California 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.

As a complement to the National UPI Report, ICER has received funding from the California Health Care Foundation to produce a state-specific report for California. In 2017, California passed SB-17, a drug transparency law requiring manufacturers to report increases to prescription drugs' wholesale acquisition cost (WAC).[2] ICER will leverage the annual SB-17 reports on brand and specialty drugs with the most significant year-over-year spending increases to evaluate whether there is new evidence that could justify the price increase. Because the SB-17 reports are published approximately 11 months after the time period they highlight, the California UPI Report will be published *after* the National UPI Report that examines the same period of price increases. By highlighting which of the top drugs with spending increases and substantial price increases lack supporting new clinical evidence, ICER will help the state of California identify specific drugs for further scrutiny and potential action.

Please see the figure below for an overview of the timeframe for the 2022 California UPI report:

Milestone	Date/Timeframe
SB-17 Prescription Drug Cost Transparency Report	2020
SB-17 Review Period	2019 – 2020
Evidence Review Period	January 2019 – December 2020
Manufacturer Notification and Initial Input Period	March 22 – April 12, 2022
Manufacturer Input Phase I	April 18 – May 16, 2022
Preliminary Individual Assessments to Manufacturers	August 18, 2022
Manufacturer Input Phase II	August 18 – September 15, 2022
Final Report Posted	October 20, 2022

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 (at least eight months) provide information in a useful timeframe for the public and policymakers. Therefore, both the National and the California 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.

2. List of Drugs to Review

As described in greater detail below, the process for ICER's review will start with two publicly available lists of drugs with the highest year-over-year increase in total spending in California: 1) the top 25 specialty drugs; and 2) the top 25 branded drugs. From these lists, the next step will be to eliminate drugs that appear to have had net price year-over-year increases that are less than 2% more than the medical Consumer Price Index (CPI). We will then rank drugs by the year-over-year absolute increase in spending in California and select up to five drugs from each list. If there are fewer than five drugs on one list, additional drugs will be selected from the other list, up to a maximum of 10 drugs for review. Further details on the process are provided below.

2.1. Creating the List of Drugs with Price Increases

2.1.1. ICER will use the lists from California of the 25 specialty drugs and the 25 branded drugs with the highest year-over-year increase in total spending in California for the years of the SB-17 Review Period.

2.1.2. ICER will examine information from SSR Health, LLC, an independent investment research firm, to examine net price increases and will eliminate any drugs that had an average year-over-year **national** net price increase that is less than 2% more than the medical CPI. Because of reporting, the exact dates of net 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).[4] 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.

2.1.3. If data from SSR Health on net price changes for a given drug are unavailable or are positive but felt to be unreliable based on information from SSR Health, the therapy will not be removed from the list at this stage. See Sections 2.1.5 and 2.1.6 for how a therapy may be removed from the list after correspondence with the manufacturer.

2.1.4. ICER will rank drugs that remain on each list by the absolute increase in year-over-year spending in California. ICER will then create a combined list of drugs for review with a goal of reviewing the top five drugs from each list. If there are fewer than five drugs remaining on one list, additional drugs will be added from the other list if available up to a maximum of 10 drugs.

2.1.5. ICER will contact the manufacturers of the 10 (or fewer) drugs on the combined final list to inform them that their drugs will potentially be reviewed as part of the California UPI process. Manufacturers will have three weeks to contact ICER with any concerns about ICER's estimates of average national net price changes. To dispute one of these estimates (other than concerns about a mathematical calculation error), manufacturers will need to provide ICER with a corrected change in national year-over-year average net price that ICER may publish as part of the California UPI report.

2.1.6. If a manufacturer provides evidence of a year-over-year average net price change that is less than medical CPI plus 2%, the drug will be removed from the review list.

2.1.7. As noted above, the National UPI Report will have been completed for the same timeframe prior to completion of the California UPI Report. Drugs that are on the California list that were previously reviewed for the same timeframe as part of the National UPI Report will not go through the process described below; the California UPI Report will re-publish the information from the National UPI Report for that drug.

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 (or fewer) drugs on the California combined list 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 assessment 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 Period 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 Period
- New evidence or analyses published or presented over the two-year Evidence Review Period 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 Period, 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 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.

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 Period 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 only review evidence that became available since the prior California review if one was performed. If evidence supported a finding of a price increase with new evidence in the prior review, it will not be considered even if it falls within the two-year 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.[5] 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 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 N of the 2021 National 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 event that a drug has an uncertain change in net price and the average WAC price did not increase between the two years of the SB-17 Report Period, the drug will be reported as having "increased spending with net price change uncertain; any net price increase with new evidence" or "increased spending with net price change uncertain; any net price increase unsupported by 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. California 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.

7.1.2. For the 10 (or fewer) drugs that comprise the final combined list, the Report will include national pricing estimates of current net sales revenue (e.g., 2020), the change in list price (e.g., average list price for 2020 vs. 2019), and, if known, the change in net price (e.g., average net price for 2020 vs. 2019). It will also include a description for each drug of how the figures led sequentially from 1) California lists of highest year-over-year increases in spending on specialty drugs and branded drugs; 2) changes in net price not less than medical CPI plus 2%; 3) largest increases in California year-over-year absolute spending. This will show how the drug list was culled from the original 50 drugs to 10 (or fewer) reviewed drugs.

The Report will present the reviews/categorizations of up to 10 drugs. As noted earlier, manufacturer comments will be published along with ICER's responses to those comments as an appendix.

8. Key Differences from the 2021 National UPI Report Protocol

Differences from the National UPI Report Protocol:

1) List begins with the California SB-17 Report
2) Drugs are only removed from consideration based on net price
3) If SSR Health does not feel they have reliable information on net price, the drug will only be removed from consideration if the manufacturer submits information on net price to ICER.

ICER expects 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 commits to flexibility within this review and to transparency about any needed changes.

References

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3. Prescription Drug Transparency - Act 165 & 193 [press release]. gmcboard.vermont.gov2016.
4. US Bureau of Labor Statistics. Measuring Price Change in the CPI: Medical care. https://www.bls.gov/cpi/factsheets/medical-care.htm. Published 2022. Updated 2/7/22. Accessed 3/14/22, 2022.
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