

2021

ADVANCED THERAPIES MEDICINAL PRODUCTS:

NEW PAYMENT & FUNDING APPROACHES

*A position paper prepared by the
EUCOPE Working Group on Gene
& Cell Therapies.*



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ATMPs: NEW PAYMENT & FUNDING APPROACHES

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2. EXECUTIVE SUMMARY

The recent years have seen a number of high-end innovative therapies becoming accessible to patients in Europe. These products offer groundbreaking new opportunities to patients living with rare diseases or cancer, with the capacity of often one-time disease-modifying and potentially curative treatments.

This new generation of therapies calls for a new paradigm of care, where it is necessary to consider the affordability issues for health systems, from a long-term perspective.

Advanced Therapies Medicinal Products (ATMPs) have the potential to have a **transformative impact**, not just in terms of **improved patient outcomes** and a reduced burden on families, but also through the **long-term savings** conferred on healthcare budgets and other sectors of the economy.

A **collaborative approach** to innovative payments models such as **outcome-based agreements** and **new funding schemes** may play a crucial role in **alleviating challenges on the uncertainties of data and affordability** and ensuring payers have the **confidence to invest** in one-time treatments, enabling patients to benefit from effective ATMPs, and position Europe as an **attractive research leader**.

To ensure timely patient access, EUCOPE calls for a **coherent approach** with the scientific community, treatment centres, payers and manufacturers to **define key parameters, criteria and assessment over time** to establish **outcome-based models**, increase the use of **Real-World Evidence** and set up specific **ATMPs funds** within the healthcare systems.



There is no single approach to ensuring access to ATMPs. A common understanding of the promise of the science of ATMPs as well as of the disruption to historic patterns of funding, payment mechanisms and healthcare delivery will help to create a more receptive environment for these therapies.

Working together to identify solutions to funding and payment models will ensure appropriate prices for ATMPs are achieved that are both affordable to healthcare systems and can incentivise research and innovation in this area.

In the past, payment considerations have proven to be barriers to timely patient access to novel therapies, a risk that may only be exacerbated for gene and cell therapies. **With pioneering approaches to reimbursement and sustainable funding models, patients can access these game-changing ATMPs.**

3. INTRODUCTION

ATMPs are medicines for human use that are based on genes, tissues or cells. They offer groundbreaking new opportunities for the treatment of disease and injury¹, bringing with them the promise not only of treatment to manage the symptoms of severe, disabling or life-limiting conditions but also the promise of one-time disease-modifying and potentially curative treatments.

These treatments can transform and save lives.

Europe plays a leading role in the scientific and regulatory innovation in the ATMPs area. The industrial footprint of ATMPs developers in Europe is becoming increasingly significant.

However, the complexity and inappropriateness of pricing and reimbursement systems in the different Member States of the European Union to fully capture the value of ATMPs may not always guarantee equal access to all patients in Europe.

VALUE PROPOSITION – LONG TERM PERSPECTIVE

This new generation of therapies calls for a new paradigm of care, where it is necessary to consider the affordability issues for health systems, from a long-term perspective. ATMPs have the potential to have a transformative impact, not just in terms of improved patient outcomes and a reduced burden on carers, but also through the long-term savings conferred on healthcare budgets and other sectors of the economy.

A collaborative approach to funding/payment mechanisms can ensure appropriate pricing schemes, where adequate incentives for research and innovation are in place.

¹ <https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview>, accessed 18 March 2020.



4. CURRENT SYSTEMS – NEED FOR A CHANGE

ATMPs offer the opportunity to change traditional patterns of delivering healthcare often focused on managing symptoms rather than potentially effecting a cure. Reimbursement processes and uptake of innovative medicines are based on more traditional medicines rather than on treatments intended for one-time use. There is a concern that these therapies coming to market over the next several years will represent a significant challenge for health care systems and payers, and that their widespread uptake would remain uncertain^{2,3}.

The transformative nature of these new therapies might have as a consequence two main issues, resulting in a challenging path to reimbursement and uptake: **data uncertainty** and **affordability**.

Innovative payments models such as outcome-based agreements and new funding approaches may play a crucial role in ensuring payers have the confidence to invest in one-time treatments, enabling patients to benefit from effective ATMPs, and position Europe as an attractive research leader.

5. DATA UNCERTAINTY

Because ATMPs predominantly aim to provide solutions for rare diseases or ultra-rare diseases, the patient population may be scarce, and the evidence generated by clinical trials can trigger some uncertainty from payers and decision-makers.

A way to alleviate the challenges from HTA and payers' institutions on the uncertainties of clinical trials outcome in real life, or on the long-term outcome, might be to tie reimbursement to patient outcomes.

OUTCOME-BASED MODEL

Reimbursement payments under this model are conditional upon the patient reaching specific clinical outcomes by set deadlines. Depending on the model, a patient's failure to meet the specified clinical outcome can result in the manufacturer having to refund payments received and/or forfeit any subsequent payments⁴. These approaches can be a way to balance the financial risks between payers and ATMPs developers.

² EUCOPE Position Paper on Gene and Cell Therapies, November 2018, accessed 9 July 2020, https://www.eucope.org/wp-content/uploads/2019/03/eucope_genecell_therapy_november2018.pdf

³ Due to large quantity of efficacy in life-threatening or severely impairing diseases, EMA gives marketing authorisations based on studies with small sample size and without waiting confirmation of life time effect – with some remaining uncertainties for the HTA and pricing steps.

⁴ Bristow, Gene and Cell Therapies, Blockbuster prices and licensing challenges, May 2020, accessed 9 July 2020, <https://www.bristows.com/news/cell-and-gene-therapies/>



The experience from CAR-T cell therapies⁵ demonstrates an interest in outcome-based reimbursements in Europe. Following their marketing authorisation approval by the European Commission in August 2018, Kymriah® (tisagenlecleucel) and Yescarta® (axicabtagene ciloleucel) managed to successfully obtain national reimbursement in Spain under a scheme including partial payment at the time of infusion, followed by a subsequent payment depending on each individual patient outcome⁶. For a country not widely known for fast patient access, this model enabled a much swifter process for patients.

Under these conditions, **the payer does not pay any longer for the breakthrough medicine, but for the health outcome proven in medical practice**, as well as for non-expenses related to health care costs that are no longer needed (savings)⁷.

Whereas these agreements based on patient-level outcomes bear great benefits for all parties, **EUCOPE call for a collaborative approach⁸ with the scientific community, treatment centres, payers and manufacturers to define the key parameters of such models for these to be completely efficient⁹.**

REAL-WORLD EVIDENCE COLLECTION



⁵ Chimeric Antigen Receptor T (CAR-T) cell therapies

⁶ APM Health Europe, 63646, 10 July 2019

⁷ Maes I, Boufraioua H, Schoonaert L., Van Dyck W, Innovative solutions for paradigm changing new therapies – Policy report based on multi-stakeholder round tables. 2019

⁸ A multi-stakeholder forum, such as the European Alliance for Transformative Therapies, could host these discussions, www.transformativetherapies.eu

⁹ The parameters to define could include, e.g.: direct or surrogate endpoint, the timeframe, the source of the outcome data, the payment flow to favour.

The collection and use of Real-World Evidence (RWE) is a useful tool to address uncertainties on the transposition of short and long-term clinical trials outcome, quality of life and financial implications for healthcare budgets, by adjusting the cost to the real value for the patients and society.

Whereas data collection models bear many advantages, we see disparities in implementation at Member States level, creating differences between countries, challenges for manufacturers and, eventually, barriers to availability for patients.

An important hurdle to the harmonisation of RWE use is the different sources and requirements for data collection¹⁰. The variation in data quality can become a significant challenge in the submission of data to payers towards the confirmation of the assumptions claim.

Data Uncertainty - Recommendations

- EUCOPE recommends agreeing on **key parameters for outcome-based models**, including on endpoints, timeframe and outcome data;
- EUCOPE recommends the creation of **a multi-stakeholder EU learning network on RWE** to generate RWE that meets the needs of patients and healthcare systems¹¹;
- EUCOPE calls for the development of a European framework to foster artificial intelligence and data mining in existing healthcare data sources such as Electronic Health Records or claims database;
- EUCOPE **calls on Member States and the EMA for more guidance on data and RWE generation** and alignment on data collected at time of marketing authorisation between EMA and HTA agencies to foster harmonization of data sets and avoid country by country data collection initiatives;
- Similarly, patient education is required on the importance of post-treatment follow-up to ensure meaningful data collection¹²;

6. AFFORDABILITY ISSUES

Even though the potentially curative nature of ATMPs and their life-changing impact can hint at long-term cost-effectiveness, the high upfront costs and the incoming wave of new therapies might raise concerns on the sustainability of some healthcare systems.

¹⁰ Payer registry, claim database, regulatory registry, company registry, etc

¹¹ RWE4Decisions Call to Action, <https://rwe4decisions.com/call-to-action/>

¹² Rare IMPACT, Country Report : Germany, 2020, accessed 9 July 2020, <https://rareimpact.eu/challenges-solutions/germany>



Payers and policymakers need to create a balance between ensuring patient access to innovation and maintaining financial sustainability¹³ for both health systems and ATMPs developers. New financing models for high-cost therapies can mitigate the short-term budget impact of high upfront cost.

The challenges caused by the affordability of ATMPs may vary from one country to another, and many solutions do exist to overcome those challenges. In this paper, we chose to focus on annuity payments and specific funds.

ANNUITY PAYMENTS



The above-mentioned outcome-based models can be blended to create payment plans which combine annuity-style payments with rebates and outcomes-dependent instalments¹⁴. Annuity models would spread up-front payments over several years, facilitating appropriate resource allocation and affordable access¹⁵ and reduce the uncertainty around long-term performance and value¹⁶.

In April 2020, Luxturna® (voretigen neparvovec) has been granted reimbursement in Denmark following an annuity model linked to outcomes. Regions in Denmark will pay in instalments, patients must check at set times, and if it turns out that the drug does not have the desired effect, the subsequent instalments are not paid.¹⁷

¹³ Hanna E, et al. Funding breakthrough therapies: A systematic review and recommendation. Health Policy (2017), <https://doi.org/10.1016/j.healthpol.2017.11.012>

¹⁴ Bristow, Gene and Cell Therapies, Blockbuster prices and licensing challenges, May 2020, accessed 9 July 2020, <https://www.bristows.com/news/cell-and-gene-therapies/>

¹⁵ Alliance for Regenerative Medicine Report, Getting Ready: Recommendations for Timely Access to Advanced Therapy Medicinal Products (ATMPs) in Europe

¹⁶ Jesper Jørgensen & Panos Kefalas (2017) Annuity payments can increase patient access to innovative cell and gene therapies under England's net budget impact test, Journal of Market Access & Health Policy, 5:1, 1355203, DOI: 10.1080/20016689.2017.1355203

¹⁷ <https://medicinraadet.dk/nyheder/2020/medicinradet-anbefaler-luxturna-som-standardbehandling>



However, the compliance of annuity payments with public accounting rules, as well as the **administrative burden** generally involved with this kind of contracts might discourage manufacturers, and other stakeholders, to enter into such negotiations.

NEW FUNDING APPROACHES

Another interesting approach to payment of ATMPs is the creation of specific “ATMP funds”. Some countries are already experimenting with such techniques¹⁸, showing interesting results.

The Cancer Drug Fund (CDF)^{19,20} in the UK, for instance, allows funding for rare cancer therapies showing promising results in trials, but without sufficient evidence for a positive decision. Should the ATMP be recommended for observation in the CDF, it gives then more time to collect evidence about its efficacy, allowing reviewers to decide whether it meets the value for money criteria set out by NICE²¹.

In Italy, a specialist fund for “expensive innovative drugs”, provides for €500m per year for oncology drugs and €500m for non-oncology drugs, valid 3 years from launch²².

A good example comes from Italy where CAR-Ts Yescarta® (Axicabtagene Ciloleucel) and Kymriah® (tisagenlecleucel) have been granted innovative medicine status for 12 months, giving access to the EUR1bn ‘innovative drugs fund’, coupled to coverage in an outcome-based model.

In Germany, new funding rules were recently implemented to adapt to the rise of ATMPs, introducing partially pooling the budget of patients with a yearly cost of care above €100.000 among all the sick funds²³.

Based on the experience from established **specific funds**, EUCOPE recommends the creation of **ATMPs funds to ensure patient access to this disruptive innovation**, addressing an important gap of the current pricing models. In this view, we **recommend close collaboration between all stakeholders to establish clear eligibility criteria and assessment over time**.

CROSS-BORDER HEALTHCARE SUPPORT

¹⁸ UK, Italy, Germany.

¹⁹ Cancer Research UK, accessed 10 July 2020, <https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/access-to-treatment/cancer-drugs-fund-cdf>

²⁰ Intended to become the Innovative Medicines Funds, with broader coverage than oncology.

²¹ National Institute for Health and Care Excellence, Department of Health, England.

²² Rare IMPACT, Country Recommendations : Italy, accessed 10 July 2020, https://rareimpact.eu/site/wp-content/uploads/2020/04/RARE-IMPACT-Country-Assessments-Italy_v1_2020-04-28.pdf

²³ <https://www.bundesgesundheitsministerium.de/fairer-kassenwettbewerb-gesetz.html>



Due to the rare nature of a large part of the diseases that ATMPs will treat, treatment centres might not become available in every Member State (not in parallel or not at all). As such, patients will be relying on **cross-border treatment** to access these medicines.

To ensure timely and easy patient access, **EUCOPE strongly advocates for Member States, the EU Institutions and stakeholders to get together and examine the opportunity to set up an EU fund enabling cross-border treatment** for ATMPs, rare and genetic diseases, building on the momentum created by the EU4Health proposal from the European Commission, and inspired by its objective of coordinated action.

Affordability – Recommendations

- EUCOPE recommends **further dialogue with accounting institutions and governments** to adjust the compliance of annuity payments with public accounting rules;
- EUCOPE recommends the **creation of ATMPs funds** to ensure patient access to this disruptive innovation;
- EUCOPE calls for close collaboration between all stakeholders to establish clear **eligibility criteria and assessment over time** of these specific funds;
- EUCOPE strongly advocates to set up an **EU fund enabling cross-border treatment**.

7. CONCLUSION

There is no single approach to ensuring access to ATMPs. A common understanding of the promise of the science of ATMPs as well as of the disruption to historic patterns of funding, payment mechanisms and healthcare delivery will help to create a more receptive environment for these therapies.

The unprecedented public health crisis resulting from the COVID-19 pandemic certainly put our healthcare systems to the test. Many Member States now realize the paramount importance of health and the long-term value of a healthy society.

While the European Commission is calling in its Pharmaceutical Strategy to consider changing business and payment models in the greater accessibility debate, we feel the time is right to initiate a discussion with all relevant stakeholders.

Working together to identify approaches to funding and payment models will ensure appropriate prices for ATMPs are achieved that are both affordable to healthcare systems and can incentivise research and innovation in this area.

In the past, payment considerations have proven to be barriers to timely patient access to novel therapies, a risk that may only be exacerbated for gene and cell therapies. **With pioneering approaches to reimbursement and sustainable funding models, patients can have access these game-changing ATMPs.**