PT22

Advanced Therapy Medicinal Products from Promise to Practice: Understanding Reimbursement and Access Disparities in Western Europe

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Objectives

ATMPs have the potential to provide significant clinical benefits, and potentially cure, for patients. However, access to ATMPs across Western Europe remains unequal.

Our key objective was to explore whether Joint Clinical Assessments (JCA) can help reduce access disparities, by identifying:

- **Country-specific and cross-national factors** that influence **successful reimbursement**
- **Factors** contributing to **access disparities** across different countries.

Methods

Identification of ATMPs
ATMPs that received marketing authorisation by the European Commission (EC) were identified by scanning the EMA website.[1] Data on ATMP subtype, orphan designation, PRIME designation, and approval were collected. MHRA status was sourced from the MHRA register.[2]

Analysis of national HTA databases
National HTA assessments and outcomes were analysed by screening databases from Belgium (RIZIV/INAMI)[3], the Netherlands (ZIN)[4], France (HAS)[5], Germany (G-BA)[6], England (NICE)[7], and Ireland (NCPE)[8]. This involved both quantitative research and qualitative desk research to examine the submitted evidence and HTA outcomes within and across the countries listed.

Results

Marketing Authorisation

- From 2009 until 17 October 2025, 29 ATMPs had received MA: 8 standard approval, 13 conditional approval, 8 MA application withdrawn or MA not renewed
- 22/29 ATMPs (76%) are orphan drugs
- 14/21 ATMPs (74%) had a PRIME-scheme
- 4 TEPS / 21 GTMP / 4 sCTMP
- Nearly one third of approved ATMPs (9/29) are in the field of hematologic malignancies

Table 1: Marketing authorisation in Europe

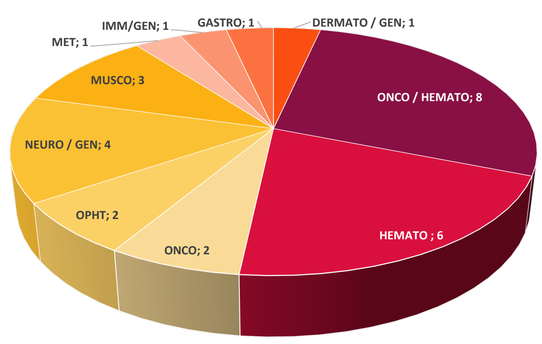
ATMP	Subtype	EMA	Orphan	PRIME	MHRA
ChondroCelect®	TEP	■		NA	■
Glybera®	GTMP	■	•	NA	■
MACI®	TEP	■		NA	■
Provenge®	sCTMP	■		NA	■
Holoclar®	TEP	■	•	NA	■▼
Imlygic®	GTMP	■		NA	■
Strimvelis®	GTMP	■	•	NA	■▼
Zalmoxis®	sCTMP	■	•	NA	■
Spherox®	TEP	■			■▼
Alofisel®	sCTMP	■¥	•		■
Yescarta®	GTMP	■	•	•	■▼
Kymriah®	GTMP	■	•	•	■▼
Luxturna®	GTMP	■	•		■▼
Zynteglo®	GTMP	■	•	•	■
Zolgensma®	GTMP	■	•	•	■
Tecartus®	GTMP	■	•	•	■▼
Libmeldy®	GTMP	■	•		■▼
Skysona®	GTMP	■	•	•	■
Abecma®	GTMP	■	•	•	■▼
Breyanzi®	GTMP	■		•	■▼
Carvykti®	GTMP	■	•	•	■▼
Upstaza®	GTMP	■	•		■▼
Roctavian®	GTMP	■	•	•	■
Ebvallo®	sCTMP	■	•	•	■▼
Hemgenix®	GTMP	■	•	•	■▼
Casgevy®	GTMP	■	•	•	■▼
Beqvez®	GTMP	■		•	■
Vyjuvek®	GTMP	■	•	•	■
Aucatzyl®	GTMP	■	•	•	■▼

■	Standard approval	•	Orphan drug
■	Conditional approval	•	PRIME priority medicine
■	MA withdrawn or not submitted	▼	Additional monitoring

Notes: ¥ Alofisel® was initially conditional approved 03/2018 and withdrawn in 12/2024.
Marketing authorisations in chronological order of EMA approval. PRIME early access scheme was launched in March 2016 hence not applicable (NA) prior to this date.

Abbreviations: GTMP, Gene Therapy Medicinal Products; MA, market authorization; MHRA, Medicines and Healthcare products Regulatory Agency; NA, not applicable; sCTMP, somatic Cell Therapy Medicinal Product; TEP, Tissue Engineered Product.

Figure 1: Therapeutic domains of existing ATMPs



Abbreviations: DERMATO/GEN, dermatology/genetic; HEMAT, hematology; IMM/GEN, Immunology/Genetics; MUSCO, Musculoskeletal; NEURO/GEN, Neurology/genetic; ONCO, Oncology; MET, Metabolism; GASTRO, gastro-enterology; OPHT, Ophthalmology; ONCO/HEMATO, Oncology/hematology.

Quantitative Analysis of HTA Outcomes

- Germany has the highest number of reimbursed ATMPs (n=18), while Ireland has the lowest (n=5).
- Ireland also has the highest number of negative reimbursement decisions (n=3), followed by Belgium (n=2), and both the Netherlands and France (n=1 each). In England, the dossiers for 4 ATMPs were withdrawn by the MAH.
- No submission or no launch was highest in Ireland (n=12), followed by Belgium (n=6), the Netherlands (n=5), France (n=4), and Germany (n=3).

Table 2: Reimbursement outcomes at the local level

ATMPs	Therapeutic Area	ENG	IRE	FR	BE	NL	GER
Beqvez®	HEMATO						
Casgevy® †	HEMATO						
Hemgenix® *	HEMATO						
Roctavian®	HEMATO						
Strimvelis®	IMM/GEN					¥ °	
Spherox®	MUSCO						
Libmeldy® *	NEURO/GEN						
Upstaza®	NEURO/GEN					°	
Zolgensma® *	NEURO/GEN						
Imlygic®	ONCO						
Abecma®	ONCO/HEMATO						
Breyanzi® †	ONCO/HEMATO						
Carvykti®	ONCO/HEMATO						
Ebvallo®	ONCO/HEMATO						
Luxturna®	ONCO/HEMATO						
Tecartus® †	ONCO/HEMATO						
Yescarta® †	ONCO/HEMATO						
Holoclar®	OPHT			¥			
Kymriah® †	OPHT						
Vyjuvek®	DERMATO/GEN			‡			
Aucatzyl®	HEMATO						
Reimbursed		14	5	15	11	12	18
Negative decision		0	3	1	2	1	0
Assessment ongoing		3	1	1	1	3	0
Withdrawn by MAH		4	0	0	1	0	0
No submission by MAH		0	12	4	6	5	3

Notes: *Assessment conducted under the Beneluxa initiative; ¥Initially reimbursed but currently unavailable; ‡Early access provided; °Decentralised agreement with health care insurers; † When multiple indications exist for a single ATMP, it is marked as reimbursed (green) if reimbursement applies to at least one indication.

Qualitative Analysis of HTA Outcomes

Country	ATMP	Key drivers of negative decisions
FR	Spherox®	• Clinical benefit (SMR) was deemed insufficient (despite high unmet need)
IRE	Tecartus®	• Not cost-effective compared to existing treatments
	Upstaza®	
BE	Imlygic®	• High unmet need not recognised (alternatives available)
	Breyanzi®	• Added value versus Yescarta® not recognized, pricing negotiations were unsuccessful. A new procedure is ongoing.
NL	Abecma®	• No survival benefit proven compared to existing treatments, not recommended
	Tecartus®	• R/R B-cell ALL: Insufficient quality of the cost-effectiveness analysis
	Yescarta®	• FL: no survival and QoL benefit proven

Common drivers of positive decisions

- High unmet need with no targeted treatment alternatives, regardless of price and clinical uncertainties

Country-Specific Reimbursement System Features

- Managed Entry Agreements with confidential rebates for interventions with added value granted and for orphan drugs
- Exemption for cost-effectiveness analysis for orphan drugs until publication of updated KCE guidelines in 2025

- Strict HTA assessments based on added value versus SoC on crucial/hard endpoints based on disease-specific PICO
- Price negotiations to reach a confidential cost-effective price

- Strict HTA assessment followed by price negotiation: reimbursed from day 1, negotiated price from month 7
- No official cost-effectiveness, difficult P4P agreements

- Frequent reassessments by HAS especially in cases of high uncertainty regarding long-term clinical efficacy
- Often reimbursement through the EAP prior to final decision

- The HST route has a higher ICER threshold than standard appraisals, however restrictive criteria may affect future UK launches
- Only 63% of oncology ATMPs have been reimbursed due to high degree of uncertainties and low comparator costs

- NCPE appraisals involve a Rapid Review stage followed by a full HTA process due to clinical and economic uncertainties
- Lack of cost-effectiveness is mitigated by complex pricing negotiations between manufacturer and HSE

Conclusion

Reimbursement outcomes are determined by **the local availability of standard of care, the appraisal of clinical evidence, and the flexibility of financial arrangements.**

- Consequently, a streamlined relative effectiveness assessment through **JCA alone** is unlikely to fully address access disparities, as **appraisal occurs at the national level**.
- Therefore, **additional measures at the country level** are necessary to **ensure faster and equitable access to ATMPs**, in alignment with the objectives of the EU **HTA regulation**.

As a pan-European strategy consultancy for the pharmaceutical and biotech industry, Kintiga offers powerful solutions resulting from our shared ambition and our agile, focused approach. Our united team brings together deep local expertise and global reach, channeling energy and experience into seamless, impactful solutions that transform patient access across Europe. Kintiga – where energy meets experience.

References: 1. EMA; 2. MHRA; 3. RIZIV/INAMI; 4. ZIN; 5. G-BA; 6. HAS; 7. NICE; 8. NCPE.
Abbreviations: ATMP, Advanced Therapy Medicinal Product; EAP, Early Access Program, EMA, European Medicine Agency; FL, follicular lymphoma, G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de Santé; HTA, health technology assessment; HSE, Health Service Executive; HTD, health technology developer; HST, Highly Specialised Technology; ICER, incremental cost-effectiveness ratio; JCA, Joint Clinical Assessments; MA, marketing authorisation; MHRA, Medicines and Healthcare products Regulatory Agency; MoH, Ministry of Health; NCPE, National Centre for Pharmacoeconomics; NICE, National Institute for Health and Care Excellence; P4P: pay for performance; PICO, Population, Intervention, Comparator, Outcomes; RIZIV/INAMI, Rijksinstitut voor ziekte-en invaliditeitsverzekering/Institut national d'assurance maladie invalidité; R/R B-cell ALL, Relapsed/Refractory B-cell Acute Lymphocytic Leukemia; SMR, Service Médical Rendu; SoC, standard of care; ZIN, Zorginstituut Nederland.

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