PERSPECTIVE

Access and affordability for all

The hope of gene therapy could be crushed by its financial burden unless there are more rational ways of paying for it, says **Michael Sherman**.

Gene therapy offers the possibility of a cure for previously untreatable diseases. But although the science and technology behind it are awe-inspiring, the costs can be daunting. Treatments are likely to have a price tag in the neighbourhood of US$1 million or more — a cost that is ultimately borne by all individuals, not just patients, through taxes and insurance premiums.

In the United States, which lacks government-administered provision of universal health care, there is a strong expectation that health insurers will pay for therapies that have been approved by the US Food and Drug Administration (FDA), particularly if a treatment is the only effective one for a given malady. In cases in which the efficacy data and value proposition are questionable, FDA approval can create enormous pressure to provide coverage.

Some stakeholders — including pharmaceutical companies and government policymakers — have been squeamish about introducing measures of cost effectiveness into the decision-making process because of concerns that such an approach could lead to putting a price on life and, ultimately, the rationing of care. Unfortunately, this has had an unintended consequence: it has led to a system that has no mechanism for imposing price ceilings. Many individuals in the United States see substantial cost increases for their medications year after year.

One possibility would be for the FDA to consider a pathway in which it expedites approval for a treatment in the absence of sufficient high-quality data, particularly for rare diseases that have no effective treatment, in return for the drug maker agreeing to a so-called value-based agreement that would tie reimbursement to the success of the drug. When treatment works, the manufacturer would receive full payment. When the patient shows a limited response to treatment, there would be a partial payment. And when the treatment fails altogether, no payment would be made.

I work for the health insurer Harvard Pilgrim Health Care in Wellesley, Massachusetts, and in January my company entered into a value-based agreement with Spark Therapeutics in Philadelphia, Pennsylvania, for the gene therapy voretigene neparvovec (Luxturna), a treatment for a form of hereditary blindness. This agreement is already driving considerable discussion between payers and pharmaceutical companies that have upcoming gene therapies and other high-cost, innovative treatments. Other firms have forged similar deals. For example, in 2016, the pharmaceutical company Novartis in Basel, Switzerland, signed a deal with several insurers, including Cigna in Bloomfield, Connecticut, and Harvard Pilgrim, for its combination drug sacubitril–valsartan, a treatment for heart failure. In the event that people receiving the drug fail to show a reduced rate of hospitalization for heart failure in clinical trials, the drug cost will be reduced. Collaborative deals such as this give hope that stakeholders will work together to ensure that all who might benefit have access to cutting-edge medical advances.

Gene therapy, which offers the potential of extremely effective but extremely expensive treatments, is a good candidate for value-based agreements. Take, for example, the high-cost biological drug eteplirsen, which targets the gene responsible for Duchenne muscular dystrophy (DMD). The FDA expedited approval of the drug in 2016 because DMD was a fatal, progressive disease with insufficient treatment options. Approval was granted despite the FDA's advisory committee voting against it and despite slim evidence of efficacy — the pivotal trial, which enrolled just 12 boys, showed very small changes in the surrogate measure used as an outcome.

The agency's decision sent shock waves through the US insurance industry and led to variability in coverage policies. Many companies agreed to pay for the drug, which costs around $300,000 per year, but others initially declined to do so.

In this case, a value-based agreement could have set out a multi-year payment model that would terminate if the effectiveness of the drug failed to persist over the long term. And because such a deal would enable broad access to the therapy, it would in turn generate robust real-world evidence of the treatment's efficacy. Such data could then be used to gain conventional FDA approval. Sarepta Therapeutics in Cambridge, Massachusetts, the company that developed eteplirsen, chose not to enter into value-based agreements for that drug, but it is collaborating with a partner to develop a one-time DMD gene therapy that is expected to be much more expensive. That therapy might present an opportunity to enter into an innovative financing agreement to promote access.

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Some pharmaceutical companies oppose value-based pricing, questioning whether the approach maximizes shareholder value. It is fair to acknowledge that any solution to improve access to health-care advances should provide a reasonable return to the companies that develop such innovations. It is also appropriate to ask whether treatments for rare conditions should be priced higher to ensure that companies will pursue the development of drugs that will always have a limited market.

Whether or not we choose to acknowledge it, there is a limit to the portion of a country's gross domestic product that can be spent on health care. To balance access and affordability over the long term and ensure that our loved ones can receive the next generation of innovative therapies, payers, pharmaceutical companies and regulatory agencies need to collaborate in a way that benefits all stakeholders. Value-based agreements from the past few years provide a model that could be applied to upcoming gene therapies and other high-cost, innovative treatments. A spirit of collaboration among industry players could ensure that everyone who needs an innovative, expensive treatment can have access to it. ■

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