# Improving patient access to gene and cell therapies for rare diseases in Europe

## A review of the challenges and proposals for improving patient access to advanced therapeutic medicinal products in Austria

**V1**

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Chaired by:

Secretariat support by:

**Reader notes:**

This document contains country-specific insights on challenges and potential solutions to patient access to advanced therapeutic medicinal products (ATMPs) for patients with rare diseases.

The purpose of the document is to provide a starting point for country-specific engagement and discussion within multi-stakeholder meetings.

The challenges and solutions were discussed and prioritised with members of the RARE IMPACT Working Group in meetings and WebEx's between September 2018 and September 2019. Country-specific challenges/solutions have drawn on global recommendations previously published by EUCOPE and ARM, both members of the Working Group.

The challenges and solutions contained within this document are those that have been proposed as priorities for discussion with local stakeholders by members of the Working Group – the report does not include all challenges identified during the secondary research or Working Group meetings.

# Contents

## Executive Summary

The RARE IMPACT initiative was launched at the European Conference on Rare Diseases and Orphan Products in 2018. It is a multi-stakeholder initiative working to improve patient access to gene and cell therapies (or advanced therapy medicinal products [ATMPs])[1]. This patient-focused initiative aims to both assess challenges and propose actionable solutions to concerns regarding patient access to these transformative rare disease treatments in Europe. Through engagement with health technology assessment (HTA) agencies, regulatory bodies, payers, patient groups, clinicians, manufacturers and other experts across Europe, RARE IMPACT partners have proposed ideas to provide better access to ATMPs in Europe.

Patient access to orphan products in Austria has been relatively good with a >90% access rate to EMA approved orphan products, similar to that seen in France. There are currently no specific assessment or reimbursement pathways for ATMPs in Austria. While there are some aspects of the current country processes that help manage barriers to ATMP access, there is recognition that changes are required in order to ensure sustainable access.

This recognition is borne out in the legislative changes taking place in Austria which are intended to create a more standard pathway of assessment and negotiation. However, it is possible that this will not include ATMPs. Within the current system, ATMPs are considered hospital products, which do not go through HTA assessment. Hospital products are instead assessed and negotiated directly between the manufacturer and the hospital, which places a large burden on the hospitals, is inconsistent, and time and resource demanding. Given that there is ongoing reform in Austria, there is an opportunity for some of these challenges to be addressed.

Under the current system, funding for ATMPs is most likely to be via reformed security funds (health insurance), but this would pose challenges, such as how to allocate funds between hospitals/treatment centres. For now, affordability does not seem to be an issue in Austria, although as the number of ATMPs on the market increases, it may represent a greater barrier, creating the need for innovative methods to reduce financial burden on regional budgets. ATMPs are also associated with higher treatment costs, and there is a lack of clarity as to what exactly these costs might include. However, since affordability is not an immediate issue, Austria is in a good position to anticipate and prepare in advance for potential future challenges.

The availability of ATMPs for rare disease in Austria is relatively good and does not pose a significant challenge under the current process. Patients have received access to treatment via cross-border initiatives, which work both ways in the country, and hospital exemption policies are in place and clearly defined.

There is recognition that future access to products for rare disease (including ATMPs) is uncertain in Austria. In response, the Austrian government has established the National Centre for Coordination of Rare Diseases (NKSE) to focus on improving access to products for rare disease. Accessibility challenges would be best managed with more standardised assessment and decision-making processes, which may not be straightforward to implement but would help in creating a sustainable pathway for patient access. These solutions are feasible with minimal interruption to current patient access procedures.

[1] Medicines for human use developed from genes, cells or tissues are classified as advanced therapy medicinal products (ATMPs) by the European Medicines Agency (EMA)

**An overview of challenges and proposals for improving patient access to ATMPs in Austria**

| Domain (Impact)* | Challenge | | Proposed solution | | Feasibility** |
|---|---|---|---|---|---|
| **Assessment**  | **AS1.** | The Austrian government is implementing legislation that ensures products are assessed and prices are negotiated in the EKO, but ATMPs are unlikely to be considered in this pathway | **AS1.** | Pharmig should request clarity on the ongoing reform pathways. Including ATMPs in the pathway would help reduce the burden on single hospitals | + |
| | **AS2.** | HTA assessment is currently not applicable to ATMPS as they are considered hospital products | **AS2.** | Creation of a clear HTA pathway and framework for hospital products, informing direct negotiations, including innovative payment options | + |
| **Affordability**  | **AF1.** | Affordability issues for hospitals have not been identified; however, more high-price products on the market may impact this, creating a need to reduce the burden on regional budgets | **AF1.** | Innovative funding options should be explored for potential future need, such as a national budget for ATMPs | ++ |
| **Availability**  | **AV1.** | Patients have received access to treatment via cross-border initiatives | **AV1.** | "Gemeinsam Grenzenlos Gesund" (Unlimited Health Together) cross-border scheme between Austria and Czech Republic could be reconfigured for ATMPs | +++ |
| | **AV2.** | Hospital exemption policies are clearly defined in Austria, but impact on commercial products is less understood | **AV2.** | EU should be pressed to provide guidelines to prevent marketed products from competing with products with hospital exemptions for the same medical indication | + |
| **Accessibility**  | **AC1.** | Access to ATMPs remains uncertain in Austria | **AC1.** | The NKSE has been established to focus on improving access to products for rare disease | + |

**Notes:** *The working group assessment of the relative impact of the challenge of each domain on patient access is represented by Harvey balls from highest (represented by a full blue Harvey ball) to lowest (represented by an empty, white Harvey ball); **Feasibility: Working Group assessment of feasibility of solutions to be implemented. + low feasibility, ++ medium feasibility, +++ high feasibility.

## The collaboration

RARE IMPACT is a collaboration of three not-for-profit organisations, two trade associations and 18 manufacturers of ATMPs brought together by EURORDIS, a non-governmental patient-driven alliance of patient organisations. The overarching objective of the collaboration is to ensure European patients with rare diseases obtain quick access to gene and cell therapies and to create a sustainable model for manufacturers and payers to maintain patient access and innovation. To achieve this objective, the collaboration has established the following goals:

- Identify challenges that are preventing rare disease patients accessing ATMPs
- Propose actionable solutions to address these challenges
- Utilise these ideas within multi-stakeholder discussions within individual countries and in pan-regional forums

## The approach

A framework for categorising barriers to patient access was developed and validated by the collaboration. The framework includes four categories, described in **Error! Reference source not found.** below.

**Table 1. Framework applied to structuring identified challenges**

| Category | Description |
|---|---|
| Assessment (magnitude of benefit) | Challenges related to the assessment of the benefit of ATMPs within pricing and reimbursement processes. This includes topics such as evidence uncertainty, generating comparative data, use of surrogate endpoints and assessment pathways |
| Affordability (price, cost and funding | Challenges concerning the pricing, funding and affordability of ATMPs, including the application of innovative payment models |
| Availability (legally available) | Non-regulatory challenges to the product being available within countries, such as those related to cross-border healthcare and hospital exemptions |
| Accessibility (accessible by patients) | Administrative, service capacity and geographic challenges that delay or prevent patient access to ATMPs |

### Identification of challenges and proposals for improving patient access

Primary and secondary research was conducted to identify challenges to patient access to ATMPs and potential solutions. Secondary research was conducted to create a database of conceptual and country-specific challenges. This research included:

- A targeted literature search
- Reviewing outputs from other initiatives (e.g., ARM's "Recommendations for Timely Access to ATMPs in Europe" and EUCOPE's "Gene & Cell Therapy – Pioneering Access for Ground-Breaking Treatments")
- Assessing pathways through which patients access ATMPs in the countries of interest
- Reviewing HTA and P&R decisions for existing ATMPs

Challenges and potential solutions were supplemented, assessed and prioritised through a review process including:

- Members of the Working Group (including EURORDIS, trade associations, affiliated NGOs and 18 member companies)
- Country-specific patient associations
- Country level decision makers, such as policymakers, HTA bodies and budget holders
- Experts and advisors, such as healthcare professionals, patient representatives, P&R system experts, ATMP technical experts, economists and academics

Following stakeholder engagement, the challenges and solutions were refined and prioritised to reflect the perceived importance in improving patient access and feasibility of implementation. Therefore, the challenges in this report are not exhaustive of all identified through primary and secondary research but represent the most important issues as determined by stakeholders.

The outputs from this process have been summarised in this report as a basis for discussion within multi-stakeholder meetings in each country and at European level.

## ASSESSMENT

**Impact**: 

| Challenge | | Proposed solution | | Feasibility |
|---|---|---|---|---|
| **AS1.** | The Austrian government is implementing legislation that ensures products are assessed and prices are negotiated in the EKO, but ATMPs are unlikely to be considered in this pathway | **AS1.** | Pharmig should request clarity on the ongoing reform pathways. Including ATMPs in the pathway would help reduce the burden on single hospitals | + |
| **AS2.** | HTA assessment is currently not applicable to ATMPS as they are considered hospital products | **AS2.** | Creation of a clear HTA pathway and framework for hospital products, informing direct negotiations, including innovative payment options | + |

The working group assessment of the **impact** of the challenge relate to all challenges in each domain. The working group assessment of **feasibility** relates to the individual or groups of proposed solutions.

### Working group identified assessment challenges

#### Challenge AS1.

***The Austrian government is implementing legislation that ensures products are assessed and prices are negotiated in the EKO, but ATMPs are unlikely to be considered in this pathway.***

Assessment of ATMPs in Austria poses a challenge to patient access, primarily due to a lack of clear assessment pathway. Although the Austrian government is implementing legislation to ensure products are assessed and prices are negotiated in the EKO (Erstattungskodex; reimbursement list), ATMPs are not mentioned explicitly and are unlikely to be considered in this pathway.

#### Proposed solution AS1.

***Pharmig should request clarity on the ongoing reform pathways. Including ATMPs in the pathway would help reduce the burden on single hospitals.***

Companies are asking for HTA evaluation of products and requesting clarity on ongoing reform projects in Austria in terms of ATMP assessment. More specifically, Pharmig, a voluntary organization representing the interests of the pharmaceutical industry, should request clarity on reform pathways that are in progress. Since the hospital route is currently relied upon for ATMP assessment, including them in the new pathway would help to reduce the burden on individual hospitals.

The solution is feasible from a manufacturer perspective, but it is uncertain if this is also the case for hospitals. The ability to consider ATMPs in this pathway also depends on the number of treatment centres available. This may pose difficulty for innovative pricing arrangements such as outcome-based agreements. Although there is recognition that there is a need for changes in the assessment process and reforms are in progress, no formal decisions have yet been made.

**Feasibility:** +
**Stakeholders:** Trade associations (Pharmig), Ministry of Health
**Timeline:** 6–18 months

**Challenge AS2.**

***HTA assessment is currently not applicable to ATMPS as they are considered hospital products.***
HTA assessment is not applicable to hospital products. As ATMPs currently carry this designation, they are assessed and negotiated on a hospital-by-hospital basis. There is a reliance on direct negotiations between manufacturers and hospitals to secure patient access. Such negotiations can be inconsistent and create a challenge for hospitals and manufacturers due to the time and resources required for each hospital.

A standardised, central process of transparent decision making, as suggested in the 2018 Austria HTA report on highly priced medicines, may need to be implemented to speed up the process of ATMP assessment. The report suggests approaches such as a central evaluation board, which uses existing infrastructure and is thus less resource intensive to implement.

A centralised national procedure would be feasible, particularly if it could be built into the existing infrastructure without the need for large structural change. However, there remains no consistent method for evaluating hospital drugs in Austria, which poses a challenge for creating standardised procedures

**Proposed solution AS2.**

***Creation of a clear HTA pathway and framework for hospital products, informing direct negotiations, including innovative payment options.***

The creation of a clear HTA pathway and framework to inform direct negotiations could help to speed up the assessment process. Such a framework should include innovative payment options, which are essential for ATMPs and should be developed with consultation from payers.

Although dedication of resources would be required to create an effective HTA pathway and framework for the hospital route, this should be achievable providing there is adequate will and agreement regarding its necessity.

**Feasibility: +**
**Stakeholders:** Trade associations (Pharmig), Ministry of Health
**Timeline:** 6–18 months

## AFFORDABILITY

**Impact:** 

| Challenge | | Proposed solution | | Feasibility |
|---|---|---|---|---|
| **AF1.** | Affordability issues for hospitals have not been identified; however, more high-price products on the market may impact this, creating a need to reduce the burden on local budgets | **AF1.** | Innovative funding options should be explored for potential future need, such as a national budget for ATMPs | ++ |

The working group assessment of the **impact** of the challenge relate to all challenges in each domain. The working group assessment of **feasibility** relates to the individual or groups of proposed solutions.

### Working group identified affordability challenges

#### Challenge AF1.

***Affordability issues for hospitals have not been identified; however, more high-price products on the market may impact this, creating a need to reduce the burden on local budgets.***

In the current system, funding is most likely to be via reformed security funds (health insurance), but this would pose challenges, such as how to allocate funds between hospitals/treatment centres. Associated costs with ATMPs in terms of treatment are high, and there is a lack of clarity as to what exactly these costs might entail. Although affordability issues for hospitals have not been identified, the increasing number of high-price products on the market may pose a future challenge for ATMPs in Austria and create a need to reduce the financial burden on regional budgets, which are the payers for hospital products. Pricing reform that is currently in progress requires products not applying for EKO inclusion to be priced at the EU average price, which may pose further challenges for expensive products such as ATMPs.

#### Proposed solution AF1.

***Innovative funding options should be explored for potential future need, such as a national budget for ATMPs.***

Innovative funding options such as managed entry agreements (MEAs) may help manage the cost of greater numbers of high-priced products as more ATMPs come forward. Pricing reforms are already in progress and hospitals have shown a willingness to use outcome-based agreements, so may also be open to other innovative funding schemes.

An additional option is to have a national-level ATMP funding option. As patients may be required to travel between regions to specialist centres, patient movement and funding is better coordinated at the national level. It is possible to incorporate ATMPs into a national process within a regional system. Spain, for example, has a regional pricing and reimbursement process, and successfully introduced a financing model for reimbursement of ATMPs and other high-cost medicines at a national level.

**Feasibility:** ++
**Stakeholders:** Trade associations (Pharmig), Ministry of Health, regional budget holders
**Timeline:** 6–18 months

## AVAILABILITY

**Impact:** 

| Challenge | | Potential solution | | Feasibility |
|---|---|---|---|---|
| **AV1.** | Patients have received access to treatment via cross-border initiatives | **AV1.** | "Gemeinsam Grenzenlos Gesund" (Unlimited Health Together) cross-border scheme between Austria and Czech Republic could be reconfigured for ATMPs | +++ |
| **AV2.** | Hospital exemption policies are clearly defined in Austria, but impact on commercial products is less understood | **AV2.** | EU should be pressed to provide guidelines to prevent marketed products from competing with products with hospital exemptions for the same medical indication | + |

The working group assessment of the **impact** of the challenge relate to all challenges in each domain. The working group assessment of **feasibility** relates to the individual or groups of proposed solutions.

### Working group identified availability challenges

#### Challenge AV1.

***Patients have received access to treatment via cross-border initiatives.***

Patients have received access to treatment via cross-border initiatives. Cross-border healthcare initiatives are used in both directions in Austria, and so are less challenging than in other countries, but improvements to the logistical structure could still be made to more specifically incorporate ATMPs.

#### Proposed solution AV1.

***"Gemeinsam Grenzenlos Gesund" (Unlimited Health Together) cross-border scheme between Austria and Czech Republic could be reconfigured for ATMPs.***

From the manufacturer's perspective, this is not considered a major challenge. For further enhancement, the "Gemeinsam Grenzenlos Gesund" (Unlimited Health Together) cross-border scheme between Austria and Czech Republic could be reconfigured for ATMPs specifically to better allow access to specialist treatment centres for patients in these countries.

**Feasibility:** +++
**Stakeholders:** Ministries of Health
**Timeline:** 6–18 months

#### Challenge AV2.

***Hospital exemption policies are clearly defined in Austria, but impact on commercial products is less understood.***

Hospital exemption policies are clearly defined in Austria, but the impact on commercial products is less understood. This could act as a disincentive for manufacturers to develop ATMPs to regulatory and manufacturing standards, as commercial opportunities could be challenged by unauthorised, individual products which have not undergone the rigorous regulatory assessment necessary to achieve Marketing Authorisation.

**Proposed solution AV2.**

***EU should be pressed to provide guidelines to prevent marketed products from competing with products with hospital exemptions for the same medical indication.***

The EU should be pressed into issuing guidelines defining more specifically the scope and requirements for hospital exemptions for ATMPs, stating clearly that when patients have access to an ATMP with a Marketing Authorisation, countries should not authorise hospital exemptions for the same medical indication. The guidelines should also address the possible interference of hospital exemption with recruitment of patients in clinical trials for the same indication. This echoes the ARM position on hospital exemptions.

**Feasibility: +**
**Stakeholders:** Patient association (EURORDIS), trade associations, EU parliament
**Timeline:** 6–18 months

## ACCESSIBILITY

**Impact:** 

| Challenge | | Proposed solution | | Feasibility |
|---|---|---|---|---|
| **AC1.** | Access to ATMPs remains uncertain in Austria | **AC1.** | The NKSE has been established to focus on improving access to products for rare disease | + |

The working group assessment of the **impact** of the challenge relate to all challenges in each domain. The working group assessment of **feasibility** relates to the individual or groups of proposed solutions.

### Working group identified accessibility challenges

#### Challenge AC1.

***Access to ATMPs remains uncertain in Austria.***

Accessibility to ATMPs in Austria poses one of the largest challenges for patient access. There is recognition that access to products for rare disease (including ATMPs) is uncertain.

#### Proposed solution AC1.

***The NKSE has been established to focus on improving access to products for rare disease.***

The National Centre for Coordination of Rare Diseases (NKSE) has been established to focus on improving access to products for rare disease. NKSE works to improve the care of people with rare diseases in Austria and to facilitate the networking of actors in the field of rare diseases. At the beginning of this initiative, a needs assessment titled "Rare Diseases in Austria" was conducted, and a report on this was published at the end of 2012. This created the basis for the National Plan of Action for Rare Diseases (NAP.se), published in 2015.

The NKSE is already established and carries responsibility for monitoring implementation of the NAP.se. This includes, for example, supporting the designation process for specialised national rare disease facilities, facilitating connection of as many facilities as possible to the European Reference Networks (ERN), mapping rare diseases in the Austrian health and social system, and improving access to therapies. As the remit of NKSE is to improve access to orphan drugs, it should be tasked with preparing the Austrian system for ATMP delivery. Engagement with manufacturers will establish the likely infrastructural, resource and expertise that will be required for ensuring ATMPs are accessible to patients in Austria.

**Feasibility:** +
**Stakeholders:** NKSE, patient associations, individual companies
**Timeline:** 6–18 months

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## Appendix

## Country profile

| | |
|---|---|
| Market type | Comparative clinical effectiveness |
| Position in launch sequence | Early |
| Previous experience with ATMPs | Yes |

| | Status | Note |
|---|---|---|
| Strimvelis | Not evaluated | ATMPs are considered hospital products only and thus negotiations take place between the manufacturer and hospitals directly |
| Holoclar | Not evaluated | |
| Zalmoxis | Not evaluated | |
| Glybera | Not evaluated | |
| Imlygic | Not evaluated | |
| Provenge | Not evaluated | |
| MACI | Not evaluated | |
| ChondroCelect | Not evaluated | |
| Yescarta | Not evaluated | |
| Kymriah | Not evaluated | |
| Luxturna | Not evaluated | |