Policy Asks on Access to Authorised ATMPs

Ensuring Safe and Timely Patient Access to Authorised ATMPs Across Europe

#MEPsforATMPs

European Alliance for Transformative Therapies

These Policy Asks reflect the current thinking of the TRANSFORM Alliance as of March 2022. The Asks will be further clarified and developed, especially in light of external policy developments, culminating in a final and integrated set of Asks outlined in a Charter in October 2022.

The European Alliance for Transformative Therapies' (TRANSFORM) Policy Asks[1] advocate for changes that offer potential solutions to unlock safe and timely patient access to authorised ATMPs in Europe[2], building on the 2021 TRANSFORM Recommendations for Action.

Currently, policy makers are giving consideration to the development, regulatory framework and access pathway for ATMPs in Europe. The European Commission is currently reviewing the EU legislation on medicines for children and rare diseases[3] and the EU's general pharmaceutical legislation.[4] The revisions will aim, among other things, to foster innovation, including in areas of unmet medical needs, and adapt to new scientific and technological developments.[5] There is recognition of the need for 'a new business model [for ATMPs] to address the shift in cost from chronic to one-time treatment'.[6]

Member States have demonstrated their commitment to the development of ATMPs - the recent Manifesto[7] for an Important Project of Common European Interest (IPCEI) commits €1.5 billion to three priorities, one being the development of innovative therapies for rare diseases, and gene and cell therapies.[8]

Transformative ATMPs represent a radical departure from current assumptions of what healthcare innovations can bring to patients and society. These treatments offer the prospect of delivering unprecedented benefits - quality of life being dramatically improved or reducing the healthcare burden of those patients over the longer-term. However, there are concerns about the sustainability of the budgetary impact on the healthcare systems due to high up-front costs associated with one-time treatments compared to lifelong treatments, which can be better accommodated within the existing healthcare funding models in Member States.

In view of the unique characteristics of ATMPs, new approaches are needed for their development, value assessment, pricing and reimbursement and, ultimately, their access by patients. Whilst pricing and reimbursement is clearly a national competence, enhanced exchange of best practice between Member States on innovative payment models would facilitate their uptake and improve patient access to ATMPs in Europe.

Fundamental to a new direction is the broader need for a **holistic approach to ATMPs that links across the access pathway:** from horizon scanning/pre-clinical work, to HTA and pricing and reimbursement decision-making. This would better equip research and healthcare systems to foresee how innovative therapies may evolve, and to plan appropriately for the future. It is important to build capacity now to deliver innovative therapies to patients and to make EU healthcare systems more sustainable. There is, moreover, a need for an **EU Rare Disease Action Plan,** to provide a coherent framework to support access to treatments like ATMPs for people living with a rare disease.

[1] The Policy Asks have been developed through a process of finding points of common agreement and majority consensus amongst Alliance members. A stakeholder meeting was held on 8 February and three rounds of consultation took place between February and March 2022.

[2] ATMP policies should correlate with oncology policies and the specificities of rare adult and paediatric cancer sectors.

[3] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12767-Medicines-for-children-&-rare-diseases-updated-rules_en

[4] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12963-Revision-of-the-EU-general-pharmaceuticals-legislation_en

[5] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52020DC0761&from=EN

[6] Ibid, page 12

[7] Signed in February 2022 by 16 Member States

[8] https://solidarites-sante.gouv.fr/IMG/pdf/220303_-_cp_-_conference_ministerielle_lancement_d_un_piiec_en_sante.pdf

Policy Asks on Access to Authorised ATMPs

POLICY ASK 1 — Improved and coordinated Horizon Scanning

Challenges

Horizon scanning of new therapies at the EU, Member State, and regional level is often fragmented. As a result, decision-makers are faced with limited information to inform planning and prioritisation of healthcare infrastructure and budgets.

Policy Asks

1.1 **Improve horizon scanning at the EU, Member State, and regional level to enable healthcare resource planning.** Consideration should be given to what more is needed to better enable healthcare systems to prepare for transformative therapies coming to the market.

Rationale / Explanation

Many countries have expressed a need for early access to information on the development of innovative therapies. The International Horizon Scanning Initiative (IHSI)[9] – involving 8 countries – is welcomed.

The Belgian Health Care Knowledge Centre (KCE) study on Horizon Scanning[10] flags the importance of broad collaboration.

[9] https://ihsi-health.org/
[10] https://kce.fgov.be/en/horizon-scanning-for-pharmaceuticals-proposal-for-the-beneluxa-collaboration

POLICY ASK 2

Extend existing early dialogues

Ensure greater transparency between regulators, HTA bodies and payers

Challenges

There is a lack of capacity at HTA/payer level which may hinder the ability to engage in early and iterative dialogue.

There is misalignment in how to best capture, demonstrate and translate the added value of ATMPs by developers, regulators, patients, HTA/payers and society.

Policy Asks

2.1 **Extend existing early dialogues** such as those between the EMA and developers (e.g. PRIME) to be more iterative and inclusive of HTA bodies, payers, patients/caregivers and ATMP developers. The joint scientific consultations (JSC) under the HTA Regulation, which will advise developers on clinical study designs, should be conducted as early as possible and offered to all developers that will undergo a Joint Clinical Assessment (JCA) at EU level. The first discussions should commence well ahead of 2025 (when the HTA Regulation will apply to ATMPs) to ensure that there is appropriate alignment on methodologies and necessary evidence, thereby avoiding unnecessary delays in evaluation and access.

2.2 **Ensure greater transparency between regulators, HTA bodies and payers** on the use of real-world data/evidence, with agreement among these bodies that where real-world data is collected by an ATMP developer, it is taken into account in decision-making.

Rationale / Explanation

Lack of HTA/payer capacity can hinder the ability to optimise clinical development plans that consider the nature of ATMPs.

POLICY ASK 3

Adapt value assessments suited to the nature of transformative ATMPs

Challenges

Current HTA methodologies are not always fit for purpose to assess the socio-economic value of ATMPs. ATMPs can be undervalued as current HTA methodologies do not account for the specificities of ATMPs - they are not sufficiently flexible to allow for decisions under uncertainty and do not adequately account for transformative or one-time treatments using cost-effectiveness or budget impact measures.

Policy Asks

3.1 **Develop methodologies for joint clinical assessment (JCA) of ATMPs, with flexibility in evidence requirements.**

- These methodologies should take a more holistic and flexible approach e.g., by considering health equity, caregiver burden and capacity of patients to work or study.[11]
- Such methodologies should also be able to evolve over time to reflect real-world data and any shifts in ethical and value proposition.
- Rigid cost-effectiveness thresholds should not be applied.

Rationale / Explanation

Prevailing regulatory, HTA and pricing & reimbursement frameworks in Europe (and globally) were developed for traditional therapies (i.e., pharmaceuticals and devices), which were predominantly focused on managing symptoms rather than transformative therapies.

Continued cooperation is needed to ensure the use of appropriate HTA methodologies, tailored to the particular nature and unique challenges of ATMPs.

3.2 **Update HTA methodologies with input from the stakeholder network.**[12] Stakeholders must be broadly involved in the EU HTA procedures. Strong coordination at EU-level is needed to help ensure: (a) JCAs for ATMPs are not duplicated at Member State level and there is a basis for common understanding of an ATMP's value, and (b) JSC for ATMPs are conducted as early as possible in a therapy's development lifecycle.

Rationale / Explanation

The establishment of the stakeholder network under the HTA Regulation, to support the work of the Member State Coordination Group on Health Technology Assessment, is welcomed.

3.3 **Develop and adopt Guidelines setting acceptable and harmonised HTA review and approval timelines for ATMPs.**

[11] See Garrison LP, Jackson T, Paul D, Kenston M. *Value-Based Pricing for Emerging Gene Therapies: The Economic Case for a Higher Cost-Effectiveness Threshold*. J Manag Care Spec Pharm. 2019 Jul;25(7):793-799.
[12] Paragraph 24 of the HTA Regulation recitals states that methodologies for performing JCA and JSC should be adapted to include specificities for new health technologies for which some data may not be readily available, which may be the case for some ATMPs.

POLICY ASK 4

Improve collection and use of RWE
Clarify governance and develop guidance
Leverage the European Health Data Space
Consider the creation of a dedicated EU Fund for RWE collection

Challenges

There are often critical uncertainties at the time of market launch which create challenges for the standard value assessment methodologies.

Gathering evidence for ATMPs can be challenging, given their long-term effects and, in the case of orphan ATMPs, small patient population sizes.

Policy Asks

4.1 **The European Health Data Space (EHDS) should develop interoperability standards for health data sets**, thereby facilitating pooling of data to increase reliability.

4.2 **Introduce recommendations on the harmonised interpretation of the EU General Data Protection Regulation (GDPR)** across all EU Member States, including clarity on the legal basis for data sharing in scientific research in the public interest.[13]

Rationale / Explanation

There are practical and ethical reasons why randomized clinical trials are challenging for ATMPs, such as small and dispersed patient populations, lack of comparators for clinical and economical evaluation, and limited treatment centres to administer investigational products where the patients are located.

4.3 **Support a multi-stakeholder learning network on Real-World Evidence (RWE) generation and its use** in innovative payment models, with a mandate to develop common guidelines for using RWE in regulatory decision-making.

Rationale / Explanation

Real-world evidence should not be considered a substitute for clinical trials but rather as a complement that provides additional information and reduces uncertainties.

[13] See further recommendations contained in SIOP Europe's review of the impact of GDPR on Childhood Cancer Research, available at: https://siope.eu/media/documents/impact-of-the-gdpr-on-childhood-cancer-research-in-europe-summary.pdf

4.4 **Fund, improve and enable better use of registries.** More specifically, stakeholders should:

- **Consider the creation of a dedicated "EU Fund for RWE collection" to finance the establishment, operation and maintenance of RWE registries.** This could support the generation and use of data and RWE for ATMPs from the point of (conditional) marketing authorisation for the appropriate timeframe.
- **Establish common quality standards for self-assessment/certification** by registry holders (as proposed by EUnetHTA[14]), which could build confidence in this type of data for decision-making.
- **Facilitate better and earlier physician and patient/caregiver involvement** (including those with limited capacity of communication) in the collection of real-world data to improve outcomes and ensure safety in the long-term. Take specific consideration of level of maturity of children of different ages.
- **Fund educational programmes on real-world data, and its importance for regulatory decision making.**

Rationale / Explanation

The precise nature, scope and implementation of any EU Fund for RWE collection is an ongoing discussion within the TRANSFORM Alliance. Further alignment and clarity is being sought on the operation and financing of such a fund, to ensure that it would address the appropriate and existing needs in the system. This concept will reflect and learn from existing EU initiatives. It is also a concept that continues to be explored with stakeholders in other fora. Whilst thinking evolves, given the need for quality data sets (including via registries) to facilitate (among other things) the implementation of innovative payment models, logic follows that such a fund could be supported with EU-level resources (e.g. from existing or new funding sources).

POLICY ASK 5 — Enable innovative payment schemes

Challenges

Misalignments remain between regulators, HTA bodies and payers in their evidence requirements such as: addressing the use of surrogate end points, small patient populations and long term efficacy/effectiveness. This is despite progress in and across Member States towards convergence and alignment.

As a result of evidence requirements for regulators differing from those of payers for managed entry agreements or other innovative payment models, they are difficult to implement effectively or across different jurisdictions.

[14] See European Network for Health Technology Assessment's Vision paper on the sustainable availability of the proposed Registry Evaluation and Quality Standards Tool (REQueST) published May 2019

Policy Asks

5.1 **Find common agreement on core parameters for outcomes-based payment models for ATMPs** to support their uptake in interested countries (e.g. appropriate endpoints, timeframe, data) in reimbursement decision-making. This should be done with consideration for specific populations such as children, taking into account the capacity of a patient to study or work and the expected additional years gained as a consequence of the ATMP.

For children, specific considerations that may be applicable for outcomes-based payment models include specific innovative development designs.

Rationale / Explanation

Disparities exist among Member States in the implementation of data collection models for outcomes-based models. These differences in approach pose problems for ATMP developers seeking to agree an implementable payment model to launch a therapy in the EU, which ultimately undermines patient access across the bloc.

5.2 **Remove structural barriers** to the implementation of innovative contracting schemes, including by adjusting **public accounting rules for annuity payments.**

Dialogue among accounting institutions and authorities at regional, national and EU level could unlock pragmatic solutions – and enable their use, as already seen in Germany.[15]

POLICY ASK 6 — Promote learnings from national funds for innovation and regional collaborations

Challenges

National innovative medicines funds have been criticized, for example because of issues around eligibility criteria, sustainability and a lack of transparency around how they are used and their impact on patient access.

Policy Asks

6.1 **Member States should learn from the achievements and shortcomings of existing innovative medicines funds** (e.g. in Scotland, England, Italy, The Netherlands) with specific regard to ATMPs, and promote continuous sharing of best practice of managed entry agreements, commercial agreements and evolving RWE and economic assessment. Using these learnings to inform best practice for funding approaches is important to ensure agile, flexible solutions are implemented across the EU.

[15] As of March 2021, in Europe only Germany had applied annuity payments, for one product. See Ronco, V., Dilecce, M., Lanati, E. et al. *Price and reimbursement of advanced therapeutic medicinal products in Europe: are assessment and appraisal diverging from expert recommendations*?. J of Pharm Policy and Pract 14, 30 (2021).

Rationale / Explanation

The English Cancer Drugs Fund (CDF) has recently been extended to non-cancer treatments via an Innovative Medicines Fund. For ATMPs, where longer-term data may need to be collected to satisfy uncertainties on clinical and cost-effectiveness, such a model could support early and timely patient access while mandated additional data collection is ongoing.

6.2 **Learnings from regional collaborations (e.g. MoCA and BeNeLuxA) and national pricing, payment and procurement policies** should: (i) support the use of innovative payment models, (ii) support health system's sustainability, and (iii) speed up pricing and reimbursement processes for ATMPs.

Rationale / Explanation

Regional collaborations have secured access to drugs for patients across countries: in 2021, Belgium, Ireland and the Netherlands jointly reached agreement on the price of gene therapy Zolgensma®, the first time this has happened with three countries.[16] Learnings from this example could inform thinking around other pricing and reimbursement approaches.

POLICY ASK 7[17] Access to cross-border care and infrastructure

Amend cross-border reimbursement rules
Extend the role of ERNs
Upscale role of NCPs
Define a European Hospital Label
Fund training and research
Upscale screening for early diagnosis

Challenges

Complex legislative framework with two different sets of authorization and reimbursement rules (Cross-border Health Services Directive (Directive 2011/24) and Social Security Regulations (Regulation 883/2004)).

Variability in the use of cross-border healthcare legal provisions (S2 form) across Member States.

European Reference Networks (ERNs) lack integration in national health systems, and are under-utilized in the definition of diagnosis and treatment pathways.

There are challenges for access to ATMPs and inequalities between Member States.

[16] https://beneluxa.org/statements
[17] See the 5 Policy Asks to optimize cross-border patient access to advanced therapies by the TRANSFORM MEP Interest Group, launched in November 2021: https://transformalliance.eu/wp-content/uploads/2021/11/TRANSFORM-MEP-Interest-Group-Five-Asks-on-Cross-border-Access-to-ATMPs-1.pdf

Policy Asks

7.1 The Commission should review both the Cross-Border Health Services Directive (Directive 2011/24) and the Social Security Regulation (Regulation 883/2004) - **merging the authorization and reimbursement rules of both under the Social Security Regulation 883/2004**, which is directly applicable.

Health services should be paid directly as if the patient is insured by the social security system of the country of treatment, and the treatment should be approved in the country of treatment basket of care.

Rationale / Explanation

This would help simplify the system and make it more transparent for patients.

7.2 **Assess the potential to strengthen the role of the European Reference Networks (ERNs)** to support best practice across Member States in decision-making for cases where cross-border care may be necessary, and continue acting as a central point of information for patients receiving cross-border care.

Areas where ERNs' remit could be bolstered include:

- **In the assessment of whether cross-border treatment is clinically justified.** ERNs could be involved in the confirmation of the therapeutic option as well as the knowledge sharing/diagnosis to facilitate the national approval process for cross-border funding.
- **In ongoing- and post-treatment care.** ERNs could develop common long-term delivery and follow-up protocols that support and follow the patient long after the delivery of the therapy.
- In the development of a **centralised repository** of clear information indicating which centres in the EU are planning, or have ongoing, clinical trials with ATMPs.
- In the **allocation of financing** for travel expenses and translation services for the patient and their family/legal representatives where they must travel long distances to a centre of treatment, thereby supporting them to stay in the host country for the required period.

Rationale / Explanation

A recent European Commission report[18] found a lack of information provision to patients in the context of cross-border healthcare, underlining this need.

The European Commission's proposed Joint Action to continue integration of ERNs into national health systems is welcomed as a way to embed the work of ERNs further.

7.3 **Upscale the role of National Contact Points (NCPs) to support the provision of information** on cross-border treatment and act as an interface between cross-border patients, treatment centres/ERNs and national social security systems to assist a patient with the application for cross-border treatment and the actual treatment pathway.

[18] See *Study on Enhancing Implementation of the Cross-Border Healthcare Directive 2011/24/EU to ensure patient rights in the EU.* Published 24 February 2022. Executive summary available here: crossborder_enhancing-implementation_exe_en.pdf (europa.eu)

Rationale / Explanation

A recent study commissioned by the European Commission found that consultation arrangements between NCPs and stakeholders have not been implemented in all Member States.[19] Training should be provided to NCPs on the specificity of some ATMPs and the need for highly specialised and multi-disciplinary teams for their administration, so that they can proactively inform their citizens about the rights they have to cross-border access when they need it and the process to follow.

7.4 Define **a (voluntary) "European Hospital" label** as a framework to support smooth cross-border access to healthcare facilities and exchange information.

Rationale / Explanation

The French EU Presidency proposal has potential for added value at the European level. It could improve coordination and sharing of information between different hospitals/Centres of Excellence across EU Member States and enable patients to be received in facilities in neighbouring countries. As discussions continue on how this concept can be applied, it will be important to consider how Centres of Excellence are established and selected. Streamlining and aligning the process at European level could improve accreditation, through shared and pre-established selection criteria, thereby accelerating access.

Moreover, Minister Véran mentioned the label could bring together health professionals to discuss good practices, especially patient care.

7.5 **Provide funding for training and research to upskill healthcare professionals across the EU** in the delivery of complex ATMPs, avoiding patients having to travel outside the EU.

Rationale / Explanation

Cell and gene therapies require formal training for healthcare professionals to have the adequate information to convey the benefits and risks to patients and to administer the treatments.

7.6 **Implement EU mechanisms funding research and support tools** to ensure more equitable access to ATMP-based therapies for **treatable rare disorders with newborn and early screening and genetic testing**.

Rationale / Explanation

Speed is essential for patients hoping to receive an approved ATMP that offers transformational treatment. In the case of genetic rare diseases, where 70% present in

[19] *Ibid*

childhood, fast diagnosis leading to treatment offers the possibility of life either free of disease, or without further progression.

Basic and preclinical research allowing increase of knowledge on human development and paediatric biomarkers targeting the rarest and still undiagnosed diseases can help bridge the gap between early diagnosis and timely access to treatment with ATMPs, to ensure that the full value of transformative therapies can be realised for paediatric patients.

These Policy Asks will be included in the TRANSFORM Charter, to be launched in the European Parliament in **October 2022**.

About the European Alliance for Transformative Therapies (TRANSFORM)

The European Alliance for Transformative Therapies (TRANSFORM) is a multi-stakeholder Alliance that connects Members of the European Parliament (MEPs) and policy-makers with patient groups, medical experts and associations, scientists, researchers, industry actors, networks and other relevant stakeholders. TRANSFORM aims to foster effective dialogue and provide evidence-based policy recommendations to enable safe and timely patient access to cell and gene therapies, whilst ensuring sustainability of healthcare systems.

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The European Medicines Agency is an Observer to the Alliance.

EFNA – European Federation of Neurological Associations

RI – Retina International

WDO – World Duchenne Organization

IPOPI – International Patient Organisation for Primary Immunodeficiencies

TIF – Thalassaemia International Federation

EHC – European Haemophilia Consortium

EURORDIS – Rare Diseases Europe

EPTRI – European Paediatric Translational Research Infrastructure

CCI Europe – Childhood Cancer International Europe

SIOP Europe – the European Society for Paediatric Oncology

EAHAD – European Association for Haemophilia and Allied Disorders

EU EYE – European Alliance for Vision Research and Ophthalmology

EUCOPE – European Confederation of Pharmaceutical Entrepreneurs