ISPOR
The professional society for health economics and outcomes research

Improving healthcare decisions

505 LAWRENCE SQUARE BLVD SOUTH
LAWRENCEVILLE, NJ 08648

P +1-609-586-4981
F +1-609-586-4982

info@ispor.org
www.ispor.org

December 21, 2018

The Honorable Alex M. Azar II
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Mr. Azar:

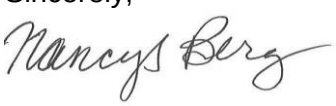
The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) is pleased to respond on behalf of its membership to the U.S. Department of Health and Human Services call for comments on "RIN 0938-AT91: Medicare Program; International Pricing Index Model for Medicare Part B Drugs." We strongly agree that these are important issues to address with input from a wide variety of stakeholders, and thank the Department for this opportunity to provide our comments.

ISPOR is a scientific and educational society with many of its members engaged in some aspect of health economics and outcomes research (HEOR) related to evaluation of pharmaceuticals. Our membership includes over 20,000 individuals across a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government (including some HHS employees), and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

As you will see below, we have chosen to respond only to selected aspects of your call for comments. We selected those areas and questions which we feel are best informed by the research and expertise of our disciplines and our membership. This response was formulated with the assistance of ISPOR's most senior and representative Council, the Health Sciences Policy Council, and informed by a survey of our full membership. It was reviewed by and approved by our current President and myself.

ISPOR would be happy to answer any questions about our response, as well as to participate in any follow-up consultations on these issues. Please consider Richard Willke, PhD, our Chief Science Officer, as the contact person in this area.

Sincerely,



Nancy S. Berg
CEO & Executive Director

ISPOR Reponse to US Department of Health and Human Services Advance Notice of Proposed Rulemaking (ANPRM): RIN 0938-AT91: Medicare Program; International Pricing Index Model for Medicare Part B Drugs

Introduction

We want to begin by congratulating CMS and CMMI for tackling issues arising from both the rapid growth of Medicare Part B spening and international differences in drug pricing [1, 2, 3]. This is a very complex issue, as the complexity of the ANPRM indicates, including the plan to conduct a pilot project rather than proceeding to immediate full-scale implementation. ISPOR is a global scientific and educational organization with a diverse membership from a range of stakeholder groups. Although it is challenging for us to reach a consensus given the different perspectives of our members, we would like to offer some input based on the scientific work in our field, which is the aim of ISPOR. In short, at this stage, we urge CMS to exercise great caution in the use of international reference pricing (IRP), as is proposed in the use of an International Pricing Index (IPI). Although we understand the appeal of short-term reductions in Part B prices via IPI, the long-term risks to innovation and thus life-saving medicines are substantial. We would urge instead exploring the use of more direct value-based approaches to determine medicine prices for Medicare Part B.

Some Perceived Advantages

First, however, we recognize that implementing IRP in Medicare Part B can be seen as having some potential advantages. We surveyed our scientific membership and some possible advantages were suggested. Use of IRP might result in overall price reductions in that program and generate some cost savings that could be used elsewhere – in other parts of Medicare, other government programs, or tax reductions. It could make pricing for these drugs more homogeneous across developed countries, which might be perceived as fairer by many U.S. citizens. It could motivate drug companies to negotiate more strongly with other countries to achieve pricing that could help share the global R&D burden cost in a way that U.S. citizens might regard as more appropriate. From a health technology assessment (HTA) perspective, the clinical and economic effectiveness of a therapy across countries and geographies might be evaluated more consistently. To date, there are significant variations across countries in the HTA methodology used to measure and understand variations in outcomes across patient populations. A more unified approach to pricing could simplify the value assessment and evidence comparisons across geographies, reducing duplicative effort by both payers and drug companies across jurisdictions, and thereby strengthening payor understanding of decision-making relative to prices as well as sending clearer signals to drug developers as to likely returns on investment.

A Challenge

We agree that there are issues related to rapidly rising Part B spending. We also recognize, however, that it is difficult to correct for the historical practices that underlie the current system. It is also necessary to recognize the investments that stakeholders have made to operate within the current system. Modifications have improved the competitiveness of the arrangements, but perverse incentives remain. It is important, however, that concerns about spending growth be balanced against the health benefits to patients that result from that spending. The GAO has found that recent growth in Part B drug spending is primarily due to introduction of innovations for treating orphan diseases and/or receiving expedited approval, both categories representing drugs that have the potential to meet significant unmet medical needs [2]. This perspective does not, of course, obviate concerns about international price differences, which deserve further discussion, as does the need to find new approaches based on the use of an assessment of product value, to generate both more price competition among, and more efficient use of, drugs.

Basic Economics of Innovative Medicines

It is useful to begin with a few points on the basic economics of innovative medicines as an important contributor to health production globally. First, as in well known, the U.S. spends more on healthcare as a percentage of GDP and in real terms per capita compared to the systems of other developed countries. Spending on medicines is a minority share of this (12% to 20% depending on measure and population) as compared to the shares spent on hospital and physician care [4]. U.S. prices for patented drugs, hospital care, and physician services are higher than in other developed countries. In recent years, the differential for drugs has widened [3].

Patented drugs are unique inputs to improving population health. They are the result of costly and risky global R&D investments [5, 6]. Most drug candidates fail in the development pipeline and only 30-40 new drugs are approved annually (though the number will be over 50 in 2018). Globally, all high-income country purchasers contribute to cover the R&D costs, but it has been clear for a long time that the U.S. has contributed more (in relation to its GDP) than other developed countries. While higher spending in the U.S. may reflect greater value placed on the health and related improvements that these medicines provide, it may also reflect—in theory—other countries "free-riding" on the global R&D investment as the ANPRM and the report by the CEA suggest [7].

Incentives for Free-Riding

Free-riding occurs when a payer suppresses its willingness to pay and seeks to use preference concealment or monopsonistic bargaining power to drive down prices to such a degree that the goods they are buying may be underprovided or not provided at all. In the context of pharmaceuticals, this would have the effect of (potentially) increasing short-term efficiency by increasing the number of patients who gain access to the treatment, but reducing long-term dynamic efficiency by reducing R&D incentives and therefore the amount of innovation. The Council of Economic Advisers (CEA, 2018) expressed the view (1) that non-U.S. markets contribute less than they should to global R&D, as, for example, the U.S. contributes more to global R&D than its share of relative GDP, and (2) that the overall amount of R&D could be higher if prices rose elsewhere, even if the U.S. contributed less [7].

However, observing different prices or different mark-ups above marginal cost in different parts of the world (i.e., "differential pricing") is not necessarily evidence of free-riding. Efficient pricing of pharmaceuticals requires prices above marginal cost during the on-patent period. However, mark-ups should reflect underlying willingness to pay which will vary by country or by population, depending on factors such as per capita income, which in turn will affect health budgets and preferences for additional health expenditure [8]. However, we would not expect poor populations in low-income countries to contribute to R&D costs by paying prices above those of off-patent generic products [9]. Given the need to use patents to reward innovation, efficient levels of expenditure on global R&D are achieved when each health system is rewarding the health gain from new innovation at prices that reflect the willingness to pay for health gain of the population they serve [8]. This could, in theory, lead to lower prices in the U.S. and a lower U.S. contribution to R&D, as the CEA suggests. For example, it has been argued that the existence of a tax subsidy for health insurance policy premiums artificially raises prices [10]. However, the impact on R&D contributions in other countries is less clear. It depends on whether prices reflect income-constrained willingness to pay for health gain, in which case the resulting amount of R&D would be efficient, or reflect the use of monopsonistic bargaining power to drive prices below willingness to pay and so not to contribute efficiently to global R&D. This is, in principle, an empirical issue, which is only partly addressed by the CEA report.

Support for Value-Based, Global Differential Pricing

There is a substantial theoretical literature in our field supporting the view that differential pricing across counties is the central element in the optimal solution to this global financing problem for pharmaceutical innovation [3,9]. However, increasingly, the global reality seems to be departing from this: adjusting for differences in national income, U.S. prices appear to be much higher than those of similar high-income countries [3]. We say "appear", in part, because price comparisons are difficult given that confidential discounts are common both among payers within the U.S. and across payers globally. Indeed, as in other sectors (e.g., air travel), confidential discounts are an efficient—perhaps the best—way to maintain prices differences across customers who value things differently. If prices are perfectly transparent, then buyers will want to free-ride and extract the lowest price.

Obviously, the use of IRP on the part of the buyers of patented medicines can result in a "race-to-the-bottom" as everyone tries to get the lowest price [11]. On the other hand, monopsonistic buyers want to counter the monopoly power of sellers (the manufacturers) in this market. While intelligent buyers understand that the short-run marginal cost of manufacturing and distributing medicines is often relatively small, they also understand that if everyone paid short-run marginal costs, under the current overall financing system, there would be no money to cover the fixed costs of R&D. Clearly, the key question is how to achieve market prices that properly transmit value signals to drug developers—with that "value" being defined in terms of how much patients and society value the health gains (and cost savings) produced by the drug treatments.

More research is needed in this area before conclusions can be drawn about variations in the willingness to pay for health gains across countries. A small number of studies have been published, but they have been criticized for the number and type of assumptions that have to be made.

Problems with the Proposed IPI

There are a number of implementation issues with any use of IRP referenced in our membership survey that hold true for the proposed IPI. The most important is the consequential changes in behavior of both payers in the referenced countries and the manufacturers supplying them.
If Country A references prices in Country B, then drug manufacturers treat the two markets as linked when they set prices. If prices in Country B were lower than those in Country A, then they may (i) increase prices in Country B, or (ii) stop supplying Country B so there is no price to be referenced by Country A [12]. Either action will reduce the impact of reference pricing on the prices in Country A. Arguably, if prices are raised in Country B, then overall returns to R&D will rise and patients in Country A will benefit from more innovation. However, two things are likely to happen, or a combination thereof. Firstly, revenues may fall (and therefore returns on innovation) because Country B buys less – for example, reducing the sub-populations for whom the drug is made available. Secondly, as noted above, the payer in Country B and the manufacturer may agree on higher list prices and larger confidential discounts, such that, the net price paid in Country B is unchanged. However, the list price rises such that Country A gains no benefit from referencing Country B.

As long as countries referencing each other have some commonality of GDP per capita and health system characteristics, and have limited local capacity for value assessment, then IRP may have merit as a policy tool. If, however, there are very substantial difference in prices, incomes, health systems, and willingness to pay for health and health related gain, then drug manufacturers will take substantial evasive action (in the form of confidential discounting and/or launch delays) and are likely to be supported by payers who do not wish to face higher prices or restrictions in product availability. Perversely the differentials highlighted in the CEA Report [7] mean that IRP is unlikely to work when

used by the U.S. This does not mean that large international price differentials should not be addressed. It means that IRP is a singularly unhelpful tool to try to use to do it.

The Need for Value-Based Approaches

Given these issues around introduction of IRP in the U.S., ISPOR would like to encourage further consideration of more direct value-based pricing approaches. A recent ISPOR Special Task Force on Value Assessment Frameworks (STF-VAF) argued for a flexible, value-based approach to assessing the economic impact of innovative medicines—in Part B and elsewhere. The STF-VAF began its work this assumption that value assessment is critical because of the signals it sends to innovators about what patients and plan subscribers care about. Simply copying or anchoring on prices in other countries is likely to be a poor estimate of value in the U.S. Value varies by the local context. For example, the other medical costs avoided by using innovative medicines can be substantial [13-14] and are likely to be even greater in the U.S. given higher unit costs of hospital and physician services [15].

To support a value-based approach, the ISPOR STF-VAF [16] made six major related recommendations with two key sub-recommendations for purposes of this discussion being:

> II.2 Value assessment frameworks that focus on health plan coverage and reimbursement decisions should consider cost-effectiveness analyses, as measured by cost per QALY, as a starting point to inform payer and policy maker deliberations. In many instances, the cost-per-QALY metric can serve well as the core component of these assessments.
>
> II.3 Elements of costs and benefits not normally included in CEA that affect individual well-being (such as severity of illness, equity, and risk protection) may be relevant for some health plan decisions; however, more research is needed on how best to measure and include them in decision making.

We do recognize that some Medicare Part B drugs are orphan and/or oncologic drugs, where standard cost-effectiveness considerations may not completely reflect patient and societal values and where some nominally high U.S. prices have attracted considerable attention.

Focusing on value-based pricing in the U.S. may or may not alleviate current cross-country price disparities and overall drug spending concerns. However, if U.S. prices do fairly reflect value considerations in the U.S., global free-riding becomes a secondary issue, parallel with almost any other technology market where there are some fixed costs of production to be borne by some consumers. U.S. consumers will not be excessively "subsidizing" other markets, and producers retain an incentive to charge prices outside the U.S. that better support their R&D investments. In addition, there are a number of arguments that support global differential pricing, as discussed above.

We do not attempt to provide answers to all of the questions in this ANPRM: many of them lay outside the ISPOR's expertise in health economics and outcomes research. Some others require more thought and research. For example, we do not discuss how value-based assessment could be embedded institutionally for Medicare Part B or how providers would be incentivized to use cost-effective drugs. Were HHS to indicate its willingness to purse a value-based approach rather than IRP, we would be pleased to contribute on these two elements. Additionally we would elaborate on other approaches to better calibrating value and net pricing worthy of further consideration including outcomes-based contracting and related types of risk-sharing agreements, indication-based pricing, and episode-of-care based pricing. Drug regulatory incentives or requirements that improve the availability of information (such as on treatment outcomes) or reduce transactions costs are important ways to allow markets to

better determine value-based prices. However, one technical point that we feel compelled to point out before closing is that international health cost comparisons should consider not only market exchange rates subject to fluctuation, but also underlying equilibrium exchange rates which will take account, for example, of "cost-of-living" differences: this is a best practice standard in our field even though it is often not incorporated into current IRP schemes [17].

We hope that these general comments are helpful as CMS crafts its approach to Medicare Part B pricing and spending. ISPOR would be happy to respond to further consultations in this area.

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