Paediatric applicatons of ATMP

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Advanced Therapies Medicinal Products (ATMP)

What is an Advanced Therapy ?

- In the EU is defined by the regulation 1394/2007

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REGULATION (EC) No 1394/2007 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 13 November 2007

on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004

(Text with EEA relevance)

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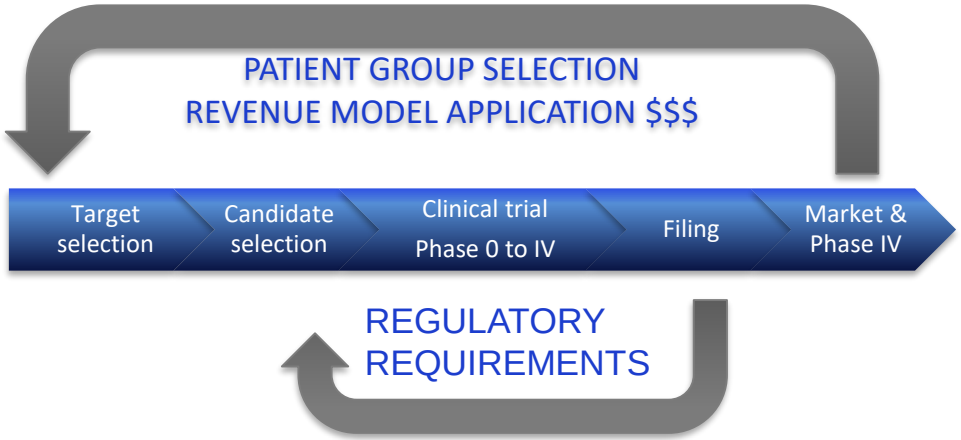
DEVELOPMENT PIPELINE for novel drugs



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Applications

- Because of the novelty, complexity and technical specificity of advanced therapy medicinal products, specially tailored and harmonised rules are needed to ensure the free movement of those products within the Community, and the effective operation of the internal market in the biotechnology sector.

Exclusion rule (so called art. 28)

- This Regulation is a lex specialis, {…}
- Advanced therapy medicinal products which are prepared on a non-routine basis according to specific quality standards, and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient, should be excluded from the scope of this Regulation {…}
- whilst at the same time ensuring that relevant Community rules related to quality and safety are not undermined.

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Reg.1394/2007 Art 2 lett. a

- Advanced therapy medicinal product' means any of the following medicinal products for human use:
  - ✓ a gene therapy medicinal product {…}, (CTMP)
  - ✓ a somatic cell therapy medicinal product {…}, (GTMP)
  - ✓ a tissue engineered product as defined in point (b). (TEP)

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TEP definition

(b) ‘Tissue engineered product’ means a product that:

— contains or consists of engineered cells or tissues, and

— is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue.

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TEP definition (2)

A tissue engineered product may contain cells or tissues of human or animal origin, or both. The cells or tissues may be viable or non-viable. It may also contain additional substances, such as cellular products, bio-molecules, bio-materials, chemical substances, scaffolds or matrices.

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Other {legal} definition

- Cells or tissues shall be considered ‘engineered’ {…..}
- ‘Combined advanced therapy medicinal product’ {…..}

Special requirements

- Centralized procedure for Marketing Authorization is compulsory
- Dedicated Committee for Advanced Therapies (CAT) at the European Medicine Agency
- Centralized national procedure for Clinical trial authorization (in most of the countries now)

Relevance for Paediatric population

- Until 2015 (CAR-T cell based products) the ATMP Research was mainly driven by Academic Groups and SME
- Especially active in marginal markets
  - Rare diseases
  - Paediatric diseases of genetic origin

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313 classification procedures

- cystic fibrosis (2)
- CLN2 disease
- mucopolysaccharidosis type II (Hunter syndrome)
- ornithine transcarbamylase deficiency
- Duchenne muscular dystrophy (3)
- Fanconi Anemia type A patients
- Hemophilia B
- Tay-Sachs disease and Sandhoff disease
- homozygous familial hypercholesterolemia caused by mutations in the LDLR gene
- patients aged 3 years and older with Leber Congenital Amaurosis type 10 (LCA10)
- Crigler-Najjar syndrome (2)
- X-linked Myotubular Myopathy
- glycogen storage disease type Ia (von Gierke disease)
- children neurological diseases: children encephalopathy (Hypoxic–ischaemic encephalopathy, immune/autoimmune encephalopathy), children epilepsy and children spinal cord injury
- childhood cerebral adrenoleukodystrophy (CCALD)

"of which 19 are for paediatric subjects"

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Few products reach the MA

List of ATMPs approved by the EMA

Name	Developer	Indication	Approval date	Status
Alofisel	TiGenix	Perianal fistulas in Crohn's disease	March 2018	Approved
Spherox	CO.DON	Cartilage defects in the knee	May 2017	Approved
Zalmoxis	MolMed	Stem cell transplantation in high-risk blood cancer	June 2016	Approved
Strimvelis	GSK	ADA-SCID	April 2016	Approved
Imlygic	Amgen	Melanoma	October 2015	Approved
Holoclar	Chiesi	Severe limbal stem cell deficiency in the eye	March 2015	Approved
Provenge	Dendreon	Metastatic prostate cancer	October 2013	Withdrawn in 2015
MACI	Vericel	Cartilage defects in the knee	July 2013	Withdrawn in 2014
Glybera	uniQure	Lipoprotein lipase deficiency (LPLD)	November 2012	Withdrawn in 2017
Chondrocelect	TiGenix	Cartilage defects	November 2009	Withdrawn in 2016

Source: European Medicines Agency

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Paediatric

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Gene therapy for ADA-SCID deficiency (Strimvelis)

- Developed by the Telethon foundation
- Rare paediatric disease
- Acquired by GSK, which paved the way to MA Strimvelis (2016)
- December 2017 - GSK announces to exit the field before a full reimbursement policy is defined
- in March 2018 GSK sold Strimvelis to Orchard Therapeutics Ltd.
- The price for the treatment was set at €594k, 2 times the annual cost of enzyme replacement therapy injections.[13] enzyme replacement therapy for ADA requires weekly injections and costs about $4.25 million for one patient over 10 years.

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Scope for a AT WG

- Diffusion of the knowledge about ATMP manufacturing in the Paediatric community
- Definition of the specific requirements for paediatric applications
- Focus on the research in human development underpinning the development of dedicated therapies
- Focus on the business model required for their application

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Scope for a AT WG (actual)

- COST project on fetal\newborn application of ATMP (feasibility?)
- Consultation on EMA guidelines

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Not yet forbidden

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