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Inspections, Human Medicines, Pharmacovigilance and Committees Division

CAT monthly report of application procedures, guidelines and related documents on advanced therapies

March 2019 meeting

The Committee for Advanced Therapies (CAT) held its 113th meeting on 20 – 22 March 2019.

The CAT Monthly Report includes statistical data on CAT scientific recommendations on Advanced Therapy Medicinal Product (ATMP) classification, certifications, initial evaluations, CAT contributions to Scientific Advice and Paediatric Investigation Plans, as well as variations, line extensions, renewals.

CAT recommends the granting of the marketing authorisation for Zynteglo

Zynteglo is a gene therapy medicinal product consisting of an autologous CD34+ cell enriched population that contains haematopoietic stem cells transduced with a lentiviral vector encoding the β-A-T87Q-globin gene. Zynteglo is approved for the treatment of patients 12 years and older with transfusion dependent β thalassaemia (TDT) who do not have a β0/β0 genotype, for whom haematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA) matched related HSC donor is not available.

Following an in-depth review of the marketing authorisation application submitted by bluebird bio GmbH., CAT concluded during its March 2019 meeting that a positive benefit risk has been demonstrated for Zynteglo. CAT adopted a positive draft opinion recommending the granting of a conditional marketing authorisation. The CHMP subsequently adopted a positive opinion for Zynteglo during its March 2019 meeting.

Zynteglo was granted access to PRIME in September 2016 and was reviewed under an accelerated timetable.

Further information can be found here.

Scientific recommendation on advanced therapy product classification

Further to consultation with the European Commission, the CAT finalised 7 scientific recommendations on the classification of advanced therapy medicinal products.

The following products were classified as gene therapy medicinal products:

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- Recombinant adeno-associated virus (serotype 5) containing the 21-hydroxylase gene, intended for the treatment of congenital adrenal hyperplasia;
- *In vitro* transcribed single-stranded messenger RNA molecules encoding human interferon-α2b, interleukin-12, interleukin-15-sushi, and Granulocyte-macrophage colony-stimulating factor, intended for the treatment of solid tumours;
- Recombinant adeno-associated virus containing a human micro-dystrophin gene, intended for the treatment of Duchene muscular dystrophy;
- Plasmid vector expressing interleukin-12 gene, intended for the treatment of advanced melanoma.

The following product was classified as a somatic cell therapy medicinal product:

- Allogeneic *ex vivo* expanded bone marrow derived mesenchymal stromal cells, intended for the treatment of graft-*versus*-host disease.

The following product was classified as tissue engineered product:

- Allogeneic *ex vivo* expanded umbilical cord (UC) blood-derived haematopoietic CD34+ progenitor cells to be used with allogeneic non-expanded UC blood-derived haematopoietic mature myeloid and lymphoid cells, intended for haematopoietic reconstitution of patients who are medically indicated for allogeneic haematopoietic stem cell transplantation.

The following product was classified as tissue engineered product and a combined ATMP:

- Autologous skeletal muscle derived cells attached to biodegradable poly(DL-lactide-co-glycolide) microparticles combined with skeletal muscle derived cells, intended for the treatment of faecal incontinence and anorectal malformation.

Organisational, regulatory and methodological matters

- CAT discussed the Question and Answer document on the use of Out-of-Specification batches of authorised ATMPs.
- CAT discussed the draft guideline on quality requirements for drug-device combination products, developed by the Quality Working Party and the Biologics Working Party.

Overview of product-related activities

The Committee discussed ongoing evaluation procedures for ATMPs and other related procedures as summarised in the following tables:

Initial Evaluation of Marketing Authorisation Applications (MAA) for ATMP												
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Submitted MAAs	3	1	2	3	2	2	1	1	4	3	0	22
Positive draft Opinion	1	0	1[ii]	1[ii]	2	1	1	2	2	3	1	15*
Negative draft opinions	1[i]	0	1[ii]	0	0	0	2[iii]	0	0	0	0	4
Withdrawals	1	1[i]	0	0	2	0	0	0	0	1	0	5
Ongoing MAAs												2

*** Corresponding to 14 ATMPs**
[i] Same product (Cerepro)
[ii] Same product (Glybera)
[iii] CAT adopted two negative draft opinions for the same product (Heparesc)

Variations (Type II) for authorised ATMP												
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Positive opinion	0	0	1	1	9	4	3	6	3	8	3	38

Scientific recommendation on advanced therapy classification												
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Submitted	22	19	12	22	20	28	61	60	46	55	14	359
Adopted	12	27	12	16	23	29	31	87	49	43	22	351

Certification of quality and non-clinical data for small and medium-sized enterprises developing ATMPs												
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Submitted	1	0	0	1	3	1	1	2	2	1	0	12
Adopted	0	1	0	1	1	2	1	1	3	1	0	11

Scientific advice procedure for ATMPs												
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Number of procedures	17	19	21	19	23	33	39	46	55	53	13	338

Paediatric Investigation Plans (PIP) for ATMPs												
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Number of procedures	3	4	4	8	5	4	3	5	3	3	0	42

Prime Eligibility for ATMPs									
	2016	2017	2018	2019					Total
Discussed	22	16	14	3					55
Granted	8	6	6	1					21

Upcoming meetings following the March 2019 CAT meeting

- The 114th meeting of the CAT will be held on 16 – 17 April 2019.

NOTE:

This Monthly Report, the Agenda of this meeting, the Minutes of the previous CAT meeting and other documents can be found on the internet at the following location: European Medicines Agency - Committee meeting reports - CAT: Committee meeting reports

Specific information related to ATMPs and the activities of the CAT (role, responsibilities and composition) can be found at: European Medicines Agency - CAT - Committee for Advanced Therapies (CAT)

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