliest drugs in those states.[13]

Based on model legislation drafted by the National Academy for State Health Policy, these state bills would enlist state departments of insurance to review publicly available data and

determine the lowest price available for a drug in Canada's four largest provinces.[14]

That lowest available Canadian price would become the highest price that participating purchasers in the state could legally pay. Participating purchasers include commercial payers, employer-sponsored plans, Medicare Advantage plans and individuals without insurance. Traditional Medicaid and Medicare plans are excluded.

Under the National Academy for State Health Policy bills, monetary penalties would apply to any pharmaceutical manufacturer that withdrew a drug or refused to negotiate prices in good faith.

Strategic Considerations

Here are a few things your organization might consider as you implement a market access strategy for your products and pipeline programs to address potential changes to the drug pricing and reimbursement landscape:

Monitor for reference pricing and other pricing and reimbursement reforms.

This should be done at federal and local levels of all key markets. In the U.S., you should expect renewed dialogue on reference or ceiling pricing for drugs during the course of the Biden administration.

This may come from the legislative branch, the executive branch, or both. Moreover, the possibility of a patchwork reference pricing regime, with different states taking different approaches, is a real and present threat to rational pharmaceutical drug pricing and contracting.

Outside of the U.S., a number of high-income countries employ external reference pricing models, including Canada, France, Germany, Italy, the Netherlands and Spain. It is important monitor for continued pressure on price in countries with existing controls and to watch for countries that might adopt new controls.

Most recently, the World Health Organization published guidelines on country pharmaceutical pricing policies, which discusses 10 pricing policies, including external reference pricing, internal reference pricing, value-based pricing, generics and biosimilars, and more.

Notably, the guidelines makes a conditional recommendation against cost-plus pricing based on several factors identified in the guidelines.

Also watch for changes in country selection for international reference pricing. For example, the Netherlands last year swapped Norway for Germany as a reference country, and drug prices decreased by 8% on average and almost 40% in some cases.[15]

Ensure you have mechanisms in key markets to identify efforts to unfairly cut reimbursement or institute price controls at their early stages.

China drug pricing is markedly different than the U.S. and E.U. regimes. Drug prices in the public hospital market, which accounts for the majority of the drug market, are mostly determined through a negotiation between drug companies and the government authorities, and drug companies have limited leverage in such negotiations.

In addition, the government authorities have increasingly used medical insurance reimbursement and procurement quantity commitment to initiate additional rounds of drug price negotiation and to press drug companies to further reduce their drug prices drastically.

The Chinese government authorities have not elaborated their methodology in these price negotiations, but it is believed that they indeed use international reference pricing as a negotiation tool.

Establish a strategy for engagement and advocacy.

Engage early with government authorities that are considering price controls or reimbursement cuts. It is important for government authorities that are considering such legislation, which would most certainly be subject to challenge if passed, to understand potential downstream impacts of price control measures or reimbursement cuts that would unfairly impact pharmaceutical investment in innovation.

Engage in discussion with relevant governmental policymakers to ensure appropriate awareness of the potential disruption to patient access, research and development programs, and provider financial viability that could be caused by such proposals.

Litigation and government investigation readiness is another critical component of a comprehensive strategy. The most-favored-nations regulation litigation demonstrates the importance of moving swiftly and possessing a deep and strategic understanding of the reimbursement regime at issue.

In the U.S., litigation readiness may include a multijurisdictional strategy and nuanced consideration of constitutional and Administrative Procedure Act arguments that may support industry viewpoints.

In E.U. member states, where litigation on pricing and reimbursement takes different forms — internal appeals, arbitration, administrative or civil courts — the readiness to litigate is becoming increasingly important as scrutiny of companies' pricing strategies increases.

Chinese authorities have attempted to use antitrust law to force multinational drug companies to reduce drug prices, though they have not issued any penalties to date. In such antitrust inquiries or investigations, the Chinese antitrust authorities in general used a cost-plus approach to determining whether the drug prices were reasonable, and also used international reference pricing as a method of analysis.

Contingency plan for alternative market access strategies.

Given the near and long-term uncertainty in pharmaceutical product cost containment efforts in various jurisdictions, consider your pricing strategy from multiple angles, including whether your organization can or must pivot to alternate market access strategies if the U.S. or another country's pricing or reimbursement regime were to dramatically change from the current approach.

For example, consider rebate and other discounting strategies, as well as value-based and outcomes-based models for pricing, which have gained popularity in the U.S. and are common in other jurisdictions such as the U.K.

In the U.K. and some countries with a national health system, it is also essential to continue to evaluate initial assumptions that may have been used to formulate strategies for health

technology appraisals. Those bodies conduct cost-effectiveness types of assessments to determine whether a specific treatment should be made available under the national health system and therefore prescribed by health care professionals.

In addition, government agencies and manufacturers are increasingly exploring novel payment and reimbursement models for innovative medicines such as the Netflix-style subscription payment model for products such as antibiotics, prevalence-based deals and hepatitis C smart deal procurements.

The recent three-part deal — large-scale trial, manufacturing and access for high-risk patients — in the U.K. for Inclisiran should be a case study, depicting both pros and cons, for market access strategy considerations going forward.

Value-based, outcomes-based or subscription model market access strategies may or may not be viable for any particular therapy.

At least asking the question "What would we do?" if reference, ceiling or other drug pricing reforms become a reality is a mission-critical question companies should ready themselves to face.

Companies that have already wrestled with these issues in preparation for a commercial launch should consider regular reevaluation of these issues in light of the shifting environment for pricing and reimbursement globally.

Companies should consider these action items from a variety of angles, including government affairs planning, research and development programs, commercial strategy, disclosures to investors, and litigation readiness, among others.

Ultimately, multinational drug and biotech companies and their owners need a comprehensive readiness strategy to address the various aspects of reference or ceiling pricing and reimbursement pressure in light of the need for fair pricing and reimbursement regimes, with country-specific focus groups for major markets.

Investors will also need to have a strategy for accounting for these risks in any diligence plan, and assessing their options in the case of proposals that are likely to gain steam.

Meenakshi Datta is a partner and global co-leader of the health care practice at Sidley Austin LLP.

Sidley partners Maarten Meulenbelt, Maria Manley and Lei Li contributed to this article.

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[13] For example, North Dakota, Oklahoma, Rhode Island, and Hawaii have introduced Canadian reference pricing bills.

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