The Difference Between Regulatory and Market Access Decisions on Treatment Availability for ATMPs Across Australia, EU4, and UK

HTA276

Authors. Giulia Fagnocchi[1], Letizia Rossi[1], Jo Atkins[2] , Carlos Balleste Martinez[3], Mariangela Prada[4]

[1] PLG Italy – Intexo Società Benefit, [2] PLG Australia – Commercial Eyes, [3] PLG Spain, [4] PLG Global

Background and Objectives.

Advanced therapy medicinal products (ATMPs) are innovative medicines for human use based on biological material, offering new opportunities for treating diseases and injuries.

ATMPs can be classified into three main types:

- **Gene therapy medicines:** that contain genes that lead to a therapeutic, prophylactic or diagnostic effect, working by inserting 'recombinant' genes into the body. They are used to treat a variety of conditions, including genetic disorders, cancer and chronic diseases. Recombinant genes are segments of DNA created in the laboratory, combining DNA from different sources.
- **Somatic-cell therapy medicines:** These contain cells or tissues that have been manipulated to change their biological characteristics or cells/tissues used for different functions than their original role. They are designed to cure, diagnose or prevent diseases.
- **Tissue-engineered medicines:** These involve cells or tissues that have been modified to repair, regenerate or replace human tissue.

Additionally, some ATMPs may include medical devices as integral components, referred to as **combined ATMPs.**

ATMPs are highly complex, and their evaluation criteria often extend beyond those applied to traditional pharmaceuticals due to the rapid advancement of scientific knowledge. To address these complexities, the **Committee for Advanced Therapies (CAT)** was established within the **European Medicines Agency (EMA)**. The CAT prepares a draft opinion, drawn up by two Member States (CAT (Co-) Rapporteurs), for each ATMP marketing authorization application. This draft is submitted to the **CHMP** for the final decision...

In **Australia**, the **Therapeutic Goods Administration (TGA)** is responsible for the marketing authorization of Advanced Therapy Medicinal Products (ATMPs). The **Pharmaceutical Benefits Advisory Committee (PBAC)** and the **Medical Services Advisory Committee (MSAC)** are independent expert bodies appointed by the Australian Government, responsible for advising on special arrangements for ATMPs, including financial risk-sharing agreements. The specific setting of care for the administration of an ATMP determines which advisory committee assesses the health technology.

Despite thorough evaluations, patient access to ATMPs can be further restricted by national or regional **Health Technology Assessment (HTA)** bodies and **Pricing and Reimbursement (P&R)** decision-makers.

This research explores variations in RWD collection and RWE uses in the health technology assessment (HTA) of Australia, EU4 (France, Germany, Italy, Spain) and the UK.

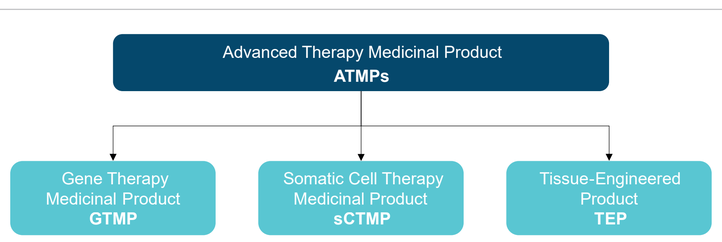

Figure 1: ATMPs medicines

Methods.

Health Technology Assessment (HTA) and Pricing & Reimbursement (P&R) assessments were reviewed for **Australia, France, Germany, Italy, Spain,** and the **UK** for the following ATMPs: **Kymriah, Yescarta, Zolgensma, Spinraza,** and **Luxturna**, all of which have been approved in these countries. Information was gathered from the websites of the respective regulatory agencies in each country.

Key points of investigation included:

- The level of restriction between the regulatory label population and the population covered by HTA/P&R decisions.
- The time taken for patients to access these treatments post-approval.

The research was coordinated centrally by **Productlife Group** global, with local research conducted by PLG's Market Access teams in each country.

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Results.

The approval dates for Australia and the European Medicines Agency (EMA) were recorded, and the time between the Australian approval date and first reimbursement date was calculated. Similarly, the time between the European Commission (EC) decision date and the first reimbursement date in **Germany, Italy, Spain, France,** and the **UK** was calculated for each drug.

The analysis revealed that the average time to reimbursement for the five drugs (**Kymriah, Yescarta, Zolgensma, Spinraza**, and **Luxturna**) was **384 days**, with the shortest being **70 days** and the longest being **1,897 days**.

Among the countries analyzed:

- **France** had the shortest time from approval to first reimbursement.
- This was followed by **Italy, Spain, Australia,** the **UK**, and finally **Germany**, which had the longest time to reimbursement.

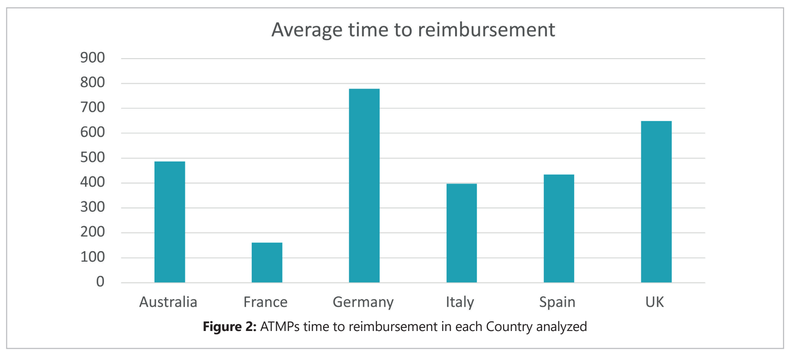

Figure 2: ATMPs time to reimbursement in each Country analyzed

For each medicine, the indications and limitation restrictions were recorded.

Medicine	Indication
Kymriah	Kymriah is indicated for the treatment of: ■ Pediatric and young adult patients up to and including 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post transplant or in second or later relapse. ■ Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. ■ Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.*
Yescarta	■ Yescarta is indicated for the treatment of adult patients with diffuse large B -cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) that relapses within 12 months from completion of, or is refractory to, first-line chemoimmunotherapy. ■ Yescarta is indicated for the treatment of adult patients with relapsed or refractory (r/r) DLBCL and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy. ■ Yescarta is indicated for the treatment of adult patients with r/r follicular lymphoma (FL) after three or more lines of systemic therapy.*
Spinraza	Spinraza is indicated for the treatment of 5q Spinal Muscular Atrophy.
Zolgensma	Zolgensma is indicated for the treatment of: ■ patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1,or ■ patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.
Luxturna	Luxturna is indicated for the treatment of adult and pediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.

*Indications not authorized in Australia

Tab 1: ATMPs indications

Except for Germany, all countries restricted the reimbursement of ATMPs to specific conditions within the authorized indications, such as diagnostic procedures, previous therapies, or subpopulations. In some cases, certain indications were not reimbursed at all.

Kymriah:

- In **Australia**, unlike in Europe, the indication for «adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy» is not authorized.
- In **France**, this indication is restricted based on patient eligibility.
- Both the **UK** and Spain further limited the eligible population by imposing age restrictions.

Yescarta:

- In **Australia**, the indication for «adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy» is not authorized, unlike in Europe.
- In the **UK** and **Spain**, Yescarta's use is subject to diagnostic restrictions.

Spinraza:

- In **Australia, France, Spain,** and the **UK**, reimbursement is limited based on both the subtype of the pathology and the diagnostic and previous treatment history of the patient.

Zolgensma:

- In **Italy**, the **UK**, and **Spain**, reimbursement is restricted based on diagnostic criteria and previous treatments.
- In **Australia** and **France**, restrictions apply to certain subpopulations.

Luxturna:

- In **Italy**, restrictions apply based on diagnosis and previous treatments.

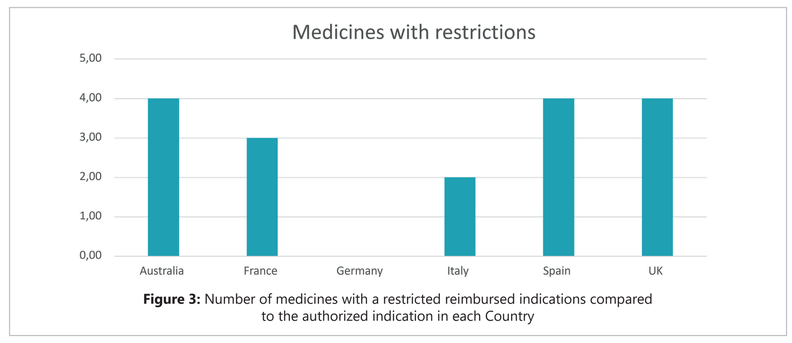

Figure 3: Number of medicines with a restricted reimbursed indications compared to the authorized indication in each Country

Most European countries reimbursed these ATMPs based on performance-based agreements, relying on registries, post-marketing studies, or re-evaluations after 2 to 5 years. There were also notable differences in how countries assessed the therapeutic added value of these drugs. In France, the price is negotiated with CEPS and not public documents are available.

Kymriah and Yescarta:

- **Australia** reimbursed the drugs on a risk-sharing arrangement that includes a single payment, a pay for performance arrangement per successfully infused patient, an annual patient cap and a post market review.
- Similarly, **Germany** set a price ceiling, which will be renegotiated based on patient outcomes.
- **Italy** reimbursed the drugs through a price discount, a payment-by-result model, and the use of a registry.
- The **UK** and **Spain** implemented performance-based agreements, while France opted for annual reassessments based on real-world data.

Spinraza:

- **Australia** reimbursed Spinraza on a risk-sharing arrangement, with a special pricing agreement.
- **France, Italy,** and **Spain** will re-evaluate Spinraza using data from registries.
- The **UK** and **Italy** negotiated price discounts, while Germany set a price ceiling.

Zolgensma:

- **Germany** identified a price ceiling.
- **Italy, Australia** and the **UK** applied price discounts, and **Italy, Australia** and **Spain** also implemented payment-by-result agreements.
- France plans to reassess the drug based on registry data.

Luxturna:

- In **Australia**, Luxturna is reimbursed under a pay-for-performance arrangement and jointly funded by the Federal and State and Territory governments
- **Germany, Spain**, and **Italy** also applied price ceilings, with **Italy** and **Spain** adding price discounts.
- The **UK** applied a price discount, while **France** will re-evaluate the drug with new data in 5 years.

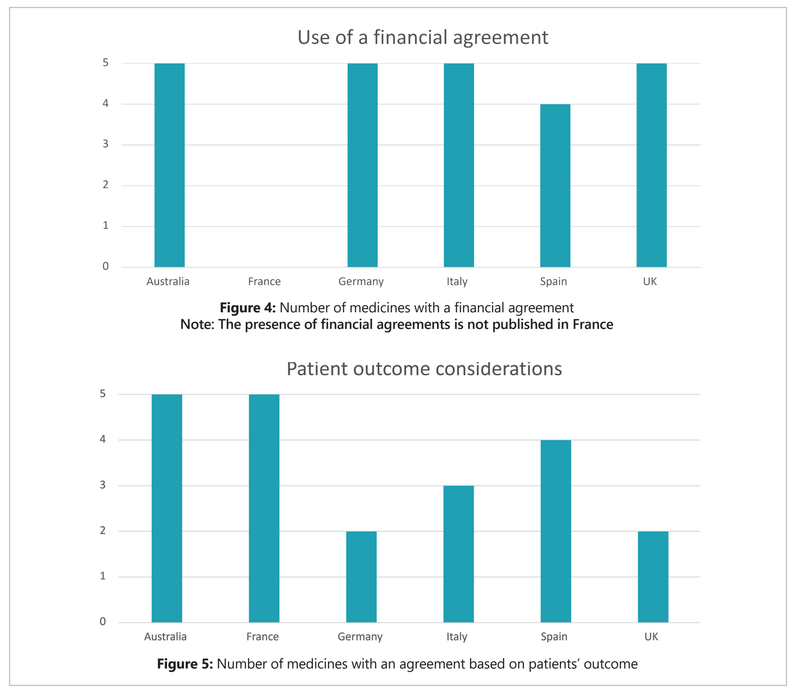

Figure 4: Number of medicines with a financial agreement
Note: The presence of financial agreements is not published in France

Figure 5: Number of medicines with an agreement based on patients' outcome

Conclusion.

The significant differences in regulatory and reimbursement decisions between Australia and various European countries have led to diverse dynamics in patient access to ATMPs. There is considerable variability in HTA and P&R decision-making at the national level, with the factors driving these discrepancies often lacking transparency. The introduction of the Joint Clinical Assessment (JCA), as part of the new EU-HTA Regulation, may help address these inconsistencies and improve alignment across European countries, potentially streamlining access to ATMPs.

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