Unsupported Price Increase Assessment

Draft Protocol

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Institute for Clinical and Economic Review

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1. Background

The price of many existing drugs, both brand and generic, can increase substantially over time, and questions are frequently raised regarding whether these price increases are justified. State policymakers have been particularly active in seeking measures to address this issue. For example, both California and Vermont now have laws tracking substantial drug price increases, requiring drug manufacturers to submit information that might justify increases above a certain threshold.[1-3] Despite these initiatives, 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. For several years, the Institute for Clinical and Economic Review (ICER) has received requests from state policymakers and others to fill this gap, but we had no dedicated funding or specified methodology to do so. Therefore, in 2017 we sought and received funding from the Laura and John Arnold Foundation to develop a new line of ICER reports evaluating selected high-impact drugs with substantial price increases. 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.

In mid-2018 we organized a multi-stakeholder advisory group to provide input into the design of a new approach for these reports. The advisory group was comprised of representatives from patient groups, drug makers, and insurers representing Medicaid and the private market. Working with this group over several months, ICER has developed a draft protocol for the UPI reports and is now seeking public comment before revising and finalizing its methods, with the first reports anticipated for mid-late 2019. Please see the figure below for an overview of the timeframe for the first UPI reports to be released later this year.

Milestone	Date
Draft Protocol	January 17
Public Comment Period	January 17 – February 13
Revised Protocol	March 8
Public Input Period on Drugs of Concern	March 15 – April 19
Manufacturer Notification and Input Phase I	May 6 – June 3
Preliminary Individual Assessments to Manufacturers	August 9
Manufacturer Input Phase II	August 9 – September 9
Final Report	October 8

As detailed below, ICER proposes to generate an annual report of up to 13 drugs that have experienced substantial price increases over a two-year time period. ICER will review changes in the evidence base for these drugs, and report on whether potential evidentiary support for price increases was found.

It is important to note 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, nor

would the time needed to develop full ICER reports provide information in a useful timeframe for the public and policymakers. Therefore, these UPI reports are not intended to determine whether a price increase for a drug is fully justified by new clinical evidence or meets an ICER value-based price benchmark. Instead, we will focus the analysis on whether or not substantial new evidence exists that *could* justify its price increase. By identifying drugs with substantial price increases for which there is no basis in new evidence we hope to make an important first step in providing the public and policymakers with information they can use to advance the public debate on drug price increases.

2. List of Drugs to Review

As described in greater detail below, the process for ICER's review will start by identifying the top 100 drugs by sales revenue (administered in any setting) in the United States (US). From this list, the next step will be to identify drugs that have had list (wholesale acquisition cost or WAC) price increases over twice the medical Consumer Price Index (CPI) over a two-year period. Drugs with list price increases that meet this threshold will also have their two-year *net* price increase determined. We then rank drugs by the expected change in budget impact due to that change in net price over two years and select the top 10 drugs whose net price increase would have generated the largest increase in budget impact at the national level. We supplement that list with up to three additional drugs with substantial price increases based in part on public input.

2.1. Creating the List of Drugs with "Substantial" Price Increases

2.1.1. ICER will obtain a list of the 100 drugs with the largest dollar sales in the US. This information will come from SSR Health, LLC, the health care division of SSR, LLC, an independent investment research firm, and may leverage other data sources for companies that are not publicly traded. To derive a net price, SSR Health combines data on unit sales with publicly-disclosed US sales figures that are net of discounts, rebates, concessions to wholesalers and distributors, and patient assistance programs.

2.1.2. ICER will determine WAC price changes for these drugs over the prior 24 months. The intent is to look at individual pricing decisions. As such, 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. For the first report we will be looking at price changes from January 1, 2017 through December 31, 2018.

2.1.3. ICER will determine which of these drugs have had a WAC price increase over the prior 24 months that exceeds two times the rate of medical care CPI (consumer price index). The medical care CPI is one of eight major components of the CPI recorded and reported by the United States Bureau of Labor Statistics (BLS).[4] Medical care CPI comprises medical care services (professional services, hospital and related services, and health insurance) and medical care commodities (medical drugs, equipment, and supplies).[5] Drugs whose WAC price increases have not exceeded two times the rate of medical care CPI will be removed from further evaluation. Our intent in choosing the overall medical care CPI and not its subcomponents is to reflect inflation in drug prices relative to inflation in the overall price of medical care.

2.1.4. Among those drugs with a WAC price increase greater than twice medical care CPI, ICER will determine *net* price changes over the prior 24 months. Net price information will be obtained from SSR Health. For drugs produced by companies that are not publicly traded, ICER will use prices from the Federal Supply Schedule (FSS).

2.1.5. ICER will rank those drugs whose net price increases have had the largest impact on US spending over the prior two years. To create this ranking, ICER will multiply the current annual

sales figure for each drug by its change in net price over 24 months. The top 10 drugs in this ranking will constitute the first part of the final list of drugs for which evidence review will be undertaken.

2.2. Additional Drugs to be Reviewed

We are aware that the public and policymakers may believe that there are drugs with significant price increases that do not meet the criteria for inclusion in this initial top 10 list. ICER may review up to three additional drugs. ICER will seek public input and consider adding drugs based on any of the following criteria:

- Drugs with extremely high price increases that do not have substantial budget impact at the national level
- Drugs used by millions of Americans with price increases that fell just below two times the medical care CPI
- Drugs whose price increases have important affordability implications for individual patients even if not for the health system
- Drugs whose price increases raise concerns about the fairness of the price increases.

2.3. Final List

The lists from 2.1 and 2.2 will be combined into a final list of up to 13 drugs for review. ICER will not publicly announce this list while the review is taking place as we heard concerns from manufacturers that being on the list would be stigmatizing when a determination has not yet been made as to whether the price increase is unsupported.

3. Manufacturer Input

ICER acknowledges that manufacturers may have information on their drugs and/or on competitor drugs that they believe justifies a substantial price increase. Manufacturers also have data on net price changes that may be more precise than data from SSR or FSS. ICER will seek to work with manufacturers to gain this information and the perspectives of manufacturers during the review process. Importantly, with the exception of clinical evidence submitted under ICER's Academic-in-Confidence policy, any information provided by manufacturers will be included as part of the final report and will therefore be transparent to the public and policymakers.

Specifically, ICER will ask each manufacturer for the following information (which may be submitted under ICER's policy on academic-in-confidence data):

- New clinical evidence over the prior 36 months that demonstrates improved clinical or economic outcomes
- New evidence relating to comparator therapies that the manufacturer believes indicate new evidence of relative clinical advantages of their drug
- Other potential justifications for a price increase, including information within the prior 36 months related to:
    - a large increase in costs of production
    - large price savings attributable to the drug in other parts of the health system
    - all other reasons deemed relevant by the manufacturers.

Additionally, manufacturers will have four weeks from time of notification to provide input.

4. ICER Review

4.1. Overview of Review Process

For each drug ICER will determine the existing or new (within prior 36 months) indication(s) that comprise approximately 10% or more of the drug's use. To determine which indications meet this threshold, ICER will seek manufacturer input and elicit input from clinical experts and payers.

4.1.1. For these indications, ICER will seek to determine a "baseline" of known safety and clinical effectiveness as reflected in the evidence contained in the Food and Drug Administration (FDA) labeling information.

4.1.2. ICER will then perform independent systematic reviews looking for *new* information over the prior 36 months about benefits and harms of the reviewed drugs within these indications. The systematic review will look for information from randomized trials, high quality comparative observational studies, and, for information on low frequency harms, from large uncontrolled studies. ICER will assess the evidence from these systematic reviews and any supplemental evidence submitted by manufacturers to determine new information over the prior 36 months.

4.1.3. ICER will rate the quality of new evidence and the magnitude of added net health benefit. The quality of evidence will be rated using three-level GRADE as low, moderate, or high.[6] GRADE is largely congruent with ICER evidence ratings and allows certainty in estimates of effect to be separated from the magnitude of benefit for this purpose.

For evidence that is rated as being of moderate or high quality, ICER will rate the additional net health benefit as none, small, or substantial using the usual ICER evidence matrix ratings.

ICER's usual evidence reports determine additional health benefit by comparing the new therapy to existing care options. However, for the UPI reports the comparison will be between previously understood net benefit for a therapy versus placebo and/or comparators and any new, additional net benefit for that same therapy based on newer evidence.

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." Drugs that have no new clinical evidence or clinical evidence that does not meet these criteria will be categorized as having unsupported price increases. As described earlier, all manufacturer information submitted to justify the price increase will be provided as a component of this report, but 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.

6. Manufacturer Review Prior to Public Release

The manufacturer of each drug reviewed will be contacted individually and sent a preliminary version of the categorization and what the UPI report says about their drug. Each manufacturer will have four weeks to submit comments about their drug(s). These comments must be emailed as a PDF attachment to publiccomments@icer-review.org, must use Times New Roman 12-point font size, and must not be longer than five pages (excluding references and appendices). ICER will have previously asked manufacturers for information on indications of the drug that comprise 10% or more of the drug's use and will not accept information on new indications for review at this stage.

7. UPI Report Public Release

7.1 Public Release Process

7.1.1. With manufacturer input and further reflection, the report will be revised as necessary to produce a version for public release. The UPI Report will be the first public presentation of the results of the analysis that began with the identification of the top 100 drugs by sales in the US.

7.1.2. For the 10-13 drugs that comprise the final list, the UPI report will include current sales, the change in list price, and the change in net price. It will also include the funnel/flow from: largest dollar sales; to largest changes in WAC; to largest changes in net price for those drugs with WAC changes exceeding two times medical CPI; to largest impact on spending. This will show how the list was culled from the original 100 drugs to the 10-13 reviewed drugs.

The report will present the reviews/categorizations of up to 13 drugs. As noted, earlier, manufacturer comments will be published along with ICER's responses to those comments as an Appendix.

8. Changes in Process

Despite benefiting from the input of our advisory group, we expect that we will encounter situations throughout the first year of the UPI review that have not been fully anticipated. Thus, it should be expected that the UPI process will change after the first year of implementation. Even during the first year of the UPI report process, ICER will be monitoring aspects of the process as it progresses and may need to alter aspects of the review if needed to maintain transparency and fairness to all parties. ICER commits to flexibility within this first review and to transparency about any needed changes.

References

1. Horvath J. Update: What's New in State Drug Pricing Legislation? 2018; https://nashp.org/update-whats-new-in-state-drug-pricing-legislation/. Accessed 01/14/19, 2019.
2. SB-17 Health care: prescription drug costs. In. Hernandez E, trans. *Health and Safety Code; Insurance Code* 2017-2018.
3. An act relating to prescription drugs, 165 (2016). Vermont General Assembly.
4. Labor USDo. Bureau of Labor Statistics. 2019; https://www.bls.gov/home.htm. Accessed 01/15/19, 2019.
5. Labor USDo. Consumer Price Index. 2018; https://www.bls.gov/cpi/factsheets/medical-care.htm. Accessed 01/15/19, 2019.
6. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clinical research ed).* 2008; 336 (7650): 924-926.