In Vivo
Informa Pharma Intelligence

Market Access 2020: Understanding US Payer Expectations

Big pharma is facing a difficult US competitive landscape as its traditional customers realign to build their own redoubts of size, scale and reach.

BY WILLIAM LOONEY

Consolidation on the payer side is changing the dynamics of success in health care.

Pharmacy benefit management groups (PBMS), far from being marginalized, are now positioned within insurers to realize with verifiable metrics what big pharma has so far only promised – lower costs and better outcomes.

So what? Big pharma moves at a slow pace, and payers face their own internal divisions, but the embrace of risk-sharing will grow as the price of many new therapies soar to seven figures – some drug-makers will surprise with market disrupting price strategies designed to win first-mover advantage even in crowded therapeutic segments like cancer.

Last month, *In Vivo* convened a roundtable of principals at one of our partner editorial advisers, Real Endpoints Inc., to examine the impact of US market structural changes on the industry's growth prospects in a world where it seems everyone else now speaks a different language: of insurance design, not drug design, of coding text, not clinical trials, and of service apps, not science.

Government pressure on big pharma is not a major factor going forward, with the industry's fate depending more on the private-sector realignments taking place in health care overall. With three major insurance players delivering medicines reliably to more than 80% of the US population, it is hard to envision a scenario where politicians agree to displace it with something untested – and, in an era of annual trillion-dollar budget deficits, absurdly expensive.

Stiff price competition is coming in all US therapeutic categories, including protected classes like cancer and rare diseases. For the industry to thrive in this environment, innovations in pricing will be as much, if not more, important than a product and the science itself. Examples of risk-sharing and other industry contracted pricing arrangements are emerging, but the pace has to pick up. Just as drug makers are exposed to huge potential losses on the R&D pipeline every year, so they must accept more risk in their commercial investments through value-based agreements.

The following are key excerpts from the roundtable discussion:

***In Vivo*: What is your take on the key developments driving market access over the past 12 months?**

Jeff Berkowitz: There's now disruption at every turn, on both ends of the pharma supply chain, and for three reasons. The first is the acceleration of vertical and

horizontal integration in key segments of the business outside pharma – namely its customer base. The second is the pressure for increased transparency on drug pricing and the explosion of information in health care overall. And the third is a side effect of the first two, posing questions for the long-term viability of the pharma business model: as the customer base consolidates and its command of the strategic asset of information grows, what should the pharma C-suite be doing to ensure its own future growth and profitability? I've been engaged on the commercial side of this industry for more than two decades, working at innovative drug manufacturers as well as payers in PBMs and retail distribution, yet these are the most drastic, fastest changes I've seen.

The most startling development is the pace of vertical integration outside the pharma space. At Real Endpoints we track developments across four segments: retail pharmacy, PBMs, drug distributors, and payers. Increasingly, we look at specialty pharmacy and the contracted patient services component too. All these businesses were once heavily siloed. But now three behemoths deliver health care services, including drugs, for over 80% of the US population. UnitedHealth Group is one, a major insurer with its own PBM, Optum; Express Scripts, the country's second largest PBM, now has its own insurer, Cigna; and finally CVS Health, the country's largest retail pharmacy chain, owns what was once the US's third largest health insurer, Aetna. Walgreens, the second largest US pharmacy retailer after CVS, is also involved in the distribution/wholesaler business due to its one-third stake in one of the largest drug distributors, AmerisourceBergen. But note that providers and patients do not figure prominently!

With this market reach comes an extraordinary level of negotiating power, especially as the pharma business remains not only vertically siloed but also highly fragmented within its own space: not one big pharma company controls more than 10% of industry sales. You have significant change and integration on one side of the coin while pharma continues to conduct business as usual.

Drug company executives say that PBMs are merely middlemen, adding little value to the system, and will eventually diminish in importance.

Berkowitz: They've been saying the same thing for the two and a half decades I've been in this business. Today, PBMs are more powerful than they've ever been. And their integration with insurers means they have no incentive to disrupt their own businesses – except that they now, integrated with payers, can try to deliver care seamlessly, toward a better outcome, hopefully at lower cost.

Silos Are Not A Strategy

What is the biggest structural challenge for big pharma faced with this consolidation in its customer base?

Berkowitz: One problem is the strangely persistent disconnect between the R&D organization and the commercial business leads responsible for securing acceptance of new products among payers. The commercial side is often still not trusted

ROUNDTABLE PARTICIPANTS FROM REAL ENDPOINTS

Roger Longman, Founder and Chairman

Jeffrey Berkowitz, CEO and Director

Susan Raiola, President

Jane Barlow, Executive Vice-President and Chief Clinical Officer (not pictured)

Ryan Walsh, Vice-President Client Services

– perhaps "valued" is a better term – by the R&D teams, whose instinct is to defend development projects that have been in the works for years. And the business side can be caustic about the scientists who lack that real-world perspective they encounter every day, outside the lab, with a changing roster of customers and stakeholders. This tension is often compounded in small biotechs, led by entrepreneurial founders convinced their science is so unique it will be embraced immediately, without question, by payers. Despite our efforts and those of other outsiders who work to help each side connect the dots and overcome the lip service biopharmas pay to cooperation, they always seem to be operating on completely separate tracks.

Roger Longman: That same disconnect appears between pharma and payers. Pharma's leaders have grown up with the physician as the principle customer. The new payer customers have very different goals and incentives – indeed they speak an entirely different language, the vocabulary of insurance design, reimbursement coding, formulary management. How many R&D executives understand it? And if they don't understand it, how can they know their customers? As elementary as it might sound, one important step forward for pharmaceutical companies would be a kind of payer boot camp – a deep dive into the structure, vocabulary, incentives and business practices of the payer and distribution world. I've seen this happen on an ad hoc basis – we just did such a program for the new president of a global pharma as well as a number of C-suite teams. But I'll also say there were no R&D execs in the room. I wish there had been.

Berkowitz: When I left Merck & Co. to join Walgreens, the

transition was – to put it mildly – challenging. I was used to a business that had an average 25% margin on marketing innovative medicines and I moved to a distribution and retail pharmacy business that was lucky to post 3%. It took me a while to understand how Walgreens made money; who was important to them and who was not. I realized that I was now working for an organization that dispensed 25% of the entire prescription volume of the US. That's huge. So why did drugmakers know so little about them? It may be that pharma is still paying lip service to a broader definition of customer centricity, beyond the provider physician. While the big pharma innovators are focused on gene therapies for those rare unmet needs, Walgreens, UnitedHealth and CVS/Caremark want solutions for cardiovascular disease, diabetes and obesity. So big pharma is on one end of the spectrum still looking inward, enamored with their own innovation, while the rest of the health care ecosystem is grappling with real-world issues, having a very different, integrated conversation. Even now, there is very little cross-sectoral dialogue taking place – at least not enough to make a difference.

Patients And Payers: Are You Leaving Money On The Table?

Aside from the disconnects between R&D and commercial are there additional areas within pharma acting at cross purposes?

Susan Raiola: Yes, there is a disconnect between what you might call the coverage side of reimbursement (getting payers to put a drug on formulary in a somewhat advantaged position) and the access side (helping patients adhere to, and afford, a new medicine). Both can be expensive, the former in terms of rebate dollars, the latter in terms, for example, of co-pay assistance or free drug provided. But both are tactics within a broader market access strategy. In the broadest sense, how hard should you push the pedal, how much should you spend, to maximize coverage and revenue through rebates – and how much should you pursue access through a free drug or co-pay? Most important, how should those two basic activities be coordinated? The problem is that the two categories of activity are often split. One group oversees patient support and service hubs, and another focuses on payers. There's no integrated strategy and certainly no integrated P&L.

Berkowitz: Exactly. It's quite common for the head of pharmaceuticals in a big US company to get a big bill for the rebates paid to the PBM in return for a place on the formulary, followed by another big expense for patient assistance and services. Yet you are still not getting much insight on whether you've optimized your investments on either side to get to a target market share at a target cost.

Raiola: I should also point out that patient assistance programs are rarely seen as strategic.But they are. They can have a significant impact in product take-up, particularly in crowded therapeutic classes where a strong patient support program is a source of competitive differentiation. Patient attitudes are also changing, in that many now want the same customer experience from pharma as they get from Amazon or Netflix, with service from one source, covering the full spectrum of needs, available at any time. We are now at the point when you can no longer refer to patient assistance as a "program." Instead it's a customized "service app" capable of serving the whole person, who just happens to be a patient too. Drug companies must adopt the mindset that the patient customer wants a different model than what he or she is currently being offered.

Innovative Contracting: A Driver Of Competitive Advantage

Step back for a moment: can we define pharma's pricing and revenue challenge?

Longman: The established brands on which pharma has depended are under extreme competitive pressure. Rebates for insulin are in the 75% range. New, highly innovative drugs in large categories are quickly seeing competition – and therefore high rebates. The anti-CGRPs for migraine are a good example. Or a great success like Regneron's Dupixent for atopic dermatitis: just a year or two after launch it will face, thanks in part to the same scientific wave of progress in immunology that enabled its creation, a group of oral JAK inhibitors with startlingly good efficacy. Meanwhile, society is less willing to tolerate the double-digit price increases which have fueled revenue growth more than they should in comparison to prescription growth and new drug introductions. And even these price increases are less valuable to pharmas thanks to clauses in virtually every major payer contract that limit price increases. A 10% nominal increase in wholesale acquisition cost (WAC) translates, in the real-world of Aetna or Optum, to maybe a 3% increase.

What is pharma doing about this?

Berkowitz: For one thing, companies are investing heavily in categories theoretically resistant to pricing restrictions: oncologics, drugs for rare diseases, and next-generation innovations like cell and gene therapy.

Jane Barlow: In the past two years, more than half of FDA approvals of novel drugs are for rare or orphan indications that impose a big cost on small populations of eligible patients. Now on top of that we have a pipeline of gene therapies promising outright cures to disease. The common theme is a high level of visibility to payers.

This also takes place against a backdrop of powerful emerging players like the Institute for Clinical and Economic Review (ICER), which stresses its independence and reliance on evidence to establish the true value of these novel treatments. Roger Longman and I were both speakers at the Alliance for Regenerative Medicine's recent summit in San Diego, a distinguishing feature of which was the near universal declaration by the attending companies that new gene therapies would be sold with performance guarantees for the payers. That's a dramatic change from the approach to pricing and reimbursement taken by the industry up to now. It demonstrates the pressure on gene therapy companies to reset the terms on how they go to market.

It is also changing the dynamics of pricing in the rare disease space, once seen as less prone to the restrictions that payers placed on chronic care medicines. Rare disease drugs faced scant competition and were intended for small target populations. But in the last three years we have seen biotech and big pharma rush into this segment, replicating many of the same conditions

we've seen in more common chronic diseases.

A good example is spinal muscular atrophy (SMA), a high-profile genetic disorder with a small cohort of several thousand patients in the US. The first effective gene-based treatment, Spinraza, was approved by the FDA in December 2016; since then, another possibly curative treatment, Zolgensma, has entered the market and three more similar products are now in pipeline. Payers may not be jumping to impose the same kind of blanket, race-to-the-bottom pricing regime as they've imposed on primary-care cardiovascular and diabetes drugs. However, payers will demand concessions from manufacturers to avoid significant restrictions. Biotechs recognize this, which is why you're seeing a proliferation of risk-sharing agreements.

Looking forward, innovation is no longer just about the science; innovation can drive the contracting structure as well. An innovative contract by itself can differentiate against a competing product in the same category, and preferred status will come precisely because the manufacturer has offered a better way to buy the product. What this means is more variety in types of contracts, not just one preferred approach. This is good for all parties.

Ryan Walsh: The embrace of integrated care models of financing and delivery creates a natural home for innovative contracting. But the situation must be placed in perspective.Although many big pharma CEOs have warmed to the idea of innovative tools like value-based contracting, there is "no one size fits all" approach. The circumstances that make these agreements feasible are often unique. Not everything is measurable. Not every outcome is achievable or meaningful within a time frame acceptable to payers and pharmas. That said, there is no question that innovative contracting is now an essential tool for pharmas and payers.

Case Study: There Is Reward In Risk

Barlow: The increasing power of payers, a consolidating marketplace, price pressures – these require companies to take a novel approach to pricing, particularly in very high-cost or competitive categories. If you think about the three basic elements of a drug's value – efficacy, safety, and cost – only cost is not an intrinsic property of the drug. And the higher the cost, the greater the need for its justification. Just as companies have to prove safety and efficacy to the FDA, they will more often have to prove value – which is what a risk-sharing agreement does. As Ryan Walsh notes, we can't minimize the complexities of these arrangements. But pharma is going to have to put its money where its mouth is. It does it all the time in R&D when spending millions on clinical trials. By the same token, it will more often have to risk its commercial investment with a value-based agreement.

Take the Illumina/Harvard Pilgrim risk-based contract for coverage of non-invasive prenatal testing (NIPT). NIPT is more expensive than traditional prenatal screens – but it's also more accurate. And, Illumina argued, using their NIPT technology would not increase costs: doctors would stop spending money ordering traditional screens and the more accurate NIPT would reduce the number of false positives and therefore the number of invasive tests, like amniocentesis. And the fewer the invasive tests, the fewer the adverse events. But payers balked at expanding coverage because of the price.

So, in a deal we helped arrange and monitor, Illlumina went at financial risk – if Harvard Pilgrim expanded coverage to average risk pregnancies, the plan's screening costs would not go up, and invasive testing would go down. And 18 months after the deal was signed in January 2018 the results are in – more NIPT tests were ordered, invasive testing and overall screening were reduced, and costs were flat. Illumina now has a trove of highly credible, real-world data it can use with other payers and Harvard Pilgrim members have access to high quality care. That's the power of risk-sharing.

Cancer Gets Competitive

When I first asked what pharma is doing about pricing, you lumped together oncology and rare diseases. But are there differences?

Longman: Absolutely. Oncology is still the most price-protected of all major therapeutic categories – which is why you see so little rebating in the category, or the kind of innovative contracting we have been describing. Payers have little ability, and less will, to force the kind of formulary or use preferences they're happy to require in other categories – and which they will use in even rare diseases when competition heats up.

For one thing, oncology has regulatory advantages. It's one of Medicare's six protected classes so it's very difficult for a plan to keep any new entity off a formulary. On the public side, oncology is THE scary disease – no payer wants a headline saying it denied "Sally Smith," mother of three, a life-saving cancer drug.Oncologists also make a significant share of their income from the buy-and-bill economics of cancer – they're still incentivized to use the more expensive therapies. Fighting motivated providers is tough. But the most important issue is payer habit. In most other specialty categories, payers can require "PA to label," that is, they'll only authorize reimbursement if the drug is being prescribed for a labeled indication. In oncology, payers will, in essence, "PA to guidelines" in the compendia, like the National Comprehensive Cancer Network (NCCN) clinical practice guidelines, which are very liberally determined. If there is even modest evidence that a drug works in an indication, it's generally listed in the compendia – and a payer will most likely approve the reimbursement.

The question going forward: how long will this situation last? Our bet is that as competition heats up, as we see more head-to-head trials within categories – say the PD-1 inhibitors – the also-ran drugs, the ones that are fourth or fifth into the category, will create strategies in collaboration with payers and providers that focus on reducing patient cost. And those strategies will begin to change oncology reimbursement.

The Great Evidence Divide

Can new information tools like real-world evidence help raise the level of confidence in the assumptions that underpin innovative approaches to contracting between pharma and payers?

Barlow: Real-world evidence is often a prerequisite for clinical approval and adoption of a rare disease therapy. It's clearly part of the fabric in how such drugs are evaluated. The problem is the disconnect between the design of a pivotal trial and linking

measurements from that to an outcomes-based metric to assess the execution of an innovative contracting arrangement. An example is the "Six-Minute Walk test" introduced some years ago to evaluate a patient's aerobic capacity and endurance. While this measure is commonly used in the clinical trial setting, it is not a practical test for use in clinical practice and rarely used. That makes it much harder to obtain verifiable outcomes linked to the trial that can be trusted as relevant by both parties to a contract. Defining those outcomes has been a large part of our recent work: can we establish an endpoint in a clinical trial that that can also be used as an endpoint in a risk-sharing contract?

Looking Forward

Cumulatively, how will the forces you have outlined shape industry prospects for market access in the coming year?

Berkowitz: It appeared for much of this year that the Trump Administration would introduce a major change in the current business model for pharma through removal of the federal anti-kickback statute's safe harbor clause for rebates on medicines in the commercial sector. Then suddenly, over the summer, it was quietly withdrawn.

The lesson we draw is that the polarization of politics today effectively prevents Congress and the White House from agreeing on a coherent strategy toward the industry, good or bad. Government is actually less relevant if we consider how the vertical integration of the past two years has inoculated key private-sector players in health care against the disruption that removal of the safe harbor clause might have caused. In fact, the consolidation of roles formerly played separately by Insurers, PBMs, retail pharmacy and distributors remove the incentives for any one actor to blow up the system. The Medicare Part D benefit has been in place for more than a decade; it's one of the more successful federal programs in terms of public support. Now that a few massive, well-integrated private-sector companies are delivering medicines consistently and safely to more than 80% of the US population, it's hard to envision a world where government displaces that system with something new and untested.

What about the rise of health technology assessment influencers like ICER? Will it and other similar institutions emerge as the true arbiters of market access by defining what constitutes value in medicines?

Barlow: It is becoming important to consider in advance the reaction of groups like ICER in pricing a new drug. How will your entry fare as ICER lays out the value landscape in a therapeutic area? ICER is influential, no doubt. But there is a bigger strategic question for industry, which is the need to assess the impact of other players with a significant customer base of their own. Are you going to Aetna, UnitedHealth, or Cigna and asking them what's on their mind and the issues you should be solving for? In many ways, this is a conversation that is much more strategic than the kind of narrowly focused dialogue one has with ICER.There is more to business than pitching the value of a particular drug. It's better to start with a broad perspective on solving the customer's problems rather than simply trying to make that customer buy what you're trying to sell to him.

What's the best course for drug-makers to take in navigating successfully through this complex political environment in 2020?

Walsh: The industry has an opportunity to pursue and, importantly, promote more rational and defensible approaches to pricing. Although drug pricing, however tempered, will always be a lightning rod for criticism, this kind of self-regulation will go down well in an election year. Interestingly, it's already underway, but rarely publicized, and even more rarely credited to the manufacturers (often other channel partners will take credit for these very actions as a result of their marketplace pressure). Many companies have moderated their traditional price increases, in both size and frequency, and others have taken opportunities to make increases contingent on meeting a defensible benchmark, like the medical inflation ratio. On launch pricing, there has also been some more deliberate, rational pricing, especially in more competitive spaces where payers are looking closely at market dynamics like generic penetration, brand saturation and differentiating therapy characteristics. Overall, self-regulation will carry the greatest impact, certainly more than government can expect to achieve given the lack of alignment in politics at the federal level.

Overall, self-regulation will carry the greatest impact, certainly more than government can expect to achieve given the lack of alignment in politics at the federal level.

Longman: Companies will continue to surprise with actions that the investment community would have dismissed as improbable – even impossible. In 2017 I was a member of an advisory group looking at the competitive outlook for the PCSK9 inhibitor class of anti-cholesterol drugs. We were about 15 people from companies and payers and the big question was whether the two companies competing in the space would opt to cut list prices to grab more market share. The verdict was unanimous – no way, never. Yet Amgen late last year slashed its price for Repatha by 60%. Lilly did something similarly bold to shake up pricing for insulin. Right now, bluebird bio is suggesting it could price its beta-thalassemia drug, Zynteglo, in a way that meets payer concerns about the durability of this curative therapy, given its likely $2m plus price tag. It's an amortization arrangement where payers pay 20% up front, with the remaining 80% spread over five years and at risk if the therapy doesn't work. This is a risky strategy, but it certainly represents an effort to meet the market more than halfway.

Comments:
Email the editor: *Lucie.Ellis@Informa.com*

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