Circulation

WHITE PAPER

Challenges and Potential Improvements to Patient Access to Pharmaceuticals

Examples From Cardiology

ABSTRACT: Patient access to a drug after US regulatory approval is controlled by complex interactions between governmental and third-party payers, pharmacy benefit managers, distributers, manufacturers, health systems, and pharmacies that together mediate the receipt of goods by patients after prescription by clinicians. Recent medication approvals highlight why and how the distribution of clinically beneficial novel therapies is controlled. Although imposed limitations on availability may be rational considering the fiduciary responsibilities of payers and escalating spending on health care and pharmaceuticals, transparency and communication are lacking, and some utilization management may disproportionately affect vulnerable populations. Analysis of the current health insurance landscape suggests mechanisms by which patient access to appropriate medications can be improved and patient and clinician frustration reduced while acknowledging the financial realities of the pharmaceutical marketplace. We propose creation of a shared, standardized, and transparent process for coverage decisions that minimizes administrative barriers and is defensible on the basis of clinical and cost-effectiveness evidence. These reforms would benefit patients and improve the efficiency of the pharmaceutical system.

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A novel medication must pass multiple milestones before it reaches a patient. Demonstration of safety and benefit in large randomized clinical trials and approval after stringent regulatory evaluation are not sufficient to successfully translate clinical discoveries into health improvements. Patient access is controlled by complex interactions between governmental and third-party payers, pharmacy benefit managers (PBMs), distributors, pharmaceutical manufacturers, health systems, and pharmacies that together control the receipt of goods by patients after prescription by clinicians. Recent novel medication approvals highlight why and how payers restrict distribution of clinically superior medications.[1] The impact is substantial. The barriers that impede patient access to pharmaceuticals likely worsen the serious problems of incomplete use of cardiovascular therapeutics and health disparities.[2] Although imposed limitations on availability may be rational considering the fiduciary responsibilities of stakeholders and ongoing escalating spending on health care and pharmaceuticals, transparency, consistency, and communication are lacking. Here, an analysis from the Heart Failure Collaboratory, a think tank formed to improve clinical care and efficiency, describes the current health insurance landscape.[3] This review of

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the processes controlling the availability and cost of pharmaceuticals for patients suggests a road map by which patient access to appropriate medications can be improved and patient adverse outcomes and clinician frustration can be reduced while acknowledging the financial realities of the pharmaceutical and healthcare marketplace.

STRUCTURE OF THE US PAYER SYSTEM

The US health insurance system is structured such that multiple intermediaries modulate patient care and accessibility of prescribed medications.[4] Although US health insurance companies originated in the 1930s as nonprofit entities mutually beneficial for medical systems and patients, legal and industry evolution established them as profit driven.[4,5] PBMs originated to manage and simplify outpatient pharmaceutical claims and to control costs as part of the burgeoning private insurance system.[6] Modern-day health insurers pay clinicians and manufacturers on behalf of patients, often through PBMs, distributors, and pharmacies.[4] Most US adults have pharmaceutical coverage through commercial insurance. When federal insurance through Medicare was established in the 1960s, third-party insurers were the fiscal intermediaries almost from the outset.[4] Medicare covers less than one-third of the number of patients covered by private payers, and 34% of Medicare beneficiaries' plans are administered by private insurers through Medicare Advantage. Although one-quarter of patients <65 years of age without a disability are covered by a public health plan (Medicaid/Children's Health Insurance Program), 65% are covered by a private plan.[7] The US Department of Veterans Affairs operates a standalone integrated health system for US military veterans but covers <5% of the US population.[8] Thus, private insurers and PBMs, whether through their commercial plans or by administration of Medicare plans, control most of the use of medical therapies, typically in response to cost, marginal safety, and marginal efficacy profiles.[9–11]

In contrast, many non-US health insurance systems are governmental programs that control therapeutic use, either as part of universal coverage or as a tightly regulated multipayer arrangement.[12] In Britain, for instance, the National Health Service typically provides only medications and technologies recommended by the National Institute for Health and Care Excellence, which both functions as the national regulatory authority and appraises cost-effectiveness of interventions.[13] Although PBMs currently possess a small share of the international market, they continue to expand their non-US presence.[14]

PHARMACEUTICAL PRICING

Prescription medication spending makes up the largest portion of outpatient cardiovascular health costs; like healthcare spending overall, it continues to rise faster than inflation, even though the United States already spends more per capita than other developed nations.[5,15] This trend has been spurred by manufacturer pricing of brand-name and specialty drugs.[4,16] The pharmaceutical industry is protected in setting brand-name drug prices by government-defined market exclusivity after US Food and Drug Administration (FDA) approval. Although it is expensive to research and develop novel pharmaceuticals, the actual cost is uncertain and does not appear to determine pricing; only 10% to 20% of pharmaceutical industry revenue is invested in research and development.[3,5] Cardiovascular drug pricing does not typically optimize value either.[17] Rather than cost-effectiveness, brand-name prescription drug pricing is typically based on market tolerability, as demonstrated by the recent pricing changes for the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors.[5,18] In these cases, Amgen appropriately dropped its initial pricing of evolocumab and Sanofi/Regeneron dropped its pricing of alirocumab by ≈60% in response to prohibitive payer restrictions and poor uptake.

However, the true prices of medications are difficult to decipher because of the opaque contracts and incentives that insurers, drug makers, pharmacies, distributors, and PBMs use to exchange money (Figure 1).[4,5,19] Because each individual party in this network maintains financial solvency by generating capital, their profit margins are in direct conflict.[9] Each thus negotiates its own set of prices, discounts, reimbursements, and rebates, none of which are released to the public or represented by the list price and all of which are variable by the regionally insured population.[16,19] Medicaid and the Veterans Affairs are federally mandated to receive the lowest commercially negotiated prices.[8] Of all drug benefits plans, >85% report growing rebate arrangements, totaling $144 billion or 31% of gross drug sales in 2016.[6,19] These deals determine the accessibility of medications to patients, including out-of-pocket costs and use within preferred pharmacy networks.

Unfortunately, this intricate system best serves these businesses and prohibits the patient and clinician consumers from being truly informed (Figure 1).[4,5,20] Hidden prices and financial exchanges create a confidential negotiation in which transparency is avoided for concern of acutely limiting payer and seller bargaining power, perpetuating the system. As exemplified by Ohio's PBMs interacting with state Medicaid managed care plans, some PBMs profit by using their intermediary status to sell medications for more than they have negotiated to pay and taking payments from industry in exchange for advantageous formulary placement

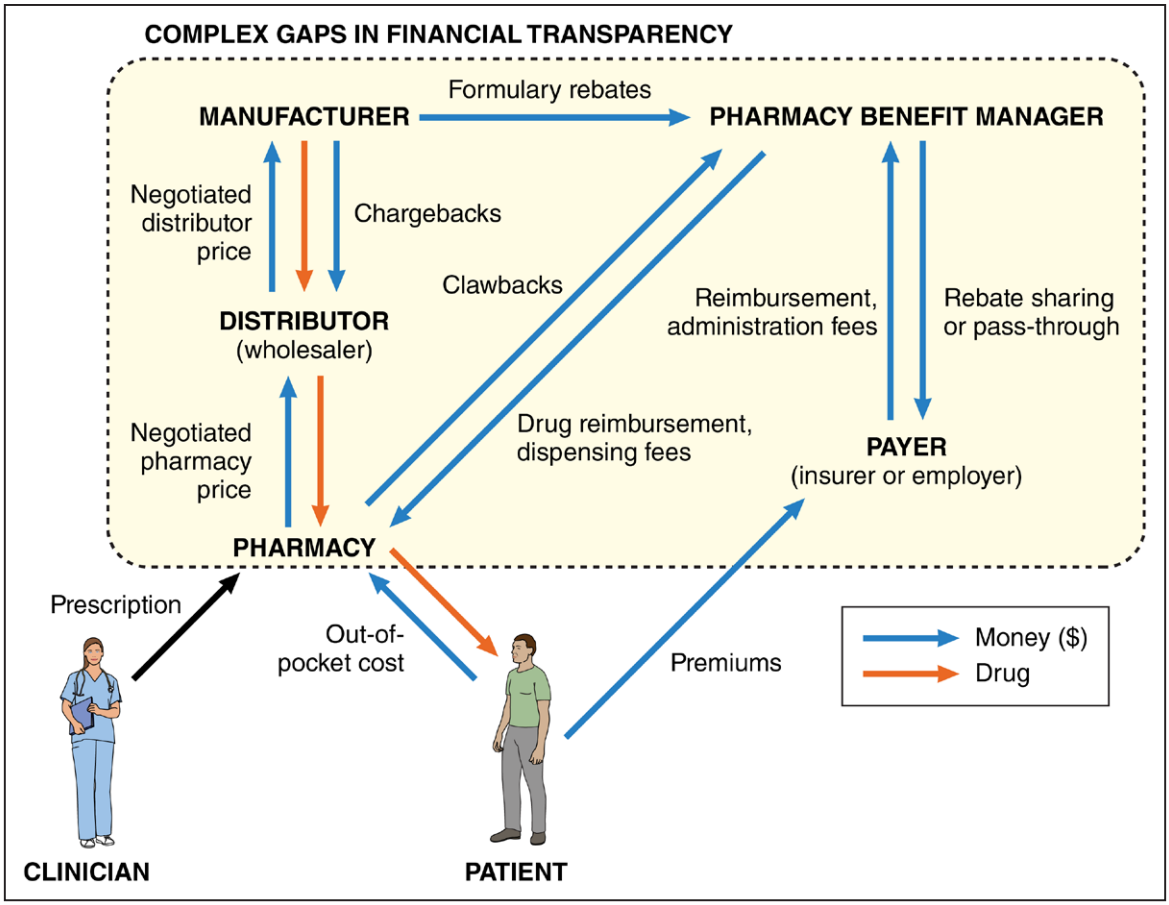

Figure 1. Complex gaps in financial transparency among transactions in the US pharmaceutical supply chain.
Negotiated prices between manufacturer and distributor and between distributor and pharmacy are typically based on the wholesale acquisition cost but may not be equivalent and do not necessarily equal list price (also known as average wholesale price), nor do they equal average manufacturer price, which includes discounts, rebates, and other transactions. These negotiated prices are proprietary. Chargebacks are payments from manufacturers to distributors that cover differences in the negotiated prices paid by distributors and those paid to the distributors by retailers such as pharmacies. Out-of-pocket cost is typically coinsurance or copayment but can be the full cost of the drug. Payers include both private and public (Medicare, Medicaid) insurers. The pharmacy benefit manager (PBM) spread is the difference in payments to pharmacies and reimbursement to the PBM from payers. The net income of the PBM additionally includes rebates from manufacturers for formulary inclusion that are not passed through to payers and clawbacks from pharmacies. Clawbacks are the excess out-of-pocket patient payment (coinsurance or copayment) above the price paid by the pharmacy for the drug.

and increased product market share.[5,21] PBMs in Ohio charged payers servicing the Ohio Department of Medicaid 9% more than the pharmacy costs, totaling $225 million in 2017.[21]

THE ROLE OF PAYERS IN PHARMACEUTICAL PROVISION AND COST CONTROL

The healthcare system relies on payers to insulate patients from financial harm by pooling risk and opposing overpricing. Payers also actively restrict some medications to medically accepted indications defined by FDA labeling or as delineated in evidence-based compendia.[22] These actions can protect patients from ineffective, inappropriate, or harmful prescriptions, for instance, by encouraging the use of generic medications if newer and more expensive options lack evidence of superior safety or efficacy. For pharmaceutical classes for which effective generic competition exists, as with statins, payers and PBMs successfully move patients to cost-saving generic alternatives.[23] However, payers and PBMs can also manage escalating drug spending, particularly of nongenerics, by impairing product use and shifting costs to patients to protect their bottom line.[19] Fewer than one-third of Medicare formularies offer unrestricted coverage of at least 1 of the directly acting oral anticoagulants.[24] Tolerance of high pricing differs widely across disease states and between corporations. For instance, opposition appears higher for medications for heart failure or cardiovascular prevention than for oncology, which may in part be caused by Medicare's designation of oncology as 1 of 6 legally protected classes that require payer coverage. Payer behavior may be influenced by the size of the target cardiovascular disease populations, which may exert greater financial stress on insurers than considerably higher priced niche medications for rare tumors, and stronger patient advocacy for cancer therapies, despite heart failure mortality

being equal to or worse than mortality from many common and deadly cancers.[3,25,26]

Insurers and PBMs typically use 3 mechanisms to control pharmaceutical use, negotiate favorable cost-containment, and control market share: formulary coverage, administrative barriers, and cost sharing (Figure 2).[19] Payers may rapidly change the mechanisms used after commercial release of a pharmaceutical as they learn how best to achieve appropriate prescribing and spending. Although these efforts might reduce total healthcare cost as with the PCSK9 inhibitors, this effect may be diminished by the direction of portions of insurer savings toward profit.

Coverage typically refers to whether the health insurance provider will offer the medication; if an agent is not covered, it is a formulary exclusion. Formulary exclusions vary by payer plan, disease state, and drug class.[19,27] When first released, coverage for the expensive PCSK9 inhibitors was shown to vary widely among commercial and public insurers.[28,29] Medicare Part D requires a minimum of 2 drugs from each medication class to be covered and essentially all available pharmaceuticals for the 6 protected classes (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants), whereas Medicaid must cover all pharmaceuticals from a manufacturer in exchange for its best prices.[8] The Veterans Affairs has its own restrictive national formulary and nonprofit PBM, despite also benefiting from legally mandated pricing discounts.[8]

Payers use several administrative and cost-sharing barriers for formulary medications (Figure 2).[19] Prior authorization (PA) is frequently enacted for high-cost novel drugs, particularly if they are felt likely to be prescribed inappropriately. Initially, 82% to 97% of plans that covered PCSK9 inhibitors mandated PA, typically requiring forms with 11 to 33 fields and submission of medical records.[28] This was also common for sacubitril-valsartan, a novel, expensive, but reportedly cost-effective survival-prolonging medication for heart failure (Table 1).[26,31] The PA process requires substantial resources and often full-time clinic staff.[32] PAs are inefficient and costly for payers as well; ≈40% of coverage denials are reversed in favor of the consumer on appeal.[33]

Cost-sharing mechanisms increasingly transfer financial burden directly to patients through copayments and coinsurance in complicated tiered formularies, along with increasing deductibles and premiums (Figure 2).[34] Copayments set fixed out-of-pocket contributions for drugs based on their cost tier; coinsurance requires out-of-pocket payment of a percentage of the drug cost. If approved after PA, the PCSK9 inhibitors assume specialty tier status 32% to 93% of the time, requiring high copayment or coinsurance, and 64% to 90% of plans require step therapy wherein a lower-cost statin must first be trialed and found to be ineffective or harmful.[28] Although increasing consumer sensitivity to medical care costs has been promoted by government legislation supporting the creation of Health Savings Accounts in high-deductible insurance plans and payers may reason that continued shifting of the cost burden to patients will reduce use, prescription drug use has continued to increase despite rising prices and out-of-pocket consumer spending.[4,16]

IMPACT ON PATIENTS AND CLINICIANS

Depending on the population and survey, approximately one-quarter to one-third of patients have reported difficulties obtaining medications because of delays,

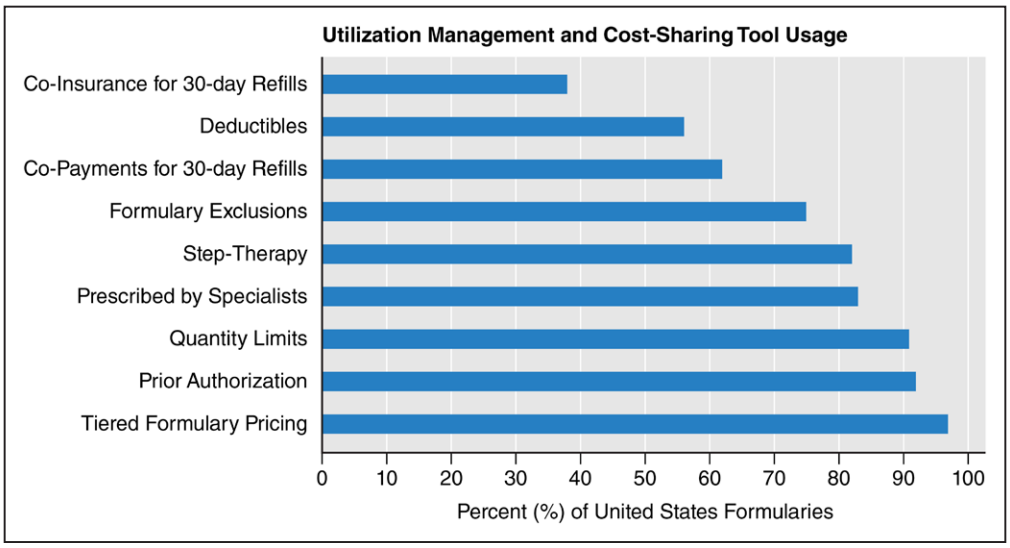

Figure 2. Use of utilization management and cost-sharing tools by US employer health insurances.
Payers and pharmacy benefit managers (PBMs) frequently use strategies to control the use of drugs and to increase cost sharing with plan members. Frequency of the use of cost-sharing and management tool inclusion by payers and PBMs. Data from the Pharmacy Benefit Management Institute survey of 318 US employers.[19]

Table 1. Coverage Barriers to Sacubitril-Valsartan by Virginia Payers as of February 2018

Payer	Plan Type	PA	Formulary Tier	Step Therapy	PA Requirements	NYHA Class	LVEF, %	Laboratory Tests	Specialist Approval	Quantity Limits
Department of Veterans Affairs	Federal	Yes	3/3	Yes	Maximum stable BB and ACE inhibitor/ARB for >4 wk and at dose equivalent to or greater than enalapril 10 mg twice daily	II or III	≤35	BNP ≥150 pg/mL or ≥100 pg/mL if hospitalized	Cardiologist	No
Aetna	Medicare	No	3/5	No	Maximum stable BB and ACE inhibitor/ARB for >4 wk and at dose equivalent to or greater than enalapril 10 mg twice daily	II or III	≤35	BNP ≥150 pg/mL or ≥100 pg/mL if hospitalized	Cardiologist	No
Aetna	Commercial	Yes	2/3	No	Authorization for 12 mo	II, III or IV	Reduced	No	No	2/d
Anthem	Medicare	Yes	4/5	No	LVEF≤40%, authorization for 12 mo	No	≤40	No	No	60/30 d
Anthem	Commercial	Yes	3/3	No	Authorization for 12 mo	II, III or IV	≤35	No	No	2/d
Blue Cross Blue Shield	Medicare	No	4/5	No	LVEF≤40%, authorization for 12 mo	No	≤40	No	No	60/30 d
Caremark	Commercial	No	2/3	No	Authorization for 12 mo	II, III or IV	≤35	No	No	No
Cigna	Medicare	No	3/5	No	LVEF ≤40%, authorization for 12 mo	No	≤40	No	No	60/30 d
Cigna	Commercial	Yes	2/3	No	NYHA class and LVEF only	II, III or IV	≤40	No	No	No
Express Scripts	Medicare	No	3/5	No	LVEF ≤40%, authorization for 12 mo	No	≤40	No	No	62/31 d
Express Scripts	Commercial	Yes	2/3	No	Authorization for 12 mo	II, III or IV	≤40	No	Cardiologist	No
Humana	Medicare	Yes	3/5	No	Approved in plan year durations or by clinical review	II, III, or IV	≤40	No	Cardiologist	60/30 d
Humana	Commercial	Yes	2/4	No	Approved in plan year durations and continues to receive benefit from sacubitril-valsartan	II, III, or IV	≤40	No	Cardiologist	60/30 d
United Healthcare	Medicare	No	3/5	No	Approved in plan year durations or by clinical review	II, III, or IV	≤40	No	Cardiologist	2/d
United Healthcare	Commercial	Yes	3/3	Yes	Stable BB; document positive clinical response to therapy; authorization for 12 mo	II, III, or IV	≤35	No	Cardiologist	60/30 d
Virginia Medicaid	Medicaid	No	1/2	Yes	Authorization for 12 mo	II, III, or IV	≤40	No	No	2/d

BNP values are expressed in picograms per milliliter, which is equivalent to nanograms per liter. Data taken from https://www.entresto-coverage.com/.[30] ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BB, β-adrenergic receptor antagonist; BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction; NYHA, New York Health Association; and PA, prior authorization.

denials, and cost.[35] In addition to the frustration and confusion of having to wait for clinician-recommended treatments or having those therapies denied as formulary exclusions, utilization management and cost-sharing mechanisms can negatively influence clinical outcomes.[19,27] Almost 1 in 10 patients does not take medications as prescribed because of cost alone.[36] Of published formulary exclusion policies, 29% correlated with negative patient impact, for instance, with increasing frequency of side effects during management of hypertension.[27] Antihypertensive step therapy was associated with increased rates of inpatient admission and emergency visits.[37] In addition, adverse effects appear to be amplified for socioeconomically vulnerable patients who are more likely to defer appropriate medication use when confronted with cost sharing in favor of nutrition, family care, and other necessities, even with small cost increases of a few dollars.[2,38–41] Disparities for underserved populations are further exacerbated because the PA and frequent appeals processes are a time-intensive burden for office staff and clinicians; thus, resource-constrained practice settings are disproportionately less able to navigate these barriers for their patients even though they may be accountable

for greater patient cost because of risk sharing.[32] These constraints can lead clinicians to spend less time providing patient care, discourage patients if they cannot receive the intended medication, and reinforce a perception that some patients may not deserve the dictated medical care.[32] These burdens and the resultant limits on the use of novel cardiovascular treatments, with diminished return on expenditures, may also be associated with declining industry investment in cardiovascular innovation relative to other fields.[3,42]

PAYER DECISION MAKING

Although few medications are excluded from formularies, the process and rationale by which payers determine utilization requirements and cost-sharing thresholds are variable and often opaque.[43] Variability in PCSK9 inhibitor payer coverage suggests that during internal coverage deliberations the same data are interpreted differently.[28,29] Payers may use a wide variety of clinical and nonclinical advisors to establish drug benefits, including consultants, brokers, PBMs, human resource departments, and contracted health plans, but the selection of advisors and analytic strategies is not standardized.[19] Physicians used by insurers are typically not endowed with the authority to make the coverage decisions outside of defined policy.[43] Patient advocates rarely play a role in this process despite desire by patients to be involved in health technology assessment.[44,45] Some payers appropriately apply clinical guidelines, clinical trial evidence, systematic reviews, and cost-effectiveness analyses during coverage deliberations.[44,46] However, reports of budget and payer cost analyses are conspicuously lacking.

Most commonly, commercial insurance drug plans rely on PBM decision making, principally through formulary construction and rebate negotiation; 73% of employer-sponsored plans enact the national preferred formulary negotiated by their PBM without change.[19] Payer drug exclusion policy decisions may appear indifferent to the clinical outcomes faced by patients: Both positive and negative effects on the targeted disease states are found in ≈30% of formulary drug exclusions.[27] These coverage decisions are also agnostic to the total healthcare system expenditures; overall healthcare spending for a disease state has increased as a result of some coverage determinations that saved money for a payer.[27]

The inconsistency in coverage and barrier decision making by payers can be seen across numerous drug classes and disease states, and evidence requirements for these decisions frequently differ between governmental and commercial entities.[47,48] Although Medicare National Coverage Determinations may be imperfect, they are generally based on sound scientific data. However, commercial payers and PBMs disagree with federal Medicare coverage decisions in 49% of cases.[49] Payers also do not necessarily use regulatory approval decisions to determine coverage; for some drug classes, coverage determinations are consistent with FDA labeling in only 15% of cases, with 69% of payers using more restrictive criteria.[47]

Non–evidence-based PA requirements may exist to decrease pharmaceutical use and payer expenditures without adequate consideration of cost-effectiveness. As an example, coverage barriers to sacubitril-valsartan by payers from early 2018 within a single US state are displayed in Table 1. Although many used criteria consistent with the PARADIGM-HF (Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) inclusions and exclusions and FDA labeling, there was substantial variability among the mandated clinical requirements and scientific appropriateness (Table 2). One-third of these major insurers required non–evidence-based ejection fraction cutoffs or step therapy with an angiotensin antagonist, even though patients in the trial tolerated angiotensin-converting enzyme inhibitors.[1,50]

SYSTEMIC CHANGES

Changes to the current system will be required to improve timely patient access to appropriate therapies and to standardize rational methodologies for coverage. Transparency in pricing, cost, quality, and relative efficacy has long been advocated; however, there is growing broad-based support for innovation among patients and active negotiation among congressional lawmakers.[51] Given regulations already being implemented by some states, stakeholders, including manufacturers, insurers, PBMs, and clinicians, should proactively strive to improve patient access before they are compelled by federal mandate.[52] Options may include but not require a governmentally driven system

Table 2. Requirements for Inclusion in the PARADIGM-HF Clinical Trial of Sacubitril-Valsartan

Trial	ACE inhibitor/ARB and BB Requirements	NYHA Class	LVEF, %	Laboratory Tests
PARADIGM-HF[1]	Maximum stable BB and ACE inhibitor/ARB for >4 wk at a dose equivalent to or greater than enalapril 10 mg twice daily	II, III, or IV	≤40	BNP ≥150 pg/mL or ≥100 pg/mL if hospitalized

BNP values are expressed in picograms per milliliter, which is equivalent to nanograms per liter. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BB, β-adrenergic receptor antagonist; BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction; NYHA, New York Health Association; and PARADIGM-HF, Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure.

for universal health coverage or vertical integration. Although these may be more distant solutions, they could lead to greater market clout on the behalf of consumers by removal of intermediaries.[53] Currently used quality metrics could be applied to calculate cost-effectiveness for clinical outcomes and to share that data with patients, allowing choice, or implemented with value-based pricing to drive use.[54]

RECOMMENDATIONS: A ROAD MAP

We suggest the following feasible improvements for the process of coverage determination, utilization management, cost sharing, and interactions with clinicians and patients. These accept the financial realities and business priorities of payers and manufacturers while rendering the process more evidence based, efficient, and transparent, as well as seeking to soothe animosity among payers, clinicians, and patients. Reformed processes may decrease PA review burden for consumers and payers, improve public opinion, increase appropriate patient access, and augment value:

1. Coalition of stakeholders: Payers and PBMs should use structured coalitions of impartial experts in clinical trial interpretation, pharmacoeconomics, and cost-effectiveness research, as well as patients, patient advocates, regulators, pharmaceutical scientists, and clinicians, to make harmonized national evidence-based coverage decisions. Heretofore, coverage deliberations have routinely excluded patients and patient advocates, individuals burdened by the disease who can directly assess the relative worth of novel interventions.[45,55]
2. Standard practices: If formulary exclusions or specific coverage requirements are constructed, they should be based on publicly cited and justifiable clinical criteria.[55] This process should acknowledge that differences in covered populations, economics, and interpretations of the evidence may confer distinct value assessments.
3. Early engagement: Improvements in patient access will need to be achieved by payers and manufacturers working together to compromise on value assessments, pricing, data availability, and coverage of novel and beneficial medications.[56] Payers should participate in the Payer Communication Task Force facilitated by the US FDA to engage in drug development early for novel therapeutics.[57] Participation during the average of 8 years required for drug development may inform clinical trial data collection and allow payers early fiscal planning and formulary preparation.[58]
4. Cost-effectiveness: Cost-effectiveness and comparative effectiveness data should continue to be generated by neutral parties to drive decision making. At least 75% of cardiovascular medications are approved in the United States with available comparative effectiveness data.[59] These data should be used for coverage and manufacturer pricing decisions as part of improved value-based care, and there is federal guidance to facilitate appropriate manufacturer communication of cost-effectiveness data to payers.[60–62]
5. Transparency: Price transparency should be a central goal. Manufacturers, payers, and PBMs should broadly enact, publicize, and integrate the basis for pricing decisions and value with transparent cost-sharing calculators to allow patients and clinicians to rationally evaluate their medication choices and cost-effectiveness to facilitate shared decision making and to eliminate waste.[21,56] Currently, only one-third of drug benefit plans offer cost-sharing tools.[19] Expanded use could reduce frustration, prevent expensive appeals, assist appropriate PA requests, return treatment decision making to clinicians and patients while facilitating evidence-based prescriptions, and invigorate medication adherence.[2]
6. PA reform: The process for ensuring appropriate use of expensive drugs, based on approved indications, evidence-based clinical practice guidelines, and analysis of cost-effectiveness, should be implemented transparently and uniformly. Payers should render their decisions to clinicians and patients in a modernized and automated system integrated with electronic health records.[56] Antiquated fax machines should be eliminated.[63] Payers should clearly state which medications are priced such that payment barriers are required and standardize the steps needed to secure the medication. Improved clarity should reduce the number of deniable PAs submitted and pressure pharmaceutical manufacturers to collaborate with payers to adjust pricing and increase patient access.
7. Monitoring: A PA reporting tool similar to the one created by the American College of Cardiology for PCSK9 inhibitors (http://www.acc.org/partool) is needed to allow tracking of PA decisions and requests. These data will allow patients to see the practice patterns of commercial insurers and return purchasing power to consumers to select the payer that provides the best care.

SUMMARY

Patient access to novel pharmaceuticals is frequently limited by administrative and cost-sharing barriers. Patients and their clinicians are frustrated by the potential for harm caused by the struggle between access to novel therapies and cost. This system is perpetuated by a fractured and

opaque drug pricing and purchasing system that involves multiple intermediaries and limits consumer market forces. We propose creation of a standardized, transparent, collaborative, and streamlined process to establish coverage decisions and utilization measures that is defensible on the basis of clinical and cost-effectiveness evidence. These reforms will, we hope, benefit patients and improve the efficiency of the pharmaceutical system.

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