Building the bridge to access: Leveraging RWE from early access schemes to reimbursement in gene and cell therapies

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Authors Molina-Ramirez LP[1]; Ivanov, L[1]; Thomas, M[1]

[1]Remap Consulting, Cheshire, United Kingdom

INTRODUCTION

Gene and cell therapies offer transformative potential for rare and severe diseases, but their high costs, small patient populations, and limited long-term data create significant uncertainty for health technology assessment (HTA) and reimbursement decisions

Real-world evidence (RWE) generated through early-access programmes (EAPs) can provide safety, effectiveness, and treatment pattern data before full market authorisation. As payer expectations evolve, RWE is becoming a strategic tool to bridge evidence gaps and support reimbursement decisions[1]

For this purpose, it is essential to understand which elements manufacturers should consider when designing their RWE strategies, ensuring that evidence plans strengthen product value without creating unnecessary operational burden or generating data that fails to address key uncertainties

OBJECTIVE

To examine how RWE generated during early-access programmes is captured, appraised, and used to support reimbursement decisions for gene and cell therapies across European markets (France, Germany, Italy, Spain, and the UK)

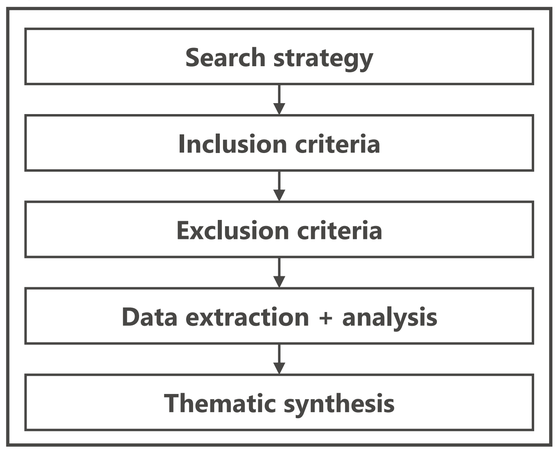
METHODS

We conducted a targeted literature review in Google Scholar (Jan 2018–Mar 2025), supplemented by hand searches.

Eligible sources included English-language peer-reviewed articles, conference abstracts, and grey literature on EAP evidence generation, RWE, payer decision-making, and reimbursement for gene and cell therapies. EAPs were defined as mechanisms providing patient access before marketing authorisation, including compassionate use and expanded access schemes. As such evidence often informs conditional reimbursement, we also included early post-approval mechanisms like coverage with evidence development (CED) and outcomes-based agreements (OBAs) when they addressed similar uncertainties.

Data were synthesised thematically across five payer-uncertainty domains: clinical effectiveness, durability, safety, budget impact, and societal value

Figure 1. Literature review process overview



RESULTS

BARRIERS TO ACCESS

- Clinical effectiveness and durability of response were the most frequently cited evidence gaps addressed by early access RWE, followed by safety and budget impact, with societal value least represented (**Figure 2**)[2-4,6-10]
- HTAs were reported to accept uncertainty at regulatory approval but sought post-launch comparative RWE to validate early data and support extrapolation of long-term benefit, especially for one-time therapies[3,4,6,8,9]
- Early-access data were most impactful when prospectively structured to align with HTA decision needs (comparators, clinical outcomes) rather than captured ad hoc[2-4,8]

COVERAGE IMPACT, INFRASTRUCTURE AND REGULATOR–PAYER DYNAMICS

- Structured early-access RWE reduced time-to-listing, lowered reassessment uncertainty, and supported outcomes-based payment triggers.[3,5–8,10] This has been shown in EUnetHTA assessments (e.g., Zolgensma). One source cited most European countries link gene and cell therapy reimbursement to performance-based agreements supported by registries and post-authorisation evidence, with reassessments typically conducted within five years of launch[6]
- Operational barriers such as administrative workload and poor data linkage limit outcomes-based agreements (OBAs), favouring simpler or hybrid agreements[5–8,10]
- Regulator–payer gap: conditional approvals often used surrogate endpoints, while HTA bodies required comparative RWE and longer follow-up before routine funding[3,4,7,9,10]

DATA-CAPTURE APPROACHES

- Registry-based capture dominate early-access evidence generation, followed by observational cohorts and expanded/compassionate access programmes; CED and OBAs were also frequently referenced. [2-4,5-10] While CED a nd OBAs are technically implemented after marketing authorisation, these approaches are described as direct extensions of the early-access evidence strategy, aimed at resolving uncertainties that underpin pre-approval access decisions
- Each modality appears to address a specific uncertainty: registries mostly address clinical effectiveness and durability of response; observational cohorts enable comparisons; CED/OBAs enable linking payment to real-world response or survival; and expanded access can support early safety. (**Table 1**) [2,3,7–11]
- Predefined data capture templates or national diseases registries streamlined the use of EAP RWE data to support reimbursement decisions compared to those using retrospective or unstructured capture[3,4,7,9]

Figure 2. Uncertainty domains addressed through early-access RWE according to the cited literature

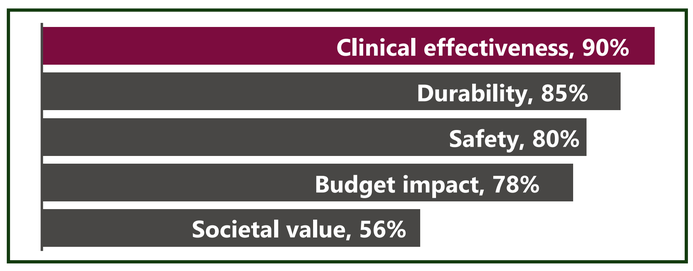


Table 1. RWE data capture modality vs uncertainty domain[a]

	Clinical effectiveness	Durability	Safety	Budget impact	Societal value
Coverage with evidence development	89%	78%	100%	89%	56%
Outcomes-based agreement	56%	67%	67%	67%	33%
Registry	44%	44%	44%	44%	22%
Observational	33%	33%	33%	33%	22%
Expanded / compassionate access	33%	11%	33%	22%	22%

[a]Including early-access and early post-authorisation evidence strategies

CONCLUSIONS

1. Real-world evidence RWE generated through early-access programmes EAPs is a strategic enabler of faster reimbursement, reduced payer uncertainty, and innovative payment models for gene and cell therapies
2. Different RWE sources solve different challenges: registries and observational studies underpin decisions on clinical effectiveness and durability, while CED and OBAs align financial risk with real-world outcomes
3. EAPs deliver their full potential **only when RWE is prospectively planned, payer-focused, and directly relevant to HTA needs**. Poorly structured approaches risk producing data of limited value beyond safety reporting

References: [1]EUCOPE Cell and Gene Therapy Working Group. Real-world evidence across the lifecycle of cell and gene therapies: facilitating patient access. Brussels: EUCOPE; 2023 Feb 8; [2]Polak TB, Baars JW, Hooft L, et al. Expanded access as a source of real-world data: overview of FDA and EMA approvals. Br J Clin Pharmacol. 2020; [3]Polak TB, O'Kane M, Hooft L, et al. Use of expanded access data in NICE technology appraisals, 2010–2020. BMJ Open. 2022; [4]Dayer R, Iorio A, Durand-Zaleski I, et al. Real-world evidence for rare disease treatments: methodological considerations for coverage. Orphanet J Rare Dis. 2024; [5]Ten Ham RM, et al. HTA considerations for ATMPs in Scotland, the Netherlands and England. Value Health. 2022; [6]Fagnocchi G, Rossi L, Atkins J, Balleste Martinez C, Prada M. The difference between regulatory and market access decisions on treatment availability for ATMPs across Australia, EU4, and UK [poster]. Presented at: ISPOR Europe 2024; November 2024; Barcelona, Spain; [7]Dabbous M, Chachoua L, Caban A, et al. Managed entry agreements in Europe: landscape, challenges and policy options. Value Health. 2020; [8]Jørgensen J, Kefalas P, et al. Outcomes-based reimbursement for CAR-T therapies in major European countries. J Mark Access Health Policy. 2020; [9]Greco M, et al. Implementing managed entry agreements for ATMPs: challenges and opportunities. Clin Ther. 2024; [10]Jommi C, Armeni P, Otto M, et al. European payer perspectives on pricing and MEAs for ATMPs. Health Policy Technol. 2023; [11]Noble-Longster N, et al. NICE HST gene therapy appraisals: uncertainties and access mechanisms. ISPOR Europe Poster. 2024.

Abbreviations: CED: Coverage with Evidence Development; EAP: Early-Access Programme;; EUCOPE: European Confederation of Pharmaceutical Entrepreneurs; EUnetHTA: European Network for Health Technology Assessment; ; HTA: Health Technology Assessment;; OBA: Outcomes-Based Agreement; RWE: Real-World Evidence