EXCERPT FROM SECTION 3
Market Access/Reimbursement/Drug Pricing

PAREXEL
BIOPHARMACEUTICAL
R&D STATISTICAL
SOURCEBOOK

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Avoiding HTA Drug Failures: The Case for Evidence-based Development Programs

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A large proportion of drugs submitted to health technology assessment (HTA) and reimbursement agencies are given restrictions that indicate either an incomplete economic argument or (locally) suboptimal pricing. It is possible, however, to anticipate and mitigate these problems in advance, while minimizing the need for additional costly trials.

Rates of failure and restriction

A quarter of recent submissions to the U.K.’s National Institute for Health and Care Excellence (NICE) were effectively rejected at submission. A further 23% received some form of restricted approval. In fact, only 52% of NICE decisions are unrestricted approvals (see exhibit below).

This is not unusual. The Canadian Agency for Drugs and Technologies in Health (CADTH) has, in recent years, rejected 44% of submissions, and has included criteria or conditions on the listing of a further 40% of submissions.

In short, the rate of rejection of new drugs through health technology assessment processes is far higher than many assume, and restrictions should be expected for a large proportion of drugs.

There are often strategic reasons for choosing to apply for restricted access. Pricing decisions are global, while reimbursement decisions are local, meaning that some markets may be effectively sacrificed in order to achieve a higher price in a larger market, or subgroups of patients may be targeted to avoid delays in the drug reaching the market.

The issue is not always price, however. While the cost-effectiveness of the drug may be weak, the strength of economic arguments is often undermined not by price, but by a lack of data and the uncertainty that this causes in both the clinical and economic argument.

A typical quote from NICE is:

At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.¹

Developing an Early Health Economic Argument

Although there are times when restriction or failure is unavoidable and unexpected, these should be very rare indeed; there is data available on both the safety and efficacy of new drugs well in advance of reimbursement submission, and the criteria used for decisions are largely transparent or at least predictable.

Given this, it is sensible to start developing a reimbursement argument at Phase II or even earlier. Indeed, any animal models used in pre-clinical development should indicate which value messages should be created, and these can be tested using a health economic model right from the start of development. There is a challenge, of course, that it is not always clear how one would model response to treatment prior to the availability of comparative trial data. The answer to this lies in using the best available data at each stage of development, incorporating new data as it becomes available, and identifying evidence gaps early to support an evidence-generation plan.

Predictive Modeling and Value of Information

The idea of an evidence-generation plan highlights the real value of early modelling—predicting how new evidence will affect our clinical economic argument, so that we can prioritize new studies or analyses.

Models developed based on early data will have a high degree of uncertainty in their outputs. In essence, as we do not know a great deal, we cannot predict with much certainty what will happen to patients. As data become available, this uncertainty should decline. However, it is not always the case that the greatest reduction in uncertainty is achieved through clinical trials. While trials are expensive and are necessary to demonstrate clinical effect, they may not be sufficient to show clinical or health economic benefit. The reasons for this may not be immediately apparent (as illustrated in the case profiled in the box below).

Summary

The failure rate of new drugs submitted to HTA and reimbursement agencies implies that the clinical and economic arguments required for market access are not being developed sufficiently.

One reason for this is that health economic models rely on more than trial and pricing data alone. As a result, models reaching reimbursement agencies often show more uncertainty than is reasonable at the specified price.

—continued—

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<th>Rejected</th>
<th>Restricted</th>
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<td>Scottish Medicines Consortium (SMC) N=167</td>
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<td>44%</td>
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*Data from 01-Jan-2010 to 01-Apr-2014 extracted from the HERON Commercialisation HTA database.

1 Accepted refers to all ‘accepted,’ ‘positive,’ or ‘recommended’ decisions. ‘Negative’ includes all ‘negative’ and ‘not recommended’ decisions. ‘Restricted’ includes ‘optimized,’ ‘research only,’ and ‘restricted’ decisions.

Source: PAREXEL Consulting, HERON™ Commercialisation

¹ This quote is found in 73 (14%) of 536 NICE decisions recorded since the agency was founded.
Uncertainty can be reduced markedly if economic models are developed early in order to plan evidence generation in advance of reimbursement submissions. This allows for a more efficient development process, and can avoid continued investment in drugs that have no realistic clinical future.

**Intensifying Regulatory Agency Interactions with HTA Bodies: A European Medicines Agency (EMA) Perspective**

“For a new medicine to reach the market and benefit patients, companies must not only ensure that they meet requirements of the regulators, but also more and more those of health technology assessment (HTAs) bodies in the Member States. The EMA recognizes that close collaboration with them is critical to allow new medicines to reach patients, and cooperation with HTAs intensified markedly in 2013...”

“Since 2010, the EMA has put in place a pilot project of parallel scientific advice with HTA bodies that allows developers to receive simultaneous feedback from both regulators and HTA bodies on their development plans for new medicines. The EMA, with the support of the national competent authorities, has so far conducted 25 parallel scientific advice procedures, with several HTA bodies taking part in this pilot project. Among the companies participating in this pilot were large pharmaceutical companies but also small and medium-sized enterprises.

“The experience gained so far has clearly underlined the need to initiate early dialogue between medicines developers, the EMA and HTA bodies to discuss and agree on a development plan that generates data that both parties can use to determine a medicine’s benefit-risk balance and value.”

*Source: EMA Annual Report, April 2014*

**Drug Prices and Placing a Value on Good Health**

“America is the pharmaceutical industry’s honeypot, accounting for a third of global drugs spending. Prices there are higher than elsewhere, and in contrast to many other rich countries, treatments are chosen with little regard for cost. Britain’s National Institute for Health and Care Excellence (NICE), for example, works to a rough threshold of $33,000-$49,000 for each additional year of good health when deciding which treatments should be available on the National Health Service.”

*Source: “Hard pills to swallow,” The Economist, January 4, 2014*

**Roche’s Schwan on Setting Drug Prices**

“The starting point always is, what is the right price for a medicine? And there is no objective answer... At the end, you are discussing, what is the price of life?”

—Severin Schwan, Roche chief executive

*Source: “Hard pills to swallow,” The Economist, January 4, 2014*
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