Market access landscape for advanced therapy medicinal products in the EU-5

PPM-11

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INTRODUCTION:

- According to EMA (European Medicines Agency) definition[1], Advanced therapy medicinal products (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 injury.
- All advanced therapy medicines are authorized centrally via the EMA.
- However, due to their specificities in terms of manufacturing and patient administration, the market access for ATMPs across European countries is complex and varies hugely depending on the country.

OBJECTIVE:

- The aim of this poster is to compare the market access for ATMPs approved by the EMA since 2015 across the EU5 countries focusing on reimbursement trends.

METHODS:

- 11 innovative ATMPs were identified with an EMA market authorization (including Zalmoxis® which was withdrawn in 2019). Since the similar analysis we done in March 2019, only one ATMP has been approved: Zolgensma®.
- A targeted research on official EU5 reimbursement / HTA agencies websites were executed in June 2020 in order to describe the current market access situation for each ATMP.

RESULTS:

- The reimbursement and pricing vary between countries: the table below describes the market access situation of each ATMP in the EU-5.

Brand name	Active substance	Indication	CHMP	France[2]	Germany[6]	Italy[5]	Spain[3,4]	UK/England[7]
Holoclar®	ex vivo expanded autologous human corneal epithelial cells containing stem cells	Deficiency caused by chemical ocular burns	19/12/2014	positive reimbursement decision / funding by hospitals	handled as procedure, reimbursed through DRG and not AMNOG assessed	reimbursed; payment by results	commercialized, but not reimbursed by the NHS. Negative reimbursement decision	reimbursed via NICE's Single Technology Appraisal pathway with some restrictions using Patient Access Scheme (Simple Discount)
Imlygic®	talimogene laherparepvec	unresectable malignant melanoma	23/10/2015	no evaluation by HAS	AMNOG assessed: no added benefit, reimbursed	not commercialized	authorized, not commercialized. Negative reimbursement decision	reimbursed via NICE's Single Technology Appraisal pathway using Patient Access Scheme (Simple Discount)I
Strimvelis®	autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence	Combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)	01/04/2016	no evaluation by HAS	At the time of data collection – no AMNOG assessment started	reimbursed; payment by results	not authorized, not commercialized.	gained full recommendation within its marketing authorisation via NICE's Highly Specialised Technology process
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)	add-on treatment in adults who have received an haploidentical transplant	24/06/2016 Withdrawn	negative reimbursement decision	AMNOG assessed: non-quantifiable added benefit, reimbursed	reimbursed; flat price per patient (withdrawn)	Withdrawn. Negative reimbursement decision	NICE has not yet reviewed
Spherox®	spheroids of human autologous matrix-associated chondrocytes	articular cartilage defects	19/05/2017	negative reimbursement decision	At the time of data collection – no AMNOG assessment started	P&R procedure not yet completed	not authorized, not commercialized	Single Technology Appraisal pathway with some restrictions
Alofisel®	darvadstrocel	complex anal fistulas in adults with Crohn's disease	15/12/2017	Reimbursed	AMNOG assessed: non-quantifiable added benefit, reimbursed	not reimbursed (class C)	reimbursed; payment by results. Restrictions in the patient population. Included in Valtermed	not recommended
Kymriah®	tisagenlecleucel	B-cell acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL)	29/06/2018	Reimbursed, MEA	AMNOG assessed: non-quantifiable added benefit, decision restricted by time and AMNOG reassessed: Hint of a non-quantifiable added benefit, reimbursed pay-for-performance Agreement	reimbursed; payment at results (ALL); obligatory discount (DLBCL)	reimbursed; payment by results. Included in Valtermed	reimbursed via Cancer Drugs Fund
Yescarta®	Axicabtagene ciloleucel	diffuse large B-cell lymphoma (DLBCL); primaryMediastinal large B-cell lymphoma (PMBCL)	29/06/2018	reimbursed; MEA	AMNOG assessed: non-quantifiable added benefit, reimbursed	reimbursed; payment at results, obligatory discount	reimbursed; payment by results. Included in Valtermed	reimbursed via Cancer Drugs Fund
Luxturna®	Voretigene neparvovec	loss of vision due to inherited retinal dystrophy	21/09/2018	Positive reimbursement decision / price in negotiation / available through post ATU program	AMNOG assessed: hint for a considerable added benefit, reimbursed	Pending decision	authorized, not commercialized. Currently being evaluated	reimbursed via NICE's Highly Specialised Technology Appraisal pathway using Patient Access Scheme (Simple Discount)
Zynteglo®	autologous CD34+ cells encoding beta A-T87Q-globin gene	Transfusion dependent beta-thalassaemia	28/03/2019	Positive reimbursement decision	AMNOG assessed: hint of a non-quantifiable added benefit, reimbursed	P&R procedure not yet completed	not authorized, not commercialized	currently being appraised by NICE
Zolgensma®	Onasemnogene abeparvovec	for the treatment of patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.	18/05/2020	Ongoing evaluation for reimbursement	The AMNOG assessment started in July 2020. Result expected in mid of December 2020.	P&R procedure not yet completed	authorized, not commercialized. Currently being evaluated	currently being appraised by NICE. Will go through the Highly Specialised Technologies evaluation

RESULTS:

France

- 8/11 ATMPs were assessed for reimbursement by the transparency committee: Six had a positive reimbursement decision (Holoclar ®, Alofisel®, Kymriah®, Yescarta®, Luxturna®, Zynteglo®). Two had a negative reimbursement decision (Zalmoxis®, Spherox®)
- Compared to 2019 analysis, two more were assessed: Zynteglo® was recognized as innovative (moderate (III) added medical benefit) and Spherox® had a negative reimbursement decision.
- Three have a public price (Yescarta®, Kymriah®, Alofisel®).
- Luxturna® and Zynteglo® are available through the post-ATU process; Holoclar can be funded by hospitals. The assessment of Zolgensma® is ongoing.

Germany

- 7/11 therapies were assessed within the AMNOG process (Imlygic®, Zalmoxis®, Alofisel®, Kymriah®, Yescarta®, Luxturna®, Zynteglo®) and 1/11 (Zolgensma®) is expected by the end of 2020.
- Kymriah® was reassessed with no change of the added benefit.
- Compared to 2019 analysis, two more therapies were assessed by G-BA (Zynteglo® which obtain a non quantifiable added benefit and Luxturna® which obtain a hint for a considerable added benefit)
- Holoclar® was taken as a procedure and it can be reimbursed through the DRG-System.
- Kymriah® was the 1st ever therapy on which a pay-for-performance deal was agreed.
- Zolgensma®, has to follow the new rule of the "Anwendungsbegleitende Datenerhebung" introduced at the end of 2019. The required Routine Practice Data Collection according §35a Par. 3b SGB V binds the manufacturer to set up a patient registry and to submit results yearly within a new AMNOG-Dossier to the G-BA

Italy

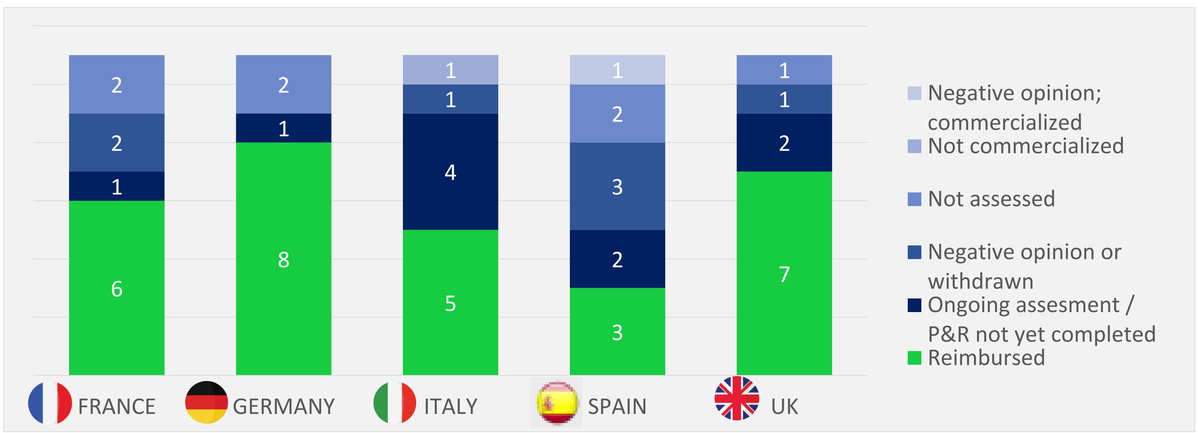
- 5/11 drugs received a positive decision on reimbursement from AIFA (Strimvelis®, Holoclar®, Zalmoxis®, Kymriah®, Yescarta®). Zalmoxis® was withdrawn in 2019 and is no longer available on the Italian market. Both, Kymriah® and Yescarta® were recognised as innovative drugs, hence they have had immediate access to regional formularies and are covered by the Innovative Drug Fund. Innovation status of Strimvelis® expired last year.
- 1/11 drug (Alofisel®) received a negative reimbursement decision (i.e. allocated in class C) but was nevertheless launched several months after it, in April 2019. 1/11 drug (Imlygic®) has not started a P&R process and is not available in Italy.
- 3/11 drugs (Spherox®, Zynteglo®, Zolgensma®) are currently under evaluation by the AIFA's Technical and Scientific Commission. Worthy to note that the P&R process for Spherox® has only started this year, although it was approved by the EMA in July 2017. 1/11 drug (Luxturna®) has completed the negotiation process with the AIFA's Pricing and Reimbursement Committee but the outcome is pending.

Spain

- 3/11 drugs (vs 2/10 in 2019) are reimbursed (Kymriah®, Yescarta® and Alofisel®; all of them included in Valtermed with a payment by results agreement). The therapeutic positioning report (IPT) of Alofisel® included restrictions in the patient population.
- Strimvelis®, Spherox® and Zynteglo® have not requested a national code. Therefore, they have not been evaluated in Spain.
- Holoclar®, Imlygic® and Zalmoxis® have a negative reimbursement decision. In spite of not being reimbursed, Holoclar® is commercialized.
- Luxturna® and Zolgensma® are currently under evaluation. National codes for Luxturna® and Zolgensma® were issued, respectively, in April 2019 and in July 2020.

United Kingdom

- 7/11 drugs (vs 5/10 in 2019) are reimbursed to date: only one of these, Strimvelis®, was reimbursed at its full list price.
- Spherox® was reimbursed via NICE's STA with some restrictions.
- The two CAR-Ts were reimbursed via NHS England's Cancer Drugs Fund.
- Holoclar®, Imlygic® and Luxturna® were recommended using a simple discount Patient Access Scheme.
- Zynteglo® and Zolgensma® are currently being appraised by NICE.
- Alofisel® was not recommended by NICE.



CONCLUSIONS:

- Most ATMPs are granted patient access in EU5 even though HTA bodies have imposed monitoring requirements to ensure the value reflects the price.
- Access to ATMPs varies across countries. Germany and the UK are the countries with the highest number of reimbursed ATMPs whereas Spain is the country with the lowest number.
- At this time, Kymriah® and Yescarta® are the only ATMPs reimbursed in the all EU-5 countries

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