Realising the Potential of Transformative Therapies

How to Optimize Cross-border Cooperation to Support Equitable Access to Advanced Therapies?

Event hosted by the MEP Interest Group on Transformative Therapies

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#MEPsforATMPs

European Alliance for Transformative Therapies

Cross-Border Access to ATMPs: Addressing the Challenges

Advanced Therapy Medicinal Products (ATMPs), such as cell and gene therapies, are highly personalised therapies with the potential to transform the lives of patients. Due to their complex manufacturing, distribution processes, the need for trained healthcare providers, and/or the rarity of the condition they aim to address, many of these therapies will be available only in a small number of treatment centres in Europe. As a result, many patients in Europe may need to travel across borders to benefit from treatment with such a transformative therapy.

In view of the European Commission's evaluation of the Cross-Border Healthcare Directive (with a report expected to be published in April 2022), MEPs, policymakers and expert stakeholders from the TRANSFORM multi-stakeholder Alliance discussed the issues at stake.

The TRANSFORM MEP Interest Group launched 5 Policy Asks to optimize cross-border patient access to advanced therapies, building on the TRANSFORM Recommendations for Action relating to cross-border access and infrastructure. These Policy Asks will be further developed in light of the discussions and will be integrated into a TRANSFORM Charter which will be launched in September/October 2022.

In 2022 the TRANSFORM Alliance will continue to support the TRANSFORM MEP Interest Group, and a series of meetings will be held to provide recommendations in view of the EU Pharmaceutical Strategy and the revision of the EU Pharmaceutical acquis, including the Cross-Border Healthcare Directive.

Key takeaways

Whilst it was highlighted that some advanced therapies treatments do not require specialist centres for administration, meaning that cross-border treatment is not the only option, for any patients that do have to travel across borders for treatment, time is of the essence and administrative simplification and cross-country collaboration is crucial for equitable and safe access to transformative therapies. Better implementation by the Member States is also essential to address some of the current challenges.

Outlined below are some of the key considerations raised in relation to each of the TRANSFORM Policy Asks (the full version of the Policy Asks is set out further below in Annex).

POLICY ASK 1

Calls upon the European Commission to review both the Cross-Border Healthcare Directive (Directive 2011/24/EU) and the Social Security Regulation (Regulation 883/2004) - merging the authorization and reimbursement rules of both under the Social Security Regulation 883/2004

The EU Cross-Border Healthcare Directive and EU Social Security Regulations, based on different articles of the Treaty, were drafted to serve patients' cross-border rights and the cross-border access to social security respectively. However, neither are fit for purpose to enable cross-border patient access to treatment and there is a need for legislative reform and simplification of procedures to make the system more transparent and workable for the patients.

It was suggested that the authorization and reimbursement rules of both the Directive and Regulation could be merged under the Social Security Regulation 883/2004 and would contain the additional rights currently provided by the Cross-Border Healthcare Directive, while the Directive would maintain its rules on HTA, European Reference Networks, National Contact Points, cooperation etc.

Given that time is often critical for patients to benefit from these treatments, it was suggested that a platform is needed to bring together all stakeholders – including payers and national Ministries of Health - to find "interim practical solutions" given that legislative changes will take several years.

The European Commission was called upon to review the cross-border healthcare legislation and is currently evaluating the Cross-Border Healthcare Directive ten years after its adoption in 2011. A report is expected to be published in Q2 2022.

It was suggested that the European Commission could prepare an ATMP-specific guideline on the current cross-border healthcare framework. Ideally, there should be clarity on why, for certain ATMPs, the only viable option for patients to access treatment abroad is under the Social Security Regulation, where no upfront out-of-pocket expenses for the patient is foreseen, provided pre-authorisation (S2 form) is obtained. The possibility of creating a list of therapies exempted from pre-authorisation was also raised.

POLICY ASK 2

Extend the role of the European Reference Networks (ERNs) to assess whether cross-border treatment is clinically justified

Structural and regional development funds should be used to increase the quality of infrastructure by developing more Centres of Excellence connected through a network. There is a need for improved funding of the ERNs in order to extend their role.

Existing Centres of Excellence in Europe (which are often also called ERNs) should be leveraged to ensure standard of care and adequate training to deliver highly specialized therapies. Clear information on which Centres in the EU are administering such specialized therapies should be provided.

POLICY ASK 3

Upscale the role of National Contact Points (NCPs) to support the provision of information on cross-border treatment for specific ATMPs and act as an interface between cross-border patients, ERNs and their national social security

Funding – for instance through EU cohesion policy – is needed to (1) train the NCPs on ATMPs specificities (in some cases, the only viable option to get access to the therapy is the cross-border movement of the patient); (2) improve cooperation between NCPs and the ERNs to improve information to patients and access to clinical expertise.

Additionally, NCPs could (3) build transparency on their national approval processes, and the information could be centralized at a European level.

POLICY ASK 4

Operationalise a pan-European infrastructure for the long-term follow-up of patients treated with ATMPs

As a case study example, the European Association for Haemophilia and Allied Disorders (EAHAD) and European Haemophilia Consortium (EHC) jointly call for all first-generation gene therapies to be managed using a 'hub-and-spoke model', prescribed and managed exclusively by expert haemophilia comprehensive care centres (as the national hubs), and monitored by haemophilia treatment centres in close communication with the primary expert hub (as spokes linking into that hub).

The need to create a European-wide research network with a legal framework integrating research infrastructures was highlighted. The European cohesion funds may further contribute to address European healthcare infrastructure needs.

POLICY ASK 5

Provide EU cross-border funding to minimize the burden on families, e.g. by covering travel and costs of stay

The idea of a European fund to enable cross-border treatment was discussed, in particular to cover for the patient and the family to travel to the centre of treatment, and to allow them to stay in the host country for the required period.

Full meeting report

TRANSFORM Co-Chair MEP Ondrej Knotek opened the meeting presenting the TRANSFORM MEP Interest Group 5 Policy Asks, building on the TRANSFORM Recommendations for Action relating to cross-border access and infrastructure. **TRANSFORM Co-Chair MEP Alessandra Moretti** defended a stronger coordinating role of the EU in healthcare, that should include a set of binding minimum standards for access to healthcare and highlighted the need for reform at every level: better information for patients, better training of doctors, simplified administrative burden and faster reimbursement, in addition to adapting the current regulatory framework.

Practical case study: the Strimvelis case

Michela Gabaldo (Head of Translational Project Management & Regulatory Affairs, Fondazione Telethon), presented learnings from the Strimvelis case, the first ex-vivo gene therapy registered in Europe in 2016. The current EU provisions for planned treatment abroad and coverage of costs are the Social Security Regulations (EC) 883/2004 and 987/2009 and the Directive on patients' rights in cross-border healthcare 2011/24/EU. She outlined that, for some specific transformative therapies, it could be safer and more cost-effective to direct European patients to the few highly specialized centres that already exist than to try to treat them all in their country of residence. As it currently stands, the Directive does not actually work in these cases, whereas the Regulation's provisions have allowed patient access to Strimvelis in Milan. She argued for a paradigm shift in approach by regulatory agencies, healthcare providers, payers and healthcare systems to realise the therapeutic potential of transformative therapies and ensure sustainable patient accessibility.

Panel discussion

MEP Tomislav Sokol (EPP, Croatia), TRANSFORM Member, highlighted:

- The need for simplification by merging the provisions on authorisation and reimbursement in the Cross-Border Healthcare Directive and the Social Security Regulations, under the Social Security Regulations, while leaving the rules on HTA, ERNs, NCPs and cooperation in the Directive.
- Rules on prior authorisation of the Cross-Border Healthcare Directive contain additional limitations, which should be abolished as they are contrary to the principles established by the case law (e.g. Kohll judgment, C-158/96; or Case C-368/98).
- Patients should have the right to a second opinion, which is in line with the recent case law (case C-538/19), and a principle that the European Parliament is also discussing in the framework of the EU's Beating Cancer Plan.
- There is a need to use cohesion policy funds to reduce cross-EU inequalities and develop infrastructure through regional excellence centres for the delivery of highly specialized therapies.

Caroline Hager (Team Leader and member of the Cross-border Healthcare Expert Group, DG SANTE) informed the audience that current challenges with the Cross-Border Healthcare Directive were discussed in the European Commission stakeholder workshop hosted on 9 November, which collected feedback on the results of the evaluation of the Directive.

- The two sets of legislation serve different objectives: the Cross-Border Healthcare Directive aims to serve patients' cross-border rights, whereas the Social Security Regulations aims to secure cross-border access to social security. Therefore, they need to remain separate.

- The European Commission would look to address the most important challenges which can be overcome with better implementation by the Member States by simplifying procedures and addressing the administrative barriers at national level in the referral system.
- Better co-operation between National Contact Points (NCPs) and with the European Reference Networks (ERNs) is needed. To do so, there is a need for improved funding.
- The European Commission adoption of the Report on the evaluation of patient rights in cross-border healthcare is planned for the second quarter of 2022.

Simone Boselli (EU Public Affairs Director, EURORDIS – Rare Diseases Europe) highlighted that:

- For rare diseases, a minimum health standard across the EU is needed that makes a difference to all European patients.
- Recent scientific developments mean that the current legislative frameworks for cross-border health are not fit for purpose.
- Structural and regional development funds are needed to increase the quality of the infrastructure, and to develop more centres of excellence connected through a network.
- Centres of excellence need to better train healthcare professionals and increase their capacity.

Christoph J. Rupprecht (Head of Department Health Policy & Health Economics, AOK Rheinland/Hamburg)

- Given the qualitative difference in access to healthcare across the EU, there is a need for European consideration of pre-authorisation and payment. He suggested that a common European fund for cross-border health could provide a solution.
- The creation of a list of therapies exempted from pre-authorisation could be another solution.
- Certification of Centres of Excellence at EU-level could be helpful to ensure standard of care and training to deliver highly specialized therapies.
- Europe-wide registries are needed for rare diseases, and federated platforms can be helpful for research.

Thomas Bols (Head of Government Affairs and Public Policy for EMEA & Asia Pacific Region, PTC Therapeutics) said that:

- Lack of information for patients and physicians and the invisibility of ERNs and NPCs creates major challenges for patients.
- National reimbursement authorities need to work together for cross-border access to specific treatments - there is a need for a revision of the legislation on cross-border treatment delivery, bringing in national payers and decision-makers.
- In the meantime, a platform could be set up to bring together all stakeholders – including payers and national Ministries of Health to find "interim practical solutions", while the EU legislation is being reviewed.

Mohit Jain (Vice President Market Access EMEA, BioMarin Pharmaceutical), pointed out that:

- Some advanced therapies (including some in-vivo gene therapies) do not require specialized centres for treatment as they are normal infusions, so while infrastructure is critical, so too are reimbursement and patient follow-up across border.
- Novel ATMPs require complex reimbursement agreements, such as payment based on performance and arrangements such as national payment caps, and rebates over time.
- Without the cross-border legislation taking these complexities into consideration, patient access to ATMPs will be impacted.

Interventions by other members of the TRANSFORM Alliance

- **Dr Giovanni Migliaccio (Scientific Director of Centro Valutazioni Biologiche e Farmacologiche (CVBF))**, focused on the role of specialized infrastructures for pediatrics care, linked to ERNs. While administration is usually a single event requiring a short time at a specialized centre, the diagnostic and follow-up for some patients may extend for decades. There is a need to create a European-wide research network with a legal framework integrating research infrastructures.

- **Dr Ioanna Psalti (Policy Advisor to the European Alliance for Vision Research and Ophthalmology (EU-EYE)),** highlighted the issue with insurance-based systems and the lack of awareness about ERNs at national level, and a need to integrate them into the national healthcare systems. In her view, it should be mandatory that national healthcare systems inform patients on their rights and possibilities and train them on how to navigate the referral system.

- **Amanda Bok (CEO of the European Haemophilia Consortium (EHC)),** explained that, for the specific case of Haemophilia, there are already certified centres for comprehensive care and a lot of expertise is already centralized, but this is not adequate for gene therapies. There is a need for a 'hub-and-spoke model' specifically for gene therapies. The EHC is currently working on defining what such a hub-and-spoke model would look like and hosted a round table on 20 November 2021 to discuss requirements for centres administering gene therapy and reflecting on gene therapies approaches in Europe.

- **Harun Šabić (Committee Member and Survivor Representative, Childhood Cancer International – Europe (CCI Europe))** stated that there is a need to increase funding for cross-disciplinary, patient-centred education. Research programmes are needed for the development of ATMPs in the field of pediatric oncology and to exchange clinical expert knowledge across European borders. Sustainable funding for ERNs is also needed.

Annex - TRANSFORM MEP Interest Group: 5 Policy Asks

POLICY ASK 1

Calls upon the Commission to 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

- Simplify the system and make it more transparent to patients by merging the two different sets of authorization and reimbursement rules (Directive 2011/24 and Regulation 883/2004) under 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 that country and the treatment should be approved in the country of treatment basket of care.
- Develop guidelines setting acceptable and harmonised review and approval timelines expedite time-to-treatment in the EU.

POLICY ASK 2

Extend the role of the European Reference Networks (ERNs) to assess whether cross-border treatment is clinically justified

- ERNs should 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.

POLICY ASK 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, ERNs and their national social security

- Provide training 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.
- Encourage NCPs to provide information on the funding paths and approval steps, taking into account their country's specificities and language. Provide clear information on which centres in the EU are administering ATMPs. This information could be centralized on the European Commission's website. The NCPs could become the interface between, patients, treatment Centre/ERN and national security system to assist a patient with the application for cross border treatment and the actual treatment.

POLICY ASK 4

Operationalise a pan-European infrastructure for the long-term follow-up of patients treated with ATMPs

- For ATMPs that require administration in specialist centres, encourage multi-stakeholder discussions to designate suitable centres and develop adequate delivery and follow-up care protocols that support and follow the patient long after the delivery of the therapy.

POLICY ASK 5

Provide EU cross-border funding to minimize the burden on families, e.g. by covering travel and costs of stay

- Allocate funding from EU4Health to the patient and the family to travel to the centre of treatment and undergo the treatment, and to allow them to stay in the host country for the required period.

About the European Alliance for Transformative Therapies (TRANSFORM)

We invite you to join the TRANSFORM Community on Twitter and LinkedIn and keep an eye on the website to continue this important discussion online and to stay updated to the 2022 plans of the TRANSFORM MEP Interest Group and Alliance of experts.

If you could not attend the event or if you want to re-watch the discussion, you can access the recording and the presentation here: https://transformalliance.eu/event/how-to-optimize-cross-border-cooperation-to-support-equitable-access-to-advanced-therapies/

You can access the TRANSFORM MEP Interest Group Policy Asks launched on 10 November here: https://transformalliance.eu/wp-content/uploads/2021/11/TRANSFORM-MEP-Interest-Group-Five-Asks-on-Cross-border-Access-to-ATMPs.pdf

You can read the TRANSFORM Recommendations for Actions launched in June 2021 here:

https://transformalliance.eu/wp-content/uploads/2021/06/TRANSFORM-Recommendations-Version1.0_June2021-1.pdf