Unsupported Price Increase Assessment

2020 Protocol

June 19, 2020

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]

In 2019, with funding from the Laura and John Arnold Foundation, we launched a new line of ICER reports, named Unsupported Price Increase (UPI) reports, to identify major drugs with substantial price increases without adequate evidence to justify the increases. To guide our work, we receive input from a multi-stakeholder advisory group comprised of representatives from patient advocacy organizations, drug makers, and insurers.

Please see the figure below for an overview of the timeframe for the 2020 UPI report to be released later this year.

Milestone	Date
Protocol Posted	June 19
Public Input Period on Drugs of Concern	June 19 – July 17
Manufacturer Notification on Price Estimates and Input Phase I	June 26 – July 17
Manufacturer Input Phase II	July 24 – August 14
Preliminary Individual Assessments to Manufacturers	October 27
Manufacturer Input Phase III	October 27 – November 24
Final Report Posted	January 8 (2021)

As detailed below, ICER proposes to generate a report of up to 13 drugs that have experienced substantial price increases over a one-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 report process, nor would the time needed to develop full ICER reports provide information in a useful timeframe for the public and policymakers. Therefore, 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 health-benefit based price benchmark. Instead, we will focus the analysis on whether 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 provide 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 one-year period. Drugs with list price increases that meet this threshold will also have their one-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 one year and then 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 timeframe 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 in 2019. 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.

2.1.2. ICER will determine average WAC price changes for these drugs over a one-year period. 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 this second UPI report, we will be looking at the average price in 2019 compared with the average price in 2018.

2.1.3. ICER will determine which of these drugs have had a WAC price increase over the one-year period that exceeded two times the rate of medical CPI. This will be calculated as the difference between the average medical CPI at the beginning and end of the time period of interest using unadjusted rates (average CPI for 2018 vs. average CPI for 2019); because of reporting, the exact dates of WAC price changes and CPI changes may be slightly different. The medical CPI is one of eight major components of the CPI recorded and reported by the US Bureau of Labor Statistics (BLS).[4] Medical 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 CPI will be removed from further evaluation. Our intent in choosing the overall medical 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 the medical CPI, ICER will determine *net* price changes over the one-year period. WAC and net price change per unit over the one-year period will be adjusted for percentage change in price across different dosing strengths for any drug, if applicable, taking into account the relative sales volume of the various dosing strengths.

Net price information will be obtained from SSR Health. 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 the average price in 2018 and 2019. If it is not possible to calculate a weighted average price (weighted by volume of sales at each price) using FSS, then the change in price from December 2018 to December 2019 will be used.

2.1.5. ICER will rank those drugs whose net price increases have had the largest impact on US spending over the prior year. To create this ranking, ICER will use calculations by SSR that dollarize the impact of net price changes year-on-year to give a representative rank-ordering of the size of the impact by product during 2019, driven by both size of the product (in terms of total net sales) and size of the net price impact.

2.1.6. ICER will contact the manufacturers of the top 15 drugs on the list to inform them that their drugs will potentially be reviewed as part of the UPI process. Manufacturers will have three weeks to contact ICER with any concerns about ICER's estimates of average price changes or budget impact. To dispute one of these estimates (other than concerns about a mathematical calculation error), manufacturers will need to provide ICER with corrected figures that ICER may publish as part of the UPI report.

2.1.7. After resolution of any concerns about estimates, the top 10 drugs remaining on the list will constitute the first part of the final list of drugs for which the evidence review will be undertaken. Drugs in positions 11 through 15 will not be included except as described in Section 2.2 below.

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 CPI
- Drugs whose price increases have important affordability implications for individual patients even if not for the health care system
- Drugs whose price increases raise concerns about the fairness of the price increases
- Drugs with net price increases that are found to be unreliable in available data sources but whose WAC price increases suggest review could be appropriate.

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 described in Section 2.1 to the extent that the data allow.

2.3. Final List

The lists from Sections 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 combined 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 evidence or analyses over the prior two years (beginning of 2018 through the end of 2019) that demonstrate improved clinical or economic outcomes compared with what was previously believed
- Older evidence that led to a new approved indication for the drug within the two-year timeframe
- New evidence or analyses relating to comparator therapies that the manufacturer believes indicate clinical advantages of their drug
- Other potential justifications for a price increase, including new information within the prior two years related to:
    - A large increase in costs of production
    - Large price savings attributable to the drug in other parts of the health care system
    - All other reasons deemed relevant by the manufacturers.

As noted below, at the time of 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 two years) 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 from randomized controlled trials (RCTs) over the prior two years on benefits and harms within these indications. However, if manufacturers have submitted evidence, ICER may choose not to perform a systematic review. ICER will not independently look for information other than from RCTs but will assess non-RCT information submitted by manufacturers. Submitted studies may include meta-analyses, economic models, and observational data. 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 relevant.

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

For the rating of new net 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. ICER will also consider evidence of economic benefits or harms.

For evidence that is rated as being of moderate or high quality, ICER will rate the new net benefit as none, small, or substantial using the usual ICER Evidence Rating Matrix.

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 be between what was previously generally believed about a therapy (whether its clinical or economic effects) and what new evidence or analyses have demonstrated. A new analysis (such as a meta-analysis) simply confirming what was previously believed or a new trial confirming the prior estimates of a drug's benefits will not result in substantial changes in what is believed about a therapy's effects (clinical or economic).

5. Designation of Drug Price Increases as "Unsupported"

Drugs found to have moderate/high quality new evidence or analyses of substantial improvement in benefit compared with what was previously believed will be categorized as having a "price increase with new evidence." Drugs that have no new evidence or analyses, or evidence or analyses that do not meet these criteria, will be categorized as having price increases "unsupported by new evidence." As described earlier, all manufacturer information submitted to justify the price increase will be provided as a component of this report, but any rationales that do not stem from new studies or new analyses will not be evaluated by ICER as a determinant in whether the drug is categorized as having its price increase unsupported by 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 evidence. Manufacturers will have four weeks to submit comments about their drug(s). These comments must be emailed as a Microsoft Word 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 report will include current net sales revenue, the change in list price (average list price for 2018 vs. 2019), and the change in net price (average net price for 2018 vs. 2019). 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. Key Changes in Process for 2020 UPI Report

In the first year of the UPI project, we correctly anticipated that there would be changes to the process both during and after the first year. Changes between the first and second year are primarily around three areas:

1) Changing the pricing lookback to one year rather than two in order to match the cadence of the annual release of a new UPI report. To align with this shortened timeframe for pricing analysis, the time window for relevant evidence has been changed from three years to two years.

2) Using the average price for a drug for a year rather than the fourth quarter price. This change was made to smooth out difficulties in measuring sales volume in a single quarter.

3) Expanding the types of studies that would be considered to provide new information. This change was made primarily to allow for certain meta-analyses and economic models, but more generally to consider any new information that alters prior beliefs about the clinical effectiveness or cost effectiveness of a therapy.

ICER continues to expect that situations may arise that were not fully anticipated in this protocol and recognizes that it may need to alter aspects of the review to maintain transparency and fairness to all parties. ICER again commits to flexibility within this second review and to transparency about any needed changes.

References

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