The Institute for Clinical and Economic Review's Use of FDA Approval Volume to Calculate Budget Impact Thresholds:
A Scenario Analysis

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Executive Summary

- The Institute for Clinical and Economic Review (ICER) is one of several organizations that analyzes evidence and assesses the value of medical interventions.
- One of the primary inputs that ICER uses to calculate and establish the budget impact threshold is the average number of new drugs approved by the U.S. Food and Drug Administration (FDA) per year, a metric that can vary materially on a year-to-year basis.
- ICER estimates a range of patient access scenarios based on the calculation of a short-term budget impact threshold. To assist stakeholders in determining if access should be managed more closely, ICER estimates the percentage of patients that could be treated by a new medicine within that pre-specified budget threshold.
- Avalere's analysis finds that because the number of FDA drug approvals can vary dramatically, ICER's reliance on the number of FDA drug approvals can lead to substantial and unpredictable variability in the budget impact threshold, which limits its reliability as a benchmark for affordability.
  - For example, utilizing the lowest, average, and highest yearly number of FDA approvals during a 20-year period results in budget impact thresholds of $1.81 billion, $1.18 billion, and $684 million, respectively, in comparison to ICER's threshold which has ranged from $904 million to $991 million.
- Payers frequently consider estimates of short-term budget impact to manage their costs. The variation in ICER budget thresholds based on an unpredictable, retrospective factor (FDA drug approvals in prior years) makes it more difficult for it to be used reliably by payers seeking to manage current-year budgets. Because payer decisions about whether, and how, to deploy utilization management techniques to manage costs are informed by these estimates, it is important for them to be as accurate and reliable as possible. Like all approaches that use a variety of data inputs, these tools have significant contextual limitations, and stakeholders wishing to rely on them may wish to carefully interpret conclusions in order to understand both their strengths and limitations.

Introduction

Over the past few decades, advances in health technologies have reduced rates of morbidity and mortality, while improving patients' quality of life. However, this steady stream of innovation has been accompanied by increased costs across the healthcare spectrum. In response to concerns about rising costs, an emphasis has been placed on ensuring healthcare budgets are spent efficiently, particularly as payers' short-term budgets are often limited. Simultaneously, value frameworks have emerged as tools to assess the benefits and affordability implications of healthcare products or services, providing stakeholders with an approach to understand and compare the value of healthcare interventions.

> "Public payer health budgets tend to be fixed in the short run and the primary aim is to maximize population health gain, subject to other modifiers, such as equity considerations"[i]
>
> - ISPOR Special Task Force

The value framework developed by the Institute for Clinical and Economic Review (ICER) includes an assessment of cost-effectiveness and short-term affordability of medical interventions. The short-term affordability of a product or service is estimated by employing a budget impact model to compare payers' costs associated with coverage and reimbursement against an internally-developed cost threshold. Over the last 3 years, ICER has revised its budget impact threshold, which has increased from $904 million to $915 million to a current value $991 million. This new ICER threshold reflects updates in number of FDA approvals, as well as US gross domestic product (GDP), total healthcare spending, and contribution of drugs to total healthcare spending. In addition, in its assessments, ICER calculates the percentage of patients that could be treated in a given year without crossing its budget impact threshold in place at the time of evidence report release.

In response to concern about the growth of the percentage of health resources allocated to drugs relative to the growth of the national economy, ICER also includes an "affordability and access alert" as a part of its value assessments if estimated utilization is "likely to exceed the budget impact threshold without active intervention by insurers and others to limit access to treatment."[ii] Although ICER's short-term budget impact analysis is reflective of payer concerns about short-term budget management, other stakeholders have voiced concerns that its methodology may rely on flawed assumptions that can cause an alert to be triggered without warrant.[iii,iv,v]

A number of key inputs inform the calculation of ICER's budget impact threshold. This paper examines the impact of ICER's reliance on the volume of new drug approvals to calculate its budget impact threshold to how significantly it affects the threshold and, if so, whether the effect is predictable. It does not examine other potential issues with ICER's method of calculating a budget threshold, such as whether the quality as well as the size of the population eligible for using the approved medications should be considered, or whether budget thresholds should

hold the value of health spending constant on current items and services (e.g., societal preference for maintaining affordability by restricting access to a new and potentially high-value technology vs. by reducing spending on existing, lower-value services).

ICER's Reliance on Average New Drug Approvals in Examining Short-Term Affordability

To calculate its budget impact threshold, ICER examines the US GDP, total healthcare spending, contribution of drug spending to total healthcare spending, and the number of new drugs approved by the FDA each year. Because the number of FDA approvals can vary widely by year, ICER's estimated budget impact thresholds can also be highly variable. ICER has updated its budget impact threshold calculations over time to incorporate the most recent estimates of US GDP, total healthcare spending, and contribution of drugs to total healthcare spending.

"The point is that when we look at healthcare, we should be assessing it the way we do education, which means thinking about the long-run returns. Thus, a singular focus on the immediate budget impact misses the point of why we consume health services"[vi]

- Dana Goldman, Director, USC Leonard D. Schaeffer Center for Health Policy & Economics

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Given the significant variability in FDA approvals over the past two decades (Figure 1), we set out to illustrate the impact of medications entering the market during periods of high, average, and low pharmaceutical approvals on ICER's budget impact thresholds. Specifically, we aimed to:

- Replicate ICER's approach for calculating the budget impact threshold and its impact on patient access for select ICER reports utilizing FDA approval data from the prior 20 years; and
- Compare these recalculations to the original ICER budget impact thresholds to illustrate the potential for arriving at different conclusions solely based on the year a drug is approved.

Methods

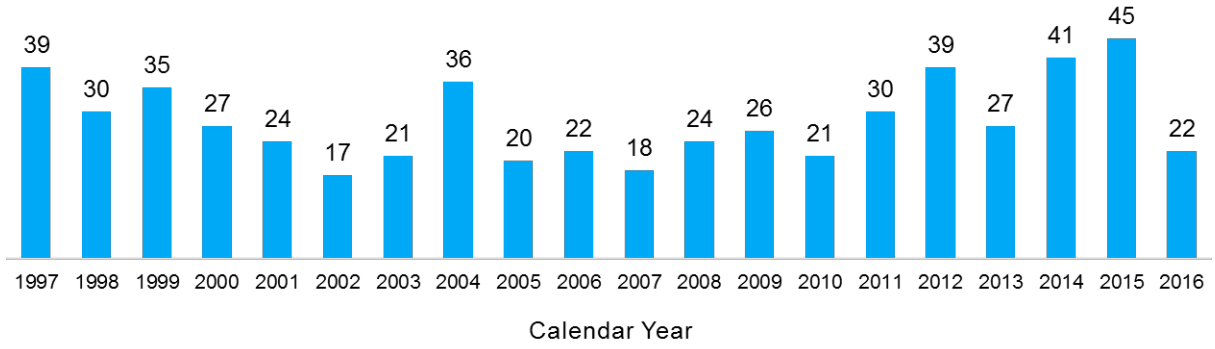
We selected 5 ICER reports, based on the clinical significance of the medications, the timing of their release, and other factors such as disease areas and media attention received since their publication, including:

- High Cholesterol (2015):[vii] PCSK9 Inhibitors
- Non-Small Cell Lung Cancer (NSCLC), (2016):[viii] Nivolumab, Pembrolizumab, Atezolizumab
- Asthma (2016): [ix] Mepolizumab
- Psoriasis (2016): [x] Ixekizumab, Brodalumab
- Multiple Sclerosis (2017): [xi] Daclizumab

FDA approval data from the past 20 years were used to recalculate the annual budget impact threshold through a series of scenario analyses.[xii] More specifically, we replaced the actual

number of newly approved drugs (**Appendix, Tables A and B, Row 6**) with the number of approvals from an alternate year between 1997 – 2016 (**Figure 1**) to examine how the year of product launch may impact the budget impact threshold for that year.[1] Patient access under multiple FDA approval scenarios was calculated by multiplying the ICER-derived patient access levels (percentages published in each report) by the recalculated budget impact threshold (in dollars) and dividing by the ICER budget impact threshold (in dollars) that was in place at the time of evidence report release.[2] The threshold referenced in ICER's high cholesterol, NSCLC, asthma, and psoriasis reports was $904 million, while in its multiple sclerosis report, ICER used $915 million.

Figure 1: Distribution of Annual FDA Approvals (1997 – 2016)



Results

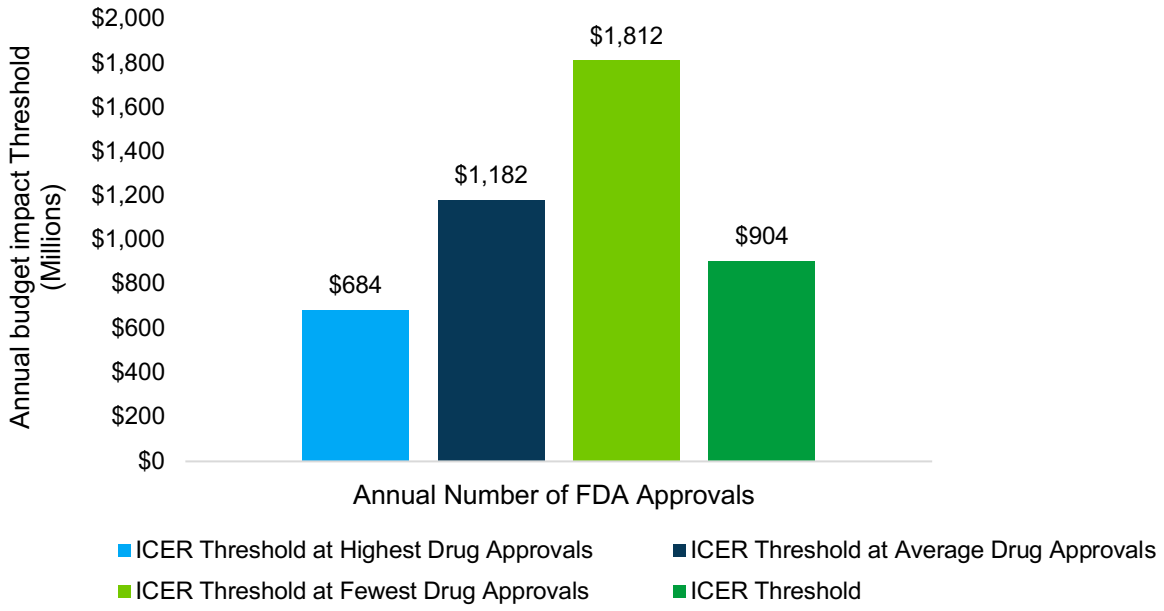
Utilizing the lowest, average, and highest annual number of FDA approvals led to recalculated budget impact thresholds of $1.81 billion, $1.18 billion, and $684 million, respectively (**Figure 2**). When the budget impact threshold is calculated based on the number of approvals in 2002 (the year with the fewest new drug approvals in the 20-year study period), the budget impact

1 We also recalculated the budget threshold using the average number of approvals in 10 2-year periods and 4 5-year periods. The threshold costs from each of these scenario analyses were compared to the ICER threshold value used in the report to capture any changes in magnitude and/or directionality due to market entry timing alone. Finally, the annual budget impact of each product was abstracted from the reports and compared with the original and recalculated annual budget impact thresholds.

2 While ICER's stated budget threshold for 2018-2019 is $991 million, reports released over the last several years use $904 million or $915 million. Avalere's calculation is relative to the threshold used in the report at the time of release.

threshold is nearly 2 times the $904 million budget impact threshold used in the 2015-2016 ICER reports analyzed.[2]

Figure 2: Recalculated Budget Impact Thresholds by Annual Number of FDA Approvals



When the threshold was adjusted to reflect the year with the highest number of approvals (resulting in the lowest budget impact threshold), Avalere's analysis found there was a commensurate drop in the percentage of patients that could be treated with each drug using ICER's budget impact threshold calculation. Conversely, ICER would have calculated increased patient access if the threshold was adjusted to reflect the year of fewest approvals (resulting in the highest budget impact threshold). Therefore, patient access to effective treatments could change significantly under ICER's model solely by virtue of the year in which the drug was approved.

To smooth variability in FDA approvals, ICER may use an average of multiple years. To reflect this approach, we also calculated thresholds using the average number of drugs approved over a 2- and 5-year time period. While these recalculated thresholds varied from the yearly approval-based thresholds, the directionality remained consistent – **as number of FDA approvals falls, the percent of patients that can be treated while remaining under ICER's budget impact threshold rises.**

3 Similar to the yearly scenario, the recalculated thresholds based on highest, average, and fewest 2-year approval data were approximately $887 million, $1.1 billion, and $1.5 billion respectively. The recalculated thresholds based on highest, average, and fewest five-year approval data were $879 million, $1.1 billion, and $1.3 billion respectively.

Highlights from our replications of ICER's calculations under various FDA approval scenarios are noted below for NSCLC, plaque psoriasis, and asthma:

- During years in which fewer drugs were approved, ICER would have estimated 94% - 100% of patients could be treated for NSCLC without triggering a budget alert, compared to 47% - 98% under ICER's threshold at the time of report release (**Figure 3**). In comparison, during years of high drug approvals, because of the lower budget impact threshold, 40% of patients or fewer could access either pembrolizumab or nivolumab for NSCLC.
- In plaque psoriasis, ICER would have estimated almost 50% of patients with plaque psoriasis could gain access to either ixekizumab or brodalumab in years of lowest drug approvals. In years of high drug approvals, fewer than 30% of patients could be treated before an affordability alert is triggered **(Figure 4).**
- ICER's mepolizumab patient access estimates vary between 11% - 30% in severe eosinophilic asthma depending on year of drug approval (**Figure 5**).

ICER's calculations for multiple sclerosis and high cholesterol were also replicated under these scenarios and demonstrate a similar relationship (**Appendix, Figures A-B**).

Figure 3: Patient Access Estimates to Non-Small Cell Lung Cancer Treatments Derived from ICER's Budget Impact Threshold Methodology

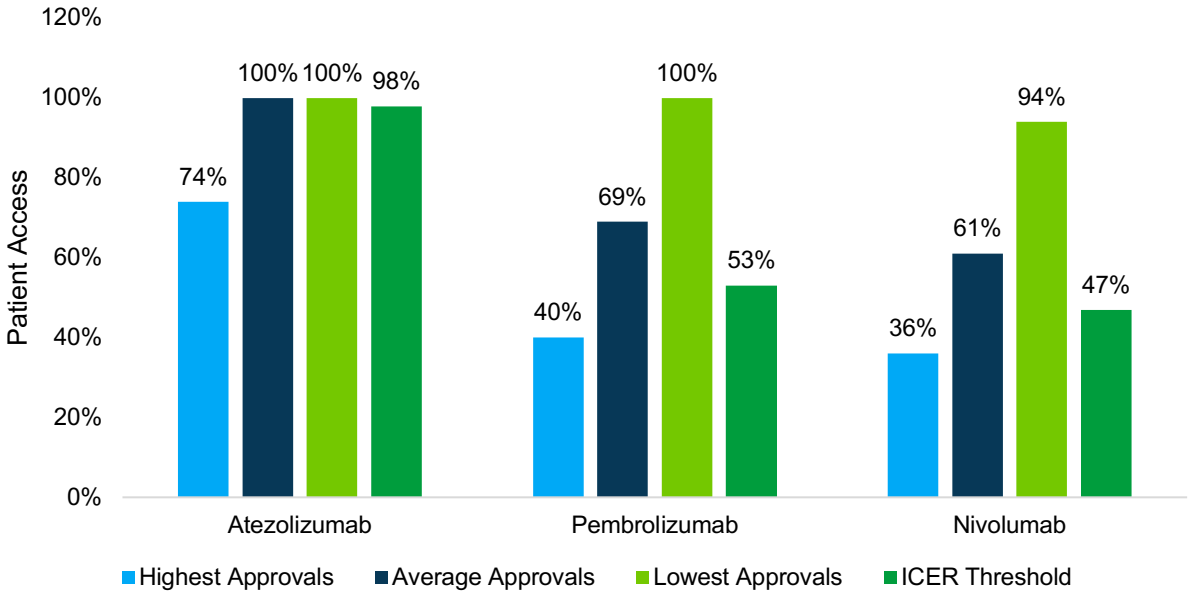


Figure 4: Patient Access Estimates to Plaque Psoriasis Treatments Derived from ICER's Budget Impact Threshold Methodology

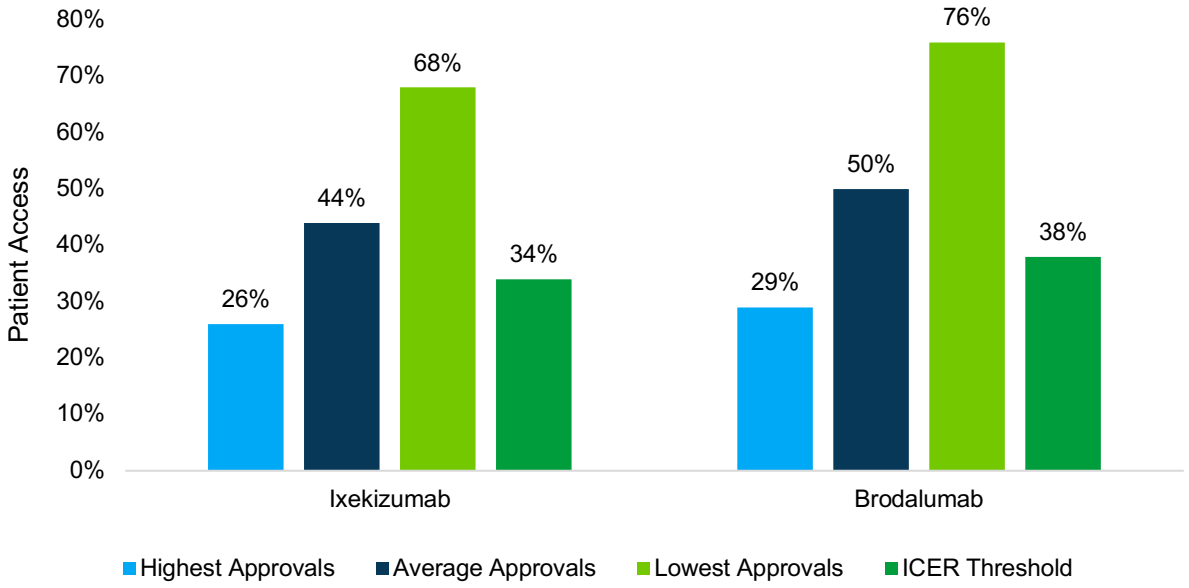
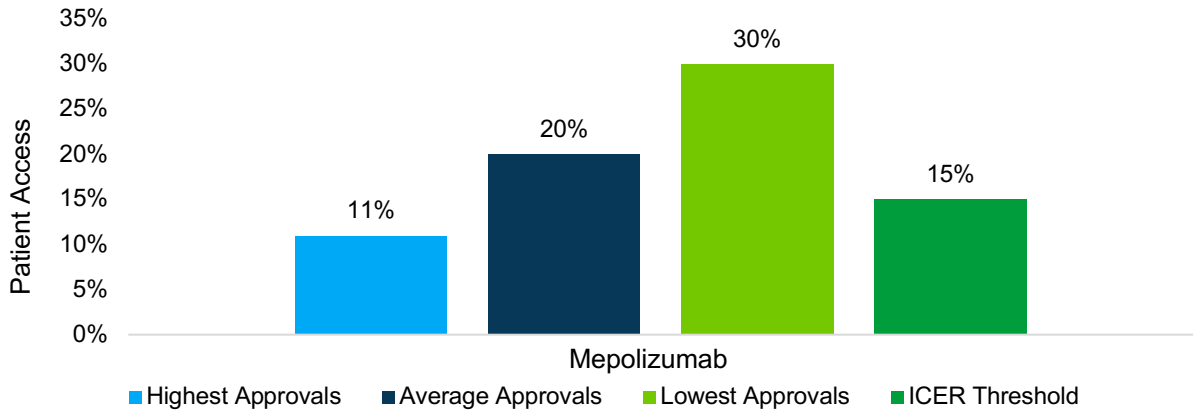


Figure 5: Patient Access Estimates to Severe Eosinophilic Asthma Treatment Derived from ICER's Budget Impact Threshold Methodology



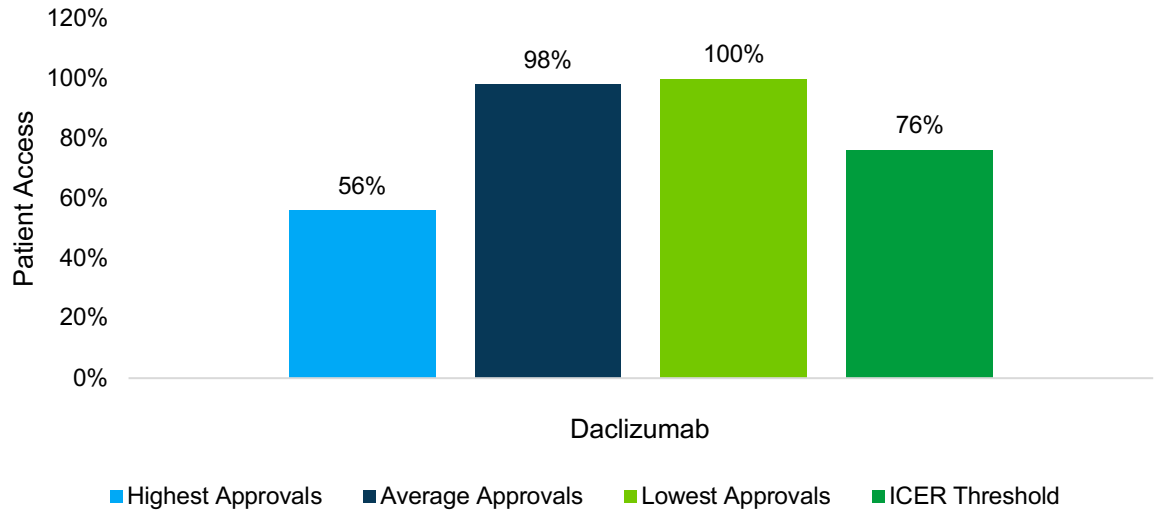
Discussion

An overarching theme emerged from our analysis of ICER's budget impact thresholds in recent reports: the number of FDA drug approvals impacts the budget impact threshold considerably. Adjusting the budget impact thresholds based on historical FDA approval data leads to considerable variation in how ICER would estimate the percentage of patients that could be treated at wholesale acquisition cost (WAC) pricing while remaining under the budget impact threshold. If the budget impact thresholds are based on the year of highest drug approvals (i.e., 2015), the percent of patients that ICER would estimate could access the drugs at WAC is reduced significantly and would trigger an "affordability alert" for a majority of the drugs evaluated in this study. However, if the budget thresholds are based on the year of the fewest drug approvals (i.e., 2002), the percent of patients that could access the drugs at WAC prices almost doubles.

In sum, under the ICER methodology, the year in which a product is approved determines the budget threshold that will be applied to it, and these thresholds vary significantly from year to year. As a result, the year in which a drug is approved plays an important role in determining whether ICER's "budget alarm" will be triggered and the percentage of patients that ICER estimates can gain access before restrictions would need to be applied. This wide and arbitrary variation in ICER's budget threshold may limit its reliability as a benchmark. Stakeholders relying on ICER's conclusions may wish to appropriately contextualize their interpretations to ensure that decisions impacting patient access to medications result from methodologically sound approaches.

Appendix

Figure A: Patient Access Estimates to Multiple Sclerosis Treatment Derived from ICER's Budget Impact Threshold Methodology*



*Note: For multiple sclerosis, ICER used $915 million budget impact threshold to calculate patient access. ICER has since updated its threshold to $991 million.

Figure B: Patient Access Estimates to High Cholesterol Treatments Derived from ICER's Budget Impact Threshold Methodology

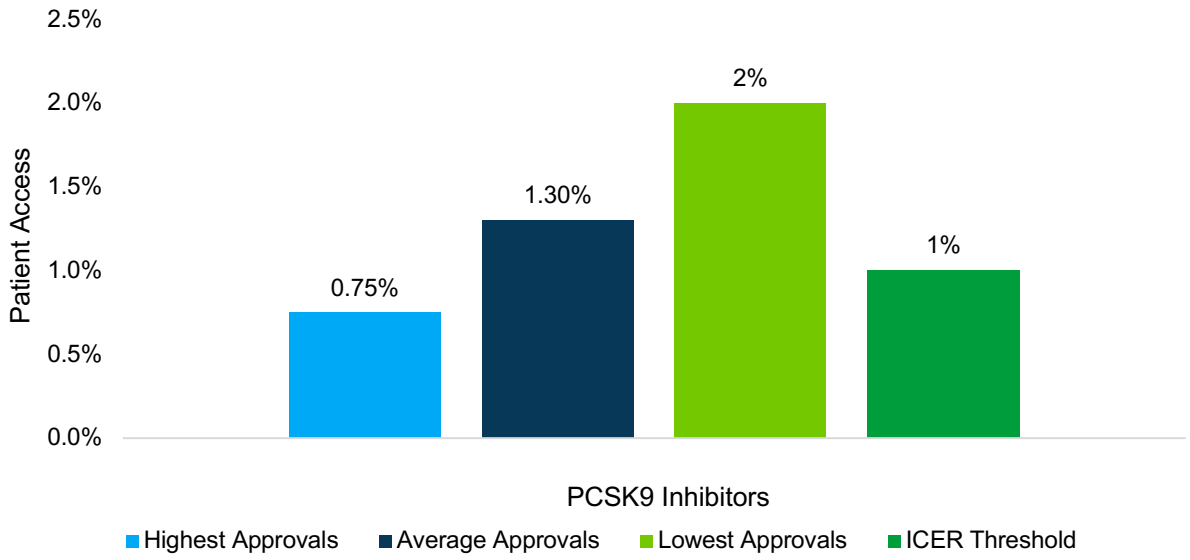


Table A: ICER's 2015 Budget Impact Threshold Calculation

Item	Parameter	Estimate
1	Growth in US GDP + 1% (2015-2016)	3.75%
2	Total healthcare spending	$3.08 trillion
3	Contribution of drug spending to total healthcare spending (%)	13%
4	Contribution of drug spending to total healthcare spending (row 2 x row 3)	$410 billion
5	Annual threshold for net healthcare cost growth for ALL new drugs (row 1 x row 4)	$15.4 billion
6	**Average annual number of new molecular entities (2-year average)**	**34**
7	Annual threshold for average cost growth per individual new molecular entity (row 5/row 6)	$452 million
8	Annual threshold for estimated potential budget impact for each individual new molecular entity (doubling of row 7)	$904 million

Table B: ICER's 2017 Budget Impact Threshold Calculation

Item	Parameter	Estimate
1	Growth in US GDP + 1% (2015-2016)	3.0%
2	Total healthcare spending	$2.71 trillion
3	Contribution of drug spending to total healthcare spending (%)	17.7%
4	Contribution of drug spending to total healthcare spending (row 2 x row 3)	$479 billion
5	Annual threshold for net healthcare cost growth for ALL new drugs (row 1 x row 4)	$15.3 billion
6	**Average annual number of new molecular entities (2-year average)**	**33.5**
7	Annual threshold for average cost growth per individual new molecular entity (row 5/row 6)	$457.5 million
8	Annual threshold for estimated potential budget impact for each individual new molecular entity (doubling of row 7)	$915 million

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