

AMGEN'S COMMENTS ON ICER'S PRICE INCREASE DRAFT PROTOCOL

Final Comments Submitted February 13, 2019

Amgen appreciates the opportunity to comment on ICER's Draft Protocol for their first Unsupported Price Increase Report. We agree that it is important to optimize the value of health care expenditure, and we have concerns with the proposed approach as outlined below. We are hopeful that ICER will make the appropriate changes to enable more meaningful results.

OVERALL POSITION

ICER is pursuing an extraordinarily complex issue and there are many factors that need to be considered for this report. Prescription drug expenditure in the US accounts for a relatively small percentage of overall healthcare spend. Singling out one component of healthcare rather than viewing the system holistically, and focusing only on the highest impact drugs rather than all drugs, distorts the underlying cost drivers in the US healthcare system. It also contradicts comments made by ICER in recent value framework updates:

*"ICER does not intend to target any particular interest group or organization. There are many areas in which the US health system fails to serve patients well, in which access to care is suboptimal, waste and inefficiency pose major problems, and costs to patients and the health system fail to align with added value. ICER believes that only through collaborative efforts, built upon a foundation of civil discourse and honest consideration of evidence on effectiveness and value, can lasting progress be made on behalf of patients today and those of the future."*¹

Moreover, the extensive methodological challenges to reliably calculate net price should not be underestimated. Challenges with the data utilized by SSR Health, LLC to derive net price include transparency, subjectivity and uncertainty in evaluation of both the quality and magnitude of evidence to support price. The proposed analysis is unlikely to have meaningful impact given the inherent limitations and challenges. Ideally, we believe ICER should expand the remit of this report to include all healthcare expenditures. By doing so, ICER would take on the greater opportunity of tackling fundamental healthcare issues and address 1). the architecture and causes of meaningful national health expenditure drivers and 2). general price transparency of healthcare services, medical equipment and treatments, which currently makes informed decision-making difficult. However, if this is not an option, then at the very least, we suggest ICER expand the remit of this report to include all drug price changes, increases and decreases, that impact net expenditures in the entire pharmaceutical sector.

Healthcare systems are plagued by inefficiencies in how care is delivered and paid for. With hospital care and professional services being dominant drivers of healthcare spending², drug spending accounts for only 14% of total U.S. healthcare costs.³ Healthcare service prices continue to grow: a majority of the growth in payments for inpatient and hospital-based outpatient care was driven by growth in hospital prices.⁴ The highest growth rates in US national expenditure in 2019 will be taken by government administration (10.2%), healthcare professional services (6%) and home healthcare (6.7%) *in contrast to pharmaceuticals, which in 2019 are only expected to grow by 5.6%: this is close to the average for all healthcare expenditure of 5.2%.*⁵ The proportion

of national expenditure from drugs at 14% is a fraction of hospital and professional (*e.g.*, physician) services which account for more than half.^{6,7} US net prices for drugs rose only 1.5% in 2018 which is lower than the rate of inflation; and this is projected to grow only 0-3% annually over the next five years.⁸ CMS projections further establish that pharmaceutical expenditure is not the highest growth area or portion of expenditure. Also, drug prices fall over time, in contrast to medical services continuing to rise due to increases in administration costs and the rising trend of provider consolidation with proven effect on prices.^{9,10,11,12} Over the past decade, generics dropped the price of pharmaceuticals after loss of exclusivity by 51-57% in the first and second year. In the next five years, generics and biosimilars are expected to reduce the sales of branded drugs by \$121 billion.¹³

Amgen understands that prescription drug cost is a concern for many people and we strive to price our medicines responsibly, in a way that ensures patient access and affordability. It is however important to differentiate between list (WAC) price growth and net price (*i.e.*, price net of rebates and discount) growth. For 2019, the weighted average list price increase across Amgen's entire U.S. portfolio of products is less than 2.0%, which is below the projected inflation rate of 2.4% for the year. In addition, net prices for several Amgen products have declined.¹⁴ This situation is echoed in recent ESI data, one of the nation's largest PBMs that revealed spending on medicines in commercial plans grew just 0.4% in 2018 net of rebates and discounts, the lowest in 25 years.¹⁵ For many Amgen medicines, there are no price increases. We are also committed to delivering new solutions that tie payments to performance (*e.g.*, lowering the cost of medicine if it does not meet identified performance targets.) With many stakeholders in our healthcare ecosystem, we, like others, have a role to play in making healthcare affordable so patients can access the medicines they need. Amgen is committed to taking a fresh look at how we can partner to test new ways to improve access and deliver more affordable care.

KEY COMMENTS ON ICER's APPROACH

ICER should consider assessing price and net expenditure changes in the entire healthcare system, since this is an under researched area and is consistent with ICER's broader mission. If ICER insists on limiting its focus to medicines, the current proposal to focus only on the price for a handful of medicines with the highest system impact is inherently biased and will not meaningfully shed light on the reasons for changes in price or impact on overall healthcare expenditures. **At a minimum, the report should look at all drug price changes that impact net prices in the entire sector.** In a health system with constant innovation, robust and changing competition, frequent price collapses due to patent expiry, and other events which impact the competitive environment for medicines, ICER's currently proposed approach misses opportunities to help promote better understanding of this complex area. Prioritizing drugs for review according to those that by virtue of high numbers of patients (volume) who receive them, even sends a negative message about the impact of the most innovative drugs for the largest populations.¹⁶ Additionally, this could create a higher bar of pricing scrutiny for drugs that most likely have the biggest positive impact to society because their value is actually increasing. Drug prices are reflective of the value drugs bring, demonstrated in studies linking greater expenditure on drugs to reduced healthcare costs in other areas.^{17,18,19,20} The Congressional Budget Office (CBO) estimates that every 1% increase in the number of prescriptions filled by beneficiaries causes Medicare's spending on medical services to fall by roughly one-fifth of 1%.²¹ In a recent Health

Affairs Study, drugs were recently shown to have a material effect on reducing Medicare spending. For Medicare beneficiaries sixty-five and older, spending has declined since 2005 with half of spending attributable to slower spending growth in cardiovascular disease with roughly 50% due to medications controlling cardiovascular risk factors.²²

One cannot determine whether a price increase is justified without looking at both the value being delivered and extrinsic effects that may have resulted in a price increase. There are many factors beyond the value of a drug that can explain price increases. The evidence base both in traditional clinical data and real-world evidence continues to evolve together with the addition of new indications, changing patterns of use, clinical care innovations, biomarkers and better understanding of patient sub-groups. In addition, various exogenous shocks to the market supply and demand curves can drive changes in the price. In unusual circumstances, this has sometimes included changes in prices for material costs and demand constraints from a given manufacturing plants capacity.^{23,24} The current draft protocol misses an opportunity for ICER to shed light on the reasons for price changes.

ICER should remove the term ‘unsupported’ from the title of the report. The use of the term ‘unsupported’ automatically suggests that all drugs in the assessment have unsubstantiated prices even before the analysis is performed. ICER can demonstrate greater impartiality and fair balance by starting with a title that does not make assumptions as to what the results of the report may be.

METHODOLOGICAL RECOMMENDATIONS

Net prices are difficult to discern given the complexity of the current system; should ICER decide to proceed with the analysis, it should account for uncertainty in the results. The walk from the wholesale average cost (WAC) to the actual price that manufacturers receive is exceedingly complex within a given payer, but this complexity grows in magnitude when taking into account over 800 different payers in the US, all with different processes and payment mechanisms.^{25,26} Significant uncertainties accompany the move from the WAC to the net price with fundamental shortcomings inherent in the data sources used, wide variations across different diseases, drugs, delivery, payers, and methodological challenges for evaluating evidence and the subjective nature by which the value of this evidence is determined. These complexities require a robust and externally validated approach for reducing uncertainty.

Given extensive variability, ICER should provide greater detail on how it derives net price. There can be significant variation between net price and list price and the data used in this analysis will not account for this. Also, this approach is in contrast to how manufacturers capture these data.²⁷

To enable a more fair-balanced assessment, ICER should also capture price changes in generics and biosimilars in addition to branded drugs. Some generic and biosimilar drugs have seen significant price growth, which is equally important in the U.S.^{28,29} Including these types of products in this pricing assessment enables a more accurate picture of historic U.S. price change.

ICER should consider evidence for all indications regardless of population size. An indication may not reach 10% of a drug's use but may be 100% of the use in the indication, and as such,

should be included due to its value in that indication. This would rule out certain populations. Pediatric evidence which provides valuable data for HCPs would likely fall under the 10% threshold. Identifying indications that form 10% or more of a drug's use can be difficult in some areas such as oncology, which have multiple tumor types, combinations and lines of therapy; this is also a significant issue in inflammation where one drug can have as many as 6 different indications.

In addition to clinical data, ICER should include factors that determine price and other determinants of patient value. Amgen continues to invest in clinical trials, new indications, new formulations, new delivery methods, disease management programs and other ways to improve the patient experience. Continuous innovations like these require significant ongoing investment, which should be reflected in ICER's report. ICER should include wider components of benefit including improvements in disease-based patient life impacts, work productivity, and product enhancements to advance patient-centered care and improve utilization. These encompass better quality of life, adherence, unmet need, severity of disease, value of hope, ability of a treatment to extend life to give time for the development of a cure (real option value), scientific spillover and other contextual criteria that form the basis of a drug's benefit.^{30,31} These data should have: a). *equal weight* to clinical data, b). *form a central part* of the consideration of data and evidence that substantiates price, and c). be *directly* reflected in the determination of price substantiation.

ICER should ensure a robust, methodologically sound and impartial method for grading the quality of evidence and the magnitude of net health benefit. It is currently unclear from this draft protocol, how ICER will rate the quality of the new evidence and the level of additional net benefit. We suggest ICER adopt a 3-step process for this.

- (1). Identify a governance board to optimize credibility and validation of this process. To complete this analysis, the public should elect a governance board of impartial experts that will monitor and control the process of this assessment. ICER's press release states consultation with a multi-stakeholder advisory group but there is little information on membership and governance.
- (2). Rate the quality of new evidence (low, moderate, or high) using an external peer-review process to validate the methodology and application to this analysis. Subsequent to this, reviewers should report their findings publicly, subject to validation by the governance board.
- (3). Rate the additional net health benefit (none, small, or substantial for evidence that has been rated as of 'moderate' or 'high' quality from above):
 - o The draft protocol should outline the criteria to determine 'small' versus 'substantial' benefits.
 - o We recommend identifying a group of independent experts primarily from treating clinicians, experts in the relevant disease and affected patients. This group should be chosen by members of the public, industry and academic experts to ensure impartiality. This group and the criteria they will use to differentiate between 'small' and 'substantial' should be validated in a transparent manner by the governance board.

To help minimize bias, ICER should remove the three additional subjectively chosen drugs. The addition of these extra products based on subjective criteria will compromise the scientific integrity of the work, invalidating the methodology and leaving the report open to criticism.

We recommend ICER apply best practices in transparency and make their methodology, evidence model, data and data sources publicly available and replicable. Specifically, ICER should give greater detail as to the methodology for more complex areas that are open to interpretation and assumption, including greater detail in the methodology for the evaluation of evidence and benefit.

CONCLUSIONS

ICER should expand the remit of this report since the current limited focus on drug pricing will not address the wider cost architecture of healthcare services and provision that drives U.S. healthcare expenditure. Net prices for medicines are lower than the general rate of inflation and this is projected to continue over the next five years.³² This report's scope necessitates including all price increases across the healthcare system. Should ICER decide to proceed with this analysis without making these changes, we have additional methodological concerns centered on the inherent complexity in calculating net prices and evaluating justified price increases. ICER should provide extensive detail on the calculation of net price and address uncertainties in their conclusions. It should ensure that it captures price changes in generics and biosimilars and remove the three additional subjectively chosen drugs. Assessing whether a price increase is justified requires a more comprehensive examination of value to encapsulate the extrinsic effects that may have resulted in a price increase. ICER should account for: market shocks to drug supply, the need to incorporate evidence regardless of population size, and include not only clinical data but other determinants of patient value. ICER should mandate a process for grading the quality of evidence and the magnitude of net health benefit that is methodologically sound and impartial and then apply best practices in transparency, making the methodology, evidence model, data and data sources publicly available and replicable. These changes will improve the general validity of the report but will not fix the uncertainty in the conclusions nor will they address the narrow scope of the report. We strongly suggest that ICER consider a more holistic approach that better aligns with their mission.

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- ²⁵ From Dusetzina *et al.*, 2017 How rebates work: *"In the United States, the net price received by the drug manufacturer can differ substantially from the sale price at the pharmacy. Figure 1 provides an overview; at the top of the figure is the net price zone, where the price that the manufacturer receives is reduced when it gives a rebate to the payer. In Medicare, the payer is the Part D plan sponsor and the pharmacy benefit manager working on its behalf. The pharmacy sale occurs in the list price zone. The pharmacy pays an acquisition price when it purchases the drug and then receives a negotiated price from the payer (inclusive of payment from the patient) when it dispenses the drug. Although the negotiated price and the list price differ, they are usually reasonable approximations of each other. Regulations define the wholesale acquisition cost of a drug as the list price from a manufacturer to a wholesaler or another direct purchaser without discounts or rebates. For branded prescription medications with no direct competitors, acquisition prices for pharmacies are typically within a few percentage points of the wholesale acquisition cost.* Source: Dusetzina SB, Conti RM, Nancy LY, Bach PB. Association of prescription drug price rebates in Medicare Part D with patient out-of-pocket and federal spending. JAMA internal medicine. 2017 Aug 1;177(8):1185-8. [Link](#)
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- ²⁷ Net prices are a **census** (no ambiguity as reported by manufacturer), Symphony data is **extrapolated from a sample**. Reliability is wholly dependent on the representativeness of the sample chosen by Symphony (including products which go through channels that are under-represented). Also, SSR methodology for net sales captures various accounting adjustments including patient assistance programs, free goods, ex-factory wholesaler adjustments, etc. The disconnect that requires greater attention is the disparity between the net sales and net units, largely that the units data from Symphony is customer-based

purchase units versus the ex-factory reported net sales figure. This combined with SSRs's method to average out variations in product packaging compositions and non-linear unit of measure conversions will likely cause variations in data.

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³¹ *“Real option value: Patients also face uncertainty about when and how future advances in medicine will occur. Thus, extending life provides patients with an option to enjoy these uncertain future benefits. This “real option value” is generated when a health technology that extends life creates opportunities for the patient to benefit from other future advances in medicine [35]. Previous economics literature has identified real option value as an additional element of value that may be relevant for specific medical products [36,37]. This element is not generally captured or reflected in the intervention-specific projections of QALYs gained, which account for a combination of expected survival and the health-related utility at any point in time during the remaining lifetime.”* From Lakdawalla et al.,

³² *Op. cit.* IQVIA.

February 13, 2019

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review

RE: Draft Protocol for Unsupported Price Increase Assessment

Dear Dr. Pearson,

On behalf of Boehringer Ingelheim Pharmaceuticals, Inc. (“Boehringer Ingelheim” or “The Company”) we are pleased to submit comments on ICER’s Draft Protocol for the Unsupported Price Increase (UPI) Assessment. Boehringer Ingelheim is a leading global research organization with extensive expertise developing therapies to treat a variety of chronic and life threatening diseases. Boehringer Ingelheim supports ICER’s continued efforts to improve the quality of evidence for decision-makers through its value assessment process. We believe that collaboration, transparency, and open dialogue throughout the development of ICER’s value assessment frameworks is critical to ensuring that they are appropriately and accurately evaluating the treatments according to what patients and other stakeholders value. We therefore appreciate the opportunity to provide feedback to ICER on this UPI Assessment.

Section 2 - List of Drugs to Review

- ICER proposes to use the SSR health data (FSS for privately held companies) to determine the net price for each drug, with input from manufacturers and other sources that may also be taken into consideration. The SSR health data methods are a crude way to assess net price and do not take into account stocking and other supply chain issues. To ensure transparency of the process, detailed guidance on when and how manufacturer input will affect net price calculations should be provided in the protocol. Moreover, this guidance should clearly state how ICER will prioritize use of a manufacturer provided net price, if it will replace the SSR health net price, and what the criteria are for determining which price will be utilized in the UPI assessment.
- ICER provides a list of criteria that will be used for considering drugs to be added to the UPI list through public input, but does not specify the weight and rating that will be assigned to each criterion listed (ie, “extremely high price increases” is listed as a criterion, but “extremely high” is not defined). In addition, there is no guidance on how these criteria are ranked relative to each other and the initial 10 drugs on the list. Boehringer Ingelheim requests increased transparency in the selection, methodology, calculations, and subsequent ranking, of all drugs included on the UPI assessment.

Section 3 - Manufacturer Input

- Boehringer Ingelheim is concerned that 4 weeks is insufficient for manufacturers to receive

notification that their product is on the UPI assessment list, gather the appropriate supporting evidence, carry out new analyses if needed, communicate any clarifying questions, and subsequently provide written and/or verbal comments to ICER. Boehringer Ingelheim strongly urges ICER to increase the timeline for manufacturer input.

- ICER states that “any information provided by manufacturers will be included as part of the final report and will therefore be transparent to the public and policymakers”. ICER’s Academic-in-Confidence policy is limited in scope, which will inhibit manufacturers from providing comprehensive information on all of the factors that determine pricing calculations, many of which are proprietary and confidential.
 - For this reason, Boehringer Ingelheim strongly encourages ICER to extend the Academic-in-Confidence policy to all information submitted by manufacturers, particularly pricing information, rather than limiting it to only clinical evidence.

Section 4 - ICER Review

- Boehringer Ingelheim requests ICER provide further detail around how “high quality” comparative observational studies will be defined and assessed during ICER’s review process. By clearly defining this criteria, ICER can aid in increasing transparency in which evidence will, or will not be considered.
- In addition, it is unclear what criteria or restrictions are placed on the evidence that ICER will accept and consider. This includes questions around whether ICER plans to prioritize US data compared to global data, the acceptability and inclusion of evidence from non-US studies, consideration of patient-centered outcomes data, and the inclusion of other factors that weigh into the overall value of the drug (ie, caregiver burden, quality of life data, patient perspective, and the potential impact on other costs).
 - We request that ICER provide more detail around how evidence provided from manufacturers will be taken into account to increase methodological transparency and ensure manufacturer readiness.
- ICER references use of the GRADE rating system alone, rather than ICER’s Evidence Rating Matrix (ERM). BI requests clarification of the rationale for not utilizing the ERM directly.
- It is further unclear how ICER will account for single products that are prescribed and utilized in combination or otherwise may be perceived differently in the context of price compared to similar drugs in the class for the same indication. For example, drugs have increased in price due to competition from other products, but still remain at a lower total cost than competitors when taking into consideration total cost of care (ie, combination therapy vs single therapy that requires add on drugs). One of ICER’s guiding principles is “evidence on added benefits, price and insurance coverage”. By failing to take into account the broader context of price increases, ICER is jeopardizing fostering innovation to create sustainable access to high-value care.

- Further, BI recommends that ICER expand the type of evidence considered for the UPI assessment beyond efficacy and safety data. By overwhelmingly focusing on efficacy and safety evidence, the UPI assessment excludes an essential component of what brings value to patients. Even in ICER's own value assessment framework (VAF), "Other Benefits and Contextual Considerations" weigh into ICER's evidence ratings as they are recognized as very important aspects of a drug's value.

Section 5 - Designation of Drug Price Increases as "Unsupported"

- It is unclear what type of data are considered "non-clinical". For example, does this refer to anything collected outside of the randomized clinical trial? Specific objective criteria for data that will or will not be considered should be clearly outlined in the protocol.
- Moreover, the nomenclature proposed by ICER alluding to "small" benefits and "unsupported" drug price increases are inherently subjective. To ensure the integrity of ICER's UPI report, it is essential that they clearly define and operationalize such terms.

Section 6 - Manufacturer Review Prior to Public Release


- ICER's UPI assessment draft protocol does not support price increases in instances where indication specific pricing exists. The use of indication-based pricing is becoming more common, with the potential to progressively impact drug pricing in the future. ICER should consider specifying how the UPI protocol will account for products that have indication specific pricing, and if resulting price increases will be factored into UPI assessment results.

Section 7 - UPI Assessment Public Release

- We recommend ICER consider delineating a protocol for drugs that may have been included in previous UPI assessments. It is unclear if drugs may be included in the UPI assessment over 2 or more consecutive years, or if drugs will only be included in the annual UPI report once and then excluded from future versions of the UPI assessment. Further, a process in which subsequent assessments will address new evidentiary findings of drugs noted as unsupported in prior years should be considered.

We respectfully request that ICER consider the above suggestions in finalizing the UPI assessment protocol.

Sincerely,



Thomas Seck
Senior Vice President
Medicine and Regulatory Affairs
Boehringer Ingelheim Pharmaceuticals, Inc.



February 13, 2019

Steven D. Pearson, MD, MSc, FRCP
President
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RE: ICER Unsupported Price Increase Assessment Protocol

Dear Dr. Pearson,

I am writing on behalf of Celgene in response to the Institute for Clinical and Economic Review's (ICER) "Unsupported Price Increase Assessment" (UPI) draft protocol. At Celgene, we have long believed that value is fundamental to price and therefore any assessment of a therapy's price should include a thorough analysis of the value that the therapy provides. It is our opinion that ICER's UPI draft protocol takes a narrow look at value and is therefore ill-equipped to evaluate the pricing of innovative medicines in any meaningful way.

This essential link between price and value is reflected in Celgene's [Principles for the Pricing of Innovative Medicines](#), updated in 2018 to include the standard that price increases for any product in Celgene's portfolio will be limited to no more than once a year and at a level no greater than medical inflation (CMS projected growth rate for National Health Expenditures for the year). Because value is a guiding principle of our pricing decisions, there may be exceptional circumstances in which additional clinical or health economic evidence demonstrates a significant increase in the value of one of our medicines where this standard would not apply.

At Celgene, we follow four value pillars to measure our own performance in creating value and to provide clarity around what we mean when we use the term:

- 1) Value to patients
- 2) Value to the health system
- 3) Value to the economy and society
- 4) Value to future innovation

These pillars are representative of our belief that value is holistic and multi-dimensional and that any attempt to measure a therapy's value in the short-term, or through the lens of only one or some of these pillars, is insufficient. Celgene's perspective on value – including how it relates to price – is further articulated in our annual [Value and Innovation Report](#) and on the company's [Value Hub](#).



Innovative medicines have played a crucial role in improving patient health outcomes and quality of life over the last century. For patients with cancer, new therapies have contributed to a 26% decline in death rates since the 1990s.¹ In multiple myeloma specifically, patients have experienced a 79% increase in five-year survival rates between 1990-2014.² And the role of biopharmaceutical companies in making these advancements possible cannot be overstated; one study found that new biopharmaceutical therapies were responsible for 73% of the improvements in life expectancy between 2000 and 2009.³

The significant gains in patient health and quality of life are at least partially due to the biopharmaceutical industry's dedication to addressing all aspects of a patient's journey. In addition to pursuing improvements in patient mortality and morbidity, biopharmaceutical companies are constantly researching ways to improve the overall patient experience, directly addressing important considerations such as drug administration, dosing frequency, and other patient preferences. All these factors are valued by patients and should therefore be deemed valuable through any value assessment methodology.

The value of a given therapy is not limited to just the patients who are the direct beneficiaries of the product, but also extends to the broader health system. As innovative medicines lose exclusivity, generic versions of the product are made available at substantially reduced costs, thereby providing an everlasting benefit to the health system. From 2012 to 2016, loss of exclusivity accounted for \$93.6 billion in savings to the health system, with the benefits of these drugs continuing to be made available to patients at a low cost.⁴

The use of innovative medicines has also been shown to reduce spending on other medical services elsewhere in the health system. For example, in multiple sclerosis, the initiation of therapy is associated with reductions of up to \$5,700 in medical costs due to the decreased use of outpatient services and inpatient hospital stays.⁵ In 2017, better adherence to medication by Medicaid patients significantly reduced hospitalizations across a number of disease states, resulting in approximately \$8 billion in savings to the system.⁶ And for newly-diagnosed multiple myeloma patients, total monthly costs of the disease – including drug and medical costs – steadily decreased after the initiation of therapy as a result of slowing disease progression.⁷ As we continue to look to optimize overall spending across the health system, biopharmaceutical innovation should increasingly be considered a high-value tool instead of a target.

Biopharmaceutical innovation provides significant value to the economy and society by increasing worker productivity. New medicines have been shown to increase worker productivity by 4.8 million work days and add \$221 billion in taxable wages per year.⁸ And in disease states with a previously high unmet need like hepatitis C, innovative medicines can mean as much as a 167% increase in worker productivity.⁹ The simple reality that innovative medicines can help patients return to being productive members of the workforce, thereby providing benefits to employers and the broader society, demonstrates the “trickle-up” effect of biopharmaceutical innovation. Any assessment that only seeks to capture the clinical value of a biopharmaceutical therapy completely ignores the important societal and economic aspects of value.



Through substantial investment in R&D, Celgene and other research-based biopharmaceutical companies are driving the discovery and development of life-altering innovative medicines. But this level of investment, and the innovative medicines that result from it, would not be possible without the incentives that reward the high-risk endeavor that is biopharmaceutical research and development.

Research for patients is what drives Celgene – in 2018, we invested \$5.67 billion in R&D, accounting for 37.1% of revenues.¹⁰ Our commitment to research and development was again recognized in the 2018 EU Industrial R&D Investment Scorecard, where Celgene ranked first among biopharmaceutical companies and third overall among the 2,500 companies, across all industries, investing the largest amounts in R&D anywhere in the world.¹¹ And this commitment to future innovation can be seen across the biopharmaceutical sector, with one recent analysis concluding that biopharmaceutical companies invest more than 12 times the amount of R&D per employee as the average for manufacturing industries overall.¹² In 2016, biopharmaceutical companies spent 159 billion U.S. dollars on R&D and this figure is expected to increase to over 200 billion dollars in 2024.¹³

In assessing the value of an individual therapy, there must be some consideration for how the biopharmaceutical research ecosystem is expected to sustain, let alone enhance, innovation in the future. Tomorrow's breakthrough therapies are only made possible by the financial rewards for today's innovative products. In an industry where only two in ten FDA-approved medicines produce revenues that exceed the average R&D investment, the value of a therapy should appropriately account for the great risks involved in biopharmaceutical innovation.¹⁴

Celgene fully supports the ongoing dialogue around how we as a country are allocating our healthcare resources, including spending on biopharmaceutical therapies. We believe that for consideration of our health system challenges to be a fruitful endeavor, it should be based upon a holistic examination of value, as opposed to a restricted assessment of price increases for one component of healthcare during a narrow timeframe. By focusing solely on the pricing of innovative medicines, combined with a limited analysis of value, ICER's UPI draft protocol is destined to underestimate the value of biopharmaceutical innovation.

Sincerely,

A handwritten signature in black ink that reads "Richard H. Bagger".

Richard H. Bagger
Executive Vice President, Corporate Affairs & Market Access

¹ Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2018. CA Cancer J Clin. 2018;68: 7-30. <https://onlinelibrary.wiley.com/doi/epdf/10.3322/caac.21442>. Accessed April 2018.



² National Cancer Institute, SEER Cancer Statistics Review 1975-2015. Difference in 5-year relative survival between the 1990-1992 cohort and the 2007-2014 cohort calculated. Data on file at Celgene.

³ Lichtenberg FR (2014a), "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-Income Countries, 2000-2009," Health Policy and Technology 3(1): 36-58.

⁴ QuintilesIMS Institute. (2017, May). Medicines Use and Spending in the U.S.- A Review of 2016 and Outlook to 2021. Retrieved from https://structurecms-staging-psyclone.netdna-ssl.com/client_assets/dwonk/media/attachments/590c/6aa0/6970/2d2d/4182/0000/590c6aa069702d2d41820000.pdf?1493985952.

⁵ Nicholas J, Boster A, Wu N, et al. Comparison of disease-modifying therapies for the management of multiple sclerosis: analysis of healthcare resource utilization and relapse rates from US insurance claims data. Pharmacoecon Open. 2018;2(1):31-41.

⁶ Roebuck MC, Kaestner RJ, Dougherty JS. Impact of medication adherence on health services utilization in Medicaid. Medical Care. 2018;56(3):266-273.

⁷ Steven R. Arikian, Dejan Milentijevic, Gary Binder, Craig J. Gibson, X. Henry Hu, Yasir Nagarwala, Mohamad Hussein, Frank A. Corvino, Andy Surinach & Saad Z. Usmani (2015) Patterns of total cost and economic consequences of progression for patients with newly diagnosed multiple myeloma, Current Medical Research and Opinion, 31:6, 1105-1115, DOI: 10.1185/03007995.2015.1031732

⁸ Chen AJ, Goldman DP. Productivity benefits of medical care: evidence from US-based randomized clinical trials. Value in Health. <https://www.sciencedirect.com/science/article/pii/S1098301518301918>. Published online March 9, 2018.

⁹ Ibid.

¹⁰ Data on file. Celgene Reports Fourth Quarter and Full Year 2018 Operating and Financial Result. <https://ir.celgene.com/press-releases/press-release-details/2019/Celgene-Reports-Fourth-Quarter-and-Full-Year-2018-Operating-and-Financial-Results/default.aspx>.

¹¹ European Commission. 2018 EU Industrial R&D Investment Scorecard. Available at: <http://iri.jrc.ec.europa.eu/scoreboard18.html>.

¹² NDP Analytics. IP-Intensive Manufacturing Industries: Driving US Economic Growth. Washington, DC: NDP Analytics. <http://www.ndpanalytics.com/s/IP-Report-2017.pdf>. Published 2015. Updated 2018.

¹³ Statista. Global pharmaceutical R&D spending 2010-2024. <https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/>. Published June 2018.

¹⁴ PhRMA. (n.d.). 2016 Biopharmaceutical Research Industry Profile. Retrieved from <http://phrma-docs.phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf>.

February 13, 2019
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109

Re: Draft Protocol for the Unsupported Price Increase Assessment
Submitted electronically to: publiccomments@icer-review.org

Dear ICER:

Genentech appreciates the opportunity to submit comments in response to the Draft Protocol for ICER's Unsupported Price Increase (UPI) Assessment. Genentech is a leading biotechnology company that discovers, develops and manufactures novel medicines to treat patients with serious and life-threatening conditions. We invest more than \$10 billion a year in research and development, exceeding that of any other health care company in the world. As a result, we have brought 14 new medicines to patients in the last 8 years and have more than 70 potential medicines in development.

We provide these comments based on our commitment to help bring long-term, system-wide solutions that can lower costs for patients while sustaining innovation and access to the life-changing medicines they need. We are concerned that limitations of the proposed methods may misinform health care policymaking and ultimately impact patients' access to important treatments. A summary of our comments is as follows:

- 1. We encourage ICER to adopt a system-wide view to identify inefficiencies and optimize resource use by assessing health care beyond medicines.**
- 2. An assessment of medicines should be value-based and comprehensively account for all available evidence to support the decision needs of patients, society and the health care system.**
- 3. The approach to identifying medicines for review is biased and has noteworthy limitations that impact the utility of the UPI Assessment.**

The remainder of this letter provides additional details and perspectives for your consideration.

1. We encourage ICER to adopt a system-wide view to identify inefficiencies and optimize resource use by assessing health care beyond medicines.

We believe that ICER's intended goal towards a more effective and efficient health care system is best achieved with a holistic assessment of the entire system. The Centers for Medicare and Medicaid

Services estimate that the U.S. spent \$3.5 trillion on health care in 2017¹. Retail prescription medicines constituted a modest share of overall health care spending (10%), while services such as hospital care (33%) and physician and clinical services (20%) comprised over half the total spend. Multiple sources support that U.S. drug price growth has slowed by remaining relatively flat (0.4% to 1.5%) or has decreased on a per capita basis when adjusting for manufacturer discounts and economic and population growth (-2.2%)^{1,2,3}. Further, we believe the investments made in biopharmaceuticals have resulted in meaningful improvements in health outcomes and value. In a recent analysis assessing the cost-effectiveness of medical interventions for the top seven causes of mortality and morbidity in the U.S. between 1995 to 2015, treatments for six of the seven conditions were found to be cost-effective or cost-saving with improved outcomes.⁴

We recommend focusing on areas where resources can be used more efficiently to reduce the overall cost of care. Approximately \$213 billion, or 8% of overall health care expenditures, was spent on avoidable costs in 2012. The largest sources of avoidable costs were additional resources required to manage negative health outcomes stemming from nonadherence, delays in applying evidence-based treatment in clinical practice, misuse of antibiotics and medication errors⁵. An evaluation solely focused on the temporal price increases of prescription drugs will yield a limited perspective on potential improvement initiatives to support the goal of a better and more efficient system.

2. An assessment of medicines should be value-based and comprehensively account for all available evidence to support the decision needs of patients, society and the health care system.

Genentech is concerned that the designation of a supported or unsupported price increase is based on a limited view of available evidence and a rating system that lacks clear criteria. The proposed approach is agnostic to value and risks not accounting for important benefits and offsets obtained by the broad stakeholder base. As our healthcare system evolves to focus on value-based care, it seems remiss to ignore whether a drug's price is justified by the totality of health, economic and patient-reported outcomes it affords. Furthermore, a review of the totality of evidence will provide ICER with an indication of the level of post-approval investment a manufacturer is making to ensure the effectiveness, safety and value of a medicine, which may be one consideration in the decision to take a price increase.

2a. The evidence review should be expanded to include clinical, economic and patient-reported outcomes from both trial-based and observational settings.

Per the draft protocol, only randomized trials, high quality comparative observational studies and uncontrolled large observational studies for low frequency harms are considered. However, we believe a limited focus on a subtype of clinical study designs will lead to inaccurate conclusions and underestimate a medicine's benefit and value to the national population. By only including clinical outcomes assessed in a highly selected group of patients, the UPI assessment will exclude important and relevant information on effectiveness, quality, patient-reported and economic outcomes. Public and policymakers are best served with a comprehensive understanding of all available evidence that reflects the outcomes most important to patients and society.

2b. Rating criteria for evidence quality are unclear and lack consistency.

We recommend that ICER provide additional clarification on how the GRADE system will be applied consistently and transparently in order to address known limitations of this framework. We are concerned that this may not be appropriate to inform population-level decision making for these specific reasons:

- The GRADE system rates evidence quality as low, moderate or high quality based on reviewer opinion and risks subjectivity.
- There is evidence to suggest that the framework is prone to inconsistencies and low interrater reliability.⁶
- Studies assessing outcomes with multiple endpoints are extremely difficult for reviewers to grade.⁶
- The grading system is limited by its lack of applicability to evidence generated from sources other than randomized clinical trials.

2c. The rating of incremental net health benefit (NHB) is prone to significant subjectivity and variable interpretation.

In the evaluation of incremental NHB, UPI raters will assess the magnitude of clinical benefit for a therapy as defined by the labeling information versus the additional benefit demonstrated from a “new” body of evidence in the prior three-year period. There are several risks associated with this approach that may result in misinforming policymakers and the general public.

- The estimation of incremental NHB as none, small or substantial is not informed by a clear and validated rating system.
- The risks and challenges are further compounded by the comparison of “previously understood net health benefit for a therapy versus placebo and/or comparators” and “any new, additional net benefit for that same therapy based on newer evidence”. Therefore, this is an assessment of differences of differences which may be further complicated by varying comparators, differing study types, and divergent study objectives.
- This approach is subject to significant variation based on the interpretation of a review panel and poses concerns around replicability.

It is important to establish clear and objective criteria in the assessment of incremental NHB given its significant importance in the final designation of a supported or unsupported price increase.

2d. The 36-month time period offers a limited view on the totality of evidence.

We suggest the evidence review encompass the entire body of available evidence for a product. ICER proposes to assess only evidence published in the prior 36 months against that described in the labeling information. The timeframe of 36 months is biased against therapies which have been on the market for several years. There may be meaningful evidence, such as post-approval subgroup analyses or long-term follow-up data, that may have been published prior to the time period of interest, but the value of which is not reflected in a product’s price until a later time

point. Additionally, this limited view may result in an underestimation of the quality or strength of evidence. Findings that are reproduced in multiple studies, which may be published at various time points, generally indicate a greater strength of evidence.

3. The approach to identifying medicines for review is biased and has noteworthy limitations that impact the utility of the UPI Assessment.

We share specific areas of concern and offer recommendations specific to the proposed selection criteria.

3a. The drug selection criteria proposed by ICER may result in an assessment that is biased, narrow in scope and repetitive.

We believe that the current selection criteria may result in unintended consequences. The selection of final drugs starts with the top 100 drugs based on U.S. sales. Although ICER seeks to determine prescription drugs with the greatest U.S. budget impact, this criterion is inherently biased against chronic conditions, diseases of high prevalence and incidence and curative therapies. While sales are partially driven by drug price, other disease-related factors, including the number of treated patients, efficacy and treatment duration, are important drivers of total sales. Therefore, this criterion risks overlooking the evaluation of drugs that target smaller populations or acute conditions. Lastly, drugs with top dollar sales are unlikely to change significantly on a yearly basis. Annual reviews will thus likely be focused on a similar list of drugs, thereby limiting the scope and increasing redundancy in ICER's subsequent reviews. We advise ICER to reconsider the value in repeating this assessment on an annual basis.

3b. Current data sources risk misidentifying the therapies that ICER seeks to identify.

The data sources that ICER intends to use to inform net price are not reliable due to the confidential nature of contractual agreements with third party organizations. There are no available sources that systematically and comprehensively capture the true net price, one that is inclusive of all price concessions given to customers and of all statutory discounts and rebates. Further, the resources that ICER proposes to use for net price do not accurately account for reporting variability amongst entities within a complex drug distribution chain including insurers, pharmacy benefit managers (PBMs), pharmacies and wholesalers. For example, SSR Health leverages algorithms from open claims data sources to project unit sales at a national level. This projection is limited by the reporting practices of specific distributors such as specialty pharmacies. In addition, the use of the Federal Supply Schedule (FSS), determined by a statutorily defined federal process outside of the commercial market, for drugs produced by companies that are not publicly traded is inappropriate. FSS prices are the result of negotiations resulting from a bidding process by class and are proprietary in nature.

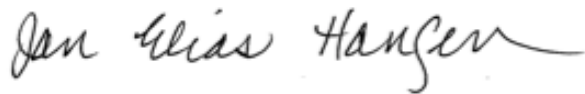
3c. Rationale for the price increase threshold, based on the medical care Consumer Price Index (CPI), should be provided.

To narrow the list of potential therapies to review, ICER proposes that drugs with Wholesale Acquisition Cost (WAC) increases greater than two times the medical CPI will be used. The rationale for the choice of two times the medical care CPI as an appropriate threshold for significant price increase is unclear, and as a key criterion in the selection process, should be further elaborated upon.

In closing, we recommend that ICER move beyond prescription drugs and adopt a broader system-level perspective, ensure an evaluation of cost is aligned with value, and address the notable limitations posed by the current approach to the UPI assessment.

We hope our comments will contribute to a more robust evaluation that is aligned with the evidence needs of a broad base of stakeholders. We welcome the opportunity for additional discussion.

Sincerely,

A handwritten signature in dark ink, reading "Jan Elias Hansen". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

Jan Elias Hansen, Ph.D.
Vice President, Evidence for Access Medical Unit
Genentech US Medical Affairs

References

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February 13, 2019

Steven D. Pearson, MD, MSc
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301-435-8717

Martin D. Marciniak, Ph.D.
Vice President
US Medical Affairs,
Customer Engagement,
Value Evidence &
Outcomes
GlaxoSmithKline

Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709-3398

Tel. 919-483-1959

Re: Response to ICER's Draft Protocol to Assess Unsupported Price Increases (UPI) Report

Dear Dr. Pearson:

GSK appreciates the opportunity to provide comments on ICER's draft protocol for the unsupported price increases (UPI) report. As a science-led, global biopharmaceutical company, GSK is dedicated to improving the quality of human life by enabling people to do more, feel better and live longer. Our commitment to patients is demonstrated by the broad range of innovative therapies and access solutions that we have delivered and continue to develop in respiratory, allergy, anti-infectives, dermatology, neurosciences, urology, HIV, and oncology. It is with patients in mind, that we offer the following methodologic recommendations for your consideration:

A. Expand the Scope of Evidence Review for UPI

At a time when US health care expenditures has slowed, including slower growth for retail prescription spending,¹ we believe that the UPI report's focus on drug prices and clinical evidence is misplaced. As proposed, ICER seeks to assess the temporal relationship between pricing increases relative to the public dissemination of clinical evidence. This approach suggests a simple, linear relationship between drug prices and clinical evidence, which is counter to the complexity of the US healthcare system and may mislead patient and policy stakeholders. We are concerned that this approach also fails to objectively value the significant commitment to extensive Phase IV evidence generation undertaken by manufacturers — not for label expansion or product differentiation but to improve appropriate clinical decision making or to ensure post-approval safety monitoring. Lastly, the UPI report's narrow focus on solely clinical evidence — underestimates the value and cost offsets that innovative therapies can deliver to the US health system, such as a reduction in non-drug related healthcare services or increased productivity. We recommend that ICER broaden the scope of its UPI report to include:

1. Detailed systematic literature reviews of both clinical and non-clinical evidence for included therapies and respective indications and
2. More robust economic analyses of all therapies identified for the UPI report

¹ Martin AB, Hartman M, Washington B, Catlin A. National health care spending in 2017: growth slows to post–great recession rates; share of GDP stabilizes [published online December 6, 2018]. Health Aff (Millwood). doi: 10.1377/hlthaff.2018.05085

Short of the recommended analyses above, the UPI report would present an incomplete assessment of the supporting evidence for included therapies and US price trends. Given ICER's mission to inform health policy decision-making with objective evidence, we believe that ICER has an important responsibility to ensure that the UPI report is robust, comprehensive, transparent and held to the same methodologic rigor and quality standards for peer-reviewed publications.

B. Accounting for Publication Bias and Timing

We concur with ICER on the need for an independent systematic literature review (SLR) to support the intended aims of the UPI report. However, GSK is concerned about the potential impact that publication bias can have on SLR and the current body of knowledge at a cross-sectional point in time.

Unfortunately, failed studies are less likely to be published in a timely manner or published at all. We are also mindful of the limitations of relying on published clinical data. Publication of a manuscript can often take between 6-12 months from journal submission. ICER proposes to accept manufacturer evidence under its academic in confidence policy to ameliorate this issue. However, the policy dictates that confidentiality will be maintained for 18-month period from the date of a public ICER meeting — a meeting that has not been included as part of the UPI protocol. We recommend that ICER further define their processes to adjust for publication bias in the proposed, independent SLR and UPI report.

C. Inclusion of External Stakeholder Input on Systematic Literature Review Protocol

As the UPI report results will rest heavily on the curation of evidence from SLR, we recommend that ICER provide all stakeholders with an opportunity to review the SLR protocol and results, including studies excluded by adjudication.

D. Assessment of Additional Net Benefit Rating

ICER proposes to use its existing Evidence Rating Matrix (EBM) to assess the quality and certainty of clinical evidence. While we concur with the need to assess curated studies from the SLR, we question the utility of the EBM to support the intended aims of the UPI report. The EBM's level of certainty is based on a "conceptual confidence interval" of existing evidence.² The five domains that are used to anchor the "conceptual confidence interval" (Level of Bias, Applicability, Consistency, Directness, and Precision) handicaps any indications wherein evidence generation is challenged by the inherent uniqueness of the disease. For example, orphan diseases, in which evidence generation is challenged by small patient populations, misdiagnoses and poor surveillance as well as discontinuous access to specialty care centers, are at high risk of being systematically disadvantaged by the use of the EBM in UPI reports.^{2,3} We recommend that ICER reconsider the use of its EBM for assessment of orphan diseases and indications with small patient populations, to account for the challenges of evidence generation in these patient groups.

Lastly, as we have recommended the inclusion of non-clinical evidence in the UPI report, we believe that it is important to note that the EBM undervalues the meaningful, evidence drawn directly from patients, using mixed - methods or other socio-anthropologic approaches. These types of patient derived real-world data — often captured by studies using surveys, interviews, and focus group discussions — are unlikely to meet the UPI EBM criteria of "moderate/high quality" new evidence due to their study

² ICER Evidence Rating Matrix. <http://icer-review.org/wp-content/uploads/2016/02/Rating-Matrix-User-Guide-UPDATED-06.30.17.pdf>


³ ICER Orphan Drug Assessment: Final Framework Adaptations. <https://icer-review.org/material/final-ultra-rare-adaptations/>

designs. We believe that ICER has a unique opportunity to expand its engagement and inclusion of patient perspectives in the UPI report. As highlighted by the recent NHC Roundtable on Patient Perspectives on Real-World Evidence, “*patients would like to see RWE generated from patients’ experiences be incorporated into value-driven decision making and policy discussions ensuring the outcomes most important to them are considered*”.⁴ GSK recommends ICER includes qualitative patient derived real-world data in the UPI report and prioritize the development of value assessment standards for qualitative evidence derived directly from patients.

As an innovation leader, GSK envisions a sustainable, evidence-based healthcare ecosystem that ensures improved patient outcomes and access, rewards innovation and fosters robust scientific discourse. We believe that value in healthcare should encompass the holistic benefits and costs as experienced by patients and society, over time. To this end, care must be taken to appropriately frame the current US healthcare challenges and advance the dialogue on holistic healthcare system solutions.

GSK appreciates the opportunity to share our recommendations with ICER. We hope that these recommendations will further ICER’s efforts on the UPI report. We look forward to exploring these and other related issues in greater depth with you. Please feel free to contact us should you wish to discuss these recommendations in further detail.

Sincerely,



Martin D. Marciniak, Ph.D.

Vice President

US Medical Affairs, Customer Engagement,
Value Evidence and Outcomes

⁴ NHC: Patient Perspectives on Real-World Evidence: A Roundtable to Gather Views, Needs, and Recommendations.
<http://www.nationalhealthcouncil.org/sites/default/files/Patient%20Perspectives%20on%20Real-World%20Evidence.pdf>

February 13, 2019

VIA ELECTRONIC MAIL

ICER
Celia Siegel

RE: Revised Draft Methodology on Unsupported Price Increase Assessments

Mallinckrodt Pharmaceuticals ("Mallinckrodt") appreciates the opportunity to comment on the revised draft protocol on unsupported price increases ("UPI") dated January 17, 2019. Mallinckrodt is a global business that develops, manufactures, markets and distributes specialty pharmaceutical products and therapies. Areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics and gastrointestinal products. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Thank you for the opportunity to comment on the draft methodology and protocol and the careful manner in which ICER has solicited comments. We appreciate the revisions made to the prior version of the draft in response to comments, and we set out a few additional comments for consideration below.

- **Glossary of Key Terms:** We continue to believe that a glossary defining key terms such as "budget impact," "largest budget impact increases," "harms" of Food and Drug Administration ("FDA")-approved therapies, "patient assistance programs," and "incremental clinical effect" would be helpful to readers of this report to ground them to ICER's approach and provide clarity regarding each term. These terms are often used imprecisely and in differing ways by industry, payers, and others, and thus, having clearly defined meanings will help to strengthen third-party understanding of ICER's methodology.
- **Section 2.1.1:** To create a list of drugs with substantial price increases, ICER will rely on net prices obtained from SSR Health, which combines data on unit sales with publicly-disclosed sales figures that are net of discounts, rebates, concessions to wholesalers and distributors, and patient assistance programs. One outstanding question is whether discounts to pharmacies will be included in the net price calculations.
- **Criteria to Assess Price Increases for Drugs Identified in Section 2.2:** We appreciate the addition of criteria to help guide the selection of the three additional drugs to be evaluated as part of this report in Section 2.2 of the draft protocol. It would also be helpful to clarify whether the methodology set out in Section 2.1 will be the same methodology used to evaluate drug price increases for the drugs publicly identified in Section 2.2. Further, please clarify that for the first report, ICER will be considering the same time frame as that identified in Section 2.1, from January 1, 2017-December 31, 2018, to assess price increases for the drugs identified in Section 2.2. We believe ICER should use the same methodology and time frame to evaluate price increases for drugs

identified in each section in order to allow for meaningful comparisons between the two lists of drugs assessed.

- **Protection from Public Release of Data/Information Held by Others:** Some of the data and information that would be helpful to ICER may be subject to intellectual property (IP) protections held by others, such as patents, copyrights, and trademarks. Under contractual arrangements to which manufacturers may be a party, such as clinical trial agreements or other arrangements, companies are bound by those IP protections often in the form of confidentiality provisions and would not be able to provide ICER the information sought without violating contractual obligations. Manufacturers would need additional time to work through those obligations in order to further share relevant information that may be useful to ICER in its evaluations.
- **Protection from Public Release of Confidential Commercial and Trade Secret Information:** The draft protocol does not sufficiently exempt from public disclosure data and information that is ordinarily protected as confidential commercial or trade secret information. For example, some data supporting a product's value proposition may result from interim analyses, unpublished data, or retrospective analyses of claims data. Each of these may be appropriate data sources. However, these data may not be available in the public domain for proprietary, competitive or other reasons meriting confidentiality and protection from public disclosure. Yet, ICER's draft protocol clearly states that any information submitted to ICER will be publicly released. As such, we believe that ICER should grant companies flexibility to provide abstracts of such data to maintain their confidentiality, without negative biases against such data. Further, ICER should clarify that information that is marked by the manufacturer as confidential commercial or trade secret information will not be publicly released.

* * * * *

Mallinckrodt appreciates the opportunity to comment on the revised draft protocol to assess unsupported price increases. Please contact Kendra Martello, Sr. Director of Public Policy (kendra.martello@mnk.com) or (202) 459-4145) if you have questions or wish to discuss further.

Sincerely,



Mark A. Tyndall,
Senior Vice President, Government Affairs

February 13, 2019

Steven D. Pearson, MD, MSc, FRCP
President
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Boston MA 02109 USA

RE: ICER Unsupported Price Increase Assessment Protocol

Dear Steven:

Merck thanks ICER for the opportunity to comment on the draft protocol for unsupported drug price increase assessment. As always, we appreciate ICER's willingness to solicit input openly from stakeholders. Attached please find Merck's comments on the protocol. These comments and our suggestions are tabulated in the order of the protocol's sections.

In general, we appreciate ICER for investing resources to investigate the important issue of drug price increases. However, we are deeply concerned about ICER's approach to categorizing price increases solely based on clinical evidence. This approach overlooks other important value factors and many business/market conditions that may justify drug price changes. We believe ICER needs to revise this approach and address the other issues we identified in the protocol to ensure insightful and fair reporting on drug price increases.

Please feel free to reach out to us if ICER has any questions about our comments. We look forward to further discussion with the Institute regarding the proposed reports and the draft protocol.

Sincerely,

Megan O'Brien, Ph.D., M.P.H

Executive Director
Center for Observational and Real-World Evidence (CORE)
Merck & Company, Inc.

Attachment: Merck Comments on ICER Draft Protocol for Unsupported Price Increase Assessment (6 pages)

Merck Comments on ICER Draft Protocol for Unsupported Price Increase Assessment

Section	Page #	Content of Concern	Merck Comments
1. Background	1	<p>“These new reports will seek to identify drugs for which there was no new clinical evidence that could support their price increases. These reports will be called Unsupported Price Increase (UPI) reports.”</p>	<p>The proposed title of the reports, “Unsupported Price Increase (UPI),” does not accurately reflect the content.</p> <ul style="list-style-type: none"> • The reports will review evidence for all 13 drugs flagged due to a price increase threshold, regardless of whether their price increases are categorized as “unsupported” or not. • It is overly simplistic and misleading to determine price increases as “unsupported” <u>only</u> because no new clinical evidence was identified. Other than clinical evidence, other value factors and business/market conditions may justify drug price changes (see <i>the next comment</i>). <p>We suggest ICER uses a different title that more accurately reflects what the reports are intended to achieve, i.e., investigating whether drug price increases are associated with substantial new clinical evidence.</p>

Section	Page #	Content of Concern	Merck Comments
1. Background	1-2	ICER's focus on clinical evidence as the only factor to categorize drug price increase as "unsupported"	Other than clinical evidence, many other value factors (e.g., benefits for patients' caregivers, increased societal productivity) and certain business/market conditions (e.g., needs for raising additional resources to accelerate innovation development, production difficulties, supply shortages) may also justify price adjustments. It is important to identify and discuss these factors and conditions in the reports to present a fair and balanced view on drug price increases.
2. List of Drugs to Review	3	ICER's approach to ranking drugs by list (wholesale acquisition cost or WAC) price increases over twice the medical Consumer Price Index (CPI) over a two-year period	To reflect real-world price increases and budget impact, net prices should be used instead of WAC. The M CPI rate should be assessed over the same 24-month period, since this can fluctuate.
2. List of Drugs to Review 2.1.1	3	ICER will use net price information from SSR Health. For drugs produced by companies that are not publicly traded, ICER will use prices from the Federal Supply Schedule (FSS).	Payers have their own mechanisms for negotiating net price that is not visible to the public or data vendors. SSR may not always have access to this sensitive price information. Using SSR data, ICER could end up with overestimating net prices. Using SSR and FSS data respectively for public and non-public companies could cause inconsistency and bias in identification of drugs for review.

Section	Page #	Content of Concern	Merck Comments
2. List of Drugs to Review 2.1.1	3	Additional concerns with SSR data	<p>1). SSR data may have significant variability for certain types of products, especially new products, LOE products, products with a low volume or shifting channel mix, and seasonal products- including vaccines.</p> <p>2). SSR data combines products that are part of a product family, for example, Janumet/Janumet XR, MMR/Varivax/ProQuad, Recombivax HB / Vaqta (Hep A & B).</p> <p>3). Some data are product-specific prior to mergers, which show the sales for each product and each manufacturer on a separate line. For example, Nexplanon data is reflected on the Schering line prior to the merger and on the Merck line after the merger, but there is a combined section further down the page</p>
2. List of Drugs to Review 2.1.5	3-4	ICER's approach to prioritizing drugs for review (e.g., ranking drugs by multiplying the current annual sales by change in net price over 24 months)	Using this approach, the ICER reports will focus primarily on drugs with larger patient populations. However, some of the most controversial price increase cases occurred for drugs treating rarer conditions (e.g., Daraprim, Deflazacort). We suggest ICER sheds more light on these cases and the irrational behavior behind it.

Section	Page #	Content of Concern	Merck Comments
2. List of Drugs to Review 2.2	4	Lack of specificity on criteria to establish the additional drugs for review	The criteria for additional drugs selection are generally vague – e.g., what metric is used to determine “drugs used by millions...”, what does it mean to have “important affordability implications” or “concerns about the fairness of price increases”? Why is MCPI benchmark arbitrarily changed for additional drugs? ICER should provide more specifics to minimize potential biases or unfair scrutiny in the drug selection process.
3. Manufacturer Input	5	Timing for ICER to seek input from manufacturers	Please clarify at what point of the review process CER will reach out to manufacturers for input.
3. Manufacturer Input	5	“Other potential justifications for a price increase, including information ...”	Please clarify how ICER intends to incorporate this information into the price increase reports. As previously commented, we believe it is crucial to discuss these “other justifications” in the reports to present fair and balanced views on drug price increases.
3. Manufacturer Input	5	Confidentiality of info	While ICER expects manufacturers to submit commercial information to justify price increase, this information may not be protected under the ICER academic-in-confidence policy. This would discourage manufacturers from sharing sensitive information. For example, when the SSR data on net prices aren’t accurate, manufacturer wouldn’t be able to share that information with ICER. So, we suggest ICER clarifies whether its academic-in-confidence policy also applies to commercial information.

Section	Page #	Content of Concern	Merck Comments
4. ICER Review	6	The 10% threshold for indications to be included	If indications are relatively new, they might not have yet met the 10% threshold, but there could be significant clinical data to support their use. We suggest ICER reviews all available data, whether the indication meets the 10% threshold or not. If the evidence supports the product, it should be part of the review.
4. ICER Review 4.1.1	6	Use of evidence from FDA labeling information to determine a baseline of known safety and clinical effectiveness	For drugs that have been on the market for several years, ICER should use more current evidence to establish the baseline.
4. ICER Review 4.1.3	6	ICER will assess net health benefits only if the new evidence is rated as being of moderate or high quality using GRADE	Some evidence may get a low GRADE rating due to single-arm design, small study sample sizes, or short follow-ups, but shows substantial health benefits (e.g., in the CAR-T cases). This type of evidence should not be ignored. We suggest ICER assesses net health benefits from all evidence bases rated as high, moderate, or low using GRADE.

Section	Page #	Content of Concern	Merck Comments
5. Designation of Drug Price Increases as “Unsupported”		Drugs found to have moderate/high quality new evidence of a substantial improvement in net benefit will be categorized as having a “price increase with new clinical evidence.”	Based on the last comment, we suggest ICER revises the categorization criterion so that drugs found to have low quality evidence of substantial net benefits will be further assessed for more appropriate categorization.
6. Manufacturer Review Prior to Public Release	8	ICER will not accept information on new indications for review at this stage	We believe ICER should maintain certain flexibility to accept information that emerges at a late stage of the review process. Some new information (e.g., safety alerts) could be too important to be ignored.
6. Manufacturer Review Prior to Public Release	8	There is no mention of how ICER will use manufacturer comments in the process	Please clarify how manufacturers review will be incorporated into the final reports.
7. UPI Report Public Release 7.1.2	9	Reporting on factors other than clinical evidence that may justify price increases	As previously commented, we believe these other factors are just as important to discuss as clinical evidence to justify drug price changes. This information should be presented appropriately in the main sections of the reports, not simply attached as an appendix.

February 13, 2019

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109 USA

Re: Draft Unsupported Price Increase Assessment Protocol

Submitted electronically via: publiccomments@icer-review.org

Dear Dr. Pearson:

Novartis appreciates the opportunity to provide feedback on ICER's draft protocol for "Unsupported Price Increase Assessment" (UPI)¹. Novartis shares ICER's interest in assessing the value of drugs to patients and society and recognizes the merit of the proposed report. However, we strongly urge ICER to provide thoughtful consideration to the complexity of drug pricing as currently only clinical evidence is used as a basis to support a price increase. This approach does not reflect the complexity of pricing decisions, nor the context of the rapidly evolving US healthcare landscape. In regards to the methodology proposed, we offer the following suggestions for consideration:

- Use consistent and transparent methodology throughout the report
- Provide clear methodology for determining the additional 3 drugs to be reviewed
- Provide a hypothetical example of the report to allow early visibility and understanding of this novel process
- Protect all confidential information provided by manufacturers
- Include broader types of evidence for new evidence assessment to fully capture the progressive value of therapies
- Limit subjective assessment or approach

We further elaborate on each of these suggestions below.

Use consistent and transparent methodology throughout the report

Novartis recommends that consistent and transparent methodology is used throughout the report, and all variables be clearly defined to avoid misinterpretation.

- ICER plans to obtain a list of 100 drugs with the largest dollar sales in the US. However, it is not clear whether it refers to gross or net sales and what year of sales will form the basis for the list.
- Consistent methodology should be applied when the price or budget increase, and the rate of medical consumer price index (CPI) are calculated. Specifically, if net price is calculated by taking a difference in two time points during a 24 months period, the rate of medical CPI increase should be calculated the same way.
- The methodology for net price derived by SSR Health is not transparent and Novartis recommends ICER provides additional information about their methodology, including the data source.
- Regarding the assessment of clinical effect size, transparent criteria for determining "small" and "substantial" should be provided. In addition, any threshold chosen for the

report should be supported by a strong rationale. For example, it is not clear why 2 times the rate of medical CPI was chosen as a threshold for price increase.

- The title of the report may suggest that the drugs included have unsupported price increase determined by ICER. Novartis recommends ICER to consider using a different title such as “Evidence-based price increase assessment” to reflect its suggested methodology and stated intent of the report.

Provide clear methodology for determining the additional 3 drugs to be reviewed

A more detailed and clear methodology regarding additional 3 drugs to be reviewed is needed. For example, currently provided criteria do not clarify how “extremely high price increases”, and “important affordability implications” are determined.

Provide a hypothetical example of the report

Novartis recommends that ICER provides a hypothetical example that permits manufacturers to use as framework and examine the calculations thoroughly. The example will illustrate the methodologies more clearly and help provide transparency.

Protect all confidential information provided by manufacturers

“ICER recognizes manufacturers may have more precise data on net prices changes than SSR or FSS, and plans to work with manufacturers to gain this information.” However, without the protection of this confidential information, manufacturers may be unable to have a full exchange of information with ICER during the review.

Include broader types of evidence for the new evidence assessment

ICER plans to perform systematic reviews for “information from randomized trials, high quality comparative observational studies, and, for information on low frequency harms, from large uncontrolled studies”. Novartis recommends that ICER consider other types of evidence such as non-comparative observational studies, and evidence presented in forms of posters, manuscripts, and grey literature.

Limit subjective assessment or approach

ICER states in the report that “UPI reports are not intended to determine whether a price increase is fully justified by new clinical evidence...Instead, we will focus the analysis on whether or not substantial new evidence exists that *could* justify its price increase”. Whether the evidence fully justifies or could justify price increases seems to be a subjective assessment without clear and established criteria. Novartis recommends that ICER interprets the evidence in an objective manner.

References

¹ ICER Unsupported Price Increase Assessment Draft Protocol. https://icer-review.org/wp-content/uploads/2019/01/ICER_UPI_Draft_Protocol_011719.pdf. Accessed January 22, 2019.



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February 13, 2019

Steven D. Pearson, MD
President
Institute for Clinical and Economic Review
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Submitted via email: publiccomments@icer-review.org

RE: Comments on ICER's "Unsupported Price Increase" draft protocol

Dear Dr. Pearson,

On behalf of Pfizer Inc, I am responding to the call for comments issued by the Institute for Clinical and Economic Review (ICER) regarding the draft protocol for its "Unsupported Price Increase" (UPI) project.¹

As a leading biopharmaceutical company, Pfizer is dedicated to the discovery and delivery of high value therapies across a variety of disease areas. It is our mission to bring innovative medicines to patients that significantly improve their lives, and our priority is to ensure patients have access to these medicines.

We have carefully reviewed the draft protocol and have significant concerns related to the perspective, assumptions and methods that ICER has applied in developing this project. In the draft protocol, ICER indicates that that UPI project is designed to inform policy makers and their decisions. We do not believe that the project as framed is suitable for this purpose, given its fundamental methodological limitations and bias.

ICER's approach is not patient-centric

In several prior comment letters, we have highlighted how ICER's approach to value assessment does not fully adopt the perspective of the patient. In the case of the UPI project, ICER has again failed to take a patient-centric approach, notably with respect to its selection of price metrics. ICER's use of list and net pricing in its analysis ignores what patients are most concerned about: their out of pocket healthcare costs. For most, these expenditures are directly impacted by their insurance premiums, deductibles, co-payments and co-insurance.

The amounts paid by most patients for pharmaceuticals differ vastly from the list prices set by manufacturers and net prices paid by insurers. Yet, ICER continues to measure drug prices in a manner that is not relevant to most patients in the US. As such, the outputs of UPI report

¹ Institute for Clinical and Economic Review. Unsupported Price Increase Assessment. Available at: https://icer-review.org/wp-content/uploads/2019/01/ICER_UPI_Draft_Protocol_011719.pdf. Accessed February 1, 2019.

will not aid policymakers in their understanding of one of the issues that matter to patients most.

We continue to encourage ICER to meaningfully engage patients, their families and their caregivers to understand the most important challenges they face, and to seek to address those critical and pragmatic questions.

ICER excludes important factors related to pharmaceutical pricing

The draft protocol indicates that the intent of ICER's UPI project is to determine whether product-specific pricing actions taken by pharmaceutical manufacturers can be rationalized by newly generated clinical data for those products. Importantly, the title of the project itself reveals a key assumption by ICER: that the timely development of new clinical evidence is a required justification for pharmaceutical price increases.

ICER notes that its planned "reports are not intended to determine whether a price increase for a drug is *fully justified* by new clinical evidence..." (emphasis added) but "...whether or not substantial new evidence exists that could justify its price increase."¹ This is an appropriate caveat, as there are important factors besides new clinical evidence that may be considered in making a pricing decision, and such factors may contextualize such a decision even in the absence of new clinical evidence.

Yet ICER's proposed framework for the determining whether a price increase is 'unsupported' specifically excludes all other considerations that may factor into drug pricing decisions. ICER does not offer any rationale for excluding factors it explicitly acknowledges may be relevant to pricing decisions. While ICER notes that it intends to ask manufacturers for "other potential justifications for a price increase,"¹ it is unclear whether and how this information will be used by ICER given that its proposed framework intends to exclude this information. We urge ICER to include in its framework all factors proposed by manufacturers in response to its inquiry.

ICER's rejection of additional factors reflects its bias and unwillingness to meaningfully consider pricing decisions in full context. This again raises significant concerns regarding the value of ICER's UPI report in a policymaking context.

ICER's UPI project ignores significant components of healthcare spending

The scope of ICER's draft UPI protocol is limited to the assessment of price increases of pharmaceutical products. This narrow focus is a missed opportunity to contextualize changes in drug prices relative to changes in other sectors of healthcare. For example, recent data suggest that the prices of hospital services and physician visits have increased dramatically in recent years.²

Understanding price increases across all sectors of healthcare would provide critical context for whether the increases observed in pharmaceuticals are 'supported' from a value perspective. Prior analysis suggests that over time, innovation in pharmaceuticals has offered the greatest value with respect to impact on patient outcomes.³ Given ICER's interest in value and sustainability, a broader examination of healthcare pricing is warranted.

² Cooper Z, Craig S, Gaynor M et al. Hospital Prices Grew Substantially Faster Than Physician Prices For Hospital-Based Care In 2007–14. *Health Affairs* 2018; 38(2): 184-189.

³ Wamble D, Ciaramentaro M, Dubois R. The Effect of Medical Technology Innovations on Patient Outcomes, 1990-2015: Results of a Physician Survey. *Journal of Managed Care and Specialty Pharmacy* 2019; 25(1): 66-71.

ICER's proposed methodology lacks validity and rigor

The UPI methodology outlined by ICER in the draft protocol suffers from critical limitations that raise serious questions about the validity of its potential findings, and their value to policy decision-makers:

- *ICER's net pricing data have not been validated:* Net pricing data are central to ICER's UPI methodology. ICER proposes to use net pricing data from SSR Health in its analysis. Because net prices are confidential, SSR Health has developed its own estimates of net prices through proprietary calculations. The use of net pricing data that have not been empirically validated will significantly diminish the validity of ICER's findings.
- *ICER's threshold rationale is unclear:* ICER proposes to establish a threshold of two times the medical consumer price index (mCPI) as an initial cutoff for its determination of 'unsupported' increases. CPI measures are used in economic analysis as a measure of inflation; ICER offers no rationale as to why the use of an inflation-based measure is appropriate in its UPI project, and further does not establish why twice the mCPI is the right value for its analysis. The use of arbitrary thresholds limits the value of ICER's output.
- *ICER's focus on individual pricing decisions ignores true patient impact:* in section 2.1.2 of the draft protocol, ICER notes that it will focus on individual pricing decisions only and will exclude price increases for a single product observed across multiple manufacturers.¹ These kinds of multi-manufacturer pricing actions may have a significant impact on patient expenditures. Given ICER's objective to assist policymakers, we believe that these types of price increases should be included in the framework.
- *ICER offers no rationale for proposed timeframes for evidence gathering:* ICER is interested in new clinical data developed in the 36 months preceding a price increase. ICER offers no justification or rationale for its approach in the selection of this time frame. The lack of a clear conceptual framework and vetted rationale for the relationship between evidence and price significantly undermines the overall quality of the project.
- *ICER's proposed net health benefit metric is not objective:* A critical element of the UPI methodology is ICER's determination of the relative value of the clinical evidence for a given product. ICER proposes to assess the net health benefit demonstrated by the clinical evidence using its own Evidence Matrix (EM) rating system. The EM system was developed in 2007 by a workgroup convened by America's Health Insurance Plans.⁴ We have significant concerns about the subjective nature of the EM system, especially given that ICER notes that "judgment remains an important component of the rating system." We strongly believe that the evaluation of the relationship between clinical evidence, value, and price should be objective, and not subject to bias.
- *ICER's binary rating system applies a subjective approach:* At the end of its assessment, ICER will label the price increases observed for the products under review as (a)

⁴ ICER Evidence Rating Matrix. Available at: <https://icer-review.org/methodology/icers-methods/icer-evidence-rating-matrix/>. Accessed February 1, 2019.

“having price increase with new clinical evidence” or (b) “having unsupported price increases”.¹ This categorization does not allow for any price increase to be deemed ‘supported’, even with compelling evidence, and pre-determines the findings of the framework in a biased manner.

Summary

We understand that ICER’s intent for the UPI project is to address concerns about healthcare spending that have garnered increased public attention from key stakeholders. However, we are concerned that the substantial flaws in the scope and methodology of UPI project, as described above, may result in outputs that will not help to advance a meaningful dialogue around price and value in healthcare, and may even undermine it.

Given that policy actions related to drug pricing could have significant impacts on patients, physicians, insurers and the pharmaceutical industry, it is critical that any assessment of price increases presented to policymakers is complete and balanced.

Therefore, we encourage ICER to reconsider its approach, and to significantly broaden its perspective on how to understand changes in healthcare prices in the U.S. Given its substantial resources, ICER has an opportunity to make meaningful contributions towards defining and measuring the value of pharmaceuticals and other health interventions.

We hope that our comments are useful as you seek to revise its proposal. We would welcome an opportunity to discuss our thoughts with you in additional detail.

Sincerely,

A handwritten signature in black ink, appearing to read 'PS', with a stylized flourish at the end.

Prasun Subedi, PhD
Senior Director
Patient and Health Impact



Sanofi welcomes the opportunity to comment on the draft protocol for ICER's new "Unsupported Price Increase Assessment Report"¹ (UPI report).

Executive Summary

- Sanofi is committed to supporting responsible prescription medicine pricing in the U.S. and elsewhere, as articulated in the three pillars of our pricing principles²:
 - A clear rationale for product pricing globally at the launch of a new medicine
 - Limited price increases in the U.S. on our medicines over time
 - Greater transparency in the U.S. around our pricing decisions.
- Sanofi understands and share patients' concerns about the affordability of medicines. We also support an evolution to a value-based health care system that provides incentives for the highest quality care and enables both affordable access to treatment and continued investment in medical innovation.
- Sanofi shares ICER's interest in assessing the value of prescription medicines and other health care services. However, we are concerned that the draft protocol for this report is narrowly focused, promotes a simplistic conceptualization of evidence and value-based pricing, and does not include robust procedures to test the precision, validity and reliability of its conclusions.
- As a result, we disagree that the proposed UPI report will contribute meaningfully to a better understanding of value-based pricing or potential solutions to medication access or affordability challenges for patients. We also do not believe the UPI report in its current format will support restraining medical care spending or more informed pricing and coverage decisions.
- The UPI report's exclusive focus on prescription medicine products and pricing and the perspective of insurers provide a limited and incomplete view of pricing and value issues in the USA. The protocol also does not sufficiently represent the key issues of interest to society and patients.
- The UPI report's proposed methodology to select the primary list of 10 products for evaluation is flawed. The proposed process for identifying up to 3 additional products is informal and arbitrary.
- The UPI report's proposed evidence review and assessment methodology and the process for designating drug prices as "unsupported" are not fully transparent and not appropriate for the purpose of optimally assessing the value of post marketed products.

- Given these limitations, we encourage ICER to revise the proposed objectives and methods of the UPI report before proceeding with this initiative.

Comments on the Intent and Objective of the UPI Report

- The report's exclusive focus on prescription medicine products and pricing and the perspective of insurers provide a limited and incomplete view of pricing and value issues in the health care system, and do not address patients' key concerns.
 - Prescription medicines represent a minority component of overall health care spending in the USA³. Moreover, prescription drug spending is currently growing more slowly than the costs of other types of health care services. As reported in the January issue of *Health Affairs*, for example, in 2017 retail prescription drug spending increased 0.4% overall, continuing a decelerating trend from 2014-2016. In contrast, hospital care spending increased by 4.6% in 2017, and physician and clinical services by 4.2%.⁴
 - Prescription drug prices increases have slowed and are anticipated to do so for the foreseeable future. Newly reported data from the IQVIA Institute estimate that list prices for brand-name drugs grew by 5.7% in 2018 while net prices increased by 1.5%.⁵ These figures mark the fourth consecutive year that net prices have grown by low-single-digit amounts. IQVIA also estimates that list price increases are expected to remain in the 4 – 7 percent range within the next five years. Importantly, net price increases for prescription medicines are expected to rise at 0 – 3% during the same period and in many individual instances net prices for products are actually declining (*ibid.*).
 - Thus, if the underlying objective of the UPI Report is to contribute positively to efforts to address medical care spending, the exclusive focus of the report on prescription medicines and drug pricing seems misplaced, does not constitute a holistic assessment of value, and is poorly conceived to support this aim.
 - The proposed narrow focus of the UPI Report is also in conflict with good principles of health technology assessment, which call for comprehensive evaluation of different types of health care technologies and explicit consideration of tradeoffs between alternative types of interventions^{6, 7, 8}, and facilitate differentiation between high- and low-value health care. Such tradeoffs cannot be readily considered within the current proposed framework of the UPI Report. The selective focus only on drugs also conflicts with ICER's own stated organizational purpose of serving as a nonpartisan evaluator of all types of health care interventions, i.e., an institution that "objectively evaluates the clinical and economic value of prescription drugs, medical tests, and other health care and health care delivery innovations."⁹
 - In general, narrow assessment periods, such as proposed in the UPI Report, give inadequate opportunity for consideration of broader societal trends in health care and other contextual factors, potentially distorting the report's conclusions.
 - Informative evaluation of pricing decisions after launch for prescription medicines necessarily requires a long-term perspective, because an understanding of clinical benefits

and harms and economic value evolves over time, and uncertainty is difficult to quantify. Moreover, drug pricing trajectories are typically unique in comparison to other non-drug health care services because of the impact of patent expirations and loss of exclusivity. For example, Fendrick and George emphasize this point by contrasting the relative pricing histories of statins vs. coronary stents, both introduced approximately three decades ago.¹⁰ A selective focus on a limited time span of pricing decisions distorts the specific assessment of a drug as well as comparisons to non-drug alternatives. Methods exist to measure and evaluate long-term costs and cost offsets of drugs^{11, 12}, but the UPI Report protocol does not consider or incorporate such approaches.

- The payer's perspective is exclusively represented in the proposed report, in contrast to the recommendations of good assessment practices for a broader focus on societal and patient interests¹³. We are especially concerned that the proposed protocol makes minimal reference to the specific concerns of patients, and does not specify types of evidence included in the evaluation process that will be meaningful to patients.

Comments on the Proposed Methodology to Identify Products Evaluated in the Report

- ICER's proposed selection process to identify the initial list of 10 drugs (Section 2.1) is problematic.
 - ICER's proposal to use the consumer price index (CPI) for medical care to establish a standard against which to gauge the magnitude of drug prices changes is insufficiently described. Please clarify how the CPI benchmark will be calculated over the proposed 24 month period.
 - We are also concerned that reliance upon SSR Health data to estimate and inform net price is problematic and may lead to erroneous conclusions. SSR data is based on a set of assumptions; if these assumptions are in error, recommendations will be similarly flawed. Moreover, SSR provides multiple net prices; it is not clear from the draft protocol which approach ICER will utilize.
 - ICER's use of estimated budget impact as part of the product selection process is flawed. It is inappropriate to evaluate a product's budget impact on US health care spending in isolation from its potential impact on savings for other health care services. ICER's proposed approach also penalizes drugs for highly prevalent conditions such as diabetes or cardiovascular disease, skewing the initial list to such therapies.
- ICER's proposed selection process to identify up to 3 additional drugs (Section 2.2) to review in addition to the primary list is informal and appears largely arbitrary, and is inconsistent with the process outlined for the primary list identification process. The few parameters listed for this portion of the report are remarkably broad and appear to encompass virtually any potential selection decision. This open ended approach is also in conflict with good technology assessment

practices, which call for explicit, systematic, and transparent evaluation objectives. This informality undercuts the overall premise of the report.

Comments on the Proposed Methodology to Evaluate Evidence in Support of Price Increases and To Designate “Unsupported” Price Increases

- ICER’s proposed methodology to evaluate and synthesize evidence in support of price increases (Section 4) is not fully transparent and is inadequately conceived to assess the value of products in the marketplace.
 - ICER’s protocol should clearly state the types of evidence that will be accepted as the basis for improved clinical or economic outcomes and the relative weighting of such evidence for the objective of the assessment. For example, will the assessment include data from all of the following: randomized controlled trials, observational studies or cohorts, real world studies based on claims/administrative databases or electronic health records or registries, and cost-effectiveness models?
 - Statistical procedures to combine findings from systematic reviews and compare drugs are not identified in the protocol. How will meta-analyses be completed? Will network meta-analyses be conducted? Will pairwise indirect comparisons be included?
 - How will outcomes for the comparisons be chosen to avoid selected outcome reporting biases? Outcomes have different clinical value, for example improvement on cardiovascular outcomes or mortality/survival is clinically more important than sole improvement in lipid levels or HbA1c in metabolic disorder trials. For other diseases, this hierarchy in outcome clinical value is more difficult to determine. When comparing two drugs, better efficacy can be statistically demonstrated for some of the outcomes while not for others. Therefore, guidance on the way outcomes will be chosen to evaluate evidence is needed in the protocol to avoid a bias when selecting the outcomes to undergo analysis.
 - GRADE¹³ is not an optimal assessment tool for observational and real world research, and thus is of questionable utility for a report designed to evaluate the evolving value of products in current clinical settings. GRADE’s evidence hierarchy privileges data from randomized clinical trials (RCTs) at the beginning of the rating process and down weights evidence from observational/real world studies¹³. The two types of studies of course provide answers to different questions: RCT answers the efficacy in a controlled clinical trial setting, observational studies (comparative) effectiveness in a real world setting. How this will be balanced to rate the overall additional net benefit in ICER’s UPI Report? For example, take the example of a drug A with slightly but significantly better efficacy in RCTs than drug B, while poor adherence/persistence in real world leads to a better effectiveness of B compared to A. By process, GRADE will tend to favor drug A over B with potential consequences for the conclusions of the Unsupported Price Increase

Assessment. ICER has previously shown substantial interest in incorporating real world evidence in its assessments¹⁴, so it is disappointing that this protocol does not sufficiently address this issue.

- ICER’s proposed process to designate drug price increases as “unsupported” using GRADE and ICER’s matrix ratings (Section 5) is unclear and appears incomplete.
 - Will the final categorization proposed in the report (“price increase with new clinical evidence” vs. “unsupported price increase”) be based on GRADE criteria, or after applying ICER’s matrix ratings for additional net health benefit? The translation from GRADE to ICER matrix ratings should be more clearly stated in the protocol.
 - There is no mention of sensitivity analyses or other efforts test the validity and reliability of the conclusions. This may give a false impression of precision to the findings. It is critical to evaluate the uncertainty associated with conclusions.
 - In general, we are concerned that the UPI report’s designations will be characterized by high levels of uncertainty and inconsistent quality, given its reliance on the creation of a large, heterogeneous list of up to 13 products using diverse methods, limited assessment period and abbreviated appraisal process. It is important that ICER appropriately characterize this uncertainty and qualify findings, to avoid over interpretation of the report’s conclusions when it is released.

We encourage ICER to revisit the premise and methodology of the report before proceeding with this initiative. Thank you for the opportunity to contribute our comments.

Citations

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February 13, 2019

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Boston, MA 02109

RE: Comments on ICER's Unsupported Price Increase Assessment *(submitted electronically via: publiccomments@icer-review.org)*

Good Afternoon,

UCB appreciates the opportunity to comment and provide feedback on ICER's draft protocol to assess unsupported price increases of therapies. UCB's comments are provided below.

Section 1: Background

- ICER's undertaking to inform the public and policymakers of drugs with substantial price increases with no evidence generated or published in the previous 36 months would be a relatively simple process. It is where ICER attempts to then determine whether the evidence provided *could* justify the price increase that is seemingly more complex. Does ICER intend on creating committees with experts, including patients, that have direct experience with the drugs and indications identified for review?

Section 3: Manufacturer Input

- The GRADE and ICER evidence matrix currently do not capture assessment of economic outcomes. How will this be integrated in the overall evaluation if the tools available do not allow for non-clinical elements to be assessed as low/high quality of evidence?
- It appears that new evidence, specifically, clinical evidence, is most important factor in determining whether an increase in price is justified or not. For other 'potential justifications,' (page 7) how is each factor weighted and can these factors alone warrant a price increase?
- How does ICER plan to assess evidence and/or manufacturer commitments related to improving patient experience and/or satisfaction? This can include evidence related to innovative delivery mechanisms or less frequent dosing, both of which can lead to improved adherence and enhanced disease control.

Section 4: ICER Review

- In ICER's review for new information, via systematic review or manufacturer input, will both prospective and retrospective observational studies be considered for review?
- How will ICER review and rate studies that indirectly inform efficacy for a specific therapeutic area? For example: randomized trials, PK studies, or retrospective observational studies that provide insight into specific patient segments that may experience an incremental benefit in efficacy or safety versus the general population with the disease in question.
- For any given indication, there may be several outcomes/endpoints that inform the incremental efficacy or safety of a drug. How will ICER consolidate information across several outcomes



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and potentially across several GRADEs of evidence to make an informed decision on whether the evidence *could* justify a price increase?

- Will clinical physician specialists review and provide GRADEs for evidence submitted? How will discrepancies be reconciled?
- Typically, ICER's evidence matrix ratings are using when comparing a common outcome across several comparators. How will the matrix be adapted to account for several outcomes with variability in GRADEs to provide a consistent rating?

Section 5: Designation of Drug Price Increases as “Unsupported”

- Does ICER intend on publishing dichotomous results as “price increase with new clinical evidence” or “price increase with no new clinical evidence?” Given the levels of GRADEs that could be attribute to the evidence provided in addition to the levels captured in the evidence matrix, should there be a scaled response based on the certainty or uncertainty of the type of evidence provided and its proposed impact on the population of interest?
- Although a full cost-effectiveness analysis is out of scope, will there be any economic modeling considered? Especially since economic outcomes are being considered.
- While economic studies are considered as new evidence, the draft framework states that “non-clinical rationales will not be evaluated by ICER.” Can ICER provide a clear framework on how economic information will or will not be reviewed and included in the assessment?

UCB respectfully appreciates this opportunity to comment and is open to continued engagements regarding this assessment. Please direct any questions to Edward Lee, Head of Health Economics & Outcomes Research, at 770.970.8393; or Edward.Lee@ucb.com.

Sincerely,

A handwritten signature in black ink, appearing to read 'Patricia A. Fritz'.

Patricia A. Fritz
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February 13, 2019

Steven Pearson, MD
Institute for Clinical and Economic Review
2 Liberty Square, Ninth Floor
Boston, MA 02109

Dear Dr. Pearson:

Aimed Alliance is a 501(c)(3) non-profit organization that seeks to protect and enhance the rights of health care consumers and providers in the U.S. On behalf of Aimed Alliance, I respectfully submit the following comment in response to the “Unsupported Price Increase Assessment” Draft Protocol (“Protocol”) published by the Institute for Clinical and Economic Review (“ICER”) on January 17, 2019.

We acknowledge that the cost of health care in the United States has become unjustifiably high and that certain brand and generic manufacturers have contributed to this problem with continued, unjustified price increases on their medications. We are pleased to see that the United States Federal Government has begun to take steps to address this issue and to craft policies that protect consumers, such as the recent proposal from the Department of Health and Human Services (“HHS”) to end the practice of pharmaceutical rebates in the supply chain.¹ Additionally, a handful of states have enacted laws to combat pharmaceutical price gouging, and many more are currently considering similar legislation.

In the Draft Protocol document, ICER proposes to generate a report of the 13 medications that have experienced substantial price increases over the past two years. While the objective of this effort is commendable, we believe that the federal and state governments are the appropriate entities to determine whether price increases are justified – not ICER. Therefore, we urge you to abandon this project. If you insist on moving forward with the Unsupported Price Increase Assessment, we hope that you will address some of the critiques of the Protocol we set forth below.

An imperfect process could produce results that have a negative downstream effect on patient access. For instance, if ICER erroneously identifies medications for which price increases are not justified, insurers and pharmacy benefit managers (“PBM”) can rely on this faulty information when imposing stricter utilization management restrictions on those medications. Additionally, if ICER’s report extracts price concessions from manufacturers, there is no guarantee that any savings would be passed along to patients and ICER lacks the authority to require savings to be passed on by actors in the pharmaceutical supply chain.

I. Study Design May Not Identify Most Egregious Price Increases

The Protocol proposes to assemble a list of the top 100 medications, determined by sales revenue in the United States. ICER will then identify the medications that have experienced a list price increase “over

¹ <https://www.federalregister.gov/documents/2019/02/06/2019-01026/fraud-and-abuse-removal-of-safe-harbor-protection-for-rebates-involving-prescription-pharmaceuticals>

two times the medical Consumer Price Index over a two-year period.”² ICER will then analyze the net price increase that these medications experienced and select the top 10 medications whose price increases would generate the “largest increase in budget impact at the national level.”³ We believe that this approach is flawed because it will not necessarily identify the medications that experienced the most unreasonable price increases. For example, several generic manufacturers have increased the prices of their products significantly, including products that have been in the market for many years.⁴ This protocol would exclude these price increases from the scope of ICER’s review. We find this troubling because generic medications should offer the most promise for increased competition and lower prices for patients. When generics fail to provide this benefit, the manufacturers are likely exploiting market forces to achieve unjustified profits. We recommend that ICER adjust its Protocol in order to identify the top bad actors in the industry, regardless of sales revenue.

II. Study Design Should Include Critical Actors in the Supply Chain

The Draft Protocol, by design, only analyzes data from manufacturers and excludes information from other actors in the supply chain who have a significant influence on the prices that consumers pay for their medications at the pharmacy counter. Without considering the behavior and trade practices of these entities, ICER’s review will be incomplete. We recommend that ICER solicit data from insurers, PBMs, distributors, hospitals, and pharmacies, which could provide additional context for the prices that consumers pay for medications, inefficiencies or waste in the supply chain, whether drug prices are reasonable, and which entities are most responsible for high prices.

III. Wholesale Acquisition Costs Are Likely to Lead to Inaccurate Assessments

ICER’s Protocol proposes to compare the wholesale acquisition cost (“WAC”) and Consumer Price Index (“CPI”) to determine the theoretical budget impact that a reference medication has on the national level. We recommend against using WAC as a variable in this calculation because other factors, such as rebates, discounts to PBMs, best price mandates, discounts to hospitals and health systems, wholesaler fees, copay assistance programs, and administrative fees to group purchasing organizations (“GPOs”) and PBMs account for a significant portion of a medication’s price. These factors are included in a medication’s net price, but not the WAC. Determining whether a price increase is reasonable based on the WAC ignores the true cost of medications and may produce misleading results. For these reasons, we recommend that ICER only use net price as a reference and exclude WAC from these calculations.

IV. Length of Time on the Market Can Impact Drug Pricing

The Protocol does not account for fluctuations in price that are typically associated with the length of time that a product has been available on the market. When medications are introduced in the market, prices are often high, but they usually come down as patent and exclusivity protections expire.⁵ Therefore, depending on the situation, a price increase after the drug has been on the market for several years may be less justified than a price increase for a medication that is new to the market.

Drug prices may also increase right before patent and exclusivity periods are scheduled to run out. We do not support tactics to keep drug prices artificially high and prevent generic drug entry into the

² <https://icer-review.org/material/unsupported-price-increase-assessment-draft-protocol/>

³ <https://icer-review.org/material/unsupported-price-increase-assessment-draft-protocol/>

⁴ <https://arstechnica.com/tech-policy/2018/05/drug-made-famous-by-shkreli-5000-price-hike-is-still-750-a-pill/>

⁵ <https://www.commonwealthfund.org/publications/journal-article/2017/sep/determinants-market-exclusivity-prescription-drugs-united>

marketplace, such as patent evergreening and other strategies that extend the life of patents without providing new clinical benefits to patients. These tactics are bad for patients and the health system overall. Therefore, investigating the length of time the drug is on the market, especially in relation to its patents and exclusivities could be helpful in assessing whether a pricing increase is justified or not. We recommend that ICER incorporate this data into its review to account for secondary factors that could influence pricing decisions.

V. Manufacturers May Not Be able to Share Requested Information

ICER proposes to solicit information from manufacturers about their medications and competitor medications that could justify a substantial price increase. Notably, ICER proposes to publish this information publicly in the final report. We caution that some of the data that ICER seeks from manufacturers may be prohibited. For example, the Food Drug and Cosmetics Act prohibits manufacturers from sharing certain data with the public if such data is not listed on the product's FDA-approved labeling because the information could be considered false and misleading.^{6,7} As such, manufactures may be prohibited from sharing information on potential new clinical indications or uses with ICER. However, such information may be critical in assessing a pricing increase.

The FDA recently released guidance titled “Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities – Questions and Answers” (“Guidance”).⁸ The Guidance notes that manufacturers may share health care economic information, including information on different dosing or use regimens, different endpoints, more-limited or targeted patient populations, with payers, formulary committees, and “other similar entities with knowledge and expertise in the area of health care economic analysis.”⁹ Therefore, we recommend that ICER request an advisory letter from the FDA that would confirm that ICER is a “similar entity with knowledge and expertise in the area of health care economic analysis” in accordance with the Guidance. ICER should delay its implementation of this Protocol until it receives this confirmation from the FDA.

VI. Non-Clinical Factors Do Not Receive Proper Consideration

In the Protocol, ICER indicates that it will request “other potential justifications for a price increase, including . . . a large increase in costs of production . . . large price savings attributable to the drug in other parts of the health system . . . [and] all other reasons deemed relevant by the manufacturers.”¹⁰ Yet, the Protocol also states that “non-clinical rationales will not be evaluated by ICER as a determinant in whether the drug is categorized as having its price increase unsupported by clinical evidence.”¹¹ It is unclear why ICER is requesting other potential justifications for a price increase when such information will not be incorporated into the final assessment of drug price increases. Considerations should be given to valid business practices that could contribute to increased drug prices, such as drug shortages due to shortages of raw materials or unanticipated demand, and manufacturing issues. This information should be given weight because unexpected increases in production costs are a legitimate reason to increase the price of a medication.

⁶ <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=312.7>

⁷ <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=201.100>

⁸ <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm537347.pdf>

⁹ <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm537347.pdf>

¹⁰ <https://icer-review.org/material/unsupported-price-increase-assessment-draft-protocol/>

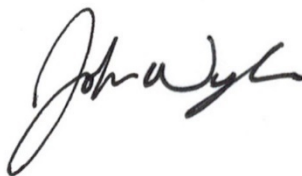
¹¹ <https://icer-review.org/material/unsupported-price-increase-assessment-draft-protocol/>

VII. Orphan Drugs

As ICER acknowledged in its Orphan Drug Assessment published in November 2017, orphan drugs should be treated differently. For individuals with rare diseases, it is typical for very few medication options to be available. Pharmaceutical manufacturers do not prioritize developing these types of medications because generally there is little-to-no return on investment. Without being able to charge prices for these medications that could potentially generate at least some level of return on investment, there would be no incentive to bring these medications to the market. Due to these factors, we recommend that ICER exclude these types of medications from its assessment.

Thank you for the opportunity to comment on the Draft Protocol.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "John A. Wylam". The signature is fluid and cursive, with the first name "John" being the most prominent part.

John A. Wylam
Staff Attorney

February 13, 2019

BY ELECTRONIC DELIVERY

Steven D. Pearson, M.D., M.Sc.
President
Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

Re: ICER's Unsupported Price Increase Assessment Draft Protocol

Dear Dr. Pearson:

We are writing on behalf of the Biotechnology Innovation Organization (BIO) to provide comments on the Institute for Clinical and Economic Review's (ICER) "Unsupported Price Increase Assessment" (UPI) draft protocol.¹ BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology companies, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes, but have also reduced healthcare expenditures due to fewer physician office visits, hospitalizations, and surgical interventions.

In this draft protocol, ICER proposes a framework for evaluating whether price increases on prescription drugs are supported by clinical evidence. The draft protocol outlines how a list of up to 13 drugs will be selected for evaluation, how ICER will consider and rate new clinical evidence related to these medicines, and how it will engage and solicit information from manufacturers during the evaluation process. ICER explicitly states that non-clinical rationales will not be evaluated as part of the UPI.

We believe the dichotomy between "possibly justified by new clinical evidence" or "unjustified" is inappropriate. This draft protocol fundamentally fails at accurately – and in a way that is helpful to policymakers and the public – describing when a price increase is "justified." How prescription drugs are priced is an incredibly complex process. Clinical considerations, supply chain dynamics, payor preferences, research and development, and market conditions all factor into how the price of a medicine is set. Yet nearly all these considerations are disregarded in the draft protocol.

ICER's approach to seeking feedback and information from manufacturers as part of this process clearly illustrates the flaws in this methodology. Many of the considerations critical to prescription drug pricing are, and have long been considered, proprietary and confidential. However, ICER states that with the exception of its standing Academic-In-Confidence policy (in which ICER will not publish data provided by manufacturers that is awaiting peer review or public presentation), any information provided by manufacturers as part of this process will be included in the final report. This necessarily limits the types of information that manufacturers could provide to ICER as part of the UPI process. By

¹ Available at: https://icer-review.org/wp-content/uploads/2019/01/ICER_UPI_Draft_Protocol_011719.pdf

definition, then, this methodology cannot provide a complete picture when it comes to how prices for prescription drugs are determined. Yet ICER seems to be framing this report as a tool for policymakers to do just that.

At best, a report produced with the proposed methodology would provide limited information devoid of context about one factor among many in how prescription drug prices are determined. At worst, its findings could be misconstrued by the public and policymakers with real consequences for market efficiency and the innovation ecosystem. Given these deficiencies, we strongly recommend ICER abandon this draft protocol and not move forward with this report.

Sincerely,

/s/

Crystal Kuntz
Vice President
Healthcare Policy and Research



National Health Council

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February 13, 2019

Steven D. Pearson, MD, MSc

Founder and President, Institute for Clinical and Economic Review

Institute for Clinical and Economic Review

Two Liberty Square, Ninth Floor, Boston, MA 02109

Re: Unsupported Price Increase Assessment

Dear Dr. Pearson:

The National Health Council (NHC) is pleased to provide comments on the Institute for Clinical and Economic Review's (ICER) solicitation for feedback on the Unsupported Price Increase Assessment draft protocol.¹

Founded in 1920, the NHC is the only organization that brings together all segments of the health community to provide a united voice for the more than 160 million people in the United States with chronic diseases and disabilities, and their family caregivers. Made up of more than 125 diverse national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient advocacy organizations, which control its governance and policy-making process. Other members include professional and membership associations; nonprofit organizations with an interest in health; and representatives from the pharmaceutical, generic drug, health insurance, device, and biotechnology industries.

This work is very much aligned with our 2017 report *Policy Recommendations for Reducing Health Care Costs*.² One of the recommendations included in that report was that the National Academy of Medicine could commission reports on price increases on selected drugs of significant interest to patients. Selection criteria would be based on lack of competition, shortages, and significant price increases. We suggested that manufacturers would submit any relevant information to provide justification for the price increase, and the National Academy would retain any confidential and propriety information. The information to be collected would include but not be limited to:

- A narrative of factors contributing to the drug's pricing
- Existing therapeutic alternatives and any information demonstrating its comparative patient value, consistent with information contained in the FDA label
- Acquisition information if the drug was not developed by the current manufacturer

¹ Institute for Clinical and Economic Review (ICER). Unsupported Price Increase Assessment: Draft Protocol (January 17, 2019). https://icer-review.org/wp-content/uploads/2019/01/ICER_UPI_Draft_Protocol_011719.pdf

² National Health Council. Policy Recommendations for Reducing Health Care Costs. Available from: <http://www.nationalhealthcouncil.org/sites/default/files/NHC%20Policy%20Proposals%20for%20Reducing%20Health%20Care%20Costs%20UpdatedFINAL052217.pdf>

- Aggregate research, development, and administrative expenditures
- Aggregate rebates, discounts, and other concessions that reduce the effective price

While the current draft protocol does not consider each of these factors, the outlined process is an important starting point. We encourage ICER to consider this additional, relevant information in future iterations of the unsupported price increase program.

We appreciate ICER's inclusion of a patient representative on the multi-stakeholder advisory committee. We encourage the consideration of additional patient representatives and engagement in the process. ICER should also outline a role for patient representatives within the individual reviews. For example, patient perspectives from those with experience in a particular disease area would provide useful insights within the scope of individual reviews. The draft protocol contains a detailed explanation of how manufacturers can submit information but is lacking in detail on how patients and patient organizations can contribute to the process in a similar fashion as ICER's therapeutic reviews.

For this initiative to be successful, processes must be rigorous, transparent and reproducible. Opportunities for stakeholder and public input will help facilitate the program's credibility. We are pleased that ICER will provide an opportunity for members of the public to identify additional drugs that do not necessarily meet the cost criteria, but nevertheless cause hardships among patients and their families. Additional details on how this input will be sought would be helpful. The NHC would be happy to disseminate calls for input.

Additionally, greater clarity on how ICER will identify "important affordability implications for individual patients even if not for the health system" is needed. Greater clarity on the intended meaning of "affordability implications" would be needed for operationalizing the program and improve transparency. The scoping document also does not describe whether or not the Advisory Committee will participate in the selection of the (up to) three additional drugs. If not, how will the drugs be selected? Since many patients struggle with the costs of drugs and only up to three public-identified drugs will be considered, transparent and detailed selection criteria would help facilitate the process.

Additional details on how the independent systematic reviews will be performed would also be useful. For example, the scoping document refers to "high quality comparative observational studies." We recommend that ICER provide a definition or characteristics of "high quality" in this context.

ICER's decision to categorize drug-price increases as either "price increase with new clinical evidence" (those with moderate/high quality new evidence of a substantial improvement in net benefit) or unsupported is a reasonable approach. However, it may be important to consider what is included under the "clinical evidence" umbrella. For example, we recommend consideration of other factors that typically fall into the "contextual considerations" category of ICER's therapeutic reviews, such as impact on adherence, social factors, productivity, quality of life, or other outcomes not typically considered "clinical." Determination of impacts to consider would be greatly benefitted by engaging with patients and patient organizations.

Finally, the NHC recommends greater clarity on the format of the public reports. We recommend that ICER publish a report that can be understood by individual patients and include information that explains what the potential impact may be for them. For example, our 2017 recommendation calls for a report that "offer[s] context around the selected drugs' pricing and attempt to characterize its health, economic, and societal benefits, measured through both short- and long-term patient outcomes, adherence, productivity, quality of life, and/or life expectancy."

Conclusion

The NHC appreciates the opportunity to comment on this initiative and agrees that methodology will need to be updated as experience in this space grows. Future iterations of ICER's Unsupported Price Increase Assessment program could also consider medical devices, surgeries, and other non-drug medical products.

Please do not hesitate to contact Eric Gascho, our Vice President of Policy and Government Affairs, if you or your staff would like to discuss these issues in greater detail. He is reachable by phone at 202-973-0545 or via e-mail at egascho@nhcouncil.org.

Sincerely,

A handwritten signature in black ink, appearing to read "MBoutin", with a long horizontal flourish extending to the right.

Marc Boutin, JD
Chief Executive Officer
National Health Council

February 13, 2019

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109 USA

RE: Draft Unsupported Price Increase Assessment Protocol

Submitted electronically via: publiccomments@icer-review.org

Dear Dr. Pearson:

The National Pharmaceutical Council (NPC) shares your interest in optimizing the value of health care spending, and we have launched the *Going Below the Surface* initiative to broaden the conversation around the use of health care resources. Hence, another ICER initiative that is focused solely on drugs,¹ rather than the entire health care system, is truly a missed opportunity. Drug spending accounts for only 16% of the U.S. health care dollar.² A fully informed and productive dialogue must consider the other 84%, too.

NPC is a health policy research organization dedicated to the advancement of good evidence and science, and to fostering an environment in the United States that supports medical innovation. NPC is supported by the major U.S. research-based biopharmaceutical companies. We focus on research development, information dissemination, education and communication of the critical issues of evidence, innovation and the value of medicines for patients. Our research helps inform critical health care policy debates and supports the achievement of the best patient outcomes in the most efficient way possible.

NPC's *Guiding Practices for Patient-Centered Value Assessment*³ are a useful lens for viewing the concerns we have with ICER's proposed unsupported price increase assessment protocol. Of particular note are the breadth, robustness, and subjectivity of the assessment process. Seven guiding practices particularly relevant to ICER's proposed protocol are presented below.

Value assessments should focus broadly on all aspects of the health care system, not just on medications. (*Guiding Practice VII*)

Optimizing our health care resources by shifting our health care system from a volume-based focus to a value-based focus requires an examination of the entire system. Medications

account for only 16% of health care spending, yet ICER puts almost 100% of its resources towards examining medications.

NPC recommends that ICER shift resources to meaningfully examine the rest of the health care system.

Sufficient time, staff and resources should be dedicated to support a thorough and robust assessment process. (Guiding Practice VI)

What ICER hopes to accomplish with this report — in a relatively short timeframe — is an incredibly time-intensive and unprecedented undertaking. ICER notes in its draft protocol that “ICER does not have the capacity to perform full economic analyses on the large number of therapies that will be subject to analysis as part of this new report process. ... Therefore, these UPI reports are not intended to determine whether a price increase for a drug is fully justified by new clinical evidence.” Considering these resource constraints, ICER should avoid making determinations, or at least add extensive caveats and acknowledge limitations.

NPC recommends that ICER add caveats to any determinations and acknowledge their limitations.

ICER notes it does not have the resources to answer the question of whether price increases are supported by new evidence and, hence, does not seek to answer this question. This approach is only designed to identify cases where ICER believes the price increases are unsupported; it does not seek to identify supported price increases.

This one-sided methodology will only present the biopharmaceutical industry in a negative way without highlighting any positives. Taking a one-sided approach runs contrary to ICER’s previously stated mission: “Our aim is not to support one side in a negotiation; it is to provide what our health care system has lacked for so long: an independent, trustworthy source of information that can bring all voices into the discussion on value.”⁴ This one-sided approach does not contribute to a constructive discussion about drug prices and health care spending.

NPC recommends that ICER undertake more comprehensive reviews that can identify cases where price increases are aligned with value.

The measurement of value should include a broad array of benefits that are important to patients and society. (Guiding Practice XIII)

While manufacturers are invited to share information based on non-clinical information, this will not be incorporated into ICER’s considerations: “... non-clinical rationales will not be evaluated by ICER as a determinant in whether the drug is categorized as having its price increase unsupported by clinical evidence.”

Patients and society value more than clinical outcomes, including economic and humanistic types of outcomes. Ignoring non-clinical information such as health care resource utilization, medical cost offsets, work productivity, patient preference and/or caregiver burden dismisses these factors. We should encourage investment in all aspects of the patient experience and not place emphasis solely on clinical development.

NPC recommends that ICER expand its analyses to include non-clinical information.

Subjective evidence should be used minimally, if at all, and its inclusion should be clearly labeled. (*Guiding Practice XXV*)

Sensitivity analyses should be performed, taking into account input from external stakeholders. (*Guiding Practice XI*)

Whether a product's price increases are labeled as unsupported hinges on ICER's subjective assessment of the size of the clinical effect demonstrated by new evidence — if the effect is deemed “small,” the increase is labeled unsupported; if the effect is considered “substantial,” the unsupported label is not applied.

There are no transparent criteria to differentiate between “small” and “substantial” effects — the categorization process lacks specificity and is not replicable. Further, there are no sensitivity analyses to explore the range of effects that lie between the binary choices of “small” and “substantial.”

NPC recommends that ICER use transparent and replicable ratings criteria and incorporate sensitivity analyses.

Methods, models and assumptions should be transparent and assessment results should be reproducible. (*Guiding Practice IX*)

ICER's proposed methodology lacks specificity. As noted above, the categorization of evidence scoring is subjective, and no complete definition or academic references have been provided by which to assess best-use cases. It is unclear how ICER will weight outcomes (overall survival vs. progression-free survival, for example), or whether evidence related to a new indication will be weighted more or less than additional outcomes or safety evidence for an older indication.

ICER should avoid using terminology and phrases that are imprecise or lack objectivity, e.g., “extremely high price increases”; “fell just below”; and “raise concerns about fairness.” Such terms may potentially alienate stakeholders, particularly in the absence of transparent and clearly stated assumptions. The normative basis of “fair,” “unsubstantiated,” “substantial,” etc., should be made explicit and transparent.

NPC recommends that ICER clarify methods and terminology to facilitate transparency and reproducibility.

Stakeholders should be given the opportunity to submit relevant evidence, such as clinical trial and real-world evidence beyond the public literature. (*Guiding Practice XXI*)

While ICER does give manufacturers the opportunity to submit relevant evidence, only some of this evidence will be protected. Proprietary clinical information will be protected under the ICER’s “academic in confidence” policy; proprietary confidential financial information, however, will not be protected. Manufacturers’ confidential commercial and trade secret information have significant trade protections under law and regulations in many contexts. These protections should be recognized by ICER and extended to information manufacturers may choose to submit in response to an ICER inquiry. Failure to provide complete protection will limit the types of information that manufacturers can submit and, therefore, provide an incomplete picture of value.

NPC recommends that ICER fully protect the confidentiality of manufacturer information.

In addition, the evidence review limits the amount of evidence considered by an arbitrary cutoff of approximately 10% or more of the drug’s use. There is a huge need for better treatment of rare conditions and many pediatric indications, and this arbitrary cutoff appears to disregard important areas such as these. This disadvantages products with multiple indications and is in opposition to Food and Drug Administration incentives to research and invest in smaller, yet high burden, disease areas.

NPC recommends that ICER reconsider the 10% utilization threshold when examining new data.

ICER states in its draft protocol: “there has been no systematic approach at a state or national level to determine whether certain price increases are justified by new clinical evidence or other factors.” ICER’s proposed approach does not achieve this objective. NPC encourages ICER to:

- focus on the entire health care system,
- undertake more comprehensive reviews that can identify cases where price increases are aligned with value,
- add caveats to determinations and note their limitations,
- expand its analyses to include non-clinical evidence,
- use transparent and replicable ratings criteria and sensitivity analyses,
- clarify methods and terminology to facilitate transparency and reproducibility, and
- protect the confidentiality of manufacturer information.

Respectfully submitted,



Robert W. Dubois, MD, PhD
Chief Science Officer

References

¹ ICER Unsupported Price Increase Assessment Draft Protocol. https://icer-review.org/wp-content/uploads/2019/01/ICER_UPI_Draft_Protocol_011719.pdf. Accessed January 22, 2019.

² Kleinrock M, et al. Reconciling the Seemingly Irreconcilable: How Much Are We Spending on Drugs? Value in Health, 2019, online ahead of print. [https://www.valueinhealthjournal.com/article/S1098-3015\(18\)36310-1/fulltext](https://www.valueinhealthjournal.com/article/S1098-3015(18)36310-1/fulltext). Accessed January 29, 2019.

³ Guiding Practices for Patient-Centered Value Assessment. National Pharmaceutical Council. <http://www.npcnow.org/sites/default/files/npc-guiding-practices-for-patient-centered-value-assessment.pdf>. Accessed January 22, 2019.

⁴ ICER FAQ. <https://icer-review.org/wp-content/uploads/2016/01/ICER-FAQ-052316.pdf>. Accessed February 11, 2019.



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ICER's new annual analyses on Unsupported Price Increases (UPIs) is a laudable effort to bring some transparency into the conversations around why the U.S. has seen dramatic price increases for some prescription drugs. However, we would like to present the following questions and considerations as the protocol for the UPI analyses is finalized.

First, what is the practical purpose of the UPI reports, and how does ICER intend for them to be used? ICER's comparative effectiveness analyses allow the public - including patients, providers, payers, and policy makers - to determine the economic value of a drug. This can practically impact decisions such as which drugs a provider prescribes, or which drugs a payer chooses to cover. Alternatively, an ICER report can influence a manufacturer's pricing decisions, as occurred when the price of evolocumab was reduced partly in response to ICER's value assessment for PCSK9 inhibitors. It is unclear whether the new UPI reports would have a similar influence, as they will be comparing a drug's current value to its historic value without offering a clear picture of what alternatives may be available. In a press release, the president of ICER mentioned that "several states have already passed laws that will generate lists of drugs with substantial price increases so that policy makers and the public can seek greater transparency," but some critics have pointed out that these laws don't empower states to take action against price increases. Instead, they mainly provide an avenue for shaming manufacturers who raise prices too quickly. It seems that ICER's UPI reports may help to focus that shame where it is most deserved, but it is not yet clear that manufacturers will actually respond to that shame.

Second, although the UPI report draft protocol states that it will seek new evidence about both benefits and harms of the drugs being reviewed, it seems to assume that overall, new evidence will primarily provide information about added health benefits. However, it is possible that new clinical evidence will bring to light safety issues that are infrequent or only occur after long term use of a drug. It is also possible that a drug that is meant to be used chronically and was approved on the basis of relatively short-term data, such as RCTs lasting 2 years, are shown to have lackluster long-term efficacy data. Has ICER considered the possibility that a drug's overall net health benefit may have actually decreased in light of new information about the long-term safety and efficacy of a drug? What conclusions about price increases might be drawn for a drug with new safety concerns or poorer than expected long-term efficacy?

Third, does ICER intend to include generic drugs in its UPI reports? If so, how? The draft protocol states "a rise in price across multiple manufacturers of a generic medication that in combination had a large change in budget impact would not be included in the review." Although the background section of the protocol states that both brand and generic drug prices are a matter of concern, it is unclear how the UPIs will be able to assess price increases for the vast majority of generic drugs, as generics typically have multiple manufacturers. In light of the December 2018 news about 16 generic drug companies being investigated over allegedly price-fixing more than 300 drugs, the question of a rise in price across multiple generic manufacturers should be given stronger consideration in the UPI protocol.



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Fourth, does ICER intend to ensure that the UPI reports cover a range of drugs that represent different aspects of the pharmaceutical market? Pharmaceutical drugs may fall into different categories, including but not limited to generic vs. brand, biologic vs. non-biologic, hospital administered vs. self-administered drugs, drugs that are delivered via a patented device such as inhalers or “pens” for subcutaneous injection, and so on. If, by chance, the top 10 drugs whose net price increases have had the largest impact on US spending over the prior two years happen to include drugs that are very similar to each other and may reflect the same market trend - e.g., if most of the 10 drugs are biologics - will an effort be made to include less similar drugs - e.g. non-biologics - in the selection of the up to 3 additional drugs?

Sincerely,

The Clinical Team at TruDataRx
Dr. James Stahl, Chief Medical Officer
Dr. Kerry Mills, Senior Scientist
Bethany Sneathen, Clinical Data Analyst

Better decisions through better data

My name is Daniel Mytelka. I have worked for the past 20 years in the healthcare industry in finance, health outcomes, strategy and policy. The comments below are my own.

Uncertainty may affect both value and our understanding of value. If the uncertainty could change whether a product is appropriate for a particular patient, it affects the true value of the product because it could lead to the patient receiving a less effective product. If there is little ambiguity regarding what product is most effective for a patient, uncertainty does not affect the true value of the product, but could make our understanding of that value uncertain. Critically, the product's own performance will not reveal its true value in the first case, but it will in the second case.

Case 1: True value will be affected by uncertainty if the appropriate treatment for patients is unclear. For example, if head-to-head trials have not been conducted between two similar products, it may be unclear whether one is superior in some or all circumstances. In this case, the true value of the products is unclear and their performance in treated patients will not resolve that uncertainty. Changes in a product's price may be appropriate in this case to the extent that the changes specifically reflect this uncertainty.

Case 2: True value is not affected by uncertainty if the appropriate treatment is clear. For example, there may only be one available product for a disease or there may be a new product available that is clearly better than alternatives. There may still be uncertainty regarding appropriate reimbursement for the product, such as for a durable therapy with potential life-long benefits for which clinical trial data only extends for a few years. In this case, it is appropriate to manage the uncertainty using tools that ultimately provide appropriate reimbursement for a product, such as performance-based agreements.

It is important to distinguish between these cases. Not all uncertainty can be resolved at launch and some of it is difficult to resolve given clinical trial sizes and durations. Treating all uncertainty similarly may create inappropriate incentives where pharmaceutical developers are more encouraged to develop products that are lower in true value, but receive higher reimbursement because there is less uncertainty. Uncertainty should be managed using tools that are appropriate for the circumstances.

Sincerely,

Daniel Mytelka, PhD MBA CFA

Massachusetts Institute of Technology

Hello:

Thank you for the opportunity to provide input on the Unsupported Price Increase (UPI) project protocol. The methods and approach are clearly described. My comments are limited to two sections of the protocol.

Section 2.1.3

The decision to use the medical care CPI as a measure of drug price inflation is not clear to me. All components of the CPI are based on a “market basket” approach to measurement that aligns most closely with out-of-pocket expenditures. While these are certainly significant (and growing) for prescription drugs, the majority of a drug’s list or negotiated price is borne by third parties. Other publicly-available indices include third-party payments, such as the Personal Health Care (PHC) index published by CMS or the Personal Consumption Expenditure health (PCEhealth) index available from the Bureau of Economic Analysis.¹ The CPI has also been found to overstate inflation as individuals substitute away from goods or services with rapid price increases.^{1,2}

Section 2.1.4

There is likely to be a need to use an alternate (FSS or other) schedule for more than just prescription drugs produced by privately-held companies. Several drugs with highly specialized distribution systems (bypassing agents for hemophilia come to mind) are also not well-captured by the SSR dataset.

References:

1. Brathwait SD. The substitution bias of the Laspeyres price index: An analysis using estimated cost-of-living indexes. *American Economic Review* 1980;70(1):64-77.
2. Dunn A, Grosse SD, Zuvekas SH. Adjusting health expenditures for inflation: A review of measures for health services research in the United States. *Health Services Research* 2018;53(1):175-196.

Please let me know if you have any questions or concerns.

Regards,

Dan Ollendorf, Ph.D.



February 13, 2019

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109 USA

RE: Draft Protocol: Price Increase Assessments

Dear Dr. Pearson:

Patients Rising Now advocates on behalf of patients with life-threatening conditions and chronic diseases for them to have access to vital therapies and services. Access is a matter of survival for those patients, and it spans affordability, insurance coverage, and physical access. To support improved access, we are committed to engaging patients, caregivers, physicians, media, health policy experts, payers, providers, and others to foster realistic, patient-centered, solution-oriented discussions for particular conditions and the entire U.S. health care system. That is, our goal is a balanced dialogue that illuminates the truth about health care in a just and equitable way.

We appreciate the opportunity to provide our comments on ICER's January 17th Draft Protocol for Unsupported Price Increase Assessments.

The cost of prescription drugs is clearly an important issue. Patients Rising Now believes in evidence-based transparent dialogues about how to balance affordability, access, and promotion of innovation in all areas of health care because all three are key to short and long-term improvements in quality for patients and society. However, we are concerned about ICER's approach described in its Draft Protocol for several reasons described below.

Rudimentary Screen Algorithm & Understating Limitations

The process described in the Draft Protocol document is limited in several ways that could lead to inaccurate assessments and conclusions because of the restricted scope of the analyses and data that will be considered. By self-limiting this process, ICER is leading itself – and any individuals or organizations that may use the output from reports generated in this process – towards warped understandings of prices and value. While it is certainly true that no research can be entirely comprehensive because of time, resource, and data constraints, wise researchers and analysts know how to carefully frame their conclusions and insights within the context of those limitations – including in their public presentations of their findings, and particularly when conveyed to the media and lay audiences. We are concerned about the limitations of the Draft Protocol because of ICER's history in this area, and the utilization of ICER's reports – including draft reports – for sensationalizing to the public and the resulting limits to patient access.

Many Changes Occurring That Make ICER's Process Misleading or Meaningless

Another shortcoming with ICER's proposed process is that it is retrograde to the movement of the U.S. health care system that is seeking to incorporate more comprehensive, integrated, and systemic analyses about the utility and cost of all forms of therapies. Beyond the evolving trend in the U.S. health care system, there are also many proposals that would accelerate that movement, and in some cases make the concepts embodied in ICER's proposed process irrelevant. Among those pending actions are changes to Medicare's reimbursement practices for biopharmaceutical treatments. Those changes (and others) are expected to seismically alter the entire landscape for pricing and payments for medicines in the U.S., and thus insert great uncertainty about the validity of ICER's proposed process. For example, one proposed change would no longer allow biopharmaceutical companies to provide percentage rebates to health plans, but would direct those discounts to be more transparently delivered to patients. This proposed change is expected to reduce patient's costs at pharmacy while leading to some increase in monthly insurance premiums. Among the uncertainties that could accompany this change are the extent of those discounts, how discounts will differ among classes of medicines, how quickly such a change in Medicare could be implemented, and how rapidly similar changes could occur in the private sector through market forces, or via state regulator or legislative changes. In fact, this proposal has so much significant uncertainty that in presenting the proposal, the government included modeling analyses conducted by not only their own actuaries, but also from two separate private organizations. Those analyses encompassed an extensive range of possible outcomes because of the uncertainties and assumptions built into each of their models.

Thus, the rapidly changing reimbursement world and market landscapes in the U.S., (which could be turbo-charged by possible government actions), makes the retrospective analyses that ICER is proposing irrelevant or misleading, and potentially very dangerous – very much like driving a car down a highway by looking out the rear window.

Patient and Family Perspectives and Issues

We are once again disappointed that ICER continues to minimize the importance to patient's perspectives in their proposed analytical methodology. For example, while the Draft Protocol does include a process for determining net prices to manufactures, it does not recognize that those net prices may have only limited connection to what patients actually pay. That is one of the driving forces behind the Federal government's proposal to shift such discounts from going to health plans to going directly to patients, as mentioned above.

We are also concerned about the Draft Protocol limiting itself to only economic analyses, which appears to preclude looking at offsetting savings related to productivity or other aspects of patients' lives such as transportation, caregiver time, and other family burdens. This is particularly perplexing since those factors are an area that ICER routinely requests input for other assessments, yet the Draft Protocol specifically states that it will not consider non-clinical factors in its analysis.¹ We believe ICER should explain in greater detail why it is circumscribing the range of inputs for its analysis in this area – and by doing so explicitly limiting the information important to patients.

Overall, the proposed type of analysis would be disconnected from progress toward value-based benefit design and other truly value-delivering changes in the U.S. health system that benefit patients. We strongly believe that the calculations ICER is considering – which only look at a specific silo of health financing – are incomplete unless they also reflect other aspects of health care value improvement.

ICER’s History of Focus on Economics and Lack of Transparency

We are concerned about the Draft Protocol process because ICER’s value assessments have consistently stressed economic aspects of treatment options and minimized patient-centered concerns. These concerns, in part, stem from ICER’s reliance on QALYs as a fundamental determinant within its analyses, and extends to largely dismissing patient reported outcomes and insights from continuation trials following blinded studies.

As you know, QALYs have several areas of serious limitations, including:

- Ethical considerations – particularly around condition for treating people with disabilities where restricting the maximum functioning or quality of life scores because of that underlying disability discriminate against certain therapies needed by vulnerable patients. Specifically, those restrictions may cross an ethical line beyond mere fiscal prudence and into what could be described as rationing.
- There are several realms of other methodological issues for calculating QALYs that have been conveyed to ICER by Patients Rising now and others. And of particular importance to Patients Rising Now is the failure to adequately consider patient reported outcomes in QALY computations.

There has also been concerns about lack of transparency in ICER’s analyses – which runs counter to the scientific process where reproducibility is key to validation. We are particularly concerned about any publications from ICER in this area being misconstrued, misinterpreted, or blatantly misused because of ICER’s history of imprecise language and analytics.ⁱⁱ

In addition, ICER’s continuing to reference the fictional concept of “budget impact at the national level”ⁱⁱⁱ is mysterious since in a country where health care financing and reimbursement spans several Federal programs, more than 50 state Medicaid programs, hundreds of insurance plans, and many thousands of self-insured employers it has little meaning beyond macro-economic and academic analyses.

Specific Issues and Suggestions

- We are concerned about the limited scope of information the Draft Protocol will include and how that could prevent consideration of larger changes to overall care protocols in a disease area. For example, as precision medicine continues to expand with greater accuracy of diagnostics and treatments, more specific diagnoses can lead to methods or criteria that would affect treatment decisions that may not be reflected in product labels or be specific to a single product. We would like ICER to explain how such information would be considered in its process, particularly if a company would be precluded from providing ICER such information because it is not reflected in any changes to an FDA approved label.

- Another aspect that is missing from the Draft Protocol is how treatments for ultra-rare conditions will be assessed. Because ICER has a modified value framework for those diseases, we recommend ICER provide insights about how any analyses and reports based upon the Draft Protocol (or a Final Protocol should one be issued) will address the differential nature of ultra-rare diseases.
- By not considering non-clinical factors^{iv} isn't the Draft Protocol inconsistent with requesting R&D and manufacturing costs under its protocol for ultra-rare conditions? For instance, once a product is on the market, it could be possible that an ingredient in a medicine (e.g., gold for Auranofin) could increase dramatically in price, or some other component required for the production of the medicine could increase dramatically in cost. That could lead a company to be in the quandary of deciding whether to produce the medicine and sell it at a loss, or to raise the price. This would be analogous to the U.S. manufacturers of washing machines who because of new steel tariffs are raising the prices for their products. If similar tariffs were imposed on key ingredients for medicines, what would that mean for the ability of some companies – particularly smaller ones with only one or a few approved medicines – to continue to produce and delivery such medicines? Would they be able and willing to do so at a financial loss?
- The Draft Protocol says that it will not consider multi-source generics,^v but a recent report showed that generics with three or fewer manufacturers can have greater than average price increases over time – particularly when there is a shortage of that medicine.^{vi} We would like ICER to respond to the findings of this study and explain why price increases in generic medicines should be beyond the scope of its activities.
- As you know, biosimilars are an emerging type of medicine that are expected to decrease the overall cost of care. However, the Draft Protocol does not address how biosimilars will be incorporated into ICER's process. We believe that biosimilars – whether declared interchangeable or not – should be considered along with the original biologic medicine that they are “similar” to when evaluating overall cost changes in a therapeutic area. We would like ICER to respond and provide an explanation about how biosimilars will be treated by ICER in potential analyses in this activity.

Conclusions & Recommendations

ICER is proposing a methodology to evaluate so-called justifiability (or “fairness”), of price increases of treatments using data inputs and an analytical scheme that ICER recognizes have significant limitations. This is of great concern if it leads to access restrictions based solely on payer economic considerations or otherwise interferes with the shared decision making among the patient and their clinicians.

Patients Rising Now remains concerned that ICER's activities will continue to lead policy makers and others (including payers and clinicians) to focus on economic analyses in erecting barriers to patients access for FDA approved treatments. As you know, this would contribute to more adverse outcomes for patients.

We are concerned that the process ICER is proposing to embark upon with the Draft Protocol will replicate many of the problems with their previous assessments, and we strongly believe that ICER needs to respond to the limitations and restrictions of its process before finalizing any protocols. And further, we strongly urge ICER to make those limitations and uncertainties expressly clear upfront in any reports or findings it develops in the future – and particularly in any public facing materials (such as press releases) it generates and distributes.

Thus, Patients Rising Now believes that ICER’s Draft Protocol inadequately reflects patients’ perspectives, it ignores market processes and is backward looking. As you know, the outputs from analytical processes are only as valid as the certainty of the data and the assumptions used to build the models. The Draft Protocol falls short on both counts: A flawed analytical framework that will rely on limited data. Because of those serious flaws we recommend ICER rethink their entire process for this questionable endeavor.

Sincerely,



Terry Wilcox
Co-Founder & Executive Director, Patients Rising Now

ⁱ Draft Protocol p. 7.

ⁱⁱ Patient Rising Now’s comments to ICER about Draft Evidence Report “Spinraza® and Zolgensma® for Spinal Muscular Atrophy: Effectiveness and Value,” January 31, 2019.

ⁱⁱⁱ Draft Protocol p. 3.

^{iv} Draft Protocol p. 7.

^v Draft Protocol p. 3.

^{vi} I Hernandez et. al., “Changes in Drug Pricing After Drug Shortages in the United States,” *Annals of Internal Medicine*, 1 January, 2019 (170), No 1. pp 74-6.

One cannot address price increases without addressing initial price at launch....if a product launches at a million a month, likely there will be little need for price increases.

So how does one make sense of initial launch....the only time it came close to making sense to me was with Allegra's launch....I was told that it was pro rated on median income similar to Coca Cola model so it's same percent of that country's income. If there's another methodology, I'd like to better understand as that reasoning may have occurred during the Common Sense Era.

The largest impact in pricing was due to OBRA 90 at which point the government required "best price" for their business. Also impacting this was "nominal pricing", 340B pricing and since, couponing and more widespread use of patient assistance programs. All of this cuts into profitability and the only place it can be underwritten is on Commercial insurance business. This profitability balloon, if squeezed on the government business requires expansion of need on the everyday payer.

The other compounding factor is that the programs mentioned above had no controls in place and were highly abused further affecting need on Commercial side.....and now the government's going to "fix it". Kind of like the opioid crisis....all the signs and data were there, but no one acts until it's a crisis.

I think the perfect example of pricing disparity is insulin.....last I knew the government was paying a penny a vial (for tracking purposes) whereas non government diabetics are paying hundreds of dollars a month.

Then there's the PBM's and other vendors with their hands out, requiring their piece of the action, which I'm not going to even begin to discuss....that said, price increases in and of itself, cannot be addressed without understanding all the other dynamics....good luck and thanks for listening.