Rising Up: Part 2

In the second of a two-part series, the challenges of rising healthcare costs are tackled, as new strategies to integrate payer needs with decision-making in R&D are established.

Payers worldwide are under increasing pressure to reign in continuously rising healthcare costs. In our previous article we outlined how this trend, in combination with three other drivers – real-world clinical data, risk-sharing schemes and health technology assessments (HTAs) – are propelling the transition from the ‘free-pricing’ of pharmaceuticals to value-based pricing, particularly in the European Union (EU) (1). The net result of this is that payers now strongly influence pharmaceutical list prices.

In this article, we will discuss a methodology that pragmatically integrates payer needs into R&D decision-making, and highlights a project’s future sales-at-risk within various payer scenarios. This then allows for the cost-benefit evaluation of various options which can mitigate this risk. Furthermore, the methodology can be used to answer important practical questions, such as: What is the estimated maximum sales value of a particular patient segment in the seven major markets (7MMs – US, UK, France, Germany, Italy, Spain and Japan)? How would this change upon introducing a value-based pricing system into a particular market?

Health Technology Assessments

The introduction of HTAs by payers has substantially raised the bar for market access in their resident countries. Notable examples of this include the National Institute for Health and Care Excellence (NICE) in the UK, the Institute for Quality and Efficiency in Healthcare (IQWIG) in Germany, the Italian Medicines Agency in Italy and the National Authority for Health in France. Previously, an EU market authorisation was granted for a novel medicine by the European Medicines Agency (EMA), subject to safety and efficacy assessments versus a placebo. This subsequently allowed the medicine to be sold at the manufacturer’s desired list price in most EU markets. Over the past decade, there has been a rise in the two-step procedure, whereby after the EMA grants a marketing authorisation, the medicine can also be subjected to a HTA by a member state. These not only require the new medicine to be evaluated against the current standard of care in the country, but also contain an economic element which imposes a maximum list price on the drug.

NICE is arguably the most well-known gatekeeper employing HTAs. Despite the relatively small size of the English market, it is undoubtedly important, as the UK Office of Fair Trading estimates that 25 per cent of global medicine sales reference English prices, while more than 90 per cent of EU states reference them directly or indirectly to some degree (2,3). NICE evaluates the efficacy of a new treatment in comparison to the current standard of care, quantifying the economic cost of any observed benefit. This is then set against a ‘willingness to pay’ threshold to determine if the medicine is recommended for use in the National Health Service (NHS).

The current method involves comparing the quality-adjusted life years (QALYs) of two medicines (or medical devices) and then deriving the additional cost of treatment for the number of QALYs gained by the new drug. If a new medicine fails to fall under the pay threshold, it can either be significantly discounted until it does, or not be recommended by NICE. The latter acts as a de facto rejection and, consequently, is not significantly prescribed within the NHS (4). These consequences are similar for all other HTA-regulated markets which – taken with the possibility of a similar mechanism being introduced to the US – means future sales of novel medicines are at significant risk, unless pharma addresses payer requirements.

Sales-at-Risk

Currently, the industry seems relatively unprepared for the changing market conditions; hence, a pragmatic approach to integrate payers’ needs into both early and late R&D decision-making has become necessary. The method can be split into three steps:

1. Identify key payer value drivers
2. Quantify the ‘sales-at-risk’ to payers for a given project
3. Identify cost-effective strategies to mitigate this risk

In step 1, key payer value drivers are identified by using a standardised checklist to ensure consistency across projects, which is supported by discussions of relevant case studies – such as recent assessments by NICE and IQWIG. As an example, value drivers for oncology include mean overall survival, clinical trial robustness, trial comparator and health related quality of life. Step 2 employs a five-dimensional innovativeness screen to review individual projects, and also addresses the following areas:

- Novelty: how novel is the project relative to competing compounds in development?
Figure 1: Based on the innovativeness screen results, a directional peak sales range can be calculated. Subsequently, the proportion of sales exposed to payer risk can then be identified. Data displayed is an illustrative example.

- Clinical differentiation: what is the clinical picture and how effectively does the project address unmet needs?
- Market attractiveness: how attractive is the targeted market segment?
- Exploitability: can the company realise the sales potential?
- Economic differentiation: how well does the current project address payers’ needs?

This tool allows for the results of the first four dimensions to be integrated into a weighted scoring model, which converts the answers into a hypothetical peak sales range in a free-pricing world. The fifth dimension of the screen allows for the evaluation of the project against the payer value drivers identified in step 1, in order to assess the likelihood of a project achieving reimbursement at the desired target price in each major market. This is then translated into the peak sales range in a payer-dominated world, which highlights the sales-at-risk, given the project’s current development status (see Figure 1). Finally, during step 3 we explore the possible options to mitigate this risk. By, for example, running another clinical trial, redesigning a planned one, changing endpoints or adding comparators.

Ultimately, the additional benefits of these options must be weighed against their cost, thus establishing if the changes are economically viable. For projects which achieved proof-of-concept (usually post-Phase 2 clinical trials), it is possible to calculate the expected net present value of the project with and without various potential modifications, in order to evaluate their relative cost-effectiveness. As a result, the company can make an informed decision regarding their overall portfolio strategy.

The List Price

Estimating a realistic list price for individual pipeline projects is critical to assessing the likelihood of payer acceptance, and thus sales in a payer-dominated world. Therefore we sought to build a model to estimate the probability of payer acceptance given a specific list price, primarily for post-proof-of-concept projects. HTAs used by payers are highly diverse in their requirements, powers and transparency, so identifying an appropriate HTA to model and benchmark this against is critical. Ultimately, we decided on the English HTAs conducted by NICE for the following reasons:

- English prices are referenced worldwide (2,3)
- The methods of assessment (for example, cost per QALY gained) are fully transparent and publicly available, as are all the documents relating to completed HTAs
- It is perceived as one of the highest barriers to market entry in the world, so penetrating the English market means the drug is likely to gain access elsewhere (5)

We created a model to support the semi-quantitative innovativeness screen by predicting the probability of a project being recommended by NICE, given its QALY and treatment cost per patient. QALYs are composed of two mathematical elements:
overall survival (OS) – usually the arithmetic mean- and health-related quality of life. In oncology, the latter was found to vary only slightly between comparator medicines in the majority of NICE technology appraisals, making OS the primary driver for QALYs in this therapeutic area. Therefore, the key input variable for our model is the treatment’s mean OS, which can be estimated based on the current understanding of the project.

For illustration, we have run a simulation of a novel treatment in first-line HER2-negative breast cancer, where the English standard of care is docetaxel. Figure 2 depicts the result of the simulation, comprised of 50 different scenarios with a total of 250,000 possible outcomes, and shows the probability of NICE accepting a treatment for several mean OS scenarios at various possible list prices per patient. The drug list price is estimated from the overall treatment cost by taking into account the route of administration, co-drugs, safety data and supportive care costs. It is also worth noting that this model can be used to answer the opposite question: What degree of mean OS benefit do I need to charge a particular list price in a given indication?

The use of this tool, in combination with our innovativeness screen, allows the assessor to form a more accurate project and portfolio assessment, while accounting for the payer-dominated market.

**Target Market**

Commanding premium prices in a payer-dominated market is challenging, requiring drugs to have a large impact on, in the case of oncology, OS. One approach to this challenge is to target smaller and more homogenous patient segments of a particular indication (for example, HER2+ in breast cancer) in order to drive an increase in responders and drug efficacy. However, since HTAs impose a maximum price on a novel medicine, a critical question regarding this strategy is how small can the 7MM population be to still generate meaningful revenue? To estimate the annual market value of a given patient segment, a model has been developed to incorporate the above strategy as a base case, the number of eligible patients, and a medicine list price database for the 7MMs.

For illustrative purposes, we continue our analysis in first-line HER2-negative breast cancer, which has an estimated 7MM population of 86,000 (see Figure 3). Firstly, the model shows that even a relatively small patient population can have significant market value – in this case €1.2-2 billion. It should be noted that this does not reflect the estimated sales of the novel medicine; since there is no competitor data, it assumes full market penetration and full patient compliance.

Secondly, it is clear from the data that the US has a huge impact on the overall market value, which is consistent with
Traditionally, market access and other corporate elements – such as strategy or portfolio management – lie in different functions, making collaboration within an organisation essential. It having the highest drug prices and largest population in the 7MMs. Under current market conditions, the result of HTAs rejecting a novel drug with merely a marginal benefit over the comparator only has a modest impact on the drug’s overall market value as the US market is unaffected. However, should the US adopt a HTA-like system, then the model forecasts that the medicine’s market value would decrease by approximately three quarters. Indeed, should the US begin discounting in a manner similar to Italy – which is likely to be the initial step before a full-blown HTA – then the estimated market value is predicted to drop by around 20-40 per cent.

Finally, in the event of the US adopting HTAs, even a highly efficacious drug would see a drop in value by approximately a third. Taken together with our discussion of the US drivers of value-based pricing, the forecasts of our model highlight the significant future sales risk of the 7MMs as they adopt, often with little warning, HTA-like approaches.

**Conclusion**
Traditionally, market access and other corporate elements – such as strategy or portfolio management – lie in different functions, making collaboration within an organisation essential. In order to accurately manage sales risk in the payer-dominated market, it is important that these discussions occur as early as possible during product development. The approach to portfolio evaluation facilitates this through multiple discussions with project teams, driven by transparent and comparable methodologies. Incorporating payers’ needs into portfolio management is likely to be a key element for the future success of the pharma industry and, therefore, should be of high importance to company executives.

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**About the authors**

Graham Scholefield is an Analyst at Catenion where he has worked on various projects in the fields of economic modelling, portfolio evaluation and strategy, and biomedical innovation. In addition, he has taken a keen interest in pharmaceutical market access, pricing and reimbursement. Graham holds a PhD in Biochemistry from the University of Newcastle in the UK, where he investigated the regulation of DNA replication initiation, for which he was awarded the University Doctoral Prize following several publications in world-leading journals. Graham also holds an MA in Medical and Molecular Biosciences from the same university. Email: graham.scholefield@catenion.com

Markus Thunecke is a founding Senior Partner of Catenion. He has helped numerous clients around the globe in the pharmaceutical and medical products industries create a competitive advantage, and is a frequent speaker at conferences on R&D strategy and portfolio management. Markus holds a PhD in Biochemistry from the University of Heidelberg, where he generated transgenic animal models for Alzheimer’s disease. He also has three years of research experience within the central nervous system field at Schering AG. Markus started his consulting career in 1997 at Mercer Management Consulting before joining a strategy consulting boutique, Theron, and setting up Catenion in 2003. Email: markus.thunecke@catenion.com

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