The arrival of gene therapies: how can payers and pharma address the budget impact problem?

A potential cure, but at what price?

The development of gene therapies represents a new frontier of science, with the potential to help many patients with serious or fatal conditions. These new treatments offer the possibility of a ‘cure’ for many devastating conditions, with remission rates of up to 94% demonstrated in severe cancer patients not responding to other available treatments.

The list of approved gene therapies and cell-based gene therapies by either the FDA or EMA now includes Glybera, Imlygic, Strimvelis, Yescarta, Kymriah and Luxturna, and this is set to further increase. Given that these products are targeted at extremely small patient populations and are complicated and expensive to manufacture, the price levels associated with these products are unprecedented. For example, Strimvelis is priced at €594k in the EU, with Kymriah and Luxturna priced at $475k and $850k in the US, respectively. Once hospitalisation and intensive care costs for treating the severe side effects of these therapies are considered, total treatment costs can reach €1.3m per patient.

However, as a gene therapy is a potentially curative procedure that offers lifetime benefits, these high prices can be justified by the cost savings of removing the need for subsequent long-term therapy. NICE’s recent recommendation of Strimvelis reflects this, where the wider (non-health) benefits of Strimvelis brought the cost-effectiveness estimate down to an acceptable level, despite uncertainties around the efficacy data.

Though gene therapies may be considered cost-effective, the key challenge facing payers is how to fund such a substantial up-front cost, whilst the health benefits are accumulated over a number of subsequent years. The Institute for Clinical and Economic Review (ICER) has described the potential cumulative budget impact of an influx of gene therapies at costs of $1-2m as unsustainable, particularly given the increasingly cost-constrained healthcare environment.

Indeed, Glybera’s failure is a rejection of the up-front payment model. Priced at €900k per patient and with no payment mechanisms evident to minimise the budget impact or refund non-responders, Glybera was used to treat only one patient before being withdrawn from the EU market. ICER perceive existing mechanisms designed to manage expenditure on high-cost treatments (e.g. discounts and rebates) as being overly restrictive, stifling towards innovation and inadequate at rewarding value; it is therefore clear that new approaches are required.

Proposed innovative payment mechanisms

The key issue around gene therapies is affordability, but also the concept of financial risk and how this should be shared with the manufacturer. A range of models have been proposed by payers that

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1 Cancer: World Best Ever CAR-T Results have Just been Disclosed: [https://labiotech.eu/world-best-ever-car-t-results-for-cancer-have-bust-been-disclosed/](https://labiotech.eu/world-best-ever-car-t-results-for-cancer-have-bust-been-disclosed/)
2 Cascade of costs could push CAR-T therapy to $1.5M per patient: [https://endpts.com/cascade-of-costs-could-push-new-gene-therapy-above-1-million-per-patient/](https://endpts.com/cascade-of-costs-could-push-new-gene-therapy-above-1-million-per-patient/)
3 Gene Therapy: Understanding the Science, Assessing the Evidence, and Payer for Value; ICER, March 2017
seek to address these challenges, with the most promising being outcomes-based agreements, amortization models and service models.

*Outcomes-based agreements*

These are becoming increasingly common in certain EU countries, serving an important function in addressing uncertainty around the long-term outcomes of gene therapy by linking payment levels to real-world treatment outcomes. However, challenges remain in establishing cost-effective long-term tracking outcomes tracking systems in countries where these are not already in place.

*Amortization models*

Similar in concept to a property mortgage or financing deals applied in the automotive industry, a customer makes regular payments over time (or to coincide with specific stages in a patient’s treatment), with or without an initial deposit. The length of the agreement would be negotiable, as would future discounts. ICER considered gene therapies as good candidates for amortization models for a range of reasons, including the fact that they provide a one-time ‘curative’ impact in a population large enough to make an up-front payment unmanageable. However, the problem of who should bear the financial risk remains, and ICER advised manufacturers to approach payers with manufacturer-financed mechanisms for instalment payments.

*Service models*

These move gene therapies towards being priced as a service, rather than as a traditional pharmaceutical. The manufacturer would provide the technology for free, and then invoice the healthcare system for the intervention avoided. For example, if a gene therapy was developed in neovascular age-related macular degeneration (nAMD), the healthcare system could be invoiced for every anti-VEGF injection avoided. This mechanism allows new technologies to be incorporated into care pathways without an insurmountable cost barrier to the healthcare system, at the same time redistributing a large portion of the financial risk onto the pharmaceutical company.

**What has Pharma’s approach to gene therapy payment models been to date?**

Despite ICER recently declaring the $850k price tag of Spark Therapeutics’ Luxturna to be too high to be cost-effective, the company has been praised by payers for its innovative approach to helping payers afford this new therapy. Spark Therapeutics’ approach has three main elements:

- A rebate program based on proving Luxturna’s effectiveness at 30 to 90 days, and again at 3 months
- The negotiation of contracts directly with commercial payers or specialty pharmacies rather than treatment centres, to reduce the financial risks for treatment centres
- The development of a plan with the Centers for Medicare and Medicard Services (CMS) to allow reimbursement of Luxturna in instalments spread over many years

For Strimvelis, GSK has offered risk-sharing schemes and payment through instalments, although the former is common in Italy (where Strimvelis is manufactured and has been primarily used so far), and GSK simply fitted in around existing payment mechanisms.

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6 ICER report critical of Spark Therapeutics’ pricing of Luxturna, The Pharma Letter. January 2018
Novartis has been more innovative with Kymriah, transporting the pay-for-performance model which is common across the EU over to the USA. In a novel deal, Novartis has entered into an outcomes-based agreement with the CMS through which the agency must only pay for Kymriah in instances in which the patient responds after a month\(^8\).

It is still early days in the gene therapy revolution, and there is a long way to go before a satisfactory solution is found that will allow patients to access these potentially life-changing treatments without creating an unsustainable impact on payers’ budgets. Pharma companies and payers must continue to work together to identify innovative payment mechanisms that will spread the financial risk fairly between both parties, acknowledging the need for gene therapies to remain commercially viable to encourage their future development.

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