



Unsupported Price Increase Assessment

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

In 2019, with funding from Arnold Ventures, 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, drugmakers, and insurers.

Please see the figure below for an overview of the timeframe for the 2024 UPI report to be released later this year.

| Timeline for Report Year 2024 | |
|---|------------------------------|
| Top 15 Manufacturer Notification and Input Period | April 22 – May 13 |
| Manufacturer Input Phase I | May 31 – June 27 |
| Preliminary Individual Assessments to Manufacturers | September 26 |
| Manufacturer Input Phase II | September 26 – October 25 |
| Final Report Posted | December 11* |
| Data Review Periods | |
| Price Increase Period | 2022 – 2023 |
| Evidence Review Period | January 2022 – December 2023 |

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 currently 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 (at least eight months) 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 250 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 that exceed the medical Consumer Price Index (CPI) over a one-year period by more than 2%. 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. The date periods are described in the table above in Section 1.

2.1. Creating the List of Drugs with “Substantial” Price Increases

2.1.1. ICER will obtain a list of the 250 drugs with the largest net sales revenue in the US in the year prior to the Report Year. This information will come from SSR Health, 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 the one-year Main List Price Increase Period described in the table above. 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.

2.1.3. ICER will determine which of these drugs have had a WAC price increase over the one-year Main List Price Increase Period that exceeded the rate of medical CPI by more than 2%. This will be calculated as the difference between the average medical CPI at the beginning and end of the Main List Price Increase Period of interest using unadjusted rates (average CPI for starting year vs. average CPI for ending year); 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 the rate of medical CPI by more than 2% will be removed from further evaluation (that is, if medical CPI were 3%, WAC increase would need to be greater than 5%). 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 more than 2% above medical CPI, ICER will determine *net* price changes over the one-year Main List Price Increase 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, considering the relative sales volume of the various dosing strengths. Net price information will be obtained from SSR Health.

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 Health 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 the Main List Price Increase Period, 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. This information must include either:

- The effect of net price changes on change in revenue over the period in question

Or

- The average net prices and total volumes of sales for each of the two years in question.

2.1.7. After resolution of any concerns about estimates, ICER will remove from the list any therapy with an increase in budget impact due to increase in net price that is smaller than \$25 million.

2.1.8. 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 below position 10 will not be included except as described in Section 2.2 below.

2.1.9. If after notification to manufacturers of the selections for the top 15 drugs (manufacturers are only notified of their own drugs on the list), a manufacturer provides ICER with information as described in Section 2.1.6 that would have led to the drug's removal from the top 10 list had it been provided by the deadline, the drug will only be removed from evaluation if the effect of net price change on revenue over the period in question is not positive.

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 large numbers of Americans with WAC increases that did not quite exceed medical CPI plus 2%

- 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 or unavailable in data from SSR Health (such as drugs produced by companies that are not publicly traded) but whose WAC price increases suggest review could be appropriate
- Drugs with large increases in budget impact due to increases in net price even in the absence of increases in WAC.

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 Lists

The lists from Sections 2.1 and 2.2 will be reviewed as distinct lists in the report. ICER will not publicly announce these lists while the review is taking place, as we heard concerns from manufacturers that being on such a 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 lists and invite submission of this information within four weeks of notification. Importantly, 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:

- New evidence or analyses published or presented over the two-year Evidence Review Periods 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 Evidence Review Periods
- New evidence or analyses published or presented over the two-year Evidence Review Periods 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 two-year Evidence Review Periods, related to:
 - A large increase in costs of production
 - Large cost offsets or other 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 the 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. Additionally, if a manufacturer notes that a combination of indications that exceed 10% of overall utilization each individually have new evidence that could provide support for a price increase, ICER will take this into consideration in deciding which indications to review.

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) on benefits and harms within these indications published or presented during our Evidence Review Period. 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 RCT and non-RCT information published or presented during our Evidence Review Periods that is submitted by manufacturers. Submitted studies may include RCTs, 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. For therapies that are being evaluated in sequential report years, ICER will generally only review evidence that became available since the prior review. If evidence supported a finding of a price increase with new evidence in the prior review, it will generally not be considered even if it falls within the two-year timeframe.

An exception to this can occur if ICER determines that more than one item of evidence was found in the prior review that would have supported a finding of a price increase with new evidence and the items addressed completely distinct aspects of the therapy, such as demonstrating new evidence for different indications for that therapy. Under these circumstances, ICER may consider evidence that was available during the prior review period.

4.1.4. 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 [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 substantially change what is believed about a therapy's effects (clinical or economic).

In the event that a drug was approved under the FDA Accelerated Approval pathway, ICER will consider new evidence that narrows uncertainty or confirms that a surrogate outcome predicted a patient-important outcome even if this evidence does not substantially alter prior beliefs.

Manufacturers and others can refer to ICER's responses to comments in [Appendix K of the 2020 UPI report](#) for examples of reasons why submitted evidence was viewed as not leading to ratings of "with new evidence."

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.

In the unusual circumstance that multiple indications of a drug that, in aggregate, exceed 10% of utilization despite no one of the indications exceeding 10% utilization, and where every one of the indications individually has moderate- or high-quality evidence of a substantial new benefit compared with what was previously believed, ICER will consider this to be a price increase with new 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.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 250 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 List Price Increase Period), and the change in net price (average net price for List Price Increase 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 medical CPI by more than 2%; 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 250 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 2024 UPI Report

Changes for the 2024 UPI report include:

1. Section 4.1.3 now describes an exception to the general rule that, for therapies that are being evaluated in sequential report years, ICER will only review evidence that became available since the prior review.
2. The mechanism for selecting up to three additional drugs, described in section 2.2, has reverted to the method used prior to 2022.

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 review and to transparency about any needed changes.

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