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Pricing and Reimbursement Challenges for ATMPs: Does Early Regulatory Approval Mean Faster Market Access?

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Advanced Therapy Medicinal Products (ATMPs) represent a cutting-edge category of innovative therapies that utilize the properties of cells, genes, or tissues to restore, correct, or modify biological functions in patients.[1] The development of ATMPs has significantly advanced the field of medicine, providing new treatment options for a variety of conditions, including rare diseases.[2] ATMPs have emerged as disruptive health technologies, presenting challenges in terms of value assessment and pricing, with their high costs raising critical concerns regarding access and affordability.[3] [2]These innovative therapies offer promising avenues for addressing unmet medical need and potentially providing cures or disease-modifying treatments across various conditions.

The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) aim to ensure that only medicines with a favourable balance of benefits and risks are authorized for marketing. This requires the assessment of three criteria: quality, efficacy, and safety.[4,5] However, conducting the necessary studies to evaluate these criteria can be costly and time-consuming. Incentives have been put in place to encourage research and innovation in areas with high unmet medical need, which can result in a flexibility of regulatory requirements and shortened assessment timelines to avoid delays in access to treatment, especially for serious and urgent illnesses.

Recognizing the transformative potential of ATMPs, the EMA has made significant efforts to expedite the approval process for these advanced therapies. The EMA has introduced the hospital exemption pathway, which allows for the approval of ATMPs under specific circumstances, such as for patients with certain rare diseases.[6]

Abbreviations: ATMP, advanced therapy medicinal product; eCTD, electronic Common Technical Document; EMA, European Medicines Agency; FDA, U.S. Food and Drug Administration; HTA, health technology assessment; HST, highly specialized technology; IMAC, International Market Access Consulting; MEA, managed entry agreements; NICE, Additionally, implementing value-based pricing models; RTOR, Real Time Oncology Review.

[7]This acceleration involves providing incentives and flexibilities to encourage research and innovation, particularly in areas with high unmet medical needs. By shortening assessment timelines and offering conditional or exceptional authorizations, the EMA aim to streamline access to ATMPs, especially for severe and urgent illnesses.

The FDA has also been implementing strategies to enhance the review process of ATMPs. Several expedited review programs exist to facilitate earlier access to novel treatments by shortening review duration, promoting the development process, and allowing conditional approval based on surrogate or intermediate clinical endpoints.[7,8] One significant improvement is the FDA's adoption of Real-Time Oncology Review (RTOR) pilot programs. RTOR allows the FDA to review individual sections of electronic Common Technical Document (eCTD) modules for oncology drugs, rather than requiring the submission of complete modules upfront, thereby expediting the review process.[9] As well, the FDA has been collaborating with the EMA to harmonize standards for the development of ATMPs, facilitating international information exchange.[10]

Rapid access to new medicines from the regulatory side means that in most cases, more uncertainty is accepted at the time of approval, However, while the accelerated approval processes from the FDA and EMA facilitate marketing approval, this does not necessarily translate in more rapid patient access to new ATMPs. In many cases, early regulatory approval brings about several challenges in the pricing and reimbursement process. The acceptance of more uncertainty at the time of regulatory approval may lead to heightened expectations and associated high prices for these therapies. In cases where there are no therapeutic alternatives available and significant unmet medical needs exist, stakeholders may perceive accelerated regulatory authorizations as indicating high value, which can result in pressure for tough negotiations and high prices.

ATMPs pose unique challenges for reimbursement due to their innovative nature, high costs, and limited long-term data on efficacy.[1] Traditional reimbursement mechanisms may not be well-suited to accommodate the high upfront costs and long-term benefits of ATMPs.[11] The unique value proposition of ATMPs, including potential long-term efficacy and reduced need for other healthcare services, complicates the assessment of their cost-effectiveness for reimbursement purposes.[11] Additionally, the limited evidence base and uncertainties surrounding ATMPs further complicate reimbursement decisions.[12]

Several strategies can be implemented to enhance HTA approaches and ensure appropriate pricing and reimbursement. Collaboration and harmonization among stakeholders, including

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manufacturers, regulators, payers, and HTA bodies, are crucial for streamlining processes.[13] By fostering collaboration, stakeholders can work together to develop standardized procedures for pricing and reimbursement, ensuring a consistent approach.[14]

Investing in real-world evidence generation post-approval is essential to address uncertainties in clinical effectiveness assessment of ATMPs.[15] By collecting data on long-term outcomes and real-world performance, stakeholders can make more informed decisions regarding the value and effectiveness of these therapies.[15]

Additionally, implementing value-based pricing models and pricing arrangements have been proposed. One strategy involves the implementation of managed entry agreements (MEAs) for pharmaceuticals, including ATMPs, which aim to address uncertainties around the value of new therapies by allowing reimbursement while gathering additional data post-launch.[16] MEAs can help strike a balance between providing patients access to innovative treatments and the need for further evidence on long-term outcomes and cost-effectiveness.[1,17] [18]

Establishing outcome-based agreements and risk-sharing mechanisms between manufacturers and payers can help mitigate uncertainties in clinical effectiveness assessment and manage risks associated with ATMPs.[19] These agreements tie reimbursement to predefined clinical outcomes, ensuring that payment is contingent on the therapy delivering the expected results.[19] Risk-sharing agreements involve sharing the financial risk based on the therapy's performance, ensuring that payers only pay for successful outcomes.[19]

In summary, adapting HTA approaches, fostering collaboration, generating real-world evidence, implementing value-based pricing, and establishing outcome-based agreements and risk-sharing mechanisms are essential strategies to address the challenges posed by ATMPs. These approaches can enhance the evaluation of ATMPs, ensure appropriate pricing and reimbursement, and facilitate access to innovative therapies while managing uncertainties and risks effectively.

International Market Access Consulting (IMAC) has been at the forefront of securing reimbursement for ATMPs, securing one of the first Highly Specialized Tehcnology (HST) positive recommendations from NICE in 2019. Since then, IMAC has supported successful reimbursement for many ATMPs for the treatment of rare diseases. IMACs senior experts, including our Principal Health Economist and HEOR team, Evidence Generation Team, Senior Strategists, and experts in international Market Access work together to overcome the special challenges that ATMPs pose for agencies tasked with pricing and reimbursement evaluations.

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ATMPs offer innovative solutions for various conditions and represent a significant advancement in medical treatment. They represent a promising frontier in healthcare, offering innovative treatment options for rare diseases and other conditions. However, their high costs, unique characteristics, and challenges in reimbursement highlight the need for continued efforts to optimize access to these transformative therapies.

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