The expediting marketing authorisation pathways for patients' access to advanced therapies

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BACKGROUND & AIM

Medicinal products based on genes, cells and tissues of human or animal origin are being developed to treat severe diseases that conventional treatments have failed to treat or that have no available and satisfactory treatments, such as rare, genetic, or neurodegenerative diseases.

The risks they raise as innovative and complex medicines but also the therapeutic promises they offer have led to their specific regulation as Advanced Therapy Medicinal Products (ATMPs) in the European Union (EU). ATMPs include 4 legal sub-categories : Cell-therapy medicinal products (CTMP), Gene therapy medicinal products (GTMP), Tissue engineered products (TEP) and Combined (Comb.) ATMPs. They are especially submitted to the centralised procedure of Marketing Authorisation (MA) issued by the European Commission. This procedure aims not only to ensure high quality, safety and efficacy for ATMPs with a positive risk-benefit balance to be commercialised, but also a wide access to these medicines for EU patients. To date, 26 ATMPs have been granted a MA in the EU. Nevertheless, this procedure alone is not always sufficient to allow the commercialisation of ATMPs, and many of them require expediting pathways or regulatory support schemes for innovative medicines to be commercialised.

What are these expediting pathways and how much have they been used for ATMPs ?

Overview of the 26 authorised ATMPs in the EU

List of ATMPs

Name	Type	Domain	MA Year	Current status
ChondroCelect	TEP	Orthopaedic	2009	Withdrawn, 29/07/2016
Glybera	GTMP	Gastrology	2012	Withdrawn, 28/10/2017
MACI	Comb. TEP	Orthopaedic	2013	Withdrawn, 01/07/2018
Provenge	CTMP	Oncology	2013	Withdrawn, 06/05/2015
Holoclar	TEP	Ophthalmology	2015	Positive
Imlygic	GTMP	Oncology	2015	Positive
Strimvelis	GTMP	Immunology	2016	Positive
Zalmoxis	CTMP	Graft. vs. host	2016	Withdrawn, 09/10/2019
Spherox	TEP	Orthopaedic	2017	Positive
Alofisel	CTMP	Gastrology	2018	Positive
Yescarta	GTMP	Immunocellular cancer	2018	Positive
Kymriah	GTMP	Immunocellular cancer	2018	Positive
Luxturna	GTMP	Ophthalmology	2018	Positive
Zynteglo	GTMP	Beta-Thalassemia	2019	Withdrawn, 24/03/2022
Zolgensma	GTMP	Muscular Atrophy	2020	Positive
Libmeldy	GTMP	Metachromatic Leukodystrophy	2020	Positive
Tecartus	GTMP	Lymphoma, Mantle-Cell	2020	Positive
Skysona	GTMP	Cerebral adreno leuko-dystrophy	2021	Withdrawn, 18/11/2021
Abecma	GTMP	Multiple Myeloma cancer of the bone marrow	2021	Positive
Breyanzi	GTMP	Blood cancer	2022	Positive
Carvykti	GTMP	Multiple Myeloma cancer of the bone marrow	2022	Positive
Upstaza	GTMP	Amino Acid Metabolism, Inborn Errors	2022	Positive
Roctavian	GTMP	Haemophilia A	2022	Positive
Ebvallo	CTMP	Lymphoprofilerative Disorders	2022	Positive
Hemgenix	GTMP	Haemophilia B	2023	Positive
Casgevy	GTMP	Beta-Thalassemia and sickle cell disease	2024	Positive

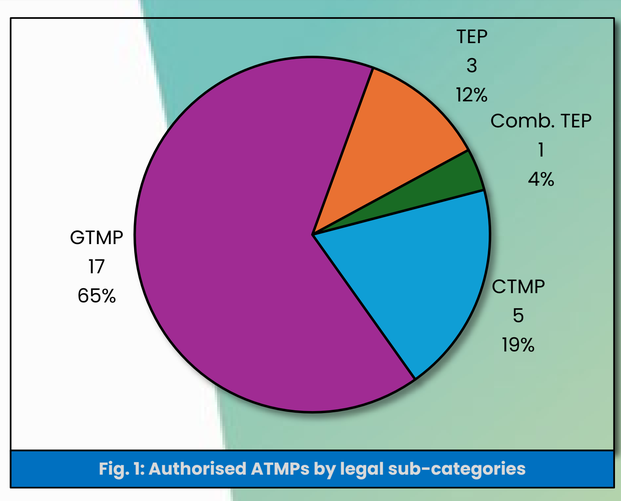


Fig. 1: Authorised ATMPs by legal sub-categories

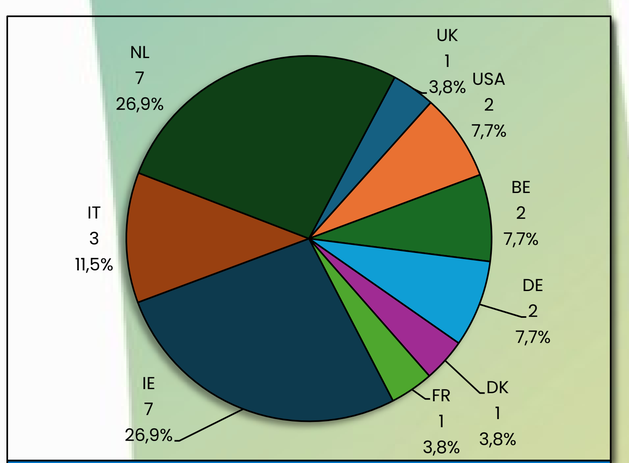
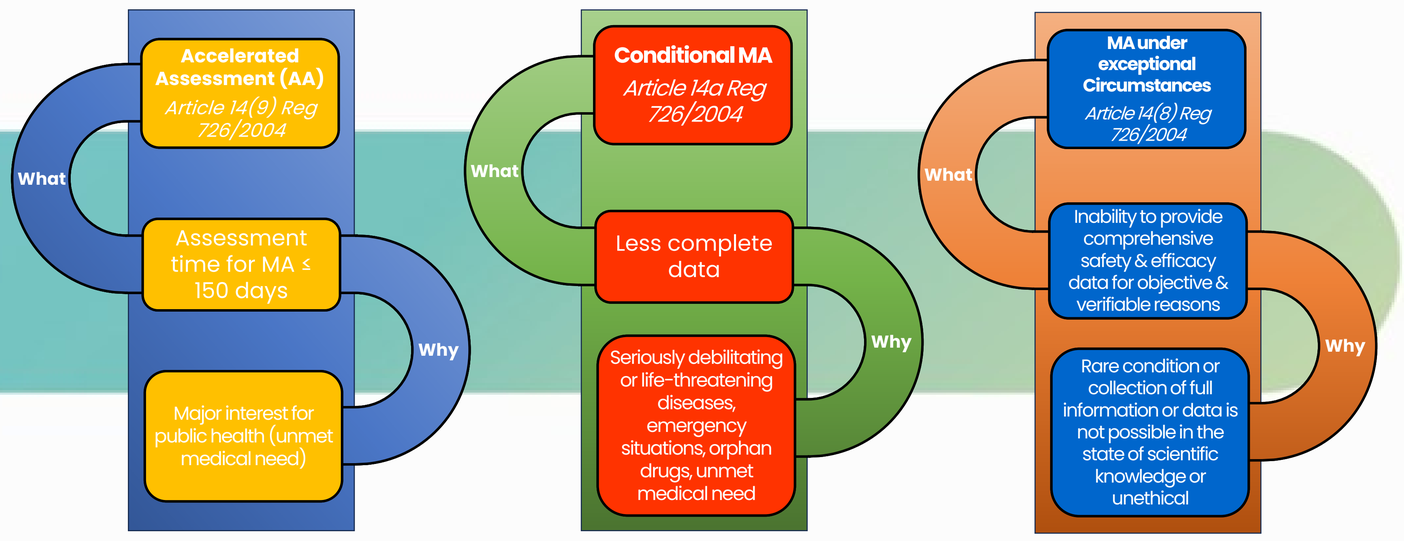
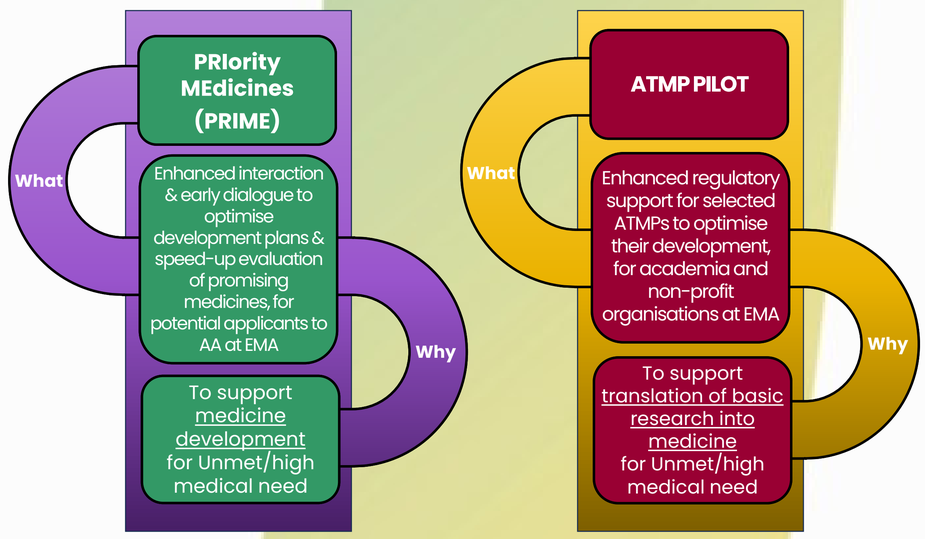


Fig. 2: Country of ATMPs MA holders

Expediting pathways



Regulatory Support schemes



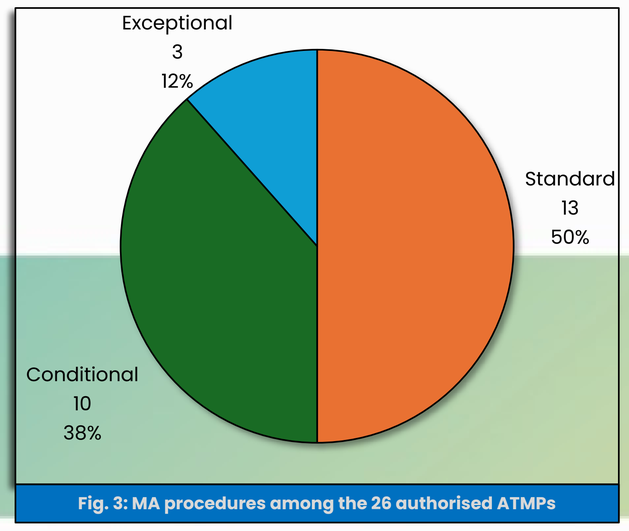


Fig. 3: MA procedures among the 26 authorised ATMPs

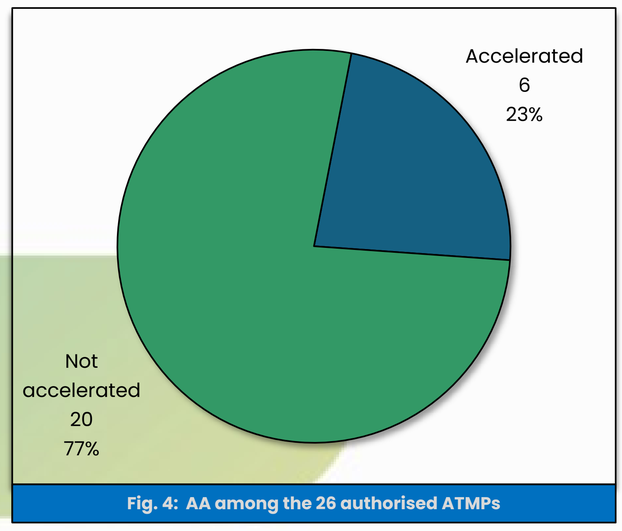


Fig. 4: AA among the 26 authorised ATMPs

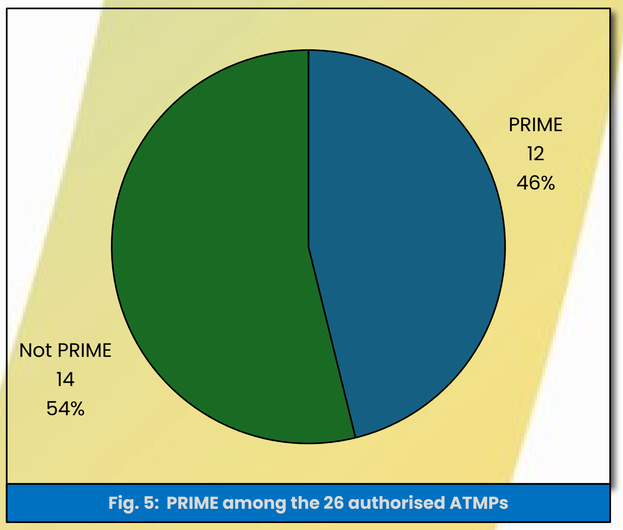


Fig. 5: PRIME among the 26 authorised ATMPs

RESULTS

- Clear increase in approvals from 2018 in various medical domains
- Most approved ATMPs are gene therapy medicinal products
- NL, where is established the European Medicines Agency from Brexit, and IE are the countries of most of MA holders among the authorised ATMPs
- Half of authorised ATMPs benefited from expediting pathways or regulatory support schemes for innovative medicines
- BUT MA withdrawn or not renewed for 7 ATMPs out of 26 authorized ATMPs

DISCUSSION/CONCLUSION

Even if the EU supports and fosters ATMPs' research, development, and access to market with regulatory tools, patients access to effective and affordable ATMP is limited by the high average cost per patient, the withdrawal of authorised ATMPs from MA holder mostly for commercial reasons, and the differences between healthcare systems and reimbursement strategies of the different Member States.

Although the standard procedure and the expediting MA pathways provide the widest commercialisation of ATMPs in Europe, patients' access to ATMPs is dependent on MA granting and on the MA holder strategy to make the product available in Europe. The latter is linked to the agreement(s) on pricing and reimbursement to provide affordable ATMPs as well as an acceptable financial benefit, including return on investment, for the MA holder.

Patients can also access ATMPs, thanks to other pathways, alternative to MA and possible under strict conditions only. However, depending on how these other pathways can be used according to the applicable national heterogenous rules (e.g., hospital exemption), they could also lead to unfair competition regarding the high requirements for MA granting.