

REAL ACCESS TO ATMPs: THE COST ISSUE

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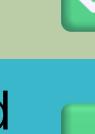
Introduction

Industry developed and manufactured Advanced Therapy Medicinal Products (ATMPs) which benefit from a centralised marketing authorisation procedure that allows commercialization in all Member States of the European Union (EU), and despite improvement in EU citizen access to ATMPs being stated as one of the two major objectives when the ATMP Regulation was released, actual patient access to ATMPs remains one of the most challenging issues to be addressed.

ATMPs include 4 legal sub-categories : Cell-therapy medicinal products (CTMP), Gene therapy medicinal products (GTMP), Tissue engineered products (TEP) and Combined (Comb.) ATMPs.

Prices of ATMPs are among the highest despite difficulties in proving long term efficacy on significant numbers of patients. Publicly accessible data show prices that vary from several hundreds of thousands euros to several million euros per treatment, with a continuous trend in increasing prices that has fuelled the concept of "financial toxicity" for those and other categories of treatments.

KNOWN PRICES OF THE 26 EU AUTHORISED ATMPs

Commercial Name	Common International Denomination (CID) & Active substance	Type	Domain(s) of application	MA Year	Current status	MA Type	Orph. Med.	Price
ChondroSelect™	Characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins	TEP	Orthopaedic	2009	Withdrawn 29/07/2016	Standard	 N/A	
Glybera™	Alipogene tiparvovec	GTMP	Gastrology	2012	Expired 28/10/2017	Exceptional	  1,318,432 €*	
MACI™	Matrix-applied characterised autologous cultured chondrocytes	Comb. TEP	Orthopaedic	2013	Expired 01/07/2018	Standard	 N/A	
Provence™	Autologous peripheral-blood mononuclear cells activated with prostatic acid phosphatase granulocyte-macrophage colony-stimulating factor (sipuleucel-T)	CTMP	Oncology	2013	Withdrawn 06/05/2015	Standard	  79,953 €*	
Holoclar™	Ex vivo expanded autologous human corneal epithelial cells containing stem cells	TEP	Ophthalmology	2015	Ongoing	Conditional	  95,000 €**  88,993 €/eye (hidden discount excluded)**  72,288 – 289,151 €* – Lauertaxe at launching: 2,398.50 €** – After negotiation: 1,220.52 €**  1,858 €/vial (hidden discount excluded)**	
Imlygic™	Talimogene laherparepvec Modified herpes simplex virus	GTMP	Oncology	2015	Ongoing	Standard	  594,000 €**  594,000 € (+ hospital costs coverage in IT)**	
Strimvelis™	Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence	GTMP	Immunology (treatment of a specific form of Severe Combine Immune Deficiency or ADA-SCID)	2016	Ongoing	Standard	  594,000 €**  594,000 € (+ hospital costs coverage in IT)**	
Zalmoxis™	Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2)	CTMP	Graft vs. host disease in the context of hematopoietic cell transplantation	2016	Withdrawn 09/10/2019	Conditional	  189,475 € – 757,899 €* – Lauertaxe at launching: 163,900 €. After negotiation: 130,000 €**  149,000 €**	
Spherox™	Spheroids of human autologous matrix-associated chondrocytes	TEP	Orthopaedics	2017	Ongoing	Standard	  11,124 € (hidden procurement discount excluded)**	
Alofisel™	Daravatstrocel Allogeneic mesenchymal stem cells to treat Crohn's disease fistulae	CTMP	Gastrology	2018	Ongoing	Standard	  71,400 €* – 60,000 €**  Submitted price: 60,083 €**  54,000 €**  60,000 €/treatment**  389,130 €* – 327,000 €**  327,000 €, discount**  Confidential price + discount**  327,000 €, recently reduced to 299,000 € + 15,000 € on top of DRG**/***1	
Yescarta™	Axicabtagene ciloleucel Autologous CAR-T Cells targeting CD19	GTMP	Oncology, haematology (lymphomas various subtypes, acute lymphoblastic leukemias) Now moving in the field of auto-immune diseases	2018	Ongoing	Standard (PRIME)	  327,000 €***  275,000 € – 320,000 €*** / ***2  320,000 €, discount for DLBC**  313,766 € (hidden discount excluded)**  297,666 € + 15,000 € on top of DRG**  320,000 €**	
Kymriah™	Tisagenlecleucel Autologous CAR-T Cells targeting CD19	GTMP	Oncology, haematology (lymphomas various subtypes, acute lymphoblastic leukemias) Now moving in the field of auto-immune diseases	2018	Ongoing	Standard (PRIME)	  275,000 € – 320,000 €*** / ***2  320,000 €, discount for DLBC**  313,766 € (hidden discount excluded)**  297,666 € + 15,000 € on top of DRG**  320,000 €**	
Luxturna™	Voretigene neparvovec	GTMP	Ophthalmology	2018	Ongoing	Standard	  702,100 €* – 345,000 €**  682,673 € (hidden Discount excluded)**  1,874,250 €* – 1,580,000 € (full price)** / 1,575,000 €***7	
Zynteglo™ in Europe	Betibeglogene autotemcel Autologous CD34+ cells genetically engineered with a lentiviral vector to express a modified version of the human beta-globin gene	GTMP	Haematology (treatment of transfusion-dependent Beta-Thalassemia or TDT and Sickle Cell Disease or SCD with severe vaso-occlusive crises)	2019	Withdrawn 24/03/2022	Conditional/Accelerated (PRIME)	  1,6 M***3  The company left Europe, after failure to reach an agreement with HTA agencies for reimbursement***3	
Zolgensma™	Onasemnogene abeparvovec	GTMP	Muscular Atrophy	2020	Ongoing	Conditional/Accelerated (PRIME)	  2,134,550 €*	
Libmeldy™	Atidarsagene autotemcel	GTMP	Metabolic diseases (Metachromatic Leukodystrophy)	2020	Ongoing	Accelerated	  2,875,000 €***7  2,875,000 £***7	
Tecartus™	Brexucabtagene autoleucel Autologous CAR-T Cells targeting CD19	GTMP	Oncology (Lymphoma, Mantle-Cell & Acute Lymphoblastic Leukaemia in adults)	2020	Ongoing	Conditional/Accelerated (PRIME)	  360,000 €*	
Skysona™	Elivaldogene autotemcel	GTMP	Cerebral adreno leuko-dystrophy	2021	Withdrawn 18/11/2021	Accelerated (PRIME) reverted to Standard	 N/A	
Abecma™	Idecabtagene vicleucel Autologous CAR-T Cells targeting BCMA	GTMP	Oncology, haematology (multiple myeloma)	2021	Ongoing	Conditional/Accelerated (PRIME)	  350,000 €*  419,500 US\$***4	
Breyanzi™	Lisocabtagene maraleucel Autologous CAR-T Cells targeting CD19 (balanced composition in CD4+ and CD8+ T-cells)	GTMP	Oncology, haematology (lymphomas various subtypes) Now moving in the field of auto-immune diseases	2022	Ongoing	Accelerated (PRIME)	  345,000 €***	
Upstaza™	Elaocagene exuparvovec	GTMP	Amino Acid Metabolism, Inborn Errors	2022	Ongoing	Exceptional	  4,165,000 €* / 3,500,000 €***7	
Carvykti™	Ciltacabtagene autoleucel Autologous CAR-T Cells targeting BCMAI	GTMP	Oncology, haematology (multiple myeloma)	2022	Ongoing	Conditional (PRIME)	  420,000 €***5	
Roctavian™	Valoctocogene roxaparvovec	GTMP	Haemophilia A	2022	Ongoing	Conditional	  2,143,960 €*	
Ebvallo™	Tableteclucel Allogeneic T lymphocytes targeting EBV infected cells	CTMP	Post-Transplant Lymphoproliferative Disorders (PTLD) induced by Epstein-Barr Virus (EBV)	2022	Ongoing	Exceptional (PRIME)	 N/A	
Hemgenix™	Etranacogene dezaparvovec	GTMP	Haemophilia B	2023	Ongoing	Conditional (PRIME)	 N/A	
Casgevy™	Exagamglogene autotemcel Autologous peripheral blood CD34+ cells genetically engineered through gene edition technology (CRISPR-Cas) to induce expression of foetal hemoglobin	GTMP	Haematology (treatment of transfusion-dependent Beta-Thalassemia or TDT and Sickle Cell Disease or SCD with severe vaso-occlusive crises)	2024	Ongoing	Conditional (PRIME)	  1,900,000 €***6	

Latest update – May 2024, MA: Marketing Authorisation; OM: Orphan Medicine; DLBC: Diffuse Large B-Cell lymphoma; DRG: Diagnosis-Related Group

*: Source Antje Behring, Gemeinsame Bundesausschuss (G-BA) German HTA Regulation: Patient access in Germany, Communication ESGCT Congress October 2023 – **: Source Price and reimbursement of advanced therapeutic medicinal products in Europe: are assessment and appraisal diverging from expert recommendations? – ***: Source Dépêches APMnews / ****: APMnews, 09/07/2019 / ****2: APMnews, 31/08/2018 / ****3: APMnews, 21/10/2021 / ****4: APMnews, 25/06/2021 / ****5: APMnews, 04/04/2023 / ****6: APMnews, 06/02/2024 / ****7: APMnews: 18/08/2022 – ****8: Source HAS – Avis économique BREYANZI®, 19/12/2023

Challenges



Payment and reimbursement mechanisms as well as decisions on the levels of healthcare expenditures are established at national level and possibly in some countries at regional levels by Healthcare Technology Assessment (HTA) agencies and other governmental bodies, with limited possibilities at the European level.

Mainly apart from the Transparency directive and the recently strengthened collaboration in the field of HTA, adoption of the HTA regulation following the HTA initiatives at the EU level, each Member State is sovereign in determining its health expenses, including to decide on the reimbursement of ATMPs by its National health insurance