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Prescription Drug Affordability Boards: Considerations to Ensure Patient Access

Overview

Prescription Drug Affordability Boards (PDABs) have been enacted by several states with an overarching goal of lowering the cost of prescription drugs. In 2024, the National Academy for State Health Policy (NASHP), in partnership with the Program On Regulation, Therapeutics, And Law (PORTAL), developed a toolkit with resources for states to use to effectively implement PDABs.[1]

The memos and white papers included in the toolkit describe several options available for state PDABs to select drugs for affordability review, determine therapeutic alternatives, establish processes for drug affordability reviews, and develop methodology for setting upper payment limits (UPLs). PORTAL's guidance differs significantly from the payer approach to drug affordability management and may overlook clinically relevant differences between available therapeutic options (eg, safety profile, variations in patient response, impact on healthcare resource utilization, and costs). The options provided present significant implications related to both patient access and clinical outcomes.

Key Concerns With PORTAL's Guidance in the NASHP Toolkit

Concern	Potential Implications for Access
Overly broad approach to identifying and defining a "drug" for affordability review—specifically, treating products with different formulations, strengths, indications, and/or modes of administration as equivalent	Not recognizing meaningful differences may: • Inflate a drug's cost estimate • Diminish incentives for ongoing research that supports expanded use or new indications • Lead to fewer treatment options for patients over time
Inappropriate use of clinical practice guidelines and ongoing or unpublished studies to identify therapeutic alternatives	Relying on premature evidence and/or considering inappropriate products to be therapeutic alternatives may: • Jeopardize access to products that are the standard of care for specific patient populations, such as those in advanced disease state or pediatric patients
Combined clinical and economic review	Combining both reviews may lead to: • Overweighting cost and budgetary impacts (that may be inaccurate due to lack of data on net price and actual out-of-pocket [OOP] costs) • Overlooking other costs such as informal caregiving or hospitalization • Proliferation of problematic "shortcut" like the cost-per-quality-adjusted life year (QALY) that is widely considered to be discriminatory

Potential Implications of Setting UPLs on Drugs With a Negative Affordability Review

- Fewer treatment options available for patients can lead to poor adherence/persistence, worse clinical outcomes, and increased healthcare costs
- Disincentive for manufacturers to research additional clinical uses or improve formulations of drugs

Drug Selection for Affordability Review

PORTAL's memo *Identifying Drugs for Affordability Review*[2] provides guidance on how drugs included for selection are defined. To ensure flexibility, PORTAL recommends maintaining a broad definition of a drug and suggests aggregating at an active moiety[3] level as an alternative to using National Drug Codes (NDCs). While this method aligns with Centers for Medicare & Medicaid Services' (CMS') approach to the Medicare Maximum Fair Price (MFP), the impacts of this broad aggregation have not yet been validated. In addition, this recommendation differs from the approach payers take in formulary management of drugs, which is generally to aggregate at the level of the clinical formulation or drug strength using commercial databases (eg, First DataBank, Medi-Span).

The PORTAL memo details various limitations of this approach to aggregate by active moiety, including the potential to "overlook clinically meaningful differences," such as different clinical uses and dosage forms.[2] Exemplifying this distinction, in January 2024, the state of Oregon reviewed the affordability of Humulin® R U-500 KwikPen®.[4] Had Oregon's PDAB elected to review at the active moiety level, all other forms of regular insulin (inhaled, Novolin® R and Humulin R® U-100 vials and pens) would have been included.[5,6] Humulin R U-500 is 5 times more concentrated than other U-100 insulins, and is specifically indicated for individuals who are insulin resistant and require larger doses of insulin.[7] In addition, the pen device may help individuals with disabilities who cannot manipulate a vial and syringe, and was developed and patented to address potential medication errors.[7] Of note, after completing the review of Humulin R U-500 KwikPen and determining that it may present affordability challenges for healthcare systems or high OOP costs for patients,[8] Oregon's PDAB voted to pause any further affordability reviews to "improve both the criteria and methods used to assess and select drugs for potential affordability reviews in 2025, using a refreshed data set."[9]

Potential Implications of Broad Aggregation for Drug Selection

Aggregating by active moiety increases the breadth of products reviewed, potentially including drugs that do not meet statutory criteria. For example, the state of Washington's authority to review drugs is limited to those that have been on the market for at least 7 years.[10] Using this method could include newer-to-market formulations or delivery mechanisms that may or may not carry different clinical indications and must not be included per state law.

Different formulations and delivery mechanisms are developed to address specific patient needs to achieve identified therapeutic goals. The failure to recognize clinical differences of various formulations and strengths and aggregating too broadly by active moiety can lead to an unfavorable affordability decision and potential UPL setting. This could affect patient access, adherence, safety, and disease management outcomes. In addition, this could undermine innovation, as it disincentivizes manufacturers to research additional clinical uses and to develop improved formulations or delivery methods that may result in better clinical outcomes and a lower total cost of care. Similarly, these concerns related to aggregation across different formulations and strengths were raised in CMS' drug selection for price setting under the Inflation Reduction Act (IRA).[11]

Therapeutic Alternative Determination

PORTAL promotes the use of clinical practice guidelines for identification and selection of therapeutic alternatives and suggests supplementing guidelines with tertiary references and ongoing studies. These practices directly conflict with the approach payers take when considering therapeutic alternatives. While payers' coverage and reimbursement of therapeutic alternatives may be informed by clinical practice guidelines and ongoing or unpublished clinical trials, identification of such treatments is typically based on pharmacologic class and therapeutic use following US Food and Drug Administration (FDA)-approved indications.

Therapeutic Alternative Determination (cont)

Identifying Therapeutic Alternatives Using Clinical Practice Guidelines and Ongoing or Unpublished Clinical Trials

The PORTAL recommendation to utilize clinical practice guidelines fails to recognize that clinical practice guidelines are not written for the purpose of identifying therapeutic alternatives for specific products, but instead to summarize evidence and provide recommendations regarding use and sequencing of therapeutic options. PORTAL's recommended approach introduces several challenges, including determining which guidelines to consider, variability and extent of guidelines depending on disease area, PDAB variability in interpretation of the recommendations and consideration of individual patient characteristics, PDAB expertise in clinical management, potential bias of the guideline authors, missing information, and currency of the included evidence and recommendations (eg, new to market drugs are often not included). For example, when conducting an affordability review of Trikafta®, Colorado's PDAB used guidelines to identify therapeutic alternatives, but later determined the alternatives were not appropriate due to FDA-approved indications covering specific subpopulations.[12]

Use of ongoing or unpublished (ie, not peer-reviewed) clinical trials on the National Institutes of Health's ClinicalTrials.gov is also problematic, as the therapies under evaluation may not ultimately be approved by the FDA or may not be FDA-approved for the use in question. Additionally, sufficient evidence to support off-label utilization may not be available. The populations and indications approved by the FDA should be at the core of therapeutic alternative identification. For example, Maryland's PDAB identified Dupixent® for affordability review. This product currently has 6 FDA-approved indications. The PDAB identified a list of therapeutic alternatives that were not specific for the different indications. They did not address that Dupixent has pediatric indications, and the alternatives selected are only FDA-approved for adults or older children. In addition, Protopic® was identified as a therapeutic alternative,[13] which is not clinically appropriate because Protopic is a topical prescription therapy for atopic dermatitis, and Dupixent is indicated for atopic dermatitis when not controlled on topical prescription therapies or when those therapies are not advisable.[14]

Therapeutic Alternatives and Off-Label Use

Payers may consider off-label uses of medications as therapeutic alternatives if they meet the benefit definition of medical necessity and have significant supporting evidence meeting evidentiary standards. Off-label uses should not be considered therapeutic alternatives unless there is robust supporting evidence, generally per CMS-recognized drug compendia establishing the use of a treatment as standard of care. Under the IRA's Medicare Drug Price Negotiation Program, CMS identifies therapeutic alternatives based on "clinical appropriateness and consideration of various sources of evidence, including clinical guidelines, peer-reviewed literature, drug compendia, and data submitted by manufacturers."[15] While this may include off-label therapeutic alternatives, CMS provides manufacturers with the opportunity to discuss any disagreements with their selected alternatives and may proactively seek consultation with various groups (eg, healthcare providers, patients or patient organizations, academic experts) to ensure appropriate selection.[15]

State Differences in Approach to Identifying Therapeutic Alternatives

Identification of therapeutic alternatives varies significantly between state PDABs. Some PDABs include all treatment options for a specific condition, while others limit review to pharmacologic class. For example, Maryland's PDAB identified Jardiance® for affordability review and determined its therapeutic alternatives broadly as SGLT2 inhibitors, DPP-4 inhibitors, GLP-1 agonists, metformin, various combination products, and insulin.[16] While the rationale for this selection of therapeutic alternatives was not detailed, these are all options for treatment of type 2 diabetes included in clinical practice guidelines; however, certain drug classes may be more appropriate for some subpopulations than others. For example, the American Diabetes Association recommends the use of drugs in specific pharmacologic classes that have proven benefits in individuals with certain comorbidities (eg, heart failure, chronic kidney disease).[17] Failure to take such considerations and patient needs into account when selecting therapeutic alternatives may lead to negative or suboptimal patient clinical outcomes.

While PDAB members are typically individuals with clinical backgrounds and PDABs may consider input from stakeholders, such as practicing providers, there may be a lack of specific clinical expertise related to the condition(s) treated by a product under review. Increased transparency and engagement with both patients and practicing clinician experts, with prescribing experience related to the treatments in question, should be considered when selecting therapeutic alternatives and conducting the affordability review. Payers frequently consult with specialists employed by their organization or practicing in a community context while conducting their clinical assessment and developing coverage policies.

Therapeutic Alternative Determination (cont)

State Differences in Approach to Identifying Therapeutic Alternatives (cont)

In addition, there are reported instances of PDABs reviewing multiple drugs that are considered therapeutic alternatives to one another. Should a review determine that multiple drugs used to treat the same condition are unaffordable, several resulting UPLs created within a therapeutic class could significantly impact available treatment options. For example, Colorado's PDAB identified Stelara®, Cosentyx®, and Enbrel® for affordability review, and it was determined that all 3 products were unaffordable.[18-20] While only Stelara and Cosentyx were considered therapeutic alternatives to each other, Enbrel had some overlapping indications (eg, psoriatic arthritis, ankylosing spondylitis).

Potential Implications of Inappropriate Therapeutic Alternative Selection

The determination of therapeutic alternatives is a critical step prior to the affordability review of a selected drug, as it will drive clinical and economic comparisons. Relying primarily on clinical practice guidelines and ongoing or unpublished clinical trials rather than defining therapeutic alternatives based on FDA approval in matched indications and populations and actively engaging clinical experts to validate can lead to an unfavorable affordability decision based on clinically inaccurate comparisons. Evaluation of multiple drugs that are used for the treatment of the same condition could result in several therapeutic options within a class that have a UPL, significantly limiting treatment options for patients. This may result in worse clinical outcomes and lead to increases in other healthcare costs.

Affordability Reviews and Setting Upper Payment Limits

PDABs are established with the aim of lowering the cost of prescription drugs. To achieve this goal, PDABs may consider the perspective of a variety of stakeholders (ie, the state, the health system, or the patient) when conducting affordability reviews. The type of data and subsequent analysis may vary depending on the PDAB's affordability perspective. The PORTAL white papers on affordability reviews and setting of UPLs provide guidance rather than prescriptive recommendations. While PORTAL includes consideration of patient costs and issues that impact access, its primary focus is the assessment of affordability at the state or health system level.

State PDABs do not have the complete data that are required to make an affordability determination as recommended by PORTAL. They do not have access to product net price as a pharmacy benefit manager (PBM) or health plan drug spend reporting does not necessarily correlate with the cost to the state. Moreover, manufacturers do not have insight into the net price at the state level as they are not privy to discounts and rebates shared between the state and PBMs or health plans. State PDABs also may not have access to benefit design information and a holistic view of actual patient OOP costs. PDABs are also unable to consider the total cost of care for a condition, due to a lack of access to that information. The economic data requested to carry out an affordability review is only related to drug spend, with no transparency into potential offsets to healthcare resource utilization (eg, hospitalizations, emergency or urgent care visits, provider encounters) and associated medical costs, quality of life, and other patient or caregiver impacts.

Conversely, payers conduct clinical and economic evaluations separately when assessing coverage, formulary placement, and utilization management. This ensures that both the clinical value of a product and how it compares to therapeutic alternatives are assessed before determining if any differences in cost are justified. For example, the Pharmacy and Therapeutics (P&T) Committee makes a clinical determination, and a value or business committee conducts an evaluation comparing net drug costs and considers potential medical cost offsets.[21] The value or business committee must adhere to the clinical finding of the P&T Committee when making coverage, formulary tier, and utilization management decisions.[21] When Colorado's PDAB reviewed Trikafta, the PDAB members made a clear clinical superiority determination for Trikafta, which significantly impacted the PDAB's view on affordability.[12] Notably, the PDAB was heavily influenced by the input of a broad range of stakeholders, including patients, caregivers, and providers active in advocacy efforts. A separate clinical and economic review is critical to ensure the clinical evidence for the drug is carefully weighed and that bias is not introduced by primarily focusing on cost and budgetary impacts.

Affordability Reviews and Setting Upper Payment Limits (cont)

Due to lack of state expertise, the clinical comparative effectiveness evaluation conducted by a PDAB is significantly diluted, with most of the focus being on cost. Similarly, it is unlikely that PDABs will be staffed with resources to conduct high-quality, long-term economic effectiveness evaluations, which are expensive and time consuming (eg, cost-effectiveness analysis). Limited resources or expertise at the state level may lead to reliance on assessments conducted by independent organizations that have various drawbacks (eg, Institute for Clinical and Economic Review's use of QALYs widely considered discriminatory and prohibited by federal law in Medicaid and Medicare because they are viewed to discount the value of life due to an individual's disability or age). PORTAL addresses the potential use of equal value life years gained (evLYG) as an alternative but notes these measurements are newer,[22] and they may have their own discriminatory implications.[23,24]

While states may include health equity impact at the drug or condition level in their affordability review, there is no assessment of how findings that may lead to a potential UPL could impact drug access and health equity. When Oregon assessed the affordability of Humulin R U-500, they did not evaluate the clinical utility of Humulin R U-500 for patients requiring large daily doses of insulin. They also did not consider the ease of use of the pen administration for patients with visual or dexterity impairments or the value of the product for patient safety compared to its alternatives before making their unaffordable determination.[5] In addition, while the price of the product was noted as high, there was not a clear notation of the determining factors that led to an unaffordable determination.

For setting UPLs, PORTAL discusses the strategic approach of reference pricing, including the use of external reference pricing such as international pricing and the Medicare Maximum Fair Price (MFP).[25] Challenges with the use of international reference pricing include accessibility of the actual net price, potential unavailability of the product for the same approved uses in other countries, and potential use of QALYs in international price negotiations and decisions.[25] The Medicare Drug Price Negotiation Program, a provision of the IRA, gives Medicare the ability to negotiate directly with drug companies for high expenditure, single-source Part B and Part D drugs.[26] The final negotiated price is referred to as the MFP, and the MFP will not take effect for the first 10 negotiated drugs in Medicare Part D until January 1, 2026. While the potential impact of this federal price control on patient access is unknown, a fall 2024 survey of independent pharmacy owners and managers from the National Community Pharmacists Association (NCPA) found that 51% of respondents are strongly considering and 40% are somewhat considering not stocking the impacted MFP drugs due to anticipated delays in refund payments.[27] A January 2025 survey reinforced the findings with 32.8% of independent pharmacists deciding to not stock one or more MFP drugs.[28] This could significantly affect access for all patients in the community, regardless of applicability of the MFP or UPL to only certain populations.

Potential Implications for an Unbalanced Clinical and Economic Review and Setting UPLs

Combining clinical and economic assessments, as outlined in the PORTAL guidance, may undervalue the clinical benefit of a product on the condition or disease and introduce bias by primarily focusing on cost and budgetary impacts that are not accurate due to lack of data on net price and actual patient OOP costs. PDAB affordability reviews should also significantly consider the impact on medical cost offsets and other costs (eg, other medications, diagnostics, laboratory monitoring) when determining the value of the selected drug. When setting UPLs, the challenge in determining accurate costs of therapeutic alternatives is similar to determining the cost of the product under review, and use of domestic and international reference pricing has significant limitations.

While UPLs could lead to restrictions on access, including formulary exclusions or utilization management requirements, PDABs do not offer solutions for patients to overcome such barriers to access their prescribed medicines, such as medical exception or prior authorization review or an appeals process. PDABs are solely focused on the drug's price and not on remedying the benefit design that dictates what a patient pays for a medicine. Depending on the patient's health plan benefit design, a drug that is assigned a UPL may result in higher patient costs compared to other appropriate therapeutic options. Consequently, costs for hospitalizations and other services could quickly accumulate when access to appropriate therapies is restricted or costs more resulting in poor adherence. Another longer-term consideration is the possible impacts UPLs may have on innovation if manufacturers are disincentivized to produce new therapeutics that may lead to better clinical outcomes.

Conclusions

Broad drug aggregation and the use of clinical practice guidelines and ongoing or unpublished evidence to determine therapeutic alternatives may contribute to clinically inaccurate or inappropriate affordability conclusions. While PORTAL's guidance in NASHP's toolkit takes into consideration differences in safety profiles and efficacy, as well as effects on health equity, these clinically meaningful patient impacts are overshadowed by the pricing considerations when combining the clinical determination and economic assessment processes. Payers generally separate these assessments to ensure all clinical factors are considered before making an economic evaluation. In addition, evaluation of costs and budgetary impacts by PDABs may be inaccurate due to a lack of data on net price and actual patient OOP costs.

Implementation of the PORTAL guidance without flexibility in those states with the authority to set UPLs could lead to decreased patient access to the therapeutic options chosen by the patient and prescriber, and possibly to all therapeutic options. **The perspectives of patients, caregivers, and providers who are experts in the disease area deserve extensive consideration prior to PDAB decision-making.**

References: 1. https://nashp.org/prescription-drug-affordability-board-toolkit/ **2.** https://eadn-wc03-8290287.nxedge.io/wp-content/uploads/2024/04/Defining-a-Drug-Memo.pdf **3.** An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=314.3) **4.** Per Oregon law, the PDAB identifies nine drugs and at least one insulin product that may create affordability challenges for health care systems or high out-of-pocket costs for patients in the state. (https://www.oregonlegislature.gov/bills_laws/ors/ors646a.html) **5.** https://dfr.oregon.gov/pdab/Documents/20240126-PDAB-document-package.pdf **6.** https://dfr.oregon.gov/pdab/Documents/20240221-PDAB-document-package.pdf **7.** https://pmc.ncbi.nlm.nih.gov/articles/PMC6187959/ **8.** https://dfr.oregon.gov/pdab/Documents/20240126-PDAB-approved-minutes.pdf **9.** https://dfr.oregon.gov/pdab/Documents/20240626-PDAB-approved-minutes.pdf **10.** https://app.leg.wa.gov/RCW/default.aspx?cite=70.405&full=true#70.405.030 **11.** https://www.statnews.com/2024/07/15/medicare-drug-pricing-rules-delay-therapies-access/ **12.** https://drive.google.com/drive/folders/1KerBUEKqexhCrr-jq9DrQTRRU7puUGfH **13.** https://pdab.maryland.gov/documents/comments/dupixent_therapeutic_alternatives.pdf **14.** https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=595f437d-2729-40bb-9c62-c8ece1f82780 **15.** https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf **16.** https://pdab.maryland.gov/Documents/meetings/2024/Jardiance.2024.07.22.List%20of%20Therapeutic%20Alternatives.docx.pdf **17.** American Diabetes Association Professional Practice Committee. Pharmacologic approaches to glycemic treatment: standards of care in diabetes – 2025. *Diabetes Care*. 2025;48(1):S181-S206. **18.** https://drive.google.com/drive/folders/1xdHNz_KHSB5uL6o2DDSqcKOZbCsmRXq2 **19.** https://drive.google.com/drive/folders/1UHaYvwQzBQgon9D28X9o5heaZUgk-fPx **20.** https://drive.google.com/drive/folders/1lliSZ288cYb3T1LwFNuy4-s4aGLjqwq7 **21.** Brogan AP, Hogue SL, Vekaria RM, Reynolds I, Coukell A. Understanding payer perspectives on value in the use of pharmaceuticals in the United States. *J Manag Care Spec Pharm*. 2019;25(12):1319-1327. **22.** https://eadn-wc03-8290287.nxedge.io/wp-content/uploads/2024/04/Affordability-Review-White-Paper.pdf **23.** https://cevr.tuftsmedicalcenter.org/news/2018/will-icers-response-to-attacks-on-the-qaly-quiet-the-critics **24.** DiStefano MJ, Zemplenyi A, Anderson KE, Mendola ND, Nair KV, McQueen RB. Alternative approaches to measuring value: an update on innovative methods in the context of the United States Medicare drug price negotiation program. *Expert Rev Pharmacoecon Outcomes Res*. 2023;24(2):171-180. **25.** https://eadn-wc03-8290287.nxedge.io/wp-content/uploads/2024/04/Upper-Payment-Limit-White-Paper.pdf **26.** https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation **27.** https://ncpa.org/sites/default/files/2024-10/NCPA-FallSurvey2024-ExecSummary.pdf **28.** https://ncpa.org/sites/default/files/2025-01/1.27.2025-FinalExecSummary.NCPA_.MemberSurvey.pdf