HTA139

Evolution of Acceptance of Evidence and P&MA Outcomes by HTA Authorities for ATMPs in Germany and the UK

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1 OBJECTIVES

Advanced therapy medicinal products (ATMPs) face inherent evidence generation challenges due to technical, ethical, and statistical constraints. By necessity, trials are short, uncontrolled and with small populations. These structural limitations raise questions about whether traditional HTA frameworks are fit to assess transformative therapies.

This research examines HTA evaluations from NICE (UK) and GBA/IQWiG (Germany) for ATMPs authorized between 2017-2025 to investigate what aspects of HTA and access have changed and to understand what, if any, trends may support access in the future.

2 METHODS

We analyzed all 17 ATMPs authorized by the EMA from 2017-2025, extracting clinical trial design parameters including from HTA assessment reports. Reimbursement outcomes and justification were obtained from NICE appraisals, IQWiG assessments, and GlobalData's HTA databases.

Time-to-reimbursement was measured from EMA authorization to positive NICE recommendation or first German pricing, post GBA review. Analyses were stratified by technology type (CAR-T vs. gene therapy) and therapeutic area (oncology vs. non-oncology rare disease). We examined associations between price, evidence characteristics, unmet need, and temporal trends across the cohort of therapies achieving positive reimbursement.

3 RESULTS

Seventeen ATMPs received MA in Europe by Q4 of 2025, with 15 remaining marketed. There was evidence that in the UK there is more acceptance of less robust evidence (small trials, open label, external comparator etc.), while Germany remains very rigid. This has affected final assessment outcomes; in Germany, most ATMPs have no proven additional benefit but not ultimate access **(Table 1)**.

Surprisingly, time-to-reimbursement increased substantially **(Figure 1)**: early approvals (2017-2019) averaged 4.8 months, whereas recent assessments (2022-2025) averaged 10.6 months—a 121% increase, driven by technology type. CAR-T therapies, predominantly targeting oncology indications, achieved remarkably consistent rapid access averaging 4.8 months with annual costs around €354,000 (Germany). In contrast, gene therapies for ultra-rare diseases faced extended negotiations averaging 9.7 months with substantially higher costs (€1.7 million), and far greater variability (ranging from 1-26 months).

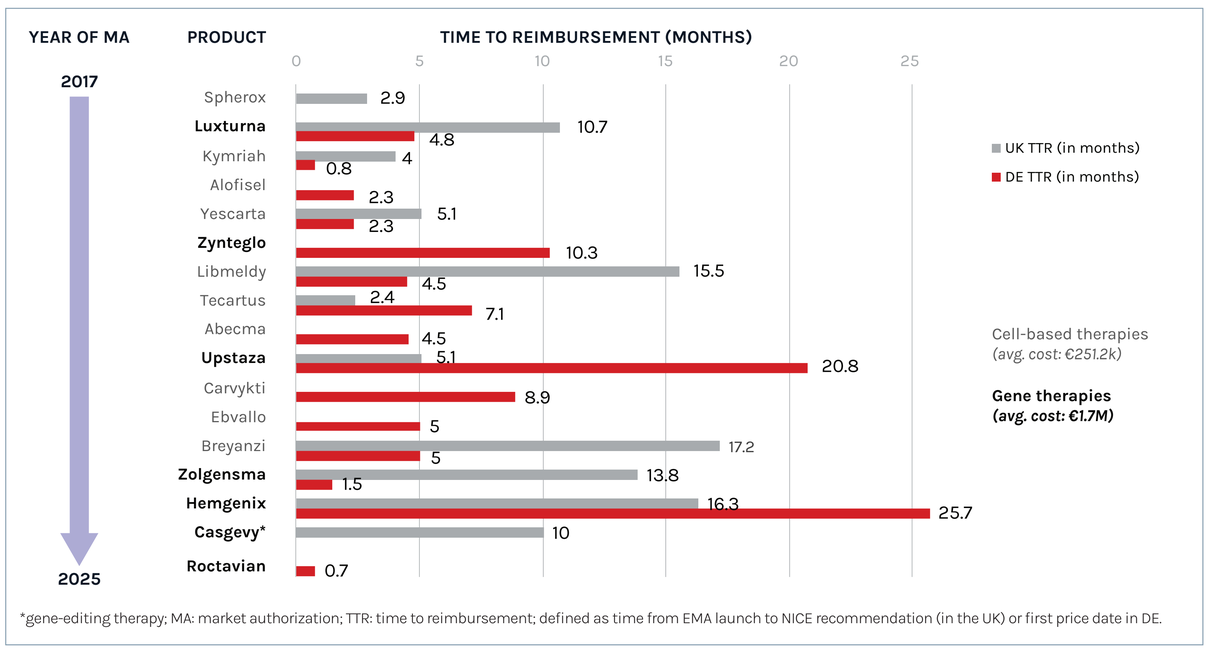
Ultra-high-priced therapies exceeding €1 million in Germany faced negotiations lasting three times as long as lower-priced products, even when demonstrating dramatic clinical effects in life-threatening conditions with no treatment alternatives.

Country-specific pathway differences revealed variation in access. Upstaza's UK assessment through the HST route led to routine commissioning within 5 months, while Germany's assessment extended to 21 months, initially rejecting indirect comparison methodology and mandating registry data collection through 2036. Notably, HST designation did not guarantee rapid access: the four ATMPs assessed via this pathway averaged 11 months to reimbursement.

Table 1. Summary of the evolution of NICE and GBA benefit assessments of ATMPs 2017-2025

EVIDENCE/ PROCESS DIMENSION	UK (NICE)	GERMANY (GBA/IQWIG)
Acceptance of ITC, external controls, & natural history	HIGH Consistently accepts for HST pathway; has begun to accept these as long as methodologically sound	LOW Rejects indirect comparisons (Upstaza, Hemgenix, Yescarta)
Small sample sizes & single-arm studies	HIGH Accepts small sample sizes (Libmeldy n=28; Upstaza n=28) for ultra-rare disease therapies	MODERATE Accepts small samples but requires additional registry data & long-term follow-up (Upstaza: registry to 2036)
Outcomes of benefit assessments	EVOLVED Initial rejections, often requires additional RWE before routine commissioning (Kymriah, Zolgensma)	RIGID Predominantly "non-quantifiable" ratings; rare reassessments (Breyanzi: NOT PROVEN considerable)
Access to ATMPs over time	IMPROVED FOR SOME HST pathway enables 5-month access (Upstaza, Libmeldy) despite evidence limitations	PROLONGED NEGOTIATIONS methodology disputes extended timelines for Upstaza (21 mos) and HEMGENIX (26 mos)
Risk-sharing & managed entry	Increased use of managed access agreements; outcomes-based models (Kymriah, Hemgenix, Casgevy)	Increasing use of outcomes-based agreements standard (Kymriah, Zynteglo); payment installments over 5 years

Figure 1. Time to reimbursement for ATMPs in the UK and Germany



*gene-editing therapy; MA: market authorization; TTR: time to reimbursement; defined as time from EMA launch to NICE recommendation (in the UK) or first price date in DE.

4 CONCLUSIONS

After 8 years both Germany and the UK have granted access to the majority of ATMPs, they have assessed. Neither NICE nor the GBA have changed in their fundamental approach, but the UK in particular has been more forgiving of necessary evidence shortfalls. Increasing exposure to these complexities has only lengthened negotiations and time to access has increased. Access speed is primarily driven by: (1) technology type and unmet need—CAR-T/oncology products are 40% faster than gene therapies; (2) price—products >€1M face 3x longer negotiations (Germany) regardless of clinical benefit or disease severity.

The evolution of financial and clinical risk-sharing over traditional benefit assessments, has resulted in pricing strategies, risk-sharing proposals, and real-world evidence commitments determining market access success.

Has the time now come to adapt assessment protocols more formally to account for clinical uncertainties, and to improve speedy access to innovative medicines for patients?

5 REFERENCES

1. European Medicines Agency, online at https://www.ema.europa.eu/en/homepage (accessed 2025). **2.** Gemeinsamer Bundesausschuss (G-BA) https://www.g-ba.de/english/benefitassessment/ (accessed 2025). **3.** GlobalData. Drug Pricing (POLI) & HTA Database, online at https://poli/globaldata.com/PricingData/Search (accessed 2025). **4.** National Institute for Health and Care Excellence (NICE), online at https://www.nice.org.uk/

Abbreviations
ATMP: advanced therapy medicinal product; CAR-T: Chimeric Antigen Receptor T-cell therapy; EMA: European Medicines Agency; GBA: Gemeinsamer Bundesausschuss (Federal Joint Committee); HST: highly specialised technology; HTA: health technology assessment; IQWiG: Institut Für Qualität Und Wirtschaftlichkeit Im Gesundheitswesen (Institute for Quality and Efficiency In Health Care); MA: marketing authorization; NICE: National Institute for Health and Care Excellence; P&MA: Pricing and Market Access; RWE: real-world evidence

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