ATMP Market Access

Overcoming cross-border restrictions

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About ARM

• **International advocacy organization**
  • Dedicated to realizing the promise of safe and effective regenerative medicines for patients around the world
  • Cell and gene therapy, tissue engineering

• **350+ members**
  • Small and large companies, non-profit research institutions, patient organizations, and other sector stakeholders
  • Across 25 countries

• **Priorities:**
  • Clear, predictable, and harmonized regulatory pathways
  • Enabling market access and value-based reimbursement policies
  • Addressing industrialization and manufacturing hurdles
  • Compile sector data, educate media and other stakeholders
Why is cross-border relevant & important for ATMPs?
More Than Half of Clinical Trials With ATMPs Are in Rare Diseases

### Clinical Trials ATMPs

**Total:** 1,066

- **Phase 1:** 252 across all tech types in rare disease
  - Gene Therapy: 62
  - Gene-Modified & Cell-Based IO: 174
  - Cell Therapy: 14
  - Tissue Engineering: 2

- **Phase 2:** 353 across all tech types in rare disease
  - Gene Therapy: 134
  - Gene-Modified & Cell-Based IO: 168
  - Cell Therapy: 49
  - Tissue Engineering: 2

- **Phase 3:** 42 across all tech types in rare disease
  - Gene Therapy: 24
  - Gene-Modified & Cell-Based IO: 9
  - Cell Therapy: 7
  - Tissue Engineering: 2

*Source data provided by: informa*
Clinical Trials for Rare Disease by Indication

72% of ATMP clinical trials for rare disease are in rare cancers, including hematological malignancies, ovarian cancers, pancreatic cancers, lung cancers, glioblastoma, and others.

6% are in endocrine, metabolic, and genetic disorders, including mucopolysaccharidosis, Fabry disease, phenylketonurias, and others.
Relevance of Cross-Border Healthcare to ATMPs

• Complex or rare diseases and conditions require highly specialised treatment and a concentration of knowledge and resources, not available in all countries.

• Ultra rare diseases affect only a few patients per year in Europe.

• ATMPs most often need to be administered by trained/certified healthcare providers or in highly specialised centers, not necessarily available in all countries.

• Many ATMPs are autologous, requiring specific logistic requirements and may be better addressed if administered only in a limited number of specialised centres.
• Brings together the views of a number of European policy makers and experts

• Recommendations:
  1. Better adapt HTA frameworks to ATMPs
  2. Favor wide application of conditional reimbursement schemes
  3. Develop pan-European initiatives (RWE, early dialogues, cross-border treatment)
  4. Favor wider application of innovative access and funding arrangements

See also ARM recommendations on cross-border and regional access to ATMPs in Europe released on 27 Jan 2020
What is the legal framework for cross-border healthcare in Europe?
Two possible routes exist for accessing and getting reimbursement for healthcare abroad

**EU/EEA citizen have the right to access medical diagnosis, medical treatment or prescription in any other EU/EEA country or Switzerland**

<table>
<thead>
<tr>
<th>Social Security Regulations</th>
<th>Cross-Border Healthcare Directive</th>
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<tr>
<td>• (EC) N° 883/2004 on the coordination of social security systems, and</td>
<td>• Directive 2011/24/EU on patients’ rights in cross-border healthcare</td>
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**Two different situations exist, under both frameworks:**

- Unplanned medical treatment: sudden illness or injury whilst abroad
- Planned medical treatment: healthcare is the reason for stay abroad (e.g. specialised treatment)
Summary of the Current EU Provisions for PLANNED Treatments Abroad - Differences

Social Security Regulations 883/04 and 987/09

- **Direct assistance** - The health services are paid directly as if the patient is insured by social security system of that country.

- Regulation => same process/requirements/conditions in all the EU Countries

- **Yes**, prior authorisation from home country required (S2 Form). Cannot be refused if treatment in the home country cannot take place within a time limit medically justifiable.

- Form S2 covers treatment costs (i.e. drugs) + clinical costs (i.e. DRG if hospitalised/clinical services). Based on tariffs in treatment country

- Logistics (i.e., travel & lodging) are not covered and are managed case by case by the insurance, social assistance, etc.

- Covers only public or private contracted with the National Health System healthcare providers in the EU.

Directive 2011/24/EU on patients' rights in cross-border EU healthcare:

- **Indirect assistance** - The patient have to pay for treatments and then to request a refund in home country with proofs of payment. Refund will be based as if the treatment was provided in home country

- Directive => may result in different national implementations with additional specific national rules

- **No**, for a wide range of treatments. Prior authorisation should be an exception, not the rule

- Costs covered are based on home country tariffs (=> country to country variations).

- Travel and lodging typically not covered.

- Not covered: Long term care, organ transplantation, public vaccination programmes

- Covers all healthcare providers in the EU, public or private
Summary of the Current EU Provisions for **PLANNED** Treatments Abroad - **Differences**

Social Security Regulations 883/04 and 987/09

- **Direct assistance** - The health services are paid directly as if the patient is insured by social security system of that country.
- Cross-border treatment under the Regulations is the only practical option, but difficulties exist
- Logistics (i.e., travel & lodging) are not covered and are managed case by case by the insurance, social assistance, etc.
- Covers only public or private contracted with the National Health System healthcare providers in the EU.

Directive 2011/24/EU on patients' rights in cross-border healthcare:

- **Indirect assistance** - The patient have to pay for treatments and then to request a refund in home country.
- The requirement of upfront payment by patients makes cross-border treatment with ATMPs under the Directive highly unlikely/impossible.
- Covers all healthcare providers in the EU, public or private.
Summary of the Current EU Provisions for **PLANNED** Treatments Abroad - **Commonalities**

- The National Contact Point can advise on both the legal paths, since these 2 EU regulatory provisions may have specific applications in the State where the patient is insured and they can be supplemented.

- National health authorities may not refuse to reimburse costs:
  - if the patient is entitled to this treatment in his/her home country
  - The treatment cannot be provided on its territory within a time limit which is medically justifiable

**NOTE** - Rare diseases: patients may be offered the possibility under the Social Security Regulation to seek treatment in another EU/EEA country even for diagnosis and treatments which are not available in the patient’s home country. **As long as the treatment concerned is covered in the country of treatment prior authorization may be granted.**

Is it working for ATMP treatment abroad?
Payer’s perspectives on providing reimbursement for ATMP treatment abroad

Major concerns & difficulties from payers on authorising S2 forms for ATMP treatment abroad:

• Biopharma companies could abuse the system to circumvent/avoid P&R procedures in some countries
• Payers from the patient’s home country do not know the details and do not benefit from the managed entry agreement that may be in place in the treatment country
• Legal limitations when the ATMP is not included in the basket of care in the home country (despite being in the basket of treatment country)

In practice, relatively few patients have benefited from reimbursement of ATMP treatment provided abroad and payers are reluctant to use such system on a routine basis
Why do similar difficulties exist in some regionalized countries?
Cross-region funding challenges in regionalized funding models when few ATMP treatment centers

Alternative funding mechanisms needed to avoid that the Regional Health Fund of the ATMP treatment center or the Treatment center itself bears the cost for patients from all regions.
What are the proposed solutions?
ARM proposed recommendations

1. **To create a one-stop shop coordination body at EU/EEA level** that will act as a broker between the different stakeholders to facilitate cross-border patient treatment and funding:
   - To assess whether cross-border treatment is justified: based on specific reasons such as the rarity of the condition, logistic issues, training & other specific requirements for healthcare providers, lack of other treatments providing similar benefit (based on pan-EU assessment of the therapeutic benefit), etc.
   - To centralize and speed up approval of S2 forms*, by signing agreements between MAH, payers and treatment centers detailing the potential market entry agreement and compensation mechanisms valid in the treatment center
   - To reduce financial uncertainty for treatment centers (no payment delays)
   - To agree on conditions to compensate for the additional travel & accommodations for patients

*As required for planned cross-border healthcare under the Social Security Regulations (EC) 883/2004 and 987/2009
2. In countries with regional funding or with multiple payers/insurers:
   • To create a one-stop shop (possibly leveraging National Contact Points)
     • to compensate regional funding authorities in the region of treatment for the costs of patients coming from other regions or
     • to anticipate potential difficulties when patients change from payer/insurer over time
   • To reduce financial uncertainty for treatment centers (no payment delays)
   • Potentially, to leverage or expand existing national funds (e.g. the innovation fund in Italy or the cancer fund in the UK).
ARM proposed recommendations

3. **More effective coordination of HTA activities:**
   
   • To align EMA and HTA post-launch evidence requirements across the different EU countries
   
   • To have a single clinical assessment with mandatory adoption by EU countries as foreseen in the original EC proposed HTA Regulation on health technology assessment and amending Directive 2011/24/EU (COM(2018) 51 final)
ARM proposed recommendations

4. Additional measures:

- Improve opportunities for cross-countries collaboration to deliver faster and broader access by removing duplicative processes at national level and adopting policy principles to enhance cross-country collaboration.

- Exclude cross-border treatments from claw-back or other pay-back mechanisms potentially in place in the treatment country (such pay-back mechanisms are typically based on the pharma expenses/sales in the country for their ‘national’ patients)
Conclusion

- Cross-border treatment will become more important and common with ATMP market adoption
- Legal instruments for cross-border healthcare exist but processes need to be adapted, such as by creating a new coordination body
- Cross-regional treatment in regionalized countries or reimbursement in countries with multiple payers/insurers causes similar difficulties and need to be addressed
- ARM proposed a series of recommendations and is willing to foster discussion with all stakeholders to see whether and how these could be implemented
Thank You!

Market access report recommendations available here

Recommendations on cross-border and regional access to ATMPs in Europe: see here

Visit www.alliancerm.org to access additional resources, including:

- Slides from this and other ARM presentations
- Quarterly sector data reports
- Upcoming near-term clinical trial milestones & data readouts
- Our weekly sector newsletter, a robust round-up of business, clinical, scientific, and policy news in the sector
- Commentary from experts in the field