Rarefied drug pricing

Orphan drug development is already difficult enough. Demanding manufacturers account for the development costs of individual drugs for reimbursement is misguided.

One cannot say this has not been coming. The prices of many new drugs are astronomical and unsustainable. And new drugs against rare diseases have prices that are among the most astronomical and unsustainable in the world. A case in point is orphan drug manufacturer Alexion Pharmaceuticals' anti-complement C5a receptor humanized antibody Solaris (eculizumab), which would set you back £340,200 ($568,583) just to provide a year's treatment for atypical hemolytic uremic syndrome. In March, as part of its health technology assessment (HTA) of Solaris, the UK's National Center for Clinical Excellence (NICE) requested that Alexion provide information on the drug's development and manufacturing costs. It also asked the company to explain how these costs relate to the drug's proposed pricing. Seeking to link the market price of a drug to the R&D investment in that drug is a Rubicon that has never been crossed by NICE—or by any other reimbursement agency. The practice runs counter to existing assessments for drug pricing in Western markets. And worst of all, it endangers future investment in orphan disease drugs.

The US Orphan Drug Act, created in 1983, applies to any rare disease that affects fewer than 200,000 people. As patient numbers in these disorders are too small to be attractive to most commercial drug makers, the legislation provides economic incentives to encourage development, such as seven years of market exclusivity for an approved product, exemptions from fees for regulatory submissions and advice, as well as certain tax credits. The European Union enacted a similar pathway in 2000.

It is safe to say that orphan drug legislation has been a resounding success. In the ten years preceding the Orphan Drug Act, only ten rare disease products were approved in the United States. Every decade since the legislation was enacted, over tenfold that number have received US approval.

Last year was a record year for US orphan drugs, with 31 registrations. Many manufacturers focus on rare disease with an eye on expanding into supplemental indications with larger patient populations once orphan approval has been obtained; indeed, several big pharma companies now tackle rare diseases that previously would have been the exclusive domain of biotech companies. No wonder then that orphan drug sales are growing at such a rapid pace. Since 2005, global revenue from orphan drugs has escalated almost 10% each year.

NICE assumed responsibility for evaluating orphan drug reimbursement last year. Because its traditional HTA assessment tools, like cost utility analysis and incremental cost-effectiveness ratio, are hard to apply to rare diseases for which little information is available, the agency created a new approach—the Highly Specialised Technology process—to evaluate orphan products. This process takes into account several factors, such as nature of the condition, clinical efficacy, budgetary impact, value for money and benefits beyond health.

In the case of Soliris, NICE gave a glowing appraisal of the drug based on the above criteria. But its guidance to Alexion also contained a bombshell. NICE stated, "the Evaluation Committee has not yet been presented with an adequate explanation for [Soliris'] considerable cost." The guidance noted that the company had provided insufficient justification for Soliris' high price "in the light of manufacturing, research and development costs" and went on to ask for clarification of the relationship between development costs and final drug price.

This is problematic on several levels. First, at no time in history has a payer asked a company to justify the list price of its drug in terms of R&D costs. This is because such an arrangement would ignore the reality that successful drugs pay not only for themselves but also for the numerous other failures in a company's pipeline. It is wrong to think about drug price just in terms of a single drug's development costs. An approved drug's price includes not only the cost of its own R&D, but also the costs of the multitude of other unsuccessful projects that are essential for any innovative drug discovery process.

Second, it is not clear that companies keep accounting records of expenses associated specifically with each drug asset as they go through the pipeline. To comply with NICE, the entire industry would have to change the way it accounts and audits R&D.

Third, with drug development efficiencies translating into a miserable nine out of every ten drugs failing human testing, no investor would take the risk of investing in an orphan drug program if the upside on profits for an approval were so low. If reimbursement authorities refuse to pay a price for a successful program that adequately covers all the (often enlightening) failures in a company's pipeline, investors will desert orphan drugs and spend their money elsewhere.

Finally, adopting such a system would perversely reward inefficiency in drug innovation. The more expensive a company can make its development process, the more money it would receive from the payer. That sounds like the wrong message to send to a drug discovery process that is already inefficient.

Basing reimbursement on R&D costs is flawed. NICE must know this. If so, it is playing a very dangerous game. Either it is hoping that the shot across Alexion's (and industry's) bow on development costs will put it in a stronger position for negotiation on price discounts. Or it is embarking down a road that means R&D costs will be applied to the pricing of all orphan products, with potential catastrophic consequences for investment and innovation.

Orphan drug legislation has transformed commercial drug development over the past 30 years. It is a truly magical thing that the free market currently serves minority patient groups—those least likely to get their voices heard. NICE should think very carefully before it tramples roughshod over orphan incentives and potentially jeopardizes three decades of progress in rare disease.