HOW DO WE PAY FOR A CURE?

The Risks and Rewards of Innovative Payment Schemes

EVERSANA™

eversana.com

EVERSANA™

Abstract

Setting drug prices is a high-stakes endeavor, and that is especially true for the latest round of gene and curative products coming to market in Europe. Drugmakers need to consider several factors that can help them set their product prices appropriately, including the risk of recurrence/relapse, differences in efficacy among cures, and comparators, including full lifecycle costs of a disease and the burden of health economic costs on budgets. They also need to design innovative payment models that will be attractive to health systems facing increased budgetary pressures as more gene and curative products enter the market. This includes outcomes- and performance-based schemes, which have gained momentum across Europe. However, drugmakers need to be cautious because such models could leave them vulnerable to "known unknowns," including whether a cure can be sustained throughout a patient's lifetime, given the lack of long-term data.

The Challenges of Paying for Curative Products

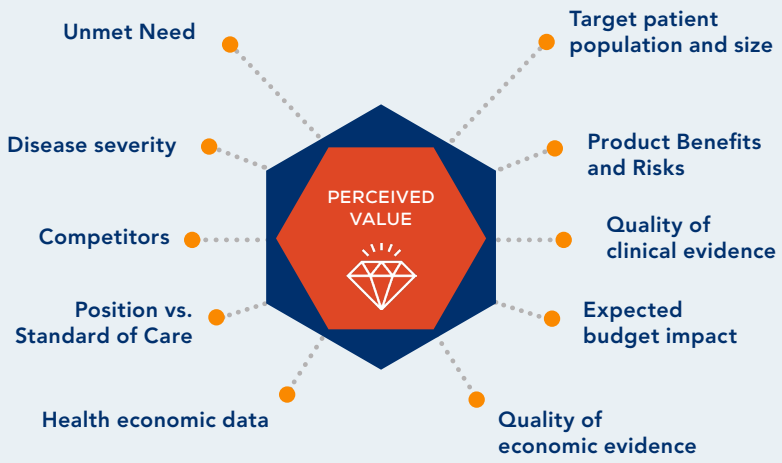
With hundreds of gene and curative products in the pipeline, patients across the world will soon have even greater access to a large number of life-changing therapies for a variety of diseases. A handful of curative therapies have already begun to come to market, offering hope for many patients with diseases such as spinal muscular atrophy (SMA), aggressive blood cancer, or Leber's congenital amaurosis, a rare inherited eye condition. These frontrunners have signaled the evolution of healthcare. However, the innovative nature of these products means they have challenged healthcare systems.

Curative therapies, specifically cell and gene therapies, bear high upfront costs, ranging anywhere from several thousands to over 1 million euros or dollars. Health technology assessment (HTA) agencies set the valuation of these drugs against willingness-to-pay thresholds. Although long-term data is limited for these novel therapies, the fact that they promise a cure which can offset future spending on treating a disease over time is pertinent when examining the drug's impact, both on the patient and health care budgets. As such, it is crucial to figure not only how to pay for a cure but who is going to pay for it.

Since supporting efficacy data are relatively immature, oftentimes only a few years old, there is a high level of risk involved, for both payers and drugmakers. Available, short-term clinical trial data show promise, but long-term efficacy remains a "known unknown," dependent on a matrix of factors, both expected and unforeseen.

Pricing Cures: Factors to Consider

A variety of factors should be considered when determining the value, and ultimately the price, of a curative therapy.



These include, but are not limited to:

- UNMET NEED
- PRODUCT BENEFITS AND RISKS
- TARGET POPULATION AND SIZE
- QUALITY OF CLINICAL TRIAL DATA
- EXPECTED BUDGET IMPACT
- MARKET COMPETITION
- THERAPEUTIC CATEGORY
- SEVERITY OF THE DISEASE

When pricing these curative therapies, some key factors need to be recognized including:

- The risk of recurrence/relapse, particularly how a payer can value a cure with recurrence or moral hazard risk
- The differences in efficacy among cures
- Comparators, including full lifecycle costs of a disease and the burden of health economic costs on budgets

WHEN PRICING A CURE, RECOGNIZE:

RECURRANCE/RELAPSE - How does a payer value a cure with recurrance or moral hazard risk?

DIFFERENCE IN EFFICACY - How does a payer value the differences in "cures" between competitors that cure?

COMPARATORS - How does a payer value a cure over full lifecycle costs of a disease? Do they bear all the health economics costs and do they budget and model them?

FIVE	100% Disease-free and efficacy No chance of disease recurrence No follow-up therapy
FOUR	100% Disease-free Recurrence and/or follow-up therapy needed More hazard a risk
THREE	Disease/impact greatly reduced, but < 90% Long-lived effect, no recurrence or follow-up
TWO	Disease/impact greatly reduced, but < 90% Recurrence and/or follow-up therapy needed
ONE	No truly curative Relapsing or recurring Semi-chronic Difficult to measure outcomes

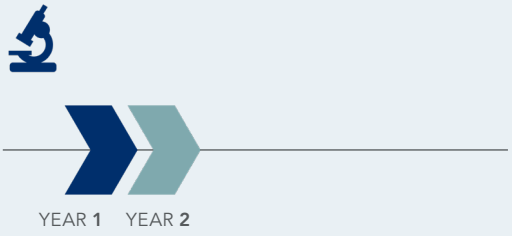
Think about this: How would a payer value a cure with 90% efficacy and an outcomes guarantee versus a therapy with 100% efficacy and no outcomes guarantee?

Ideally, curative therapies would result in a 100% disease-free outcome, with no chance of disease recurrence and no need for follow-up therapy. However, even the most effective curative therapies might not work with such efficacy, potentially leading to relapse or disease recurrence and requiring follow-up therapy.

When pricing gene and curative therapies, drugmakers also need to consider the market size for their products, which require substantial investments in research & development, as well as distribution, once approved. They also need to consider how the market for their products may shrink over time. Curative treatments might cause the disease prevalence (the proportion of cases in the population) to decrease rapidly until the number of patients initiating treatment each year is closer to the incidence rate (the number of new cases). As a disease is cured, the annual incidence rate becomes the determining factor in a product's annual revenue potential and the manufacturer's ability to recoup its costs.

Known Unknowns

Current outcomes-based payment schemes for gene and curative therapies suggest that national health systems in Europe are opting to pay for these drugs over time — the payments, of course, contingent on the drug's efficacy. By entering such contracts with drugmakers, health systems ensure patient access despite the uncertainties and high costs of these curative treatments.



DURATION OF CLINICAL TRIALS FOR A GENE THERAPY

ACTUAL DURATION OF BENEFIT

For drugmakers, these arrangements can help ensure access to their products, but they do have risks. If patients die early — even if mortality is unrelated to therapy — drugmakers would forgo payment, as is the case with Germany's deal for Kymriah. In addition, models that involve payment over time with rebates and outcomes guarantees can be burdensome because they require tracking outcomes over an extended period of time, and drugmakers could be at a disadvantage if outcomes targets are not straightforward.

Adding to drugmakers' vulnerability is the fact that there is limited long-term data on gene and curative therapies, yet the curative effect of these drugs is intended to last a patient's lifetime. When forecasting the impact of these payment models, drugmakers must accept the "known unknown," recognizing that some patients may experience relapse/recurrence or need additional treatment.

Drugmakers also must consider the potential impact of outcomes-based arrangements on their market capitalization. Long-term contracts likely favor companies with strong balance sheets. For example, when Bluebird announced its five-year payment plan for its beta-thalassemia gene therapy, some analysts expressed disappointment. In fact, such financing schemes could have short- and long-term effects on companies with smaller balance sheets. For Bluebird, the short-term impact included a 6% drop ($400 million) in its market capitalization. Over the long term, the effect will be unclear until financing models are better understood. Still, this example would suggest that for companies with stronger balance sheets, outcomes-based contracts could prove to be a competitive advantage.

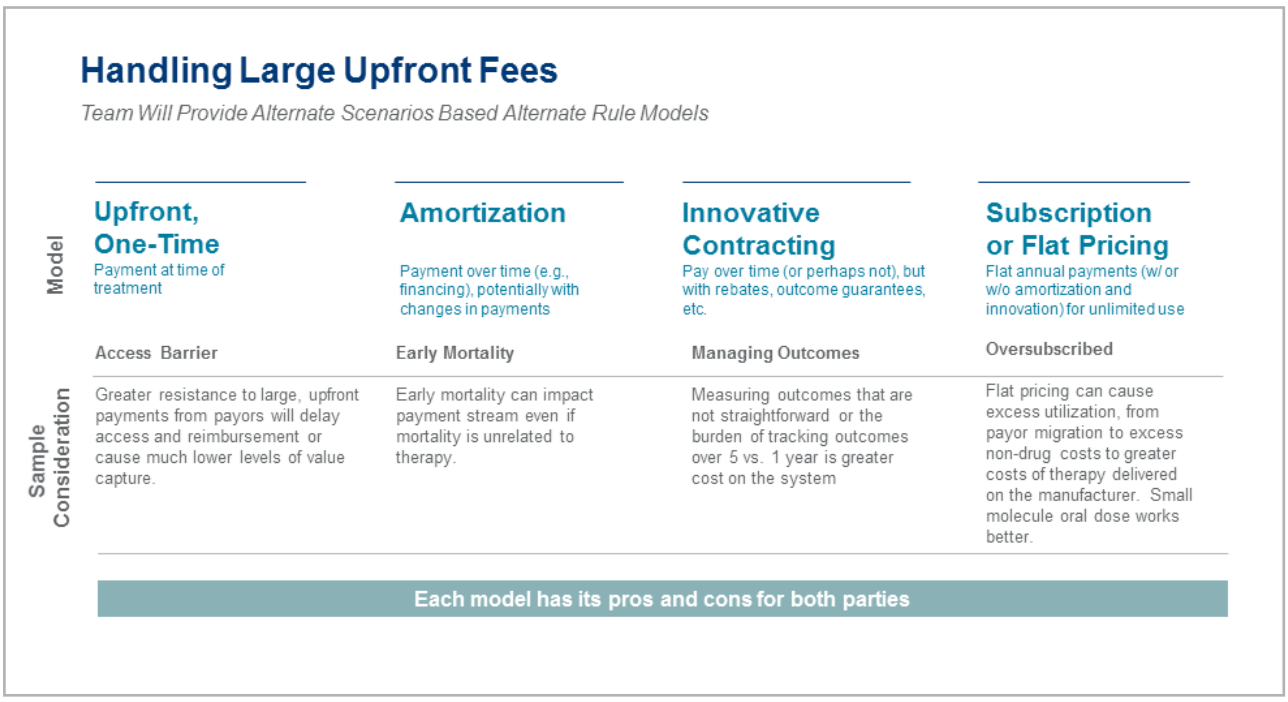
Barriers to Pricing a Cure

If payers are willing to enter innovative pricing models, which has been the case of late, drugmakers have a lot to keep in mind when pricing a curative therapy. They must consider all of the factors that can determine their product's value, including those that are apparent only later in the treatment's lifecycle. There is risk not just for payers but also for the industry. Drugmakers must quell uncertainties over the lack of long-term efficacy data as well as concerns about cost. Nevertheless, innovative payment schemes seem to be the preliminary steps toward tackling how to finance cures going forward.

Beyond Upfront Pricing

Beyond setting the right price, drugmakers also need to consider what type of payment models might be attractive to each healthcare system. Increasingly, payers are becoming resistant to making upfront, one-time payments at the time of treatment, which delays access and reimbursement.

Given these considerations, both payers and drugmakers are exploring innovative contracts in which healthcare systems pay (or not) over time through models that use rebates, outcomes guarantees, and other mechanisms.



The Shift to Long-Term, Outcomes-Based Contracts

Amortization models, which involve payment over time, are one option for gene and curative therapies. In fact, many payers prefer to engage in long-term contracts to mitigate their risk. Because these contracts are contingent upon checkups over time, the industry must prepare for potential adverse impacts, such as early mortality, which could affect their payment stream and leave them vulnerable.

Several European countries have implemented new outcomes-based payment schemes for gene and curative therapies to safeguard payers from misinvesting funds while ensuring drugmakers receive payment.

In particular, several countries are testing outcomes-based agreements on CAR T-cell therapies for several cancer indications. In Germany, payers entered outcomes-based payment schemes for CAR-T therapies in order to mitigate risk. Under this agreement, health funds will reclaim part of the treatment cost if a patient dies.

In Spain, stakeholders have agreed to a risk-sharing agreement for Yescarta in which half of the cost is paid upfront, and the remainder is paid 18 months after treatment but only if the therapy is effective.

In France, Yescarta earned an ASMR III rating, demonstrating a moderate improvement over the standard of care. In this country's agreement, payment is based on patient survival and performance.

In Italy, the Italian Medicines Agency (AIFA) penned a novel "payment at results" deal for Kymriah, under which Italy will pay the drugmaker at 6 months and 12 months. For diffuse large B-cell lymphoma, AIFA requested a mandatory discount.

Focus on Collaboration

For today's climate, outcomes-based payment models are attractive, conciliatory even, suggesting that payers in Europe are beginning to accept the high prices of gene and curative therapies.

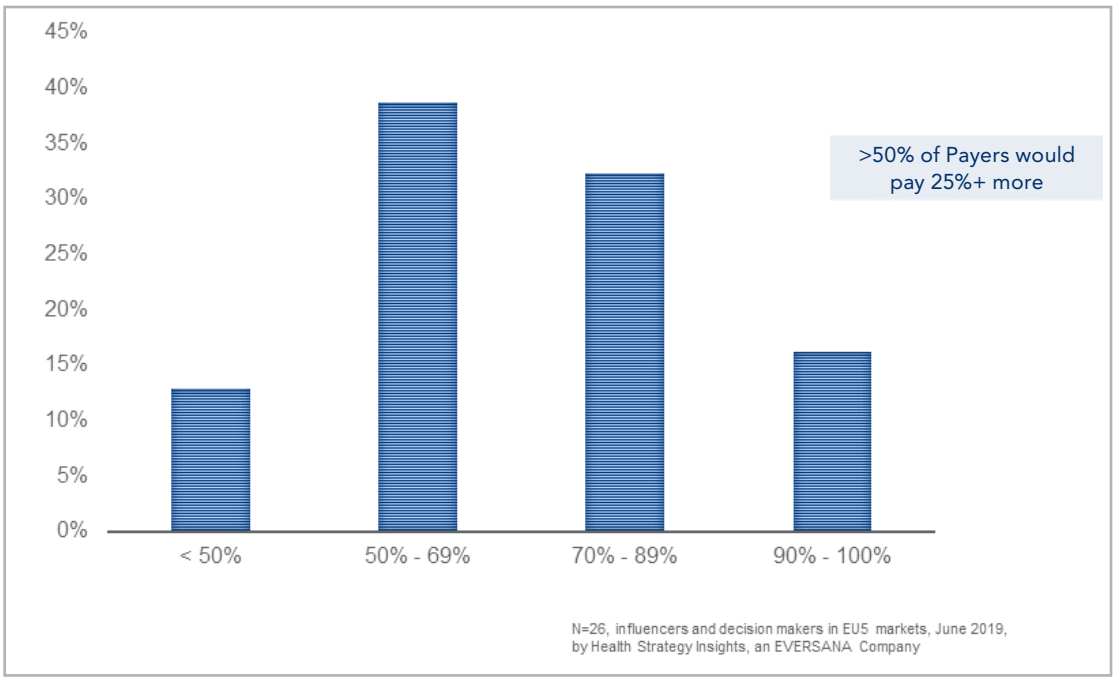
N=31, influencers and decision makers in EU5 markets, June 2019, by Health Strategy Insights, an EVERSANA Company

Back in 2016, the Economist Intelligence Unit found that European payers overall are showing high to very high interest in outcomes-based payment approaches for treatments. Recent contracting activity between healthcare systems and drugmakers supports this trend.

	Alignment with value-based healthcare	Enabling context, policy and institutions for value in healthcare	Measuring outcomes and costs	Integrated and patient focused care	Outcome-based payment approach
France	Moderate	Moderate	Moderate	Moderate	Very high
Germany	Moderate	High	Moderate	Low	Very high
Poland	Moderate	Moderate	Moderate	High	High
Spain	Low	Low	Moderate	Moderate	Low
Sweden	Very high	High	Very high	Very high	Very high
United Kingdom	High	High	High	Very high	High
Australia	Moderate	Moderate	Moderate	Moderate	High
China	Low	Low	Moderate	Moderate	Low
India	Low	Low	Low	Moderate	Low
Japan	Moderate	Moderate	Moderate	Very high	Low
United States	Moderate	Moderate	High	Moderate	Moderate

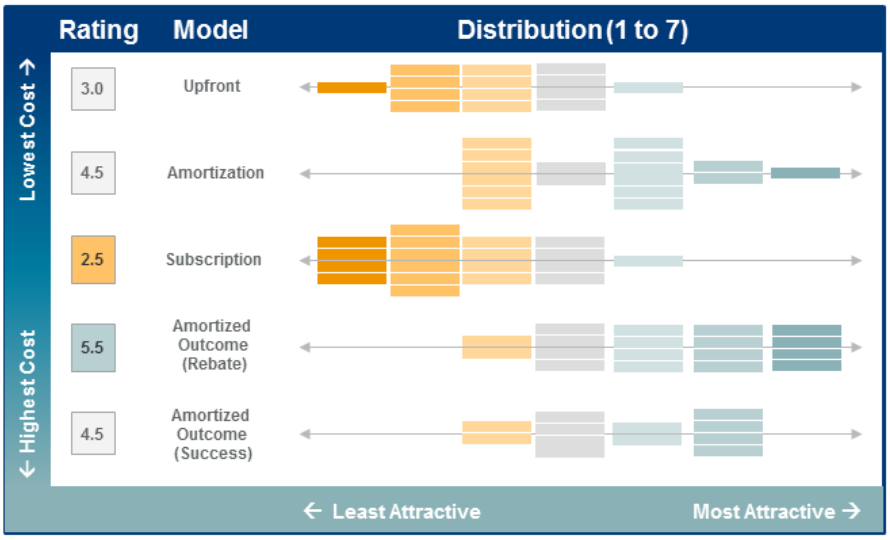
Source: Economist Intelligence Unit, 2016

Novartis' Zolgensma, the first gene therapy for a neuromuscular disease, is a good example. Zolgensma is priced at a 50% discount to the lifetime cost to treat spinal muscular atrophy with Biogen's Spinraza, according to some estimates. If the outcome was guaranteed, 85% of influencers and decision makers in EU5 markets said they would pay the same or more for Zolgensma related to Spinraza than the proposed discount (assuming proven efficacy and guaranteed outcomes).



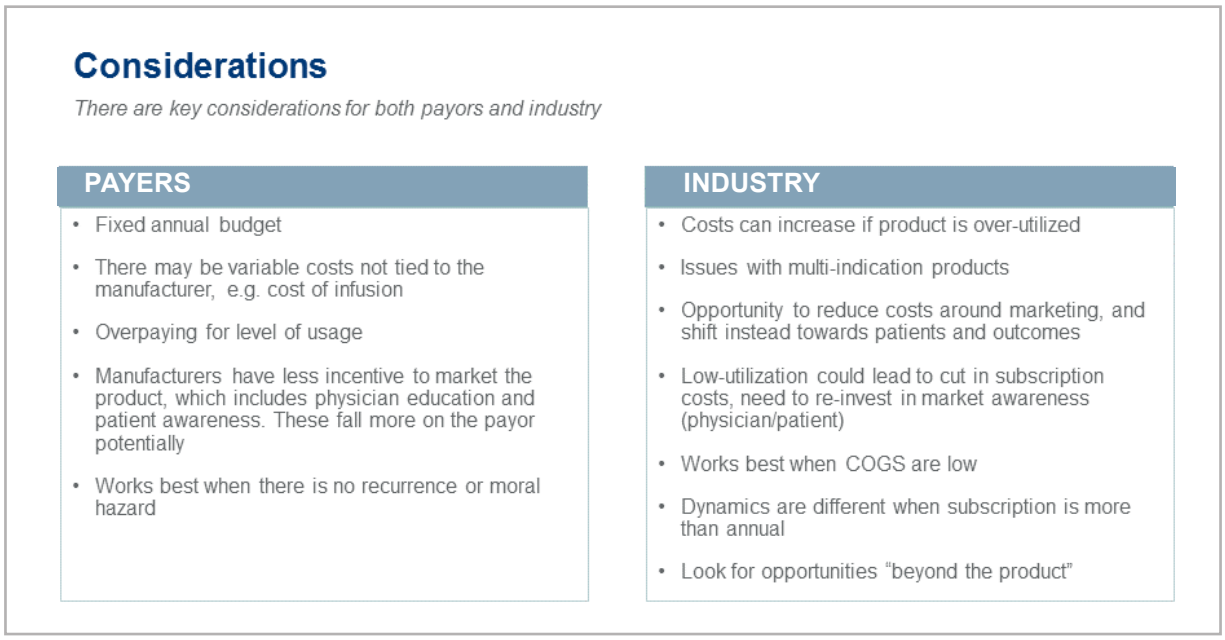
Advanced Innovative Contracts: Subscription Pricing

Subscription or flat pricing, which involves flat annual payments (with or without amortization for unlimited use) for an unrestricted supply of a curative medicines. This subscription model has been used in the United States by state-level Medicaid programs to purchase hepatitis C drugs. Yet payers and drug makers recognize its drawbacks—namely, that it can cause excess utilization, which may be of particular concern for higher-cost curative therapies. For this reason, the subscription model does not seem attractive for many. Payers have a clear preference toward amortized and outcomes-based payment models, and claim to be willing to pay for them. This is true even when subscription models are less expensive.



N=31, influencers and decision makers in EU5 markets, June 2019, by Health Strategy Insights, an EVERSANA Company

Still, the use of flat-fee contracts for unlimited usage is growing, especially for high-cost therapies like those that treat hep C. In the United States, both Washington and Louisiana were granted Medicaid waivers to implement flat pricing for hepatitis C. In Australia, the government signed a five-year confidential agreement with four manufacturers that aims to promote lower costs and higher utilization.

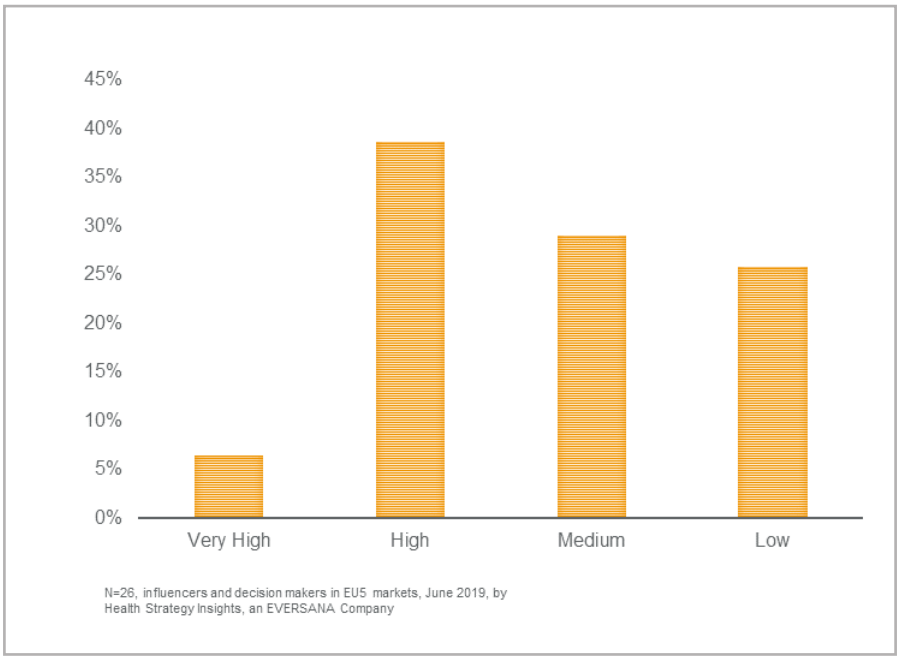


Looking ahead, one consideration for manufacturers and payers interested in pursuing subscription pricing is its potential impact on the market. In some cases, flat pricing sets up "winner-take-all" dynamics, meaning a single drugmaker secures the drug supply. Stakeholders would need to carefully consider the following questions:

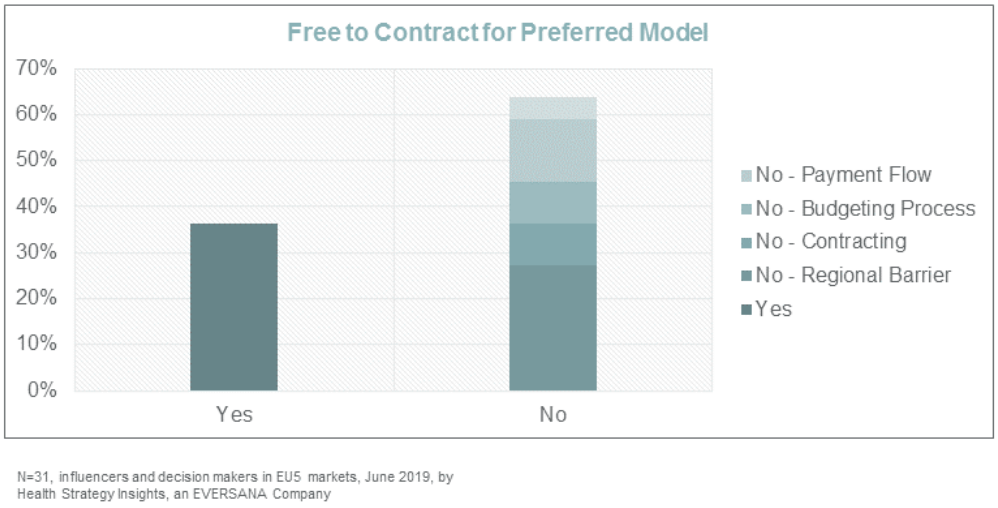
- Would marketing costs for competitive share shift to the payer for finding patients and educating physicians?
- If costs and benefits shift, how would this affect pricing models?
- What are the risks to both the payer and the manufacturer if not enough patients use the service without promotion?

Barriers to Innovative Contracting

While more payers are opting for outcomes-based arrangements that shift some of the risk to the drugmakers, the models do have at least one major drawback: they require tracking outcomes over several years, which can place a financial and administrative burden on healthcare systems. Influencers and decision makers in EU5 markets (France, Germany, Italy, Spain, and the United Kingdom) agree that there is a high burden to administering even small patient population-based programs that impacts costs. In fact, almost 45% said administering outcomes-based programs, even in small patient populations, is a burden that affects price beyond value. This may become a barrier for implementation.



Another barrier may be the country's own regulations. The overwhelming majority of influencers and decision makers in EU5 markets still feel that they cannot easily pursue innovative contracting models for gene and curative therapies. Many healthcare systems are slow to fund newer treatments, even those with better efficacy than older drugs. By continuing to fund these comparator therapies, payers leave little room in the budget to finance newer therapies that promise greater efficacy.



What's more, providers within the country may be so familiar with existing treatments that they resist a "cure." This resistance could lead to inertia that could stall the adoption of new, innovative treatments, including gene and curative therapies.

The hurdles may be especially steep for small countries with tighter budgets. For example, gene and curative therapies could cause a large variance in the annual budget. So a key question is, how should small payers handle the financial risk when the annual variance can be large? In the United States, payers have the option of purchasing reinsurance or using risk-pooling models to reduce the impact of such variances. Another issue would be an unexpected variation in regional epidemiology. Not all rare diseases are well understood globally, and unexpected variance in incidence could have a negative impact on the budget. In this case, a utilization cap or subscription model that reimburses for costs but not value of overages in the first year — until true incidence is understood — might be preferred. Lastly, small countries might need to address the effect of mobile work forces and differential coverage as patients cross borders. In this scenario, joint regional HTA negotiation and residency requirements can address this issue. This is one of the aims of the Beneluxa Initiative, which promotes greater collaboration between HTAs.

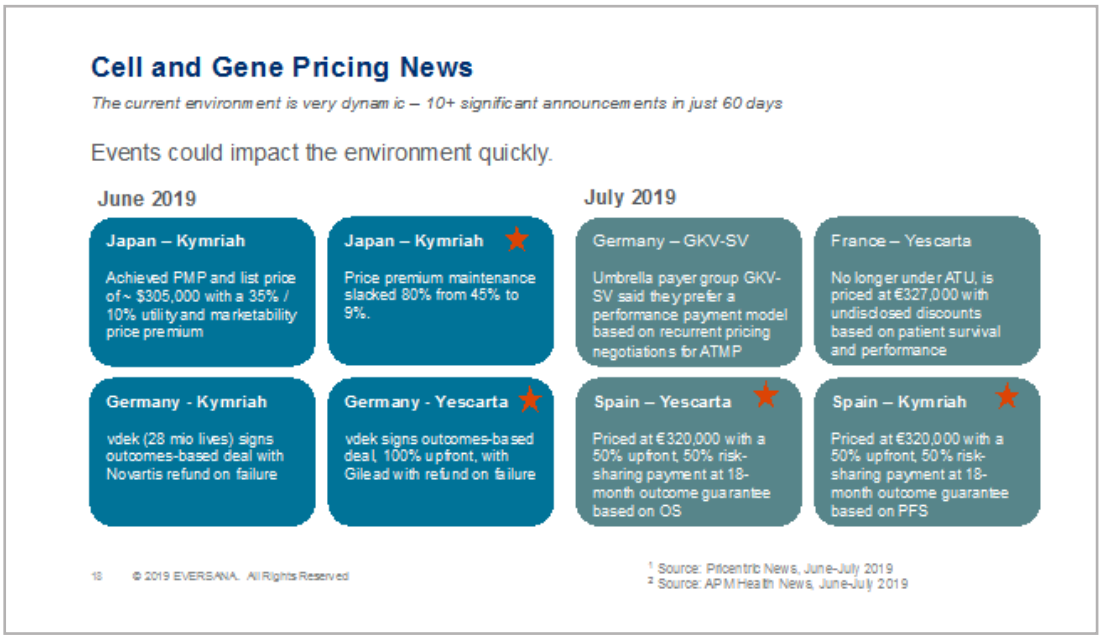
In the future, small European countries may follow the lead of states in the United States, which are looking to test innovative drug contracting to curb costs. For example, Louisiana gained support for a subscription-based service for hepatitis C drugs to control costs and ensure access. Meanwhile, Colorado can now negotiate drug prices for Medicaid and enter contracts with drugmakers voluntarily for value-based supplemental rebate agreements.

Another barrier relates to the nature of indication-based pricing. Stakeholders need to consider how pricing might vary for different indications, given that the value will likely vary as well. For now, there is no precedent for how payers should handle indication-based pricing.

Implications for Operational Pricing Teams

So far, we have primarily focused on the strategic impacts of pricing and payment models for gene and curative therapies. However, drugmakers need to consider the operational impacts of their decisions as well. One of the most significant is price referencing, which can cause issues even if the price is effectively the same across markets.

The current environment for cell and gene therapies is very dynamic, and stakeholders should expect that new payment models will continue to make headlines.



In outcomes-based arrangements, incentives are aligned for healthcare systems and drugmakers, providing a rich opportunity for collaboration. To ensure the success of these arrangements, stakeholders can coordinate in several ways. Specifically, they can:

- Develop patient hubs and support programs to improve adherence to therapy.
- Create robust patient registries that track how patients respond to therapy.
- Collaborate on longer-term outcomes studies to track a drug's efficacy.

With payers willing to enter innovative payment models, such as outcomes-based contracts, drugmakers have a lot to keep in mind when setting prices for their gene and curative therapies. By devising a collaborative strategy with payers, they can mitigate the impact of uncertainty, ensure an optimal launch, and help patients receive the curative treatments they need to live longer, healthier lives.