Novel payment models to facilitate patient access to gene therapies

Pfizer

Alliance for Regenerative Medicine

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Introduction

Innovative treatments like gene therapies provide high value but also pose unique challenges for health technology assessment (HTA) and pricing and reimbursement (P&R) processes. These challenges stem from the fact that gene therapies can be associated with particular clinical and economic uncertainty:

- **Clinical uncertainty:** gene therapies offer possible long-term, transformational health gains from a potential one-time administration – a significant divergence from conventional long-term treatments[1]. Because treatment outcomes could be lifelong, it is not possible to fully capture them during clinical trials[2]. Gene therapies also currently target rare or ultra-rare diseases[1], which are characterized by small patient populations, disease heterogeneity, and lack of established endpoints, with treatments often being assessed through single-arm trials[3].

- **Economic uncertainty:** the inherent characteristics of gene therapies, including the possibility of long-term benefit from a potential single administration, are associated with high upfront costs and uncertainty around budget impact and cost-effectiveness, since the treatment effect is expected to last longer than the trial duration[1,4].

Payment models are contractual agreements between payers and manufacturers that can address clinical and economic uncertainty at the time of launch. There are two types of payment models: financial and outcome-based[5,6,7].

- **Financial-based agreements** address economic uncertainty. These agreements can be simple discounts, but can also have more novel forms such as annuity or split payment models, which spread the total treatment cost over multiple budget cycles.

- **Outcome-based agreements (OBAs)** link P&R status to therapeutic outcomes over time as evidential certainty evolves, allowing more time to generate the required clinical evidence while providing patient access to transformative therapies. OBAs can generally be considered novel payment models, as they are used less often than financial agreements, but become increasingly important for innovative medicines like gene therapies.

Novel payment models have the potential to improve the speed and breadth of patient access to gene therapies, and have been increasingly implemented to address clinical and economic uncertainties, as well as budget impact.

OBAs, for example, have been used in Germany, France, the United States (US), and Australia for several products, including gene therapies[8,9]. In Germany, reimbursement for a gene therapy for spinal muscular atrophy (SMA) included outcome-based rebates linked to individual patient data. In France, a CAR T-cell therapy for cancer was granted reimbursement based on a coverage with evidence development (CED) agreement. This type of payment model grants reimbursement, but re-appraisals and price re-negotiations are required based on further evidence collection. In the US, the company offered insurers an OBA for the CAR T-cell therapy based on patient response at 30 days.

Financial models combined with an outcome-based component have also been increasingly used in recent years. In Italy, reimbursement of a gene therapy included annuity or split payments linked to efficacy assessment, with checkpoints at 12, 24, 36, and 48 months[10]. Based on this model, payment is stopped if the efficacy criteria are not met[10]. In Australia, funding for CAR T-cell and gene therapies (which are jointly funded by federal and state governments) is linked to both financial and individual patient outcomes at defined timepoints after therapy infusion[9]. The adoption of novel payment models has contributed

to advancing patient access to gene and cell therapies. For example, initiatives in several European countries (e.g., France, and Spain) have facilitated the uptake of novel payment models to support the achievement of agreements during P&R negotiations[6,11,12].

Despite optimism and progress, barriers to the implementation of novel payment models remain[6]. In some countries, there is a lack of laws and regulations regarding the adoption of such models (e.g., annuity). In other cases, the governance structure may be insufficiently defined in terms of roles and responsibilities, data collection process, etc. Furthermore, several practical aspects can hinder adoption, such as organization and availability of data collection infrastructure, and lack of consensus on the choice of appropriate outcomes.

In this context, roundtable participants discussed areas of focus, along with opportunities and best practices for two prominent domains related to improving the adoption of novel payment models:

- Better understand and mitigate barriers to uptake of novel payment models
- Account for relevant contextual factors to support implementation of novel payment models

Better understand and mitigate barriers to uptake of novel payment models

In the case of gene therapies, there is often substantial debate around clinical uncertainty and affordability of these potentially one-time, long-term treatments, especially when compared to conventional medicines[1,7].

Manufacturers and payers share the common goal of enabling patient access to effective medicines, while also having different viewpoints when assessing the potential value and P&R risks of a new therapy[7]. These divergent views can translate into difficulties in arriving at a mutually acceptable agreement, prolonging P&R negotiations and, ultimately, delaying patient access[13].

Although many factors can contribute to access delays, the need for early and continuous conversations between payers and manufacturers plays a key role in facilitating access, particularly when agreements need to be reached for novel treatments like gene therapies[7]. A mutual understanding and collaborative work towards the common goal of access may facilitate more efficient negotiations and improve access to promising gene therapies.

Such collaborative work requires the inclusion of some key considerations:

- The costs and complexity of development make the economics of gene therapies particularly challenging. Manufacturing is complex and resource-intensive, and it is more difficult to scale production compared to conventional medicines[14]. Additionally, investment in specialized centres, equipment and skills is required to administer approved gene therapies[14].
- Manufacturers will potentially receive only one payment per patient compared to standard treatments administered over a patient's lifetime, and these patient populations are small. Therefore, the price of gene therapies needs to reflect their one-time nature and the rarity of the conditions they currently treat.
- In terms of clinical uncertainty, there is often a lack of clarity around the duration of treatment effects, which patients may benefit from a treatment, patient uptake, and the extent of those benefits[7,15].
- Payers need to reconcile budget impact and clinical uncertainty of gene therapies and find an agreement that provides confidence in a manageable budget impact and sufficient treatment benefit[7].
- It is crucial for healthcare systems to be able to allocate sufficient resources to cover the administration and acquisition costs of innovative therapies, including gene therapies. To avoid treatment delays and

additional healthcare costs, it is essential that funding includes all resources necessary for treatment administration and follow-up[16].

Novel payment models can support a balance between patient access and economic sustainability for manufacturers, while helping alleviate uncertainties for payers. Those models, thanks to additional data collection and financial mechanisms that spread payments over time, can alleviate both clinical and budget impact uncertainties.

There is thus an opportunity to build a clearer understanding and enhanced collaboration between manufacturers and payers when trying to bring gene therapies affordably and sustainably to patients. An open dialogue among all stakeholders, including patients, can promote this understanding.

Best practice

RARE IMPACT, is a multi-stakeholder initiative organized by EURORDIS to improve patient access to advanced therapy medicinal products (ATMPs), including gene therapies[17]. As part of the initiative, the topic of ATMP pricing and economics was explored in a series of three stakeholder dialogue workshops, attended by representatives from member companies, patient organizations, policy makers, payers and physicians[18]. The workshops had the following objectives:

- To help contextualize prices within the broader ATMP innovation model through collective exploration
- To explore the economics of ATMP development in rare diseases
- To enable an open dialogue across stakeholders and advance mutual understanding of the pricing issues of ATMPs

The collaboration raised awareness about the need for collaboration to approve access to gene therapy, and opened a conversation on potential ways forward.

Such clarity and collaboration between manufacturers and payers can build a higher level of trust. This, in turn, may improve the ability to agree on novel payment models and overcome uptake barriers.

Account for relevant contextual factors to support implementation of novel payment models

The acceptance and feasibility of novel payment models may vary across contexts for two main reasons: implementation complexity at the healthcare system level or characteristics of a certain disease or indication.

- At the **healthcare system level**, some payment models, e.g., OBAs, may be difficult to implement if there is a lack of appropriate data collection infrastructure or personnel resources to effectively track treatment outcomes over time[19].
- Regarding the **characteristics of a certain disease or indication**, if the number of patients is extremely limited, it may be complex to set up a dedicated data collection infrastructure to support OBA implementation[6].

Therefore, there is an opportunity to support the successful implementation of innovative payment models by considering their acceptance and feasibility in each context.

Novel financial models, such as annuity or split payment models, allow the upfront cost of therapy to be paid in pre-specified installments, which can help overcome issues around affordability in each budget cycle and address payer concerns about budget impact[19]. There have been difficulties implementing these payment models, mainly due to accounting rules (e.g., even though the payment is spread over a number of years, the cost is fully accounted for when the gene therapy is administered)[6,20].

Despite these concerns, interest in split payments is increasing[21]; this type of payment has become more accepted and has been successfully implemented in various countries[6].

For example, in France, the 2023 Social Security Finance Bill (PLFSS) allowed the implementation of split payment models for innovative treatments[6,11], although actual implementation is currently being delayed.

OBAs are generally complex to implement compared to financial agreements, as they require specific legislation and sufficient data collection infrastructure[19]. In terms of legislation, several policymakers have established regulations or processes to facilitate the uptake of novel payment models (e.g., in Belgium, France, Italy, Spain, and the UK)[5,22].

In the US, 29 states have received approval from the Centers for Medicare & Medicaid Services (CMS) to implement Value-Based Purchasing (VBP) supplemental rebate agreements with drug manufacturers through a State Plan Amendment (SPA). Agreements can be evidence-based, where the cost of a covered outpatient drug is linked to existing evidence of its effectiveness, or outcomes-based, where payment is tied to the drug's real-world outcomes or its ability to reduce other medical costs.

Additionally, the presence or absence of data collection infrastructure largely influences the implementation of OBAs.

For example, in the UK, OBAs for chimeric antigen receptor (CAR) T cell therapies were associated with an estimated administrative burden of ~£900,000, mainly associated with the management of registries over ten years[19,23]. Conversely, the cost was estimated to be minimal in the Spanish region of Catalonia due to the presence of available infrastructure[19].

Several trends have enhanced the uptake and efficiency of data collection. For example, clinical institutions are increasingly involved in OBA data collection, and electronic health records (EHR) have evolved to provide a reliable source of information. This has allowed several countries to implement OBAs[6].

Best practice

Italy was one of the first countries to implement a system of national registries funded by pharmaceutical companies but governed at the healthcare system level to support the implementation of payment models[24]. Two CAR T-cell therapies and one gene therapy were reimbursed under OBAs at launch[6,8].

In France, CED payment models have been widely implemented. These models can address evidential uncertainty associated with one-time administration therapies, allowing data to be collected over a longer period of time to monitor the durability of treatment effects and long-term safety[8]. CED was adopted when CAR T-cell therapies were launched, and the Lymphoma Academic Research Organization Registry was used to collect patient outcomes[8].

In 2019, Spain introduced 'Valtermed' (Sistema de Información para determinar el Valor Terapéutico en la Práctica Clínica Real de los Medicamentos de Alto Impacto Sanitario y Económico en el SNS) to collect real-world data for reducing uncertainty associated with innovative therapies[12]. A gene therapy was reimbursed in 2021 under an OBA and treatment outcomes are collected via Valtermed[25].

Since the introduction of the German Law for More Safety in the Supply of Medicines (GSAV), the Federal Joint Committee (G-BA) can require pharmaceutical companies to collect real-world data for certain drugs, including orphan medicines and gene therapies[26]. Data collection addresses evidence gaps while allowing patient access to innovative treatments[27]. The drug can then be re-assessed based on the additional data[27]. Currently, data collection is ongoing for gene therapies targeting hemophilia and spinal muscular atrophy[28].

It is also worth noting that the adoption of novel payment models requires a dynamic and evolving approach as evidence matures. As the evidence for a particular therapy is generated, agreements may transition from OBAs to simpler financial agreements (e.g., simple discounts)[6,29]. .

In Italy, OBAs were initially implemented for CAR T-cell therapies and a gene therapy. A reassessment of the products done in 2022 and 2023 removed the OBAs in favor of simple discounts[30,31,32]. .

With regard to specific conditions or indications, the ability to identify appropriate endpoints to measure gene therapy efficacy can influence willingness to engage in innovative contracts[19,33]. In this context, greater collaboration among payers, clinicians, patients and health economics experts may offer the opportunity to identify appropriate, patient-relevant endpoints[29].

Adoption of novel payment models will, therefore, need to take into account multiple contextual factors. Policymakers are increasingly recognizing this need and regional initiatives are promoting the adoption of payment models tailored to specific contexts.

The Health Innovation Next Generation Pricing Models (HI – PRIX) project funded by the European Union aims to map and formulate payment models that could be used across different technologies and healthcare systems and provide guiding principles to adapt these in a flexible way[34,35], .

Enhancing transparency can support efforts to improve the implementation of novel payment models

The complexity of novel payment models requires transparent and detailed governance to support their implementation[19]. This can be separated into transparency of *process* and transparency of *content*[5].

Process *transparency* refers to clarity around roles, responsibilities, and incentives across every step of novel payment model implementation. Increased process transparency can:

- Ensure stakeholders are accountable for successfully implementing payment models.
- Clarify aspects such as who is bearing the cost of implementing innovative contracts (e.g., payer or industry), particularly in the case of OBAs, which require the establishment of data collection infrastructure[19].

Content transparency, to the extent possible, can support consistent decision-making. Although it is often necessary for some elements to be confidential (e.g., prices and commercial clauses), there can be benefits in making other information available[5]. For example, a survey of 37 European payers and market access experts highlighted that more than 50% of respondents are in favor of improving content transparency for novel payment model agreements (e.g., endpoints and time to evaluation)[36].

An opportunity discussed during the roundtable was to improve a different kind of transparency, *operational transparency*. This refers to transparency around how agreements for novel payment models are implemented, and encourages the sharing of both successful and unsuccessful examples to provide valuable insights for improving future implementation strategies[29].

Novel payment models are an essential element for ensuring access to gene therapies. Continuing to build on existing best practices and developing new ones as time progresses can provide increasingly useful blueprints for effective implementation of these agreements, and ultimately contribute to gene therapy access for patients.

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