# How could ATMPs demonstrate an economic benefit for payers and what are the real-world examples of this?

## An analysis of payer considerations underlying HTA decisions for Yescarta and Alofisel in the UK, Italy and France

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## INTRODUCTION

Advanced therapy medicinal products (ATMPs) such as cell, gene, tissue-engineered, and somatic-cell therapy medicines are often administered as one-time treatments and often claim long-term or even curative potential for difficult-to-treat conditions.

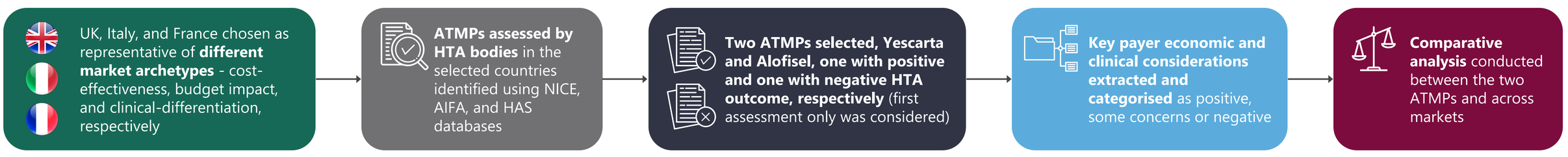
However, due to their high costs and the greater evidentiary uncertainty compared to other medicinal products, they pose significant challenges for manufacturers in demonstrating their economic benefit to payers.

## OBJECTIVES

- Explore the role of economic benefit in the HTA decisions across markets representing different payer archetypes
- Which domain, clinical or economic, yields most of the key payer considerations underlying these decisions and does this vary across different market archetypes?

## METHODS

**Figure 1. Methodology**




## RESULTS

- Payers consistently had concerns over long-term clinical outcomes for both products, which translated into economic uncertainty (see Table 3)
- For Yescarta, across markets, outcomes-based managed-entry agreements were required to address uncertainty and gain patient access (see Table 2)
- For Aloifesl, clinical uncertainty was considered too high to result in access in both Italy and the UK. In France, reimbursements were granted only to a restricted population (see Table 2)
- Economic evaluation for Alofisel was conducted only in the UK (see Table 3)

**Figure 2. Selected ATMPs based on HTA decisions in France[1], Italy[2] and the UK[3]**

| Selected Treatment | Indication | France | Italy | UK |
|---|---|---|---|---|
| **Yescarta** | R/R DLBCL and PMBCL after two or more lines of systemic therapy | **Coverage with evidence development** | **Payment by results** | **Cancer Drugs Fund** |
| **Alofisel** | Complex perianal fistulas with inadequate response to at least one conventional or biologic therapy in adults with non-active/mildly active luminal Crohn's disease | **Only for patients who failed at least one biologic therapy in the last 6 months** | | |

Full population | Restricted population | No reimbursement

**Figure 3. Key payer considerations underlying HTA decisions in France[2], Italy[3] and the UK[4]**

| Treatment | | Yescarta | Alofisel |
|---|---|---|---|
| **Evidence** | | **Zuma 1, phase 1/2 - non controlled** | **Admire-CD, phase 3 placebo-controlled RCT** |
| **Key payer considerations on drugs' value and evidence package** | France | • ASMR III - moderate added clinical benefit<br>• Unmet need and clinical efficacy recognised | • ASMR IV – minor clinical benefit<br>• Unmet need recognised |
| | | • Uncertainty over clinical benefit (lack of direct comparative evidence), long-term outcomes and generalisability<br>• Toxicity and no long-term tolerability data | • Lack of long-term data |
| | | • ICER: €114,509/QALY gained<br>• It was considered "very high" and uncertain due to short follow-up, survival extrapolation, and lack of direct comparative data | Lack of evidence in patients with inadequate response to conventional therapies alone due to small sample size |
| | Italy | • Moderate unmet need, important added therapeutic value, moderate quality of evidence<br>• Full innovation rating | • Moderate unmet need, scarce added therapeutic value, low quality of evidence<br>• Uncertainty over the generalisability and significance of the efficacy results |
| | | ICER: €54,699/QALY gained, once confidential discounts and effect of payment at result are considered | |
| | UK | • Unmet need and clinical efficacy recognised<br>• Met criteria be considered a life-extending treatment at the end of life | • Only modest benefit vs placebo<br>• Uncertainty over long-term benefit and generalisability of the results to UK clinical practice |
| | | • ICER: > £50,000/QALY gained<br>• It was considered uncertain due to short follow-up, survival extrapolation, and lack of direct comparative data | • Uncertain ICERs due to clinical data limitations<br>• Unlikely to be cost-effective |

Positive | Some concerns/ uncertainties | Negative | Clinical domain | Economic domain

## CONCLUSIONS

1. Across markets, the level of clinical benefit is the key determining factor in HTA decisions for ATMPs, and any concerns about economic aspects are primarily driven by uncertainties in clinical benefit
2. Moreover, in markets where clinical benefit is evaluated first and acts as a gateway for economic discussions, these discussions don't take place when clinical uncertainties are too high
3. While ATMPs could potentially offer long-term economic benefits to payers by reducing the need for ongoing treatment, the clinical uncertainty present at launch is typically too high to demonstrate such advantages
4. Therefore, for manufacturers to effectively demonstrate the economic benefits of ATMPs to payers, they must first overcome the challenge of proving sufficient clinical benefit
5. A limitation of this research is the analysis of only two ATMPs. Further work should explore key payer considerations on the evidence package at launch across a broader range of ATMPs and how these evolve post-launch with generation of new evidence

## REFERENCES

1. France HTA agency: https://www.has-sante.fr/
2. Italian HTA agency: https://www.aifa.gov.it/
3. UK HTA agency: https://www.nice.org.uk/

***Abbreviations:*** *AIFA: Italian Medicines Agency; ASMR: Improvement in medical benefit; ATMP: Advanced therapy medicinal products; CDF: Cancer Drugs Fund; CE: Cost-effectiveness; DLBCL: Diffuse large B cell lymphoma; HAS: Haute Autorité de Santé; HTA: Health technology assessment; ICER: Incremental cost-effectiveness ratio; NICE: National Institute of Health Care and Excellence; P&R: Price and reimbursement; PMBCL: Primary mediastinal large B cell lymphoma; QALY: Quality-adjusted life year; RCT: Randomised controlled trial*

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