Unsupported Price Increase Assessment

Revised 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 protocol for the UPI reports, 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 15
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 whether there is, or is not, new evidence for drugs with substantial price increases 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 net sales revenue in the United States (US), administered in any setting, across all insurers. 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 24-month period. Drugs with list price increases that meet this threshold will also have their two-year *net* price increase determined. We will 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. Based in part on public input, we will supplement that list with up to three additional drugs with price increases over the same time frame that have not led to placement within the top 10 drugs by budget impact. Further details on the process are provided below.

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 net sales revenue 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 December 31, 2016 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). This will be calculated as the difference between the medical CPI at the beginning and end of the time period of interest using unadjusted rates (January 2017 to January 2019); because of reporting, the exact dates of WAC price changes and CPI changes may be slightly different. 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. WAC and net price change per unit over the

24-month period will be adjusted for percentage change in price across different dosing strengths for any drug, if applicable, as well as change in sales volume. Net price information will be obtained from SSR Health. Price changes using the SSR database will be based on three-month (quarterly) average WAC and net price, with price change calculated over the eight quarters from January 1, 2017 to December 31, 2018. For drugs produced by companies that are not publicly traded, or where SSR Health does not have adequate information on price changes, ICER will use prices from the Federal Supply Schedule (FSS). Price changes using the FSS database will be calculated using prices in January 2017 and December 2018.

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 annually. 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.

2.2.1. ICER will report on price changes and budget impact changes for these drugs in the same way and over the same time period as in Section 2.1.

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. ICER will contact manufacturers of the 10-13 drugs on the initial list and invite submission of this information within four weeks of notification. 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, if necessary, 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 new 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.

As part of response to initial outreach, manufacturers may inform ICER if they believe the SSR methodology for calculating net price changes and/or net sales revenue changes was applied incorrectly. Manufacturers can submit revised inputs (such as net revenue that they believe was incorrectly recorded or transcribed from SEC filings) and ICER will review this information. If, in consultation with SSR, ICER feels that the SSR calculations had been performed incorrectly, ICER will update its calculation of price increase and budget impact in the UPI report list. If the revised figures would move the drug below the 15th position on the list, ICER will drop the drug from the review. Otherwise, it will be included.

As noted below, at the time of initial outreach ICER will also seek manufacturer input on which indications result in approximately 10% or more of overall utilization of that drug. If manufacturers report that an indication is currently below 10% of overall use but is rapidly increasing and evidence related to that indication is one justification for a price increase, ICER will consider reviewing evidence related to this indication.

4. ICER Review

4.1. Overview of Review Process

For each drug ICER will determine all existing or new (within prior 36 months) indication(s) that are responsible for approximately 10% or more of the drug's utilization. To determine which indications meet this threshold, ICER will seek manufacturer input and also elicit input from clinical experts and payers. If manufacturers report that use for an indication is rapidly increasing and is the justification for a price increase, ICER will consider reviewing evidence related to this indication even if current use is below 10% of overall utilization.

4.1.1. For all included indications, ICER will 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 on benefits and harms within these indications. However, if manufacturers have submitted evidence, ICER may choose not to perform a systematic review. Systematic reviews will look for evidence from randomized trials and high quality comparative observational studies. Studies reporting patient-reported outcomes and other real-world data will be highly relevant. For information on low frequency harms, evidence from large uncontrolled studies will also be included. As described above, evidence submitted by manufacturers will also be evaluated.

4.1.3. ICER will assign separate ratings to the quality of new evidence and to the magnitude of added "net" health benefit demonstrated by the new evidence. 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 the rating of added "net" health benefit, ICER will use its usual approach to take a comprehensive view of both benefits and harms, including anything that appears to be evidence of new patient-important benefits or harms.

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 drug value assessment reports determine additional net health benefit by comparing the new therapy to placebo or to alternative treatment options. However, for the UPI reports the comparison will generally be between any additional net health benefit for a drug based on newer evidence and the net health benefits of a therapy as previously described in the labeling information. Occasionally, previous net health benefit will be informed by evidence submitted or encountered during the review that does not appear in the drug label.

5. Designation of Drug Price Increases as "Unsupported"

Drugs found to have moderate/high quality new evidence of a substantial improvement in net health 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 price increases "unsupported by new clinical evidence." 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 and sent a preliminary analysis of the evidence and ultimate categorization of whether the price increase for their drug is unsupported by new clinical evidence. Manufacturers 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 net sales revenue, the change in list price (list price at the beginning and end of the 24 month period, and the change in net price (net price at the beginning and end of the 24 month period). It will also include a description for each drug of how the figures led sequentially from 1) largest net sales revenue; 2) changes in WAC exceeding two times medical CPI; 3) largest changes in net price; 4) largest increases in net sales revenue. This will show how the drug 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 report 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

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