



CERTARA STAKEHOLDER INSIGHTS

Payer-Pharma Perspectives on Outcomes-based Contracting



EVIDENCE & ACCESS

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Certara Stakeholder Insights

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Methodology

This paper is part of a series based on 15 semi-structured interviews with managed care experts and pharmaceutical executives, a comprehensive review of secondary research, survey data and grey literature including more than a dozen contract case studies and industry presentations.

Data analysis was supported by an innovative contracting team of Certara consultants with experience in the design of performance agreements in the US, Italy, France and UK. To preserve confidentiality, the managed markets interviewees for this research are not quoted in this release of the report. Any specifically attributed statements in this document are sourced from media reports or other material already available in the public domain.

Views from

We've outlined in the first part of this report that the adoption of OBA as a contracting mechanism is poised to grow given the urge among payers to reduce their exposure to risks of uncertainty in clinical value and budgetary impact, and the demand for manufacturers to demonstrate real world value in order to justify new, high-priced therapies as well as to guarantee access to existing products exposed to increasing rebate levels. Structural challenges for OBA uptake remain but market forces are demanding change. The US healthcare system has embraced the move to value-based purchasing, a transformative process that has marshalled heightened expectations for the pharmaceutical industry to "put skin in the game" – economically speaking, and in no small part reputationally, as a demonstration of civic responsibility to address concerns among patients, managed care stakeholders and policymakers about a rising cost of medicines in the US.

Prior to discussing a number of practical considerations for the OBA implementation in the third chapter, it seems prudent to look beneath the veneer of corporate declarations and examine the voices and rationales of those who have sat at the negotiating table. Since we are often asked what these negotiating partners "really" think about OBA, we'll give the floor to two seasoned OBA pioneers and let you be party to their personal reflections: Dr. Michael Sherman, Chief Medical Officer at Harvard Pilgrim and Mohan Balan, Vice President of Product at Tesaro. Both kindly participated in a stakeholder session conducted by Analytica Laser in April 2017 at ISPOR and we have decided to feature their unfiltered perspectives in their own words opposite.¹

the Negotiating Table



MICHAEL S. SHERMAN
MD, MBA, MS
Senior Vice President & Chief
Medical Officer, **Harvard Pilgrim
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"We are a regional health plan that does business in four states here in New England. We spend about 2.8 billion dollars every year on drugs, on services, on hospitalizations, et cetera. I'm sometimes asked recently, how come we're spending so much time worrying about pharmaceutical costs? And yes, that actually is a change. We now spend about one out of every four dollars on drugs. Twenty-five percent of the healthcare dollars – it's growing faster than any other slice of the pie. Now, twenty-five percent is not intrinsically good or bad. If we see more drugs that save lives, that keep people out of the hospital, that serve people's needs, maybe it should be thirty percent. However, that's clearly not true of all the drugs. There are wide differences, in many cases, in responsiveness, which means that some of the dollars we're spending don't do any good.

What you should understand is that, first up, we're a not-for-profit organization and just struggling to break even. So, it means that when you see high-cost drugs hit the market, and they add cost to the system, it means that the payer, the insurer, is not paying for it. Ultimately, everyone is paying for it. Either the individual who needs a drug, which, when you're talking about drugs that are hundreds of thousands of dollars a year, it's only a small fraction of that but matters. And it goes into increasing the cost of insurance premiums, which no one is happy about. I spend a lot of my time being worried about how we balance access to drugs, which we care a lot about, with affordability. And just to be clear, nowhere in our mission is there a statement about keeping our members from high-cost drugs. It's not our mission. But we do need to think about the value of the drugs that they're taking and ensure that we balance access against that cost issue.

I've been in my current role for six years. Up until three years ago, I spent about ten percent of my time dealing with drugs because again, I have a lot of other areas. Now, I spend about fifty to sixty percent of my time, personally took over chairing our P&T committee which makes the critical decisions. Quite frankly, that's where the fun is. If you think of this as an opportunity, how do we work together to balance affordability and access and think about different types of models or underlying incentives, it's a great time to be doing this.

I get excited, not about saying "no" to different indications, whether it's cancer or rare diseases, but working with pharma companies to figure out how do we actually make it a win-win situation. Health plans like mine don't want to keep people from drugs that do work, but they worry about spending money on drugs that don't work.

One way to address that is through value-based agreements. We've been doing this, actually, with the whole rest of the health care delivery system, and this part of the country and the US is fairly advanced. In Massachusetts, for example, 75% of the physicians and hospitals have some types of outcomes-based agreement. So, it's not really that surprising that we're talking about doing this with pharma companies as well, to move beyond being paid for a pill to being paid for outcomes.

The other thing I'll add is that pharma companies spend a lot of time and money trying to reach physicians and trying to reach the public so that they're drugs are used. I will tell you that the physicians who are being paid for outcomes, really, really like when they see that the pharma companies are going to share the risk and really believe in their drugs. That may actually impact the type of the decisions they're making, which is another benefit.

So this is a big opportunity. We now have eleven outcomes-based agreements. Let's look at some of the characteristics that enable them: One, there should be variability in the response. For example, we do not have an outcomes-based agreement for hepatitis C. That has a significant budget impact, but it works over ninety, ninety-five percent of the time. It's pretty

unusual to have a failure, so why should we spend time and energy putting together an agreement and capturing data for something that we know works? Where we need this are on cancer therapies and other drugs where there's a variability of response. Adding to that, some people will do well with the drug and others won't.

And I will argue that, particularly with some high-cost drugs, they're priced for perfection. When you see some of these drugs come out for cancer or rare diseases, and they cost a hundred fifty thousand a year or three hundred thousand, maybe they're worth that, maybe they're not. That's a value framework discussion for a different day. So maybe they are. But, if the patient doesn't respond, maybe it's worth a whole lot less. Like, enough to cover the cost and a little bit more. Such a system doesn't exist in this country today. To the extent that we can pay for effective treatment and not for ineffective treatment, OBA free up the dollars and allow us to be less restrictive.

Second, there should be the ability to collect data. When you look at our agreements, and I'll mention a few of these shortly, one thing that really comes across is they're for lab values, they're for data that can come out of claims date, hospitalizations... It doesn't cost a lot of money or time and energy to collect the information. That's pretty important. Now, I can see, if we were doing something for a rare disease that cost maybe half a million dollars a year, if it worked, and we were paying a hundred thousand dollars and it doesn't work, I can hire a pharmacist to go out and get that information, polling the physician or the patient, whatever it takes.

There should also be a clear relationship between the drug and the outcome. So in many disease states, there are. In others, and this is why I think this is something we'll see in maybe twenty to twenty-five percent of the conditions but not for many, is because you need to have that relationship between the drug being given and the clinical response, and there are many clinical conditions that can be highly variable, where you're not quite sure.

And then, there needs to be a reasonable period of time between giving the drug and being able to measure whether or not there's a response. Whether it is a proxy like a lab test or a cardiovascular event, if there's five or ten years in the future, it's going to be very hard for us to do an agreement and make it work.

Finally, and most importantly, we need good partners. You need organizations that want to do this, whether it's on the payer side like mine, or on the pharma side. And I will say that, although there is a lot of debate in the press today, finger-pointing, if you like, about why costs are high, on a personal basis, when I'm sitting down with my colleagues that work for some large and small pharmaceutical companies, they're very productive. They're good people. We're going from arguing to pay more versus less, to how do we line the incentives and enable success. And that's leading to different kinds of discussion. One of the positive things about our eleven agreements aren't just the eleven agreements. It's that, it's the tip of an iceberg, and there are many more discussions underway, which I think will lead to more successes.

Now for some examples of some of the type of things that we're doing, let me give you three different flavors. 🍷

¹ "Deal or no Deal? When and how to forge an outcomes-based agreement". ISPOR 22nd Annual International Meeting. Note that the verbatim narrative featured above is a transcription of the participants prepared remarks during the ISPOR educational symposium. Both contributions have not been edited for content in attempt to offer an authentic reflection of the shared viewpoints.

One is with Novartis for their drug Entresto for congestive heart failure. Again, it costs a lot more than the ACE and ARBs that it replaced, but there is data suggesting that it can be more effective, and we want to make it available to our members. Well, we have an agreement by which the price of the drug is aligned with value, and it's adjudicated through a rebate, which is kind of how we do things in this country. The important point here is that if we see the reduction in hospitalizations that were promised and presented to the FDA and seen the clinical trials, we pay the price as is. If we do not see that, if the hospitalization rate, which is easy for us to measure for congestive heart failure related admissions, which have costs involved, if they are higher, or if they don't go down, then we pay less for the drug. It seems reasonable for us and reasonable for the pharma company to really put their money where their head is. Again, that's the whole discussion around the fact that payers seem to be skeptical about whether the mileage will vary in the real world. In other words, what happens in best-case conditions, you're not going to extend it to a busy clinical practice that does nothing but one type of care. Whether we will see the same outcomes in a broader, busier, more general clinical practice in a nonacademic setting without clinical research associates and others following the patient.

A second example would be with Lilly for Trulicity. I really like this agreement, because it's one of the few that's actually about comparing effectiveness. And of course, Trulicity is a GLP-1 drug used to treat diabetes. What we do is we look over a six-month period at the percent of patients who hit a target in respect to hemoglobin A1C control. If those on Trulicity do better than those on other

GLP-1's, they get paid a little bit more. If they do less well than those other GLP-1's, they get paid less. It seems to be the right thing to do. And you can imagine, the physicians like it. I think Lilly's gotten a lot of good attention they deserve recently. I think that's a very good approach.

And then a final example, with Amgen for their PCSK9-inhibitor Repatha. That was actually our first and our most recent one. We did one agreement when the drug came out, which was really tied to a guarantee about reduction in cholesterol level, again, similar to what they promised. When it comes to patient with uncontrolled high cholesterol levels, we are completely at risk. [According to the most recent, 2017 agreement] if the patient taking Rapatha suffers a cardiovascular event, either a thrombotic stroke or an MI, a heart attack, both the payer and the patient get all their money back that they paid for the drug. And again, that sends a positive message, and it makes us more willing to support them in driving access of the drug. I think those are just some examples.

I'll just say briefly that where I'd like to go with this are for cancer or high-cost, rare disease drugs. Now, we haven't seen any of these cases yet, because of the complexity and, quite frankly, because the fact that a drug is priced very high probably suggests the fact that there is little competition, and so the pharma companies haven't felt the need to hear this. But again, where there is less than stellar data, and they're looking for expansions for indications, that's one way to get there. I had a meeting with a company just last week about a drug that's not even out yet for a year. It's for a rare disease, and I won't get into specifics, but they already talking with us about the measures you're at risk for.

They've even suggested that if their drug is ineffective at preventing liver transplants, which are a benefit, that they would go at risk for that. Again, the right kind of discussions to be having.

With cancer, again, we try to drive toward guidelines, but as we know, those are changing as we move from where there's a body of evidence to some based on genetic mutations, going to diagnostics, where there's not as much data. Health plans are likely to say let's be cautious, not because they want to keep people from cancer treatment, but because they don't want to spend money, on high-cost drugs where it's unknown if they will work. I've already offered up opportunities to pharma companies whereby we can explore. Perhaps we do go to the pharma companies and say, 'you know, we're not going to limit your drug at all. We can try to find any, or any type of cancer. We're not going to have any restrictions like most payers do – but there's a catch. We don't want to see a bill unless there is an agreed upon clinical result commensurate with what you've shown in the data.' Whether it's a four-month, remission-free survival or some other metric that is tied to what they got the drug approved for.

The point behind these types of approaches is that they are not just good to driving toward value, but I think that they can offer some benefits to all the stakeholders, including the patients and the pharma companies. I'll just close by saying this may reduce costs, but that's not even our main goal. If these don't reduce our spend on drugs, but they change the spend, so that the dollars are spent on on high-value, effective treatment and not on drugs with no impact, I think then we can consider these a success.



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I'll start with a disclaimer. Opinions that I express are mine, not those of my current or past employers. But I have worked in the industry for twenty-plus years, and over those years, I have designed many deals and implemented a few. What I will share with you is my experience. And what I say is as much, or even more, about what I've learned from my failures, as it is about what I've learned from my successes.

So let's start by taking about, "if you're a pharmaceutical company, why would you think of doing an outcomes-based agreement?" When I think back to all the things that I've worked on, those reasons fell into three buckets. These are my three buckets: One situation is where you really have access barriers or problems because there's uncertainty about the clinical value of your product, and you see this as a way to overcome that uncertainty and gain access. The second bucket is where there is really an issue of budget impact. The customer perceiving your drug to be costing too much money, and this is a way for you to mitigate the budget impact without having a price referencing issue by changing the price. The third reason is to really get competitive advantage. By doing this, you can get a differential or preferential access position relative to your competitor. And it's also kind of a PR objective, and we have to acknowledge it.

Sometimes, to be honest, it's a mix of the three or four, right? It's not always just one.


Looking back at reasons for failure, one of the issues that I faced is that we often enter into discussions of doing this without a clear understanding of why we are doing it. That really results in conversations that go in circles because there's not enough organizational alignment around why you are pursuing an outcomes-based agreement. So, let's talk a bit more about my first bucket, which is the uncertainty bucket.

What causes uncertainty? I like to think of it in groups of three again. There are three potential reasons that are drivers of uncertainty. One is really kind of obvious, there are more and more products that are coming to market with either accelerated or conditional approval based on simulated tests/ single arm studies. It's very challenging for health technology assessment agencies prepared to understand what the added value for this drug is really, relative to what else these patients would be getting. The second is the product comes to market with data on a certain endpoint but may lack data on those that are the key drivers of value. This happens in the case of accelerated approval in oncology, where often it's based on overall response to treatment. But it can happen even in a full approval setting where a drug could be approved based on PFS, or areas where it could be approved based on LDL, so it could still be based on a certain endpoint, and we really don't know what the impact is on the true outcome that we care about. The third potential driver of uncertainty is that the clinical trial data is generated in a limited population in a

controlled setting. There's uncertainty around how this drug will perform in actual clinical practice, and whether the trial data going to be applicable. When you're looking to mitigate uncertainty, it's essentially one of these kinds of drivers that you're trying to address.

How do you mitigate this uncertainty and what contracts do people usually enter into? If you look at the agreements, they're usually going to fall into one of two buckets. First is coverage with evidence development. So this is where you enter into an agreement where the payer agrees to provide access and pay for the product for a limited period of time, with the condition that you come back with evidence which would allow them to decide whether they would continue to pay for it. This was introduced by CMS many years ago, and in many European countries they are either doing it or moving towards doing something like this.

In other type of agreement, from the very beginning, you say, you're really going to pay for performance. You're going to tie the reimbursement of the drug to how the drug performs in the real world setting. If you're going to do this, you have to make a few decisions: Are you going to do this at population level, or at the individual level? What outcome are you going to measure, and how are you going to tie outcome and reimbursement?

Of course, one of the key challenges here is thinking about the outcome measures. Do you measure what we can measure, or do you measure what matters? The problem often is we cannot measure what matters. I am thinking of an example of something that I have implemented in hematology. 

➤ The advantage in hematology is that the outcome is usually measurable, or much more easily, because it's based on a blood test. But when you go to solid tumors, how can you tie your reimbursement to a response rate?

As I am looking back, let me think of what were reasons for failure, so if I said "Why did I fail so often, and succeed so few times?" Well, when I look at it, the reasons for failure, I'd identify three once again. The first is the inability to quantify risk with confidence. The problem was that you have clinical trial data, you have no idea how the drug is going to perform in the real world setting. That makes it very difficult for you to quantify the risk that you're taking when you're moving forward with an agreement. That's not so great from a company, internal perspective, when you're putting forward a proposal, and you have no idea how much it is going to cost. The second is the outcome that you are trying to measure is very difficult to measure. It becomes a pragmatic issue in terms of 'is this feasible to do'. The third is that measuring the outcome costs too much money. The cost of actually operationalizing the plan outweighs the potential benefit you get from it.

Stepping back, what would I have done to maybe not fail so much? I could identify a few potential points that could be done. First is, I think, you need to have organizational alignment on how an outcomes-based agreement is going to be important for this product. And, you need to stop trying to curve. Really think about what data you can collect in phase III.

Do you need to run phase III new trials to collect data? So, start early and build infrastructure, and keep building. If you really, really need to collect data, are you putting in place the infrastructure to do this? And finally, be creative. This is not a well beaten path - you have to be creative. Think of anything. Doing things like, for instance, risk quarters. Look for what I call pragmatic surrogates. Italy is a very good example, where, for solid tumors, what they've said was 'we'll pay based on whether the physician decides to continue treatment or not'. That's not recessed, but it is a very practical, meaningful assessment of the product's benefit, where the physician sees whether this product is going to continue to be helpful to this patient or not. Another creative question is something that rarely hear people talk about, which is who will be your sample? Do we have to assess every single patient that goes on this product, or can we get representative centers or regions or other ways to sample so that we can reduce the cost of actually doing this?

So, some of the key success factors here are: One, know why you're doing it. Two, have organizational alignment. Three, plan ahead. Four, build the infrastructure. And five, be creative. And probably most important is having a partner like Dr. Sherman across the table from you, someone who is willing to work with you to do this. And that is, for me probably the most important single success factors after all.

Strategic Pharma Considerations

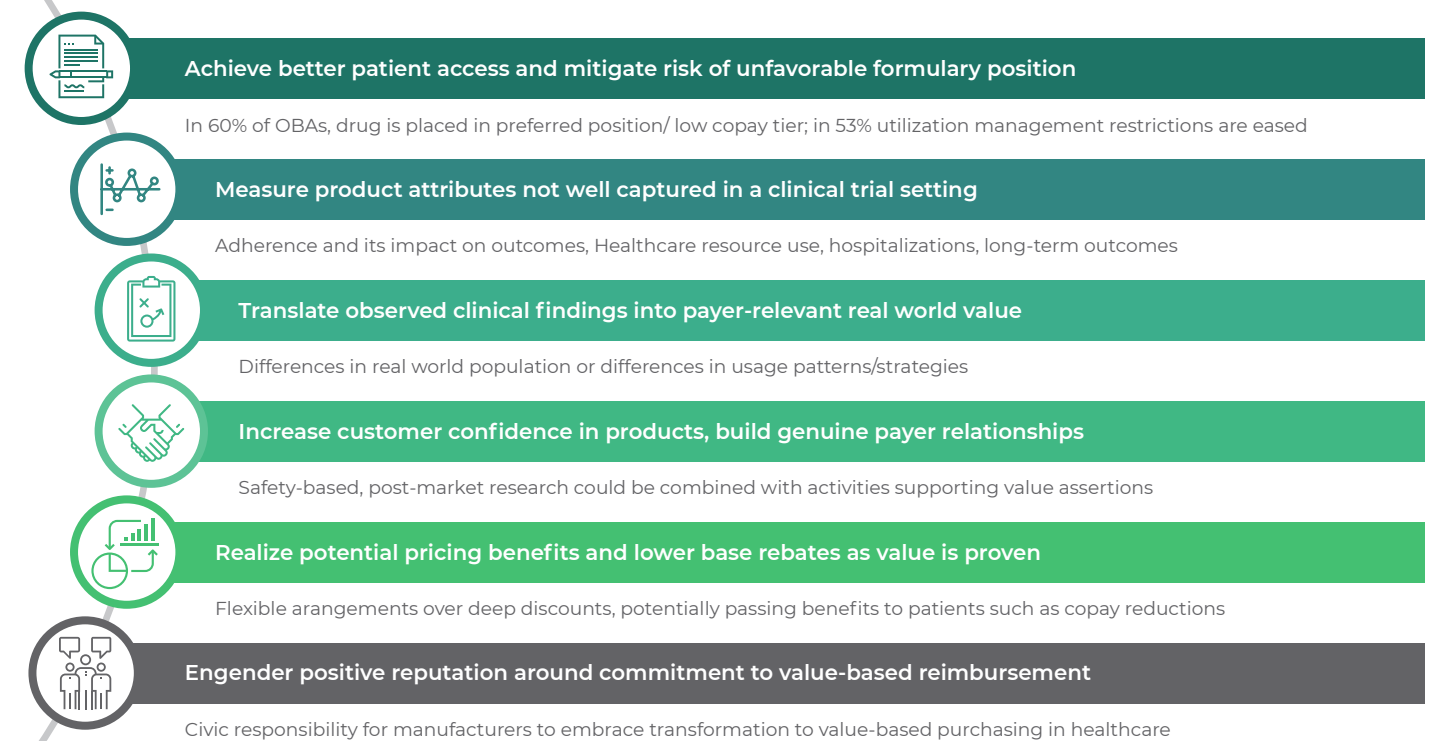
Based on our experience, developers of pharmaceutical products are motivated by a variety of business objectives to pursue OBA (Figure 13). The exact rationale varies by product and particular business case, but factors generally include the opportunity to ensure greater patient access to new medications (and potentially mitigate the impact of tiered formulary placement) and the attempt to demonstrate the full clinical and financial value of products in the marketplace, so as to ultimately increase market share in crowded therapeutic classes for instance. For brand teams, the ability to improve prescriber confidence in the products is certainly an upshot of well-executed OBA contracts we witnessed. Payers see it as a benefit to be able to give physician and members choices in medication selection.

Pharma strategy goes beyond product specific advantages. Deep relationship building, as described by Harvard Pilgrim's Dr. Sherman above, is understood to be a natural consequence of the concerted payer-pharma engagement, even in cases that may not ultimately lead to a contract in the market.

Executives at pioneering companies would add that the early investment in the OBA approach has already resulted in economies-of-scale for later contracts, in terms of both useful learnings and building infrastructure to reduce future time and resource needs during negotiation and execution. One of our clients, a leader with more than a dozen agreements in the market, was able to report an efficiency factor

of 90%, meaning resource needs shrunk to 10% of what they had been for an early benchmark pilot. Such remarkable efficiency gains are driven by growing cross-functional expertise, the setup of analytics platforms and use of guiding frameworks, templates and best practices. We refer to this as an OBA approach at scale.

FIGURE 13
Common benefits pursued by manufacturers entering OBA negotiations



Strategic Payer Considerations

From the health plan perspective, a core promise of an OBA is to provide members with access while reducing risks around budgetary uncertainty: The list of available innovative therapies can be expanded while patients with the greatest need are prioritized, generating positive reception by consumers, media and patient associations alike. In reality, OBAs are only one of many value initiatives and US payers spend the vast sum of time and resources on provider-driven value-based models, network optimization, integration and consolidation. However, increases in the cost of specialty medications

have sharpened payer rhetoric around OBA. Interestingly, most of the payer executives we spoke with are not outright dismissive of the overall costs of high-value pharmaceuticals but point to misgivings about paying premium prices for treatments that turn out to provide little value in real world use. Looking forward, those budget holders have concerns about specialty pharmacy utilization costs, but they are even more worried about the emergence of innovative combination therapies priced markedly above existing standard cost of care. They are open to better formulary placements and removal of

utilization restrictions, but only if such will result in reduced drug spend for non-responders, optimized treatment durations and overall cost savings. This puts value-based contracting squarely into the payer toolkit for achieving value for money. We would argue that this actually represents an opportunity rather than a threat for manufacturers in view of the most likely counterfactual (considering measures to manage budgets payers tend to consider at their disposal such as drastic increases in rebate levels, potentially heavy utilization restrictions and unfavorable formulary placement or even list exclusions).

“Just 2% our members account for 20% of our drug costs – largely driven by the high-cost of specialty pharmaceuticals. This disparity is expected to grow even larger... with 2% of members projected to account for 50% by 2020.¹”

WILLIAM FLEMING, President, Humana Pharmacy Solutions

Historically, when payers began to create value for money analyses, their initial basis relied on the “known” aspects of the drug’s reported value proposition – that is, using data based on completely controlled populations, placebo-controlled, double-blind research. The advent of real world evidence has changed the equation. For plans, the critical question becomes not only ‘What will it cost?’ but more importantly ‘Which members are most likely to respond, and when should we stop therapy when it becomes clear is it not working and what types of controls would be acceptable to accomplish this?’ To develop a meaningful value proposition in the construction of OBAs with respect

to payer budgeting, manufacturers are well-advised to develop population-based models that capture total medical costs (utilization, diagnostics, medical costs, hospital beds, and more) and show impact on quality and efficiency of care. Judicious use of diagnostic markers and advanced modeling can help to identify the right patients (for instance, those for whom the drug is most likely to work and those who are likely to be non-responders). As we outline further in chapter III, resulting models around real world effectiveness must be brought to bear during OBA contract negotiations so that optimum clinical and financial outcomes for both payers and drug manufacturers can be achieved.

KEY FACTORS

What they care about – Selection of typical considerations among US payers

- Which patients will be most likely to respond to therapy?
- What other conditions do those patients present?
- Is this drug expected to replace existing therapies? At what unit costs?
- How intensely would patients need to be managed (e.g., in Oncology) and what does this mean for total cost of care?
- How exactly will the drug impact utilization of other services? Who realizes potential savings?
- Does the risk score compensate for additional cost?
- What is the forecast of utilization per 1000 members/ cost per member per month?
- Who realizes longer term benefits and how does this match with upfront payment?

Payer representatives we spoke with would urge manufacturers aiming to enter OBA negotiations to develop strategies and evidence that supports actuarial and population-based decision-making and where possible go beyond product or even disease-specific analyses. This is born out of the simple but compelling fact that health plans carry fiscal responsibility for “full” members (as opposed to patients of a certain therapeutic intervention only). Such perspectives are of course neither new nor exclusive to innovative contracting, but it can

be advantageous to see OBAs and the intense collaborations that enable them as a unique vehicle to bridge divergent understandings. As one of our interviewees on the pharma side told us, “OBAs are the best investment in payer intelligence we currently have”. To understand OBAs as an exercise and opportunity in mutual trust building cannot be overemphasized.

Figure 14 shows how payers with existing OBAs see the benefits these have brought to their organization. The list synthesizes responses of the most recent

US survey research but also reflects that at this stage, plans are still on a learning curve when it comes to outcomes-based contracting. Generally, payers have an eager interest to obtain real-life insights on disease management and treatment pathways, and active partnerships that include pharma responsibilities “beyond the pill” are welcome. Dissatisfaction with the contracting process mostly sets in when negotiations become lengthy and impenetrably complex, when talks get lost in contractual minutia and trust erodes as the other side is believed to show no ability to make any concessions.

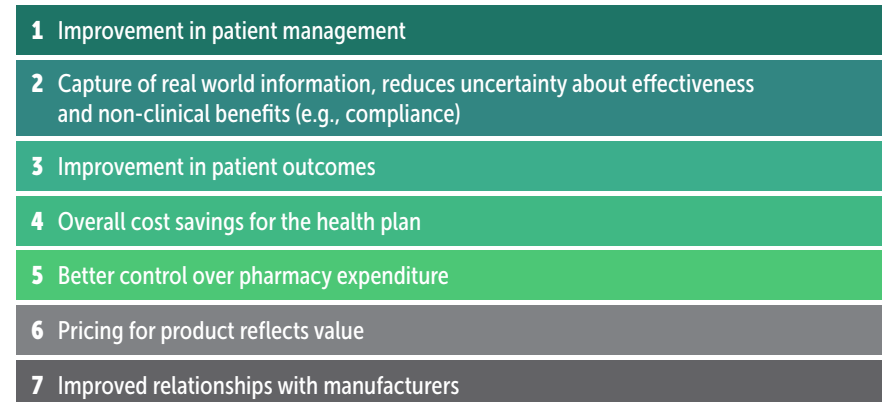


FIGURE 14
How payers see the benefits OBA bring them^{2,3,4}

We noticed that the use of clinical and actuarial analytics platforms is growing when it comes to the understanding (and definition) of meaningful endpoints and the range of factors that modify real world usage, including adherence, persistence, therapeutic selection bias – information payers expressly value.

Those drawing on outcomes-prediction technology report that internal analytics teams may end up in the contract design stage for up to six months. External expertise is often requested to accelerate the path to OBA launch.⁵

Pharmaceutical advances hold great promise for improving the health of Cigna customers, and outcomes-based agreements help to ensure that the promise is delivered. Innovating through the contracting approach is one way we are helping our customers

CHRISTOPHER BRADBURY, President, Cigna Pharmacy Solutions

Preferences for OBA – Therapeutic Areas and Commercial Scenarios

Our analysis of existing agreements shows a spread across several therapeutic areas. Consider the recent wave of US contract launches which includes products in:

- Oncology, e.g., NSCLC (i.a. Genentech’s Avastin, AZ’s Iressa) or leukemia (Novartis’ Kymriah)
- Immune/Inflammatory diseases, e.g., MS (i.a. Bayer’s Betaseron; EMD’s Repiff, Biogen’s Tecfidera),
- Endocrine, e.g., diabetes (i.a. Merck’s Januvia & Janumet; Lilly’s Trulicity; Novo’s Victoza),
- Cardiovascular, e.g., hypercholesterolemia, heart disease (i.a. Amgen’s Repatha, Novartis’s Entresto; Sanofi’s Praluent, Lilly’s Effient, AZ’s Brilinta)

The category of PCSK9 inhibitors is a good example for OBAs outside the specialty field – while not as highly priced on a per unit basis, new agents in this class are potentially applicable to much broader patient populations (even if not in first-line therapy), thus resulting in high total expenditure. Wholesale acquisition cost for both competing PCSK9 entrants, evolocumab (Amgen’s Repatha) and alirocumab (Sanofi/Regeneron’s Praluent) are above \$14,000/year. In 2015, ICER initially concluded that only a 67% discount would justify pricing noting that cost-effectiveness ratios for PCSK9 inhibitors far exceed commonly accepted thresholds and have limited clinical differentiation to justify the list price. If budget impact was considered, discounts would have to be even higher.⁶

Other more recent cost-effectiveness studies on Repatha all conclude that the product would not be cost-effective at the current list price, albeit with significant differences in the ICER (cost per QALY gained), thus resulting in discount recommendations between 30%-70%.⁸ One critical discrepancy in the assessments rest on whether a late survival benefit will or will not be reached. With a two-year follow up in the clinical trials (Fourier), it could not be shown but only assumed that prevention of nonfatal MI and strokes through the treatment will translate into a reduction of mortality over time. Without the mortality benefit in the model though, ratios obviously change dramatically. Many KOLs in the field of cardiology practice had celebrated the clinical benefit of the new agents for high-risk patients (specifically

those with pre-existing ASCVD who don’t respond to statins and require additional lipid lowering therapy). But given budgetary concerns, US payers reacted with extreme caution and put significant access restrictions in place.

2016 claims data analyses in the drug class show initial rejection at rates of 88.4 % in commercial plans and 72.8% in Medicare.⁹ After a standard 14-day look forward, final approval stands at 27.2% (Commercial) and 38.7% (Medicare) of patients who were able to receive the products they had been prescribed. These levels may not be unheard of and correspond with payer dynamics post the launch of PDE4 and HCV drugs for instance, but they obviously pose a significant challenge for manufacturers’ objectives and patient access. Troublesome is the fact that the data shows no major difference in patient characteristics between

those who were rejected and those who were approved, leading to the concern that utilization is not driven by clinical management and treatment objectives.^{2 10} In order to guarantee access to their product, Amgen began to aggressively negotiate a series of outcomes-based contracts for Repatha with key payers, including Harvard Pilgrim, Cigna, CVS Health, and Prime Therapeutics (Figure 15). According to those at the negotiating table, “Amgen put their money where their head is” and in return for guaranteeing the outcomes promised in the respective clinical trials, Repatha was granted improved formulary placement and some easing of utilization restrictions within participating plans. A valuable discussion considering payer concerns likely began here with an evidence- and data driven discussion of how such access would influence utilization cost, assuming the product performed in line with expectations.

FIGURE 15
In need for patient access:
Two generations of OBA for evolocumab (Repatha)

Date	Partnering Payers	Agreed Outcome	OBA Terms	Pivotal Clinical Trials
2015/2016	e.g., Cigna, Harvard Pilgrim	LDL-c reduction	Discount for tier 1-2 formulary placement + enhanced rebate if drugs fails to reduce LDL-C at RCT levels + additional rebate if the drug exceeds certain utilization levels	DESCARTES ¹¹ and other clinical studies 2014-2017 measured LDL-c reduction
2017/2018	Harvard Pilgrim, Abarca (PBM), Prime Therapeutics (PBM)	Heart attack or stroke	Full refund via rebate if an eligible patient has a heart attack or stroke while on Repatha for at least 6 months	FOURIER clinical trial ¹² for cardiovascular (CV) events (read out in 2017) has Primary endpoint: composite of CVD death, myocardial infarction (MI), stroke, unstable angina, revascularization; secondary: composite of MI, Stroke, CVD death

² The Symphony data shows that 48% of prescriptions for patients with LDL levels below 190 mg/dL were rejected, but so were 58% of the prescriptions for those with LDL cholesterol levels 190 mg/dl or higher.

KEY FACTORS

Common criteria: When OBAs make “strategic sense” for payers

- An objective and measurable outcome exists
- Outcomes can be analyzed at scale
- Related to significant expenditure: High cost per treatment or large budget impact (total potential population, on/off label), now or expected in the future
- Innovative treatment with uncertainty over expected risks and benefits
- Uncertainty related to appropriate patient population
- Populations with high unmet needs
- Access to therapy for severe or life-threatening conditions

The PCSK9 experience offers the exemplary case where an OBA is being considered as a commercial strategy to expand access after severe restrictions have reduced the treated population while payers receive a guarantee for improved patient outcomes and some degree of financial risk-relief. While actual financial performance results haven't been published, recent simulations modelled after the Repatha OBA suggest that despite the exposed risk for manufacturers, improved patient access would result in a net increase in reimbursement (vs. not

having an OBA) while payers would see improved effectiveness and still realize savings on the net medical cost per patient (over not having an OBA).¹³ Win-win agreements can be designed. Of course, assumptions matter a great deal: One, if not the, critical success factor during the negotiations is confidence in the projections around effectiveness, medical cost offsets and size of population receiving treatment under the deal. Principally agnostic to therapeutic indication, successful OBA strategies are thus product-specific and context-driven.

Another example that we talk about is PD-1 inhibitors and lung cancer, where those with high expressed levels may respond forty to fifty percent of the time. Most payers are approving for that reason. Now, for those who have low levels, it's not zero. It's some single digit percentages. Most payers don't cover that today. You can make a case that if you're the one with that tumor, maybe that percent looks pretty good compared to the alternative. One way to bridge that would be to agree that we will allow for those cases, but again, with payment only if they're successful.

MICHAEL SHERMAN, Senior Vice President & Chief Medical Officer, *Harvard Pilgrim Health Care*

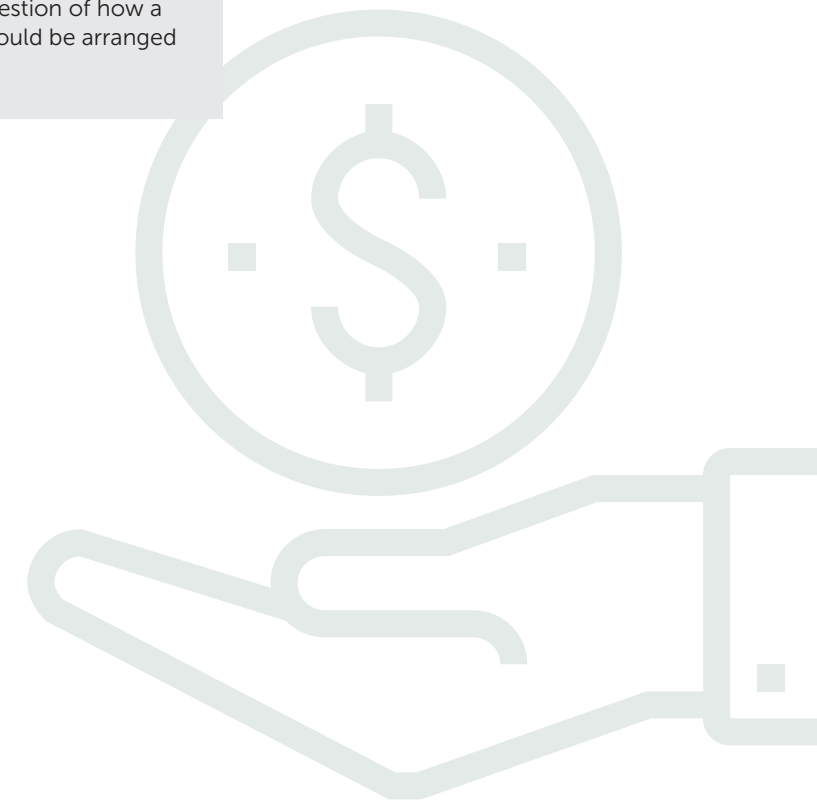
Apart from a few obvious exceptions, there is no simple checklist for which products should qualify. In our experience, OBAs generally make sense where significant budget impact (high cost/ high prevalence) is associated with uncertainty on the value from a payer perspective. Products subject to some kind of formulary management tend to be better candidates since there is an outright incentive to accept a new risk equation on the part of the manufacturer.

KEY FACTORS

The final question: Will patients realize affordability benefits from OBAs?

A critical question for innovative contracting is whether any of the assumed financial benefits, such as in co-pay reduction and discounts, will ever reach the patients who are not at the negotiating table, and thus drive affordability benefits to the consumer as well. Results-driven pricing should ultimately have a positive relief effect on premium levels. Interestingly, a recent formulary analysis of exchange plans to examine tier placement, cost sharing and utilization suggests that OBAs can produce additional saving, not just to payers due to saved expenditures for spared utilization management, but to the patient costs-sharing burden as well.¹⁴

According to the analysis of the data, those commercially insured patients covered by payers with OBAs had to pay 28% less in co-pays for the same medicines, when compared to market average silver-level plans, suggesting a significant copayment reduction effect from 2015 through to 2017. Further analyses are warranted to prove that OBAs offer a financial benefit to consumers and pose the question of how a “money-back” warranties in an individual agreement could be arranged to ultimately benefit the patient, not just the payer.



Checklist for Both Pharma and Payers

- Worked hard to establish trust between both parties
- Secured solid legal counsel to develop the contract
- Strived to balance the need for simplicity versus administrative complexity during contract development and execution; for instance, wherever possible, agree to straightforward measurement criteria and data collection
- Engaged policy makers to promote understanding and advocate for infrastructure changes that support larger concepts of population health management rather than just strict focus on medication spend alone
- Worked to agree on what measurements/data will be monitored and collected, and by whom
- Developed explicit language related to technical details of the implementation of contracts in the field
- Worked to agree on the appropriate time frame for the assessments and financial adjudication to be carried out (every month, every six months, yearly, every three years and so on)
- Agreed upon details for a reasonable statistical analysis plan for assessing clinical outcomes data, and identify data standards and interoperability requirements related to data content, definitions, and more
- Developed standardized data-reporting procedures to streamline capture of both clinical and financial data, and the ultimate financial reconciliation
- Developed reasonable escape clause provisions that would let either party terminate the agreement
- Developed explicit details related to non-disclosure of data, as the disclosure or non-disclosure of various aspects of the agreement or ongoing results has the potential to have significant positive or negatives business ramifications for both parties
- Considered bi-directional reimbursement flows that allow for up- and downstream risk-share payments between payer/pharma

Key Steps for Manufacturers

- Enlisted the right internal corporate and brand-level support
- Fostered engagement with payers as early as possible
- Studied clinical data and understood how that performance may deviate from ideal RCT scenarios under real world conditions
- Especially for new or investigational therapies, debated with payers to explore the most meaningful patient-centered outcomes or validated surrogate or proxy outcomes. Agree on other value attributes (such as quality-of-life issues) that can be measured and aggregated both to support proper use of the medication in the marketplace
- Got directly involved in monitoring, data generation and analytics
- Shared responsibility for outcomes, increasing trust and credibility longer term
- Worked to define those patients for whom the medication is most likely to work and those for whom it will not
- Defined critical threshold values that will become part of the final contract terms
- Found ways to expand patient eligibility that can be directly related to coverage criteria
- Explored options for partnership on post-approval studies to reduce residual uncertainty about the safety and effectiveness of new therapies
- Where relevant, worked with clinicians, patient advocacy groups, regulators and payers to establish Patient Registries to facilitate collection of real world evidence
- Considered the potential benefits (and risks) of carrying out additional studies (such as comparative and cost-effectiveness studies against competing products or quality-of-life studies), especially to differentiate drugs in the same therapeutic class or with a similar mechanism of action
- Analyzed and understand the gaps or unmet needs associated with a current standard of care in relevant therapeutic categories to strengthen OBA negotiations
- Depending on negotiated non-disclosure agreements, considered developing brand messaging to showcase positive product benefits demonstrated in the context of the OBA contract

Key Steps for Health Plans

- Made sure to be well informed before coming to the negotiating table; determine which outcomes and assessment metrics are needed most for a particular therapeutic class or patient population before engaging with drug developers
- Sought to obtain consensus on a common set of principles, policies, and technical methods for the data-collection programs
- Obtained consensus on the payment or reimbursement mechanism (for instance, for some therapies, having the drug maker provide initial therapy at no charge for some initial duration might be preferable to settling financial penalties later if the key clinical outcome threshold is not reached)
- Explored methods to determine patient eligibility that can be feasibly translated into coverage criteria
- Depending on the negotiated non-disclosure agreement, considered publicizing information about the OBA contract, to showcase the plan's willingness to ensure broad patient access to promising-yet-costly therapy options
- When defining the OBA approach, evaluated exactly how different payer types are positioned towards different OBA structures and investigate benefits a value-based agreement could entail for them
- Modeled mutual benefit by projecting break-even thresholds with/without OBA for both contract parties so as to quantify the win-win value upfront

THE NEW FRONTIER IN US CONTRACTING

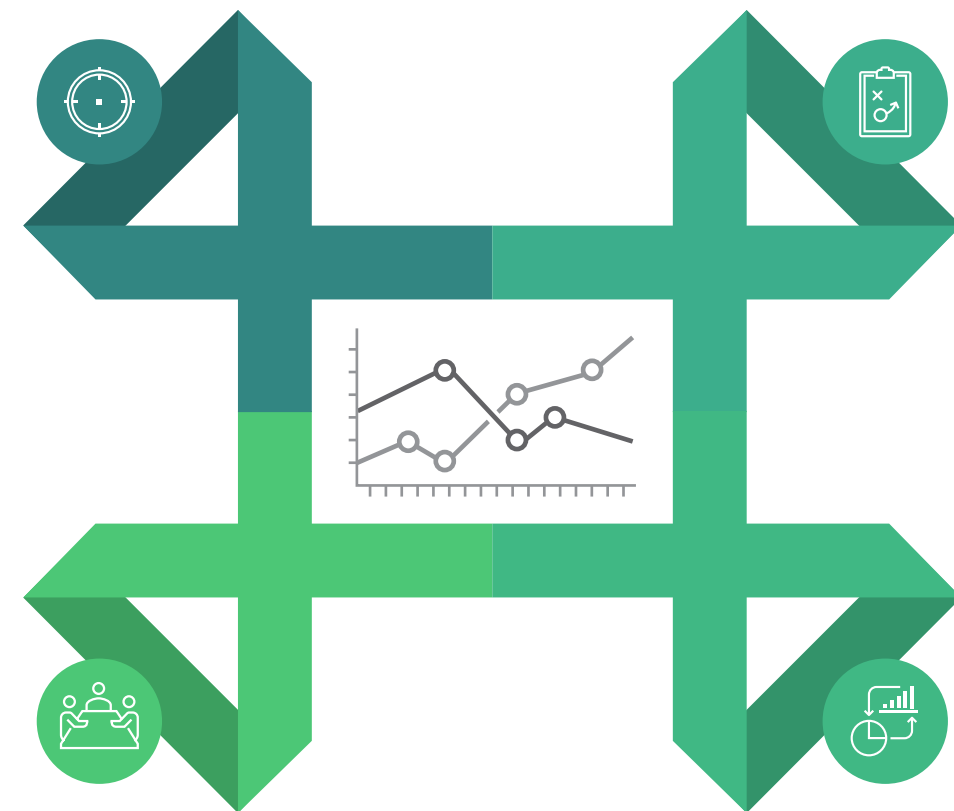
HOW YOU CAN SET UP FOR OBA SUCCESS

Definition of the Contracting Approach

- ✓ Evaluation of payers/health system position regarding different types of innovative agreements
- ✓ Clearly set out the benefits of the OBA for the respective payers
- ✓ Setting expectations in terms of improved access, lower base rebates, increased customer confidence in products, payer relationship building

Selection of the Right Design

- ✓ Investigation of outcomes interesting to respective payer(s)
- ✓ Assessment of which outcomes can be monitored
- ✓ Selection of time horizon and most adequate type of agreement
- ✓ Consideration of legal issues such as impact on Medicaid best price, Medicare Part D payment rates



Implementation and Adjudication

- ✓ Selection of data sources and methods most adequate to monitor real-world performance
- ✓ Developing plans to adjudicate results and trigger payments and define exceptional events that should lead to renegotiation
- ✓ Analysis of re-insurance modalities
- ✓ Decision of governance to ensure the long-term success of the agreement

Testing and Refining Deal Modalities

- ✓ Definition of key factors that could influence the outcomes/risk
- ✓ Simulation of the expected performance in the real world for the selected outcomes in the population covered by the plan
- ✓ Modelling of the expected financial impact compared to traditional pricing/rebating approaches
- ✓ Evaluation of contractual terms needed to limit risk



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Evaluated the real world risk of hospitalization for the implementation of innovative contract in asthma

Prepared and facilitated senior management workshop on design and implementation of OBAs for top 5 global PharmaCo

Measured real world outcomes in the context of an OBA for new treatment in schizophrenia

Evaluated new price structures and financial risk-sharing scenarios for treatment in multiple solid tumors

Led various educational symposia, i.a. ISPOR 21st (2016) and 22nd Annual Meeting (2017)

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