

# Health economic considerations for early drug discovery

The use of health economics in early phase development, while not an exact science, can, when conjoined with clinical evidence, be a very valuable information tool enabling companies to identify whether there is a market worth pursuing while identifying issues that need to be addressed in future trials and for launch.

Companies need blockbuster drugs to maximise their share price, which means a huge investment in research and development (R&D). It was estimated that the pharmaceutical industry invested approximately \$24 billion in R&D in 1999<sup>1</sup>. Despite this huge investment, the chances of developing such a blockbuster drug are small. As little as 4% of new chemical entities (NCEs) will achieve world sales in excess of \$200 million, and only 3% may achieve world sales of between \$100-200 million<sup>2</sup>. The role of health economics in this R&D process has traditionally been confined to the late discovery phases (Phase III and IV) and it has often been considered as an afterthought to the clinical trials. This traditional role is changing however, with health economics becoming an integral part of the R&D process from the early drug development phases onwards. The recent experiences with bodies such as NICE (National Institute of Clinical Excellence) in the UK have proven to many companies that if they cannot show that their product is cost-effective, it will not sell. Many companies are now performing economic evaluations for their products much earlier in the product's development for a number of reasons:

- Classic drug discovery has largely been a process of trial and error, with a myriad of failures for every minor breakthrough and a significant time period between discovery, development and launch. The average R&D period for a drug lies between 10 and 12 years, a period of high investment and no return for the industry. Recent devel-

opments in scientific and medical technology are striving to speed the R&D process up, getting drugs to the market quicker and therefore earning a return on investment. As this process is accelerating, it is in the interests of the pharmaceutical industry to develop their health economic hypotheses earlier, ensuring they have time to fully prepare for the cost-effectiveness data that they must capture during the later phases of development.

- It is always important to make the most informed decisions when considering the 'go: no go' decisions which pepper the R&D process, especially given the increasingly competitive environment the pharmaceutical industry competes in. These decisions traditionally focused on issues regarding the safety, tolerability and efficacy of the potential compound. While these issues remain of paramount importance, economics is also now a key consideration. For example, any new compound at this early stage of development may have multiple possible indications for which it may be potentially developed. It will be important to therefore consider the economics of each possible indication. This will answer a number of questions. Is my product cost-effective against what is currently on the market in each indication? Why will my product be more cost-effective in the future (eg, side-effect profile, efficacy, convenience)? What are the cost savings associated with my product's advantages? What pricing and reimbursement hurdles might be expected? At my product's launch, who will actually be the key decision-maker for drug prescribing and what will be

**By Dr Ann-Marie  
Craig and Dr Lisa  
Kennedy**

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**Figure 1**  
Health economics throughout  
the development phases

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| <b>Phase IV:</b>  | <b>Objectives</b><br>Increase product experience<br>Support lifecycle management<br>Demonstrate long-term outcomes<br>Study QoL or HE specific endpoints | <b>Approaches</b><br>Cost-effectiveness trials<br>Registries<br>Claims analysis<br>Stand-alone HE study  |
| <b>Phase III:</b> | <b>Objectives</b><br>Support regulatory submission<br>Facilitate coverage and payment  | <b>Approaches</b><br>Piggyback studies<br>Modelling studies/interactive interfaces   |
| <b>Phase II:</b>  | <b>Objectives</b><br>Build market need<br>Finalise data collection endpoints<br>and instruments  | <b>Approaches</b><br>Cost-effectiveness scenario analysis<br>Literature review to identify outcomes<br>research endpoints<br>Instrument development and validation |
| <b>Phase I:</b>   | <b>Objectives</b><br>Integration of outcomes research<br>Into product development  | <b>Approaches</b><br>HE strategic plan<br>Burden of illness<br>Retrospective chart analysis  |

the key messages that will influence them? Indeed, even at these early stages of development, health economics can help the company identify whether it is really worth pursuing particular avenues of development from a market perspective. Given that the average drug costs £350 million to develop over a 10-12 year period, the right decisions at the right time are crucial to a company's success.

- Because of the increasingly competitive environment in which pharmaceutical companies compete, it is important to provide strong, transparent economic arguments for new products, especially if a premium price is sought. By introducing health economics at the earlier phases of development it is easier to tailor later phase studies to fully address identified issues and therefore enhance the strength of the information gathered to support product launch. Health economic studies performed in Phase II, for example, can shape the data collected in Phase III. In essence, the increased depth of knowledge provided at the earlier phases of development will strategically guide later development tactics.

- Increases in expenditure on medicines that are higher than the level of increases in healthcare are generally a feature of all Western health systems<sup>3</sup>. As such, there is an atmosphere of cost containment and a need for evidence of 'value for money' throughout all of the markets the pharmaceutical industry trade in. National pricing and reimbursement bodies now request health economic evidence to support the drug approval process. Australia, Canada, Germany, Belgium, Finland, Norway,

France and the UK are all examples of countries that have published health economic guidelines. While not all of these countries have formally adopted such guidelines within their regulatory procedures, there is a growing trend for prescribers, formulary gatekeepers and formal pricing and reimbursement authorities to ask for and consider health economic arguments alongside clinical data in their evaluation of a new health technology. Clinical trials have increasingly become viewed as the proper setting for prospective economic data provision at launch<sup>4</sup>. This need for additional information has added to the competitive pressures faced by the industry. However, it has also meant that many companies are now introducing health economics into the development phase much earlier on to ensure they have the correct information at the later phases of development to support the regulatory requirements.

- Finally, health economics is becoming a much better understood subject. More healthcare providers as well as those in the industry recognise that high quality, relevant health economic evaluations can add considerable value to the decision-making process. As this has become more universally accepted, so has the use of health economic evaluation at all levels of product development.

### Common health economics studies undertaken in early drug development

Health economics draws upon a wide cross-section of economic theory including cost-benefit literature,

welfare economics, public finance, consumer theory and industrial economics. Measuring health and the effects of medical interventions upon health are not new, however over recent decades this branch of economics has received much more attention and its value has become more recognised. The type of studies undertaken during the early drug development phases necessarily differs from those conducted in later development due to the different levels of knowledge at each respective stage of development (see Figure 1). The focus at this early stage is much more on information gathering and scenario analysis to help future strategic decisions. Early health economic evaluation forms part of a cohesive product development and marketing strategy.

The most common strategy for developing economic evaluation in Phase I and Phase II is economic modelling. The general approach is to collect data from a number of sources on the current market and then use these together with the currently known profile of a new product for comparison. Essentially, these model simulations build a view of the current market and simultaneously project the future market. A new product is then placed within this context. Because of how these models are built, they are valuable tools for both clinical development and marketing. A model will show someone in clinical development the current efficacy rates of products on the market and the levels of different efficacy and adverse events their product will need to address. Hence, supposing a company had a new product that treated chemotherapy-induced nausea, a model could capture the probability of nausea for each chemotherapy cycle for current treatment and allow new product comparisons. Likewise, suppose that a company had a new product that treated a side-effect of cisplatin: a model might show that in a number of cancers, cisplatin would be replaced by carboplatin by the time the new product came to market.

Capturing the path of the patient from diagnosis to resolution, these models contribute to a full understanding of the therapeutic area, potential market and whether it is economically viable and the possible positioning of the compound if it reaches launch. They further capture the anticipated impact of the product on the market and associated potential pricing and reimbursement hurdles to overcome. Such models can be an essential tool for both 'go: no go' clinical decisions and early marketing strategy (see Figure 2).

In order to build a model simulation for early economic evaluation it is necessary to evaluate both the burden of illness and the therapeutic market:

● **The Burden of Illness.** For every compound in the early development phases it is essential to fully

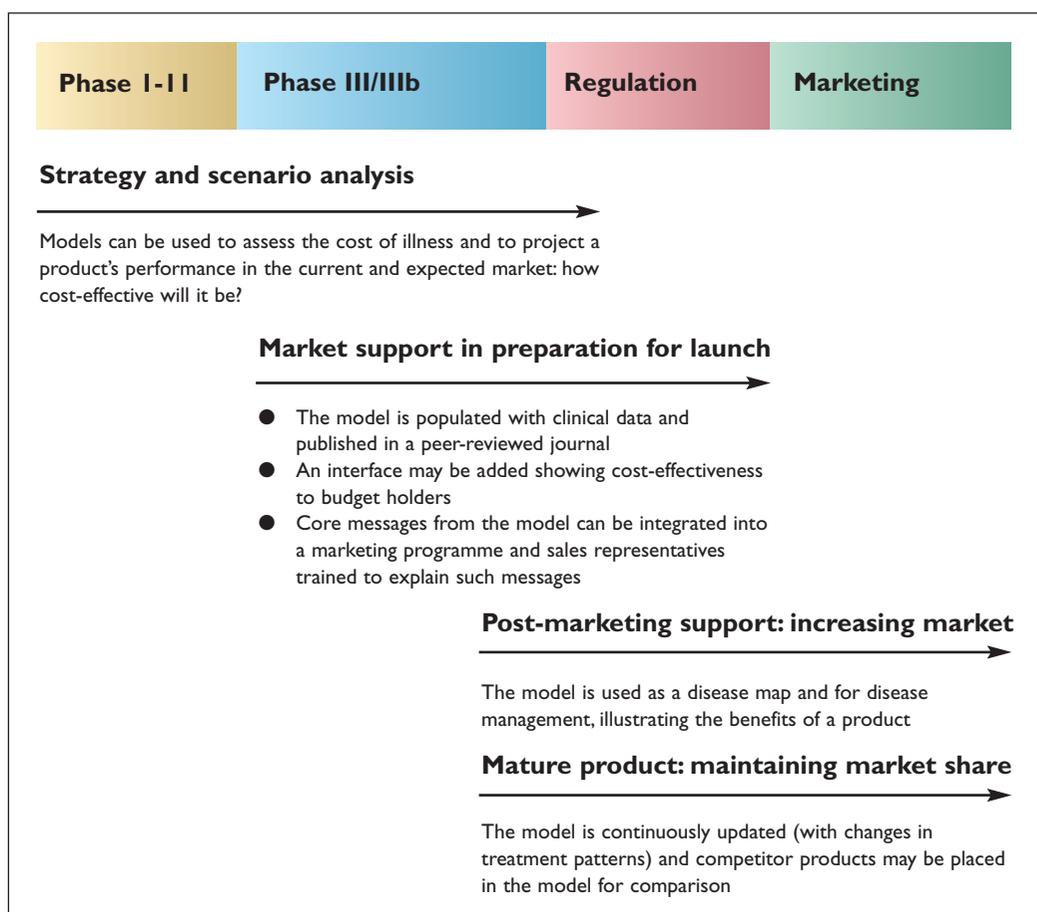
understand the illness for which it may be indicated. Who are the patients? What are the prevalence, incidence, co-morbidities and mortality rates? How does this illness impact the patient, the healthcare system and society both from a clinical and economic perspective? What are the short-term and long-term implications of the illness; are both a consideration? What healthcare resources are used in the current treatment of this illness – medical personnel, outpatient visits, hospitalisation, medication, etc? Such studies identify the current treatment pathways for a particular disease, and the most relevant clinical outcomes and economic considerations to help guide future studies. A company can find these data through literature, retrospective patient chart analyses, database analyses and expert opinion. Often these data also form part of the communication process of sensitising the market to the unmet need that a new product will fill.

*Example:* Male erectile dysfunction (ED) has been defined as a failure to achieve and maintain an erection sufficient for satisfactory sexual performance. This medical condition has a significant negative impact on quality of life, being associated with a loss of self-image, self-confidence, relationship difficulties and even chronic anger<sup>5</sup>. In 1995 it was estimated that more than 152 million men worldwide experienced ED and this number would increase to approximately 322 million by 2025<sup>6</sup>. Current treatments for ED can be classified as oral, intracavernosal injections, intraurethral suppositories, topically applied creams, external vacuum devices and surgical and psychological therapy. Prior to 1998 treatments for ED were predominantly local, including injection therapy and suppositories; mechanical vacuum devices were rarely used. In April 1998, Viagra™ (sildenafil citrate), became the first approved orally active treatment for ED.

● **The Therapeutic Market.** It is essential to consider the market place that any compound may eventually be launched into. Is it worth the investment in development to put a product into this market in the future? Where are the major markets for such a potential drug? Who are the current key players in this market, how can this be quantified and what is the status of their products (brand, near patent expiry, generic, prices, etc)? What is the current product pipeline like for this area and when are other potential competitors due to be launched? Who are the key decision-makers in this therapeutic area – the GP, the consultant, the formulary gatekeeper? What information do these decision-makers require to prescribe a new product? What guidelines

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**Figure 2**  
Modelling throughout the development phases



currently exist on a local, national or international level and what are their key concerns (quality of life, clinical outcome, value for money, hospitalisations, etc)? What is the unmet need within the therapeutic area: no known cure; treatments available but with significant side-effects and therefore implications on quality of life and cost. How are treatments administered: intravenous versus oral, once daily versus twice or more daily? What are the current pricing and reimbursement hurdles in each market and how might these change in the foreseeable future?

**Example:** Considering the number of men experiencing ED worldwide (potentially 322 million by 2025) the market might look enormous. In the UK it was estimated that the NHS spent approximately £12 million annually on impotence treatments. However, there are subtleties within each market that may make it a much more difficult place to compete in. Although the prevalence of ED among men aged 40 to 70 years has been estimated to range between 15-20%, only a small percentage of men actually seek medical help and therefore, the market potential may not be as substantial as first anticipated. In addition, the financial implications

of providing medical treatment to such numbers of ED patients has been seen as a serious challenge to already under-funded national health systems. This is especially true as the diagnosis of ED depends on self-reporting, and there is a concern that men who do not have ED but who wish to enhance normal performance will present seeking pharmacological treatment. Governments and third party payers are concerned about the affordability of treatment for a condition that is neither life threatening or causes physical pain. This was highlighted with the introduction of sildenafil in Europe. Considering the UK, the impact of oral sildenafil might have led to an annual drugs bill for this drug alone in excess of £1 billion (\$1.6 billion) a year if all men who might benefit were prescribed the drug<sup>7</sup>. This possibility led to very restrictive prescribing conditions for sildenafil in the UK to control prescribing and cost. In France, Spain, Italy and Germany there is no state reimbursement despite evidence of clinical and cost-effectiveness<sup>8</sup>. In contrast, however, the drug is free for anyone under the healthcare services in Ireland and Sweden.

### Assessment of economic viability

Given the availability of the information above it is possible to assess the economic viability of a new compound even at this early stage of development. Anticipating the characteristics of the product in comparison to current products available on the market it is possible to conduct a full scenario analysis with a model simulation. The probabilities for a new product's efficacy, side-effects and even price can be varied to show their impact on a product's outcome and cost-effectiveness. In addition, the relative impact of each market element can be assessed together through what is referred to as a model tornado analysis (see Figure 3). For example, the length and subsequent cost of hospitalisation will most likely have a large influence on the expected cost of a treatment. Indeed, as the compound progresses through the phases of development, the additional information can be fed into this model to keep the decision-making process informed of market potential. In addition, such assessments will identify areas where key information is potentially lacking. For example, to convince prescribers, formulary gatekeepers and pricing and reimbursement bodies, a company might need to better capture and communicate the incidence of ED in the general population. Another company might need to prove the link between the progression of ESRD and the control of hyperphosphatemia. Identification of such information gaps during the early development phases will allow sufficient time to design and validate such instruments for use in later phases of development.

### Conclusion

The demands of both formal and informal pricing and reimbursement authorities have meant that economic evaluation is necessary much earlier in a product's development. While NICE brought this to the consciousness of many in industry, the demands for this data will only intensify. In the future, the EC Commission would like to set up a network of health technology assessment (HTA) agencies as part of its new public health programme. There are now 20 country-based HTA agencies in the European Union and their role will be to advise governments and clinicians on health policy-making and practice in terms of the effectiveness and cost-effectiveness of health technologies.

Health economics is not an exact science and will not give a simple answer to whether a product should continue down the development pathway, but at the early phases of drug development it can be a very valuable informational tool in combination with the clinical evidence to hand. In simple

terms it can help identify whether there is a market worth pursuing and prepare the company for potential issues that they need to address in future trials and for launch. Introducing such concepts within early phase development allows the product specific health economic evaluations conducted in phases III and IV to be tailored to the issues most important to the market. As previously noted, the best decisions are the most informed decisions, therefore there is a role for health economics throughout the whole development process. **DDW**

*Ann-Marie Craig, PhD is the director of operations for the Lewin Group, UK. Dr Craig joined The Lewin Group in 1999 after spending more than two years as a health economist with a leading pharmaceutical company and prior to that was a senior research fellow at the PharmacoEconomic Research Centre, St Andrews University. Ann-Marie continues her close ties to academia through her position as honorary research fellow at St Andrews University.*

*Lisa M. Kennedy, PhD is vice-president for Lewin, Europe. Dr Kennedy completed her PhD at the University of St Andrews and started the UK operations for The Lewin Group in 1997. Dr Kennedy has been involved in health economics policy initiatives for eight years and has worked in the field of applied economics for more than 10 years.*

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**Figure 3** Tornado analysis of variables affecting the expected cost of a treatment

