Meeting the Analytic Challenges of Value-Based Agreements in Life Sciences

An EntityRisk White Paper

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Uncertainty about the real-world effectiveness and value of a new product or a new indication can hinder market access, especially for products with no real-world data available or relatively small clinical trials. Value-based agreements (VBA) can help reassure payers in these circumstances and ensure that manufacturers earn an appropriate return in the event the product works as they expect it to [1]. Implementing VBAs requires that manufacturers answer a series of somewhat complex questions:

1. What is the value of a treatment with uncertain effectiveness?
2. How well do alternative VBA designs capture the value to the manufacturer?
3. How will the VBA influence cash flow and revenues for the manufacturer?
4. How will the VBA be adjudicated in practice?

EntityRisk has brought together a team of recognized experts uniquely positioned to answer these questions in any life sciences context.

Value Assessment Under Uncertainty

What is a new product or indication really worth to patients? For decades, cost-effectiveness analysis proceeded under the assumption that clinical benefits are known and predetermined. This assumption is surely wrong, because different patients respond differently to treatment. Ignoring the variance in treatment outcomes is becoming increasingly problematic, in part because estimates of mean treatment benefits are harder to come by, making variation around the mean even more important.

EntityRisk has pioneered the rigorous assessment of value under this kind of uncertainty. In a series of peer-reviewed publications, our team has developed a more general and robust approach to cost-effectiveness under uncertain efficacy, called Generalized Risk-Adjusted Cost-Effectiveness (GRACE)[2-4]. Notably, GRACE relies on the same framework as traditional cost-effectiveness, but it relaxes the traditional assumption that efficacy is known. Since GRACE does not depart from traditional CEA, it requires no special “buy-in” from analysts or payers. Using the GRACE framework, EntityRisk can help manufacturers measure the value of their therapies even when effectiveness is uncertain.

Ensuring Fair Value from a VBA

The measurement of value provides a set of guardrails for pricing, but the design of the VBA is crucial for determining the extent to which manufacturers can earn a fair return on the value created.

The likely net present value of the VBA for the manufacturer should fall within the guardrails defined by value as appropriately estimated. This provides a benchmark against which anticipated revenues can be measured. However, measurement of expected revenues is not straightforward. The manufacturer's returns in the real world from any VBA will depend on its design, and the endpoint that the manufacturer and payer have chosen to contract upon – e.g., survival, non-response, discontinuation, etc. There are many possible choices of contract design, and the expected returns can vary significantly based on seemingly trivial choices. Sophisticated statistical methods are needed to forecast real-world outcomes like these and, in turn, both the expected value of a VBA contract and the resulting expected revenue to the manufacturer associated with alternative contract designs.

Mitigating Financial Risk from VBA Design

The expected value of a VBA is only one dimension of its value to a manufacturer. Risk also matters. Indeed, since VBAs are designed to provide insurance to the payer, they will necessarily involve some financial risk to the manufacturer. Intuitively, the manufacturer is "providing insurance" and, just like any other insurance provider, the manufacturer will bear financial risk.

Manufacturers therefore need accurate forecasts of revenue and variability in cash flows. Revenue-recognition poses particular challenges in the context of a VBA, because manufacturers must provide a credible reason to believe that its revenue estimate is likely to be achieved with 90% probability or more. Careful evaluation of alternative VBA designs is critical to maximize revenue recognition potential and minimize financial risks. EntityRisk has developed unique tools to translate health economic outcomes into predictions about financial cash flows that make sense to accountants and finance managers.

Estimating Treatment Value and Forecasting Outcomes for VBAs

EntityRisk provides a modeling platform that uses techniques from economics and biostatistics to predict health and financial outcomes under uncertainty. The design of the platform leverages the EntityRisk team's considerable experience building robust software at scale [6-8]. Rather than just estimating means or medians, the platform uses probabilistic statistical modeling to estimate the entire distribution of health outcomes among patients in a population. These models provide a level of depth and flexibility that few biopharmaceutical companies can develop with internal resources. The models leverage the totality of the available evidence inclusive of both clinical trial and real-world data. Clinical trial data are typically best able to predict how well a new treatment causally compares to existing treatments, while real-world data make predictions more representative of the target population of interest.

For example, since novel therapies are increasingly indicated for rare disease, EntityRisk uses a technique known as Bayesian dynamic borrowing to maximize the information that can be extracted from sparse data [9]. Dynamic borrowing techniques combine real-world and clinical trial data in a data-driven way to mitigate the amount of bias caused by use of non-randomized

data. As increasingly more real-world data becomes available for new treatments, predictions become more accurate. In these cases, EntityRisk utilizes techniques that it has pioneered for combining clinical trial and real-world data to forecast real-world outcomes with larger datasets [5]. Our data-driven statistical modeling not only make the parameters underlying value assessment models more reliable, but also help minimize risk from VBAs and maximize revenue recognition potential. Accurate predictions of uncertainty are critical for comparing and contrasting the expected value and the financial risks associated with alternative VBA designs and allow EntityRisk to advise its clients on how best to structure VBAs in collaboration with their customers. Similarly sophisticated techniques are available for any therapeutic area or treatment modality.

Adjudicating VBAs

Once a VBA is designed and fielded, it must be operationalized, adjudicated and updated. Real-world data arrive on the performance of the therapy and competing therapies in the field, which can be used to update estimates of cash flow and revenue recognition risks, allowing manufacturers to understand, update and proactively manage the degree of financial risk in their portfolio. At the same time, VBAs require an approach to assess whether a contractual endpoint has been reached for a patient or a set of patients. A unified solution is consequently needed that enables both real-time updating of financial risk and adjudication that is timely and efficient.

EntityRisk's partnership with HealthVerity provides a turnkey solution for adjudication. HealthVerity's expertise in real-world data collection and monitoring enables rapid and efficient adjudication. EntityRisk's analytic expertise enables real-time updating of financial risk. Together, clients are supported over the entire life-cycle of a product-specific VBA.

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