3

The Access Journey

Introducing the "Access Journey"

Ensuring access for patients to a prescription drug that has gained market authorization from the U.S. FDA, European EMA or another regulatory agency requires a concerted effort as many hurdles and endorsements will impact actual prescribing and patient use. As described in the previous chapter, the prescription drug market environment has dramatically changed over the last decade. The cost of healthcare and particularly the cost and price setting of prescription drugs has been an area of high concern among politicians, medical community, the media and patient organizations. It has elevated the role of a much more cost concerned medical community in access decision making. The return on investment for pharmaceuticals has steadily declined since 2010 to only 1.9% in 2018 (Deloitte, 2018). Meanwhile, FDA approvals in 2018 were at an all-time high. Are all these drugs designed to address customer value needs or do they merely satisfy the wrong productivity metrics with limited impact on patients and shareholder value?

Focus on physician prescribing as the main commercialization event, supplemented with contracting to payers to broaden access, is no longer enough to maximize the commercial success of drugs. We need to more comprehensively consider all stakeholder decisions that can enable or hinder patient access to treatments in consideration of its value and cost.

Consider the "Access Journey" in Figure 3.1 as a sequence of hurdles that need to be addressed to optimize the commercial success of a drug through broad and extended use at an attractive net price. Each of these steps can be considered a financial risk equivalent of a dangerous curve on a mountain road. Every "miss" results in loss of patients and revenue from what's formally authorized through the approved label. For each of the Access Journey steps, we need to consider a different decision maker with different values and preferences, which we will discuss in more detail.

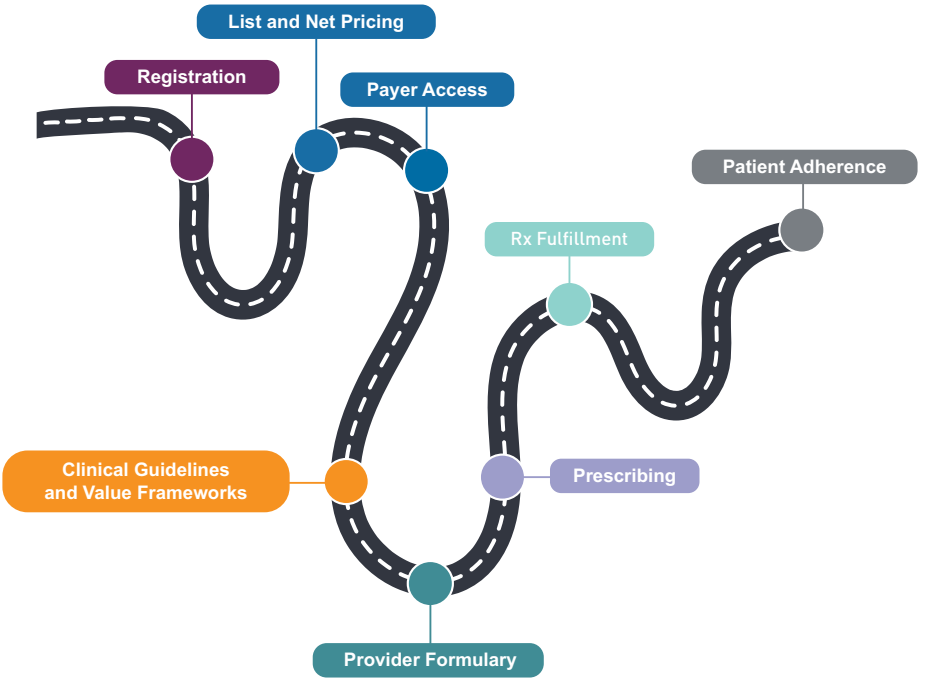

Figure 3.1 The Access Journey

The impact of imperfect value demonstration on net revenues is illustrated in Figure 3.2. While it's not realistic for a drug class or treatment to be used in all patients within label, minimizing losses from the narrowing of the funnel is essential. Each of the Access Journey steps may influence each other, and decisions aren't necessarily taken in a sequential order. For example, clinical guideline decisions are usually not formalized until some time after launch when sufficient treatment experience is gained. However, medical expert opinions carry their weight in payer decision making long before guidelines are formalized.

How do we best shape our development program so that each of these steps in the Access Journey are considered – with respect to their impact on the funnel – so that we limit restrictions and ultimately retain a large share of eligible patients? How do we ensure a proper trade-off between results and the underlying investments, clinical risk, and impact on timeline with the forecasted revenue? Doing so requires a structural evaluation of each of the steps on the Access Journey.

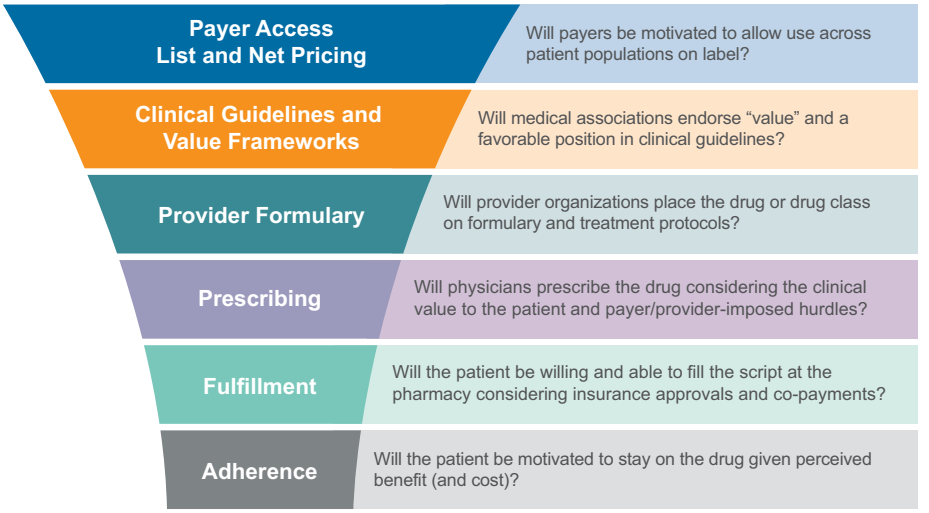

Figure 3.2 The Access Journey's impact on utilization and revenue

LIST AND NET PRICING

Differences between official list price and actual net price can be substantial, particularly in highly competitive therapy areas. In the U.S., PBMs and MCOs can extract significant rebates when choices are deemed sufficiently interchangeable by the medical community knowing that exclusion lists and co-payment differences can substantially shift prescribing behaviors. Figure 3.3 shows how list and net prices have changed over the 2011 to 2019 period, illustrating an increasing divergence between list and net pricing since 2012 and even declining average net prices in 2018 and 2019.

U.S. pharma companies spend well over $100 billion on rebates annually – more than twice all other selling, general and administrative expenses. As rebates are confidential between manufacturer and payer, it's hard to provide exact insights by drug or therapy area, but we know that many rebates in diabetes and hepatitis C exceed 50%. In other areas, where there are few similar options, rebates may be very small or non-existent. In other countries, discounts can be agreed upon, usually on a basis of confidentiality. For example, in France, periodic negotiations between the French government and pharmaceutical companies often include confidential rebates and contractually agreed upon further rebates when, for example, certain sales revenues are exceeded. In Germany, the government insists on transparency of net prices. The future will tell how this debate will further evolve in the U.S.

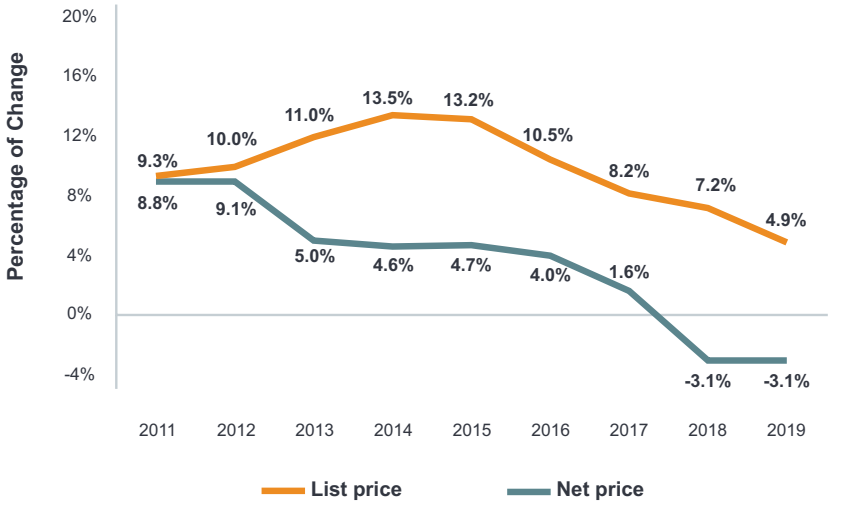

Figure 3.3 U.S. gross and net price growth for all branded drugs
Source: IQVIA data

PAYER ACCESS

Formulary adoption by public and private payers is obviously a critical step in reaching a patient. In price-controlled markets, this is essentially an all-or-nothing event, where the outcome is largely driven by the provided evidence of benefit over the existing treatment standard at the time of negotiation. Criteria for approval are different by country, but the critical issue is usually whether the demonstrated patient benefit is deemed significant by payer accepted standards. Approval criteria have gradually become more stringent over time, particularly in terms of head-to-head comparisons with standard of care and demonstrated benefit across the label population.

In the U.S., the stakes have increased as payers are no longer routinely putting new drugs on a third formulary tier with a higher co-payment. Large PBMs and many MCOs often exclude new drugs from formulary until closer review or on a more permanent basis when it is placed on an exclusion list, favoring similar drugs with better rebate terms.

PROVIDER FORMULARIES AND TREATMENT PATHWAYS

Provider organizations include a large range of integrated healthcare systems, specialty clinicals, hospitals and physician groups that put policies in place that influence treatment and prescribing behaviors of its associated

physicians in varying degrees. Payment mechanisms and performance metrics are important drivers of provider organization preferences and related decisions.

Provider performance metrics are increasingly visible to the public and can influence the ability to attract patients, as well as directly impact reimbursement rates. Hospitalization rates, re-hospitalization rates and cardiovascular outcomes metrics are among the most commonly monitored metrics but more detailed Healthcare Effectiveness Data and Information Set (HEDIS), ACO and other metrics are increasingly used in payment decisions. Broader public awareness of health outcomes performance of provider organizations and their individual physicians is likely to further evolve. In the age of TripAdvisor, it may soon only require a few clicks to access specific statistics such as hospitalization rates and cardiovascular event rates and direct patient feedback on each institution and physician.

Treatment pathways have emerged to encourage efficient use of resources in the treatment of patients. Pathways have been primarily used to optimize treatment and thus improve outcomes efficiently in cancer care. Treating physicians get a payment depending on the degree of adherence with the treatment options that are specified in the pathway guidelines. Some pathways, such as AIM (part of Anthem), select specific drugs within a recommended class. The actual impact of pathways on physician prescribing is still not fully clear. However, we expect that payers and providers may seek economic opportunities to make choices between options where they are deemed medically interchangeable.

A slightly different variation of the pathway is found in Germany, where regional physician groups agree on "quota," dictating that the least expensive drug option in a class is used for a specified percentage share of diagnosed indication. One of the earlier examples was the mandatory use of risperidone in 85% of patients with a need for an atypical antipsychotic. Quotas have proven to be an attractive tool where physicians claim to need discretion for a different option for some patients.

Funding for new technologies, including drugs, is often a challenge for providers in cases where a capped reimbursement rate, such as a diagnosis related group (DRG) rate, is resulting in institutional losses. New technologies can sometimes qualify for additional payment, such as the new technology add-on payment (NTAP) in the U.S. and the equivalent Neue Untersuchungs und Behandlungsmethoden (NUB) in Germany, but qualification has very high

hurdles. Reimbursement payments are usually adjusted over time, but in cases where the treatment involves a substantial share of patients, providers will look to limit treatment numbers or move patients, where possible, to an outpatient setting with often different reimbursement mechanisms.

CLINICAL GUIDELINES AND VALUE FRAMEWORKS

Medical communities have provided clinical guidelines to the physician community for many years. In recent history, these guidelines were purely clinically oriented and rarely included treatment and drug cost considerations. As an illustrative example, the American College of Cardiology (ACC) and the American Heart Association (AHA) published the ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures. It states, "The need for greater transparency and utility in addressing resource issues has become acute enough that the time has come to include cost-effectiveness/value assessments and recommendations in practice guidelines and performance measures."

Oncologists have been most vocal on the impact of cost and affordability on patients. Various value frameworks by the American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology (ESMO) and the National Comprehensive Cancer Network (NCCN), as well as the "Drug Pricing Lab" by Memorial Sloan Kettering Cancer Center's Dr. Peter Koch have attempted to measure and communicate benefits of drugs, or lack thereof, in relation to their cost. While the value frameworks have sensitized physicians and the public on drug cost, they have not provided clinicians with clear guidelines on when to use what treatment option.

In heath-economics-driven markets, such as the U.K., Canada and Australia, health technology evaluations provide a basis for price or reimbursement. These cost-effectiveness-based guidelines provide payers significant control through direct linkage to price or reimbursement decision-making. The Institute for Clinical and Economic Review (ICER) is using a similar method to communicate cost-effectiveness of drug treatments in the U.S. However, both methodology and financial perspective are not well aligned with U.S. PBM and MCO decision-making. The question is whether and how ICER cost-effectiveness reviews will be adopted by payers, and whether these initiatives will be endorsed by the medical community and patients.

In the U.S., a more likely scenario through which the evolving value frameworks may impact prescribing is through a linkage with treatment pathways and reinforcing incentives. This way, treatment value is better linked to a specific treatment stage and its related choices rather than for a drug overall.

The evolution of value frameworks and their impact on prescribing will continue to be an area of uncertainty for some years to come.

PRESCRIBING

The actual physician prescribing decision will continue to be the central factor in the market adoption of any drug. No drug will perform well without the physician's endorsement of its value in treating individual patients. As such, the prescribing decision is the resulting transaction under influence of decisions and communications provided by medical communities, payers, provider organizations, and other potential stakeholders and influencers.

A lack of demonstrated value can have a strong negative impact on prescribing due to payer-imposed restrictions in addition to the direct impact of a less compelling message to prescribers. Commercial success may not be achieved by merely passing minimum hurdles to gain access. In the U.S. we may gain FDA approval for an undifferentiated drug with a placebo-controlled study. However, we will subsequently be forced to offer either significant rebates or intensive co-pay offset programs in the commercial market to overcome patient co-payment hurdles and related hesitance of physicians to prescribe.

A key question is whether we adequately represent the impact of demonstrated value, or lack thereof, on the forecasted physician prescribing. Forecasts are only as good as the options that we consider in predicting performance. Unless we explicitly consider the impact of multiple value proposition options on peak market share and forecasted revenues, decision-making teams will typically favor adhering to the minimum FDA requirements.

PRESCRIPTION FULFILLMENT

What happens when the patient leaves the doctor's office? Will the patient go to the pharmacy to pick up the prescription? What if there is a substantial co-payment? If so, was the patient made aware of any coupons that may offset

the co-payment? As co-payments have been rising in the U.S. and some other markets, prescription fulfillment is an increasing area of concern.

Pharmaceutical companies have been offering an array of patient support services to help eliminate paperwork, cost and co-pay hurdles that payers have instituted to limit access to high-cost prescriptions drugs. Payer adoption of new management strategies such as drug exclusion lists and recent co-pay accumulators require adjustments in brand strategies.

PATIENT ADHERENCE

Does the patient adhere to the drug treatment over time and how is this different across patient populations? Adherence is strongly dependent on efficacy and the safety/tolerability profile and can also be impacted by patient co-payment and the associated financial burden. Particularly for non-symptomatic, chronic conditions, adherence can be a major challenge.

Value strategy implications

As a pharmaceutical company, our commercial success is hinging on our ability to optimize each of the elements of the Access Journey. It does not help us if after a favorable FDA approval, payers restrict drug access, medical associations don't recommend it on their guidelines, providers don't place it on formulary, physicians don't prescribe, or the patient decides not to pick it up in the pharmacy or ends the treatment early. Therefore, it's essential that we closely evaluate each of the Access Journey steps to determine what it takes to secure success. Who is the decision maker and what development strategy and resulting evidence will positively influence that decision?

As illustrated in Figure 3.4, each of the Access Journey steps involves a different set of decision makers with different value preferences and needs. Payers are generally focused on long-term outcomes and related economic impact. They tend to put limited significance on direct clinical metrics unless it has a sustained and long-term health impact. Provider organizations are likely to want to see an impact on quality metrics, such as (re-)hospitalization rates, other outcomes metrics and patient satisfaction. These differences may not seem fundamentally large, but they can have a significant impact on clinical development programs. For example, whether measuring a tumor response rate, progression free survival or overall survival has large implications on

	WHO TO INFLUENCE	WHAT THEY VALUE
List and Net Pricing	+ Government and Private Payers + PBMs, GPOs, Trade	+ Demonstrated long-term outcomes + Limited budget impact, rebates
Payer Access	+ Government and Private Payers + PBMs, GPOs, Trade	+ Benefit/value evidence vs. unmet needs + Economic and budget impact
Clinical Guidelines and Value Frameworks	+ Medical Associations + Compendia, Pathway Companies	+ Clinical and outcomes evidence + Appropriate place in therapy
Provider Formulary	+ Provider Organizations + Hospitals, Treatment Centers	+ Impact of treatment on relevant outcomes metrics + Impact on organization's financials
Prescribing	+ Physicians	+ Address patient clinical and humanistic needs + No access hurdles/hassle, patient affordability
Prescription Fulfillment	+ Patients/Caregivers + Pharmacies	+ Patient understanding of value across options + Address deductibles, co-pays
Patient Adherence	+ Patients	+ Managing side effects + Address patient affordability

Figure 3.4 **Decision makers and preferences for each Access Journey step**

trial design, investment need and probability of success. Similarly, HbA1c management in diabetes and low-density lipoprotein (LDL) control in hypercholesteremia may be accepted metrics for success to a clinician, but payers and provider organizations may want to see additional evidence of long-term impact on outcomes and related cost.

Even where stakeholders are aligned on a meaningful metric, the level of evidence required can be very different. Payers typically require head-to-head trials versus an appropriate long-term endpoint. Provider organizations prefer real-world evidence that demonstrates improvements on meaningful outcomes metrics in their specific population. Patients want to feel a response, improvements in their symptoms and confidence in the long-term prognosis.

Understanding what drives decisions for each of the Access Journey elements is of critical importance when devising a development plan and ultimately a launch marketing strategy. We can use our benefits analysis methodology to systematically assess priorities to stakeholders in each of the benefit domains. This is discussed in more detail in Chapters 12 and 16.

Summary: the Access Journey

As a result of the prescription drug market entering into an "*Age of Value and Affordability*," a new approach is needed to identify and meet value and evidence needs that are required for successful development and commercialization of prescription drugs. The *Access Journey* framework is describing a sequential set of hurdles that need to be addressed to ensure ultimate patient access for the drugs that he or she needs.

Each of the Access Journey steps: payer access, provider formularies and treatment pathways, clinical guidelines and value frameworks, physician prescribing, prescription fulfillment and patient adherence involve different decision makers with very different needs, perceptions of value and evidence requirements. The framework provides a systematic approach towards identifying value and evidence needs, which can assist in trade-offs related to development and commercialization decision-making.