A Review of Managed Entry Agreements and Innovative Payment Models Established for Gene Therapies in England, EU4, US, Canada and Japan

HPR124

Dabbous M.[1], Olid Gonzalez A.[1], Griffiths J.[2], Lingois N.[3], Sullivan N.[1]
[1]Evidera Inc., Needham, MA, USA [2]Evidera Ltd., London, UK [3]Evidera Ltd., Paris, France

Introduction

Gene Therapies, transformative therapies with high price expectations

- While Gene Therapies (GTs) represent transformative therapies for patients, they require a complex manufacturing and delivery process. This, coupled with small target populations, is associated with high price expectations reflecting the product's value. However, benefits of GTs are frequently only realized in the long-term, posing affordability challenges for payers.
- To manage uncertainty around long-term benefits and high prices associated with GTs, payers have entered into managed entry agreements (MEAs) and adopted innovative payment models with GT developers to facilitate timely patient access.

Objective

- This study aimed to review MEAs and innovative payment models that have been implemented for GTs in the 8 countries of scope: England, France, Germany, Italy, Spain, United States (US), Canada and Japan.
- This review aimed to detail current trends, including any publicly available data on the key drivers and obstacles in implementing MEAs for these unique therapies

Methods

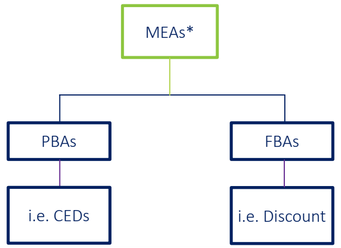
A Retrospective Analysis of Gene Therapies with Health Technology Assessments (HTAs)

GT and HTA Assessments identification

- All GTs with regulatory approval in the 8 countries of scope to date were identified.
- To identify MEAs for these GTs, a review of these approved GTs in the 8 countries of scope to date was performed on December 13th 2023 and updated on April 14th 2023 via:
  - Official government and payer websites, including HTAs;
  - Grey literature search, to supplement the website data.
- GTs' pricing and reimbursement (P&R) decisions and additional official health authority data and information were analysed to determine if they had a MEA, either a finance-based agreement (FBA) or a performance-based agreement (PBA) in place (**Figure 1**).

Methods (Cont'd)

Figure 1. MEAs Taxonomy



*There are various types of MEAs, including subtypes of FBAs and PBAs as well as "innovative payment models," such as annuity and instalment payments (which are currently being employed for GTs)

Abbreviations: MEAs: Managed Entry Agreements; FBAs: Finance-Based Agreements; PBAs: Performance-Based Agreements; CEDs: Coverage with Evidence Development

MEAs and innovative payment model

For the purposes of this study, a simplified taxonomy is presented

- MEAs are agreements between developers and payers addressing either the high cost and/or the uncertainties surrounding the effectiveness of highly-priced therapies. The main two types of MEAs include finance-based agreements (FBAs) and performance-based agreements (PBAs).[1,2,3,4]
- FBAs focus on addressing high product prices, payers' concerns, and the affordability of these products.[1,2,3,4]
- PBAs focus on therapy effectiveness, with the reimbursement directly linked to the outcome of the data collection and the performance of the product.[1,2,3,4]
- Coverage with Evidence (CED) is a type of PBA where a product is reimbursed conditionally upon the further generation of evidence to address uncertainty. This evidence may be used in re-assessments for the product and may result in adjustments in data requirements, price, and/or reimbursement rates.[1,2,3,4]

Descriptive analysis

- We conducted a descriptive analysis of all GT's in Table 1. P&R decisions, payer information, and supplementary grey literature to identify possible MEAs and innovative payment models.
- Key data fields extracted during the descriptive analysis included country, presence of MEA, type of MEA, and conditions applied via the MEA.

Methods (Cont'd)

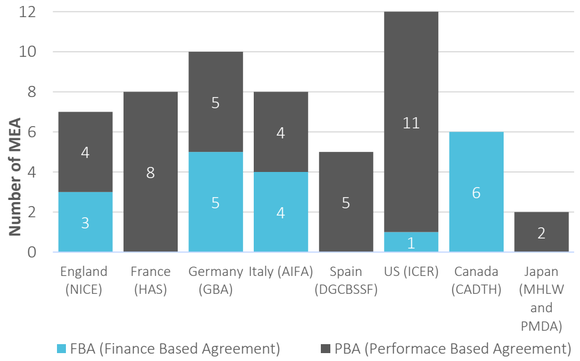
Table 1. GTs approved in the US, UK, and Europe and year of approvals

Hemgenix® (2022)	Tecartus® (2021, 2020)
Adstiladrin® (2022)	Zynteglo® (2022)
Roctavian® (2022 in the EU only)	Collategene® (2019)
Carvykti® (2022)	Zolgensma® (2022, 2021, 2019)
Skysona® (2022)	Luxturna® (2022, 2017)
Abecma® (2021)	Yescarta® (2021, 2019, 2018, 2017)
Breyanzi® (2022 , 2021)	Kymriah® (2022, 2021, 2020, 2017)
Libmeldy® (2020 in the EU only)	Imlygic® (2021)

Results

- A total of 18 GTs were identified. At time of the analysis, 72% of therapies were available in at least one of the scoped markets; it is important to note that Zynteglo® withdrew its EU marketing authorization.
- The majority of GTs approved and appraised in the countries of scope had a PBA in place (**Figure 2**).
- Yescarta® and Kymriah® had the highest number of PBAs, but this can be attributed to products being approved and appraised for multiple indications; Zolgensma® followed next with highest number of PBAs in a single indication.
- Figure 2 details the distribution of FBA and PBA across countries.
- The majority of MEAs in place or recommended are PBAs, with most being in the EU4, England and the US.

Figure 2. Distribution of FBA and PBA across countries



Discussions

- The majority of GTs that have been appraised by HTA bodies in the countries in scope have launched with some form of MEA between the developer and the HTA. The experience with MEAs varies widely across country. Italy has traditionally engaged in MEAs; yet recent challenges have resulted in a decrease of MEAs in the market, potentially explaining why it only has the second highest number of MEAs currently in place for GTs after Germany. Canada has the least experience, explaining why most GTs have launched with more straightforward FBAs instead of PBAs. In the US, ICER provided consistent recommendations across GT that manufacturers should negotiate PBA with payers and consider the substantial uncertainty when pricing GT therapies.
- Variations in types of MEAs and experience is not the only difference between markets. Several of the MEAs identified have a fixed duration, after which either a re-assessment is triggered or the contract finalizes. However, this duration can vary between countries and within a market. For example, several MEAs identified had a 12- to 24-month duration, but, in England, duration varies from 12 months to 5 years. This is critical for developers to consider, as it has important commercial implications.
- Some similarities were identified. The most common MEA across all markets was PBA, with several being CEDs. This stems from the uncertainty that often surrounds the evidence submitted by GT developers, frequently based on single-arm studies and small populations. Evidence for CEDs is almost always collected via RWE. Some markets, such as Italy, Spain and Japan, have already established registries from which to collect GT outcomes. Other markets do not have specific registries defined, although RWE collected may need to be validated with the HTA body e.g., HAS.
- PBAs on their own do not address another key challenge for GTs: their high cost. In reality, MEAs are a mixture of PBAs and FBAs or other types of innovative payment models, such as the annuity payment model for Zolgensma® in the US.

Conclusions

- MEAs have been used in most countries to manage the cost and long-term uncertainties of GTs. However, there are still logistical challenges in implementing MEAs consistently and successfully across key stakeholder groups
- Considering the GT market is forecast to grow from $5.33Bn in 2022 to $19.88Bn by 2027, it is critical for government and payer institutions to tackle these challenges, heavily supported by GT developers, to ensure patients have timely access to transformative therapies.

References

1. Garrison et al. PBRS Agreements 2013
2. Adamski et al. RS arrangements 2010
3. Dabbous et al. MEAs 2020
4. Facey et al. MEAs for Rare Diseases 2021
5. Jorgensen et al. Innovative Payments for GTs 2021

Presented at ISPOR US • May 7–10, 2023 • Boston, MA, US

Funding provided by Evidera