16 March 2022
EMA/CAT/110649/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 16-17 February 2022

Chair: Martina Schuessler-Lenz; Vice-Chair: Ilona Reischl

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in these minutes are considered commercially confidential or sensitive and therefore not disclosed. Regarding intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CAT meeting reports once the procedures are finalised.

Of note, these minutes are a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Chair welcomed the new alternate from the Slovak Republic.

1.2. Adoption of agenda

The CAT agenda for 16-17 February 2022 meeting was adopted.

1.3. Adoption of the minutes

The CAT minutes for 19-21 January 2022 meeting were adopted.

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

2.5.1. Tabelecleucel - PRIME - Orphan - EMEA/H/C/004577

Accelerated assessment

Atara Biotherapeutics Ireland Limited; treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV$^+$ PTLD)

Scope: Day 80 assessment report

Action: for information

The information was noted.

2.6. Update on ongoing initial applications

No items

2.7. New applications

No items

2.8. Withdrawal of initial marketing authorisation application

No items

2.9. Re-examination of initial application procedures under Article 9(2) of Regulation No. 726/2004

No items

2.10. GMP and GCP inspections requests

No items

2.11. Type II variations and variations of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Kymriah - tisagenlecleucel - PRIME - Orphan - EMEA/H/C/004090/II/0049/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.2. Yescarta - axicabtagene ciloleucel - PRIME - Orphan - EMEA/H/C/004480/II/0040

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark

Scope: Clinical. Opinion

Submission of the final study report for the non-interventional study KT-EU-471-0116 (Quantitative Testing of Healthcare Provider Knowledge about Yescarta (axicabtagene ciloleucel) Risk Minimisation Measures) in fulfilment of an additional pharmacovigilance activity (Category 3) listed in the EU Risk Management Plan for Yescarta.

Action: for adoption

Request for Supplementary Information adopted on 10.09.2021.

The opinion was adopted.

2.11.3. Yescarta - axicabtagene ciloleucel - PRIME - Orphan - EMEA/H/C/004480/II/0042

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, PRAC Rapporteur: Anette Kirstine Stark

Scope: Clinical. Request for Supplementary information.

Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC, Annex II (Section D) and package leaflet are proposed to be updated. As a consequence, the RMP (version 5.1) has been updated to align with the indication extension. In addition, the applicant has taken the opportunity to make minor editorial corrections throughout the SmPC and package leaflet to align with the current Quality Review of Documents (QRD) template.

Action: for adoption

Request for Supplementary Information (RSI) adopted on 05.11.2021.

The Rapporteur presented the outcome of the assessment of the response to the RSI. The comments from the member states were discussed. A second RSI was adopted to allow the applicant to address the SmPC issues.

2.11.4. Yescarta - axicabtagene ciloleucel - PRIME - Orphan - EMEA/H/C/004480/II/0046

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, PRAC Rapporteur: Anette Kirstine Stark

Scope: Clinical. Request for supplementary information

Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) as second line treatment for Yescarta; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 5.3 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the product information with minor editorial changes.

Action: for adoption

The Rapporteur presented the outcome of the assessment. The request for supplementary information was adopted.

2.11.5. Tecartus; Yescarta - autologous anti-CD19-transduced CD3+ cells; axicabtagene ciloleucel - PRIME - Orphan - EMEA/H/C/WS2197

Kite Pharma EU B.V.

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Kymriah - tisagenlecleucel - PRIME - Orphan - EMEA/H/C/004090/REC/015

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Quality.

Action: for adoption

The outcome of the post-authorisation measure was adopted.

2.13.2. Kymriah - tisagenlecleucel - PRIME - Orphan - EMEA/H/C/004090/REC/016

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Quality.

Action: for adoption

The outcome of the post-authorisation measure was adopted.

2.13.3. Libmeldy - atidarsagene autotemcel - Orphan - EMEA/H/C/005321/REC/007

Orchard Therapeutics (Netherlands) BV

Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

Scope: Quality

Action: for adoption

The outcome of the post-authorisation measure was adopted.

2.13.4. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/R/0024

CO.DON AG

Rapporteur: Lisbeth Barkholt, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year Renewal of Marketing Authorisation

Action: for adoption

Request for Supplementary Information adopted on 10.12.2021.

CAT adopted the renewal of the marketing authorisation. It was agreed that no further renewal of the marketing authorisation is required.

2.13.5. Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - PRIME - Orphan - EMEA/H/C/005102/ANX/002.2

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Scope: MAH Response to ANX-002.1 [Study No. KTE-EU-472-6036: Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)]

Action: for adoption

The protocol for the post-authorisation efficacy study (PAES) was agreed. The outcome of the post-authorisation measure was adopted.

2.13.6. Zolgensma - onasemnogene abeparvovec - PRIME - Orphan - EMEA/H/C/004750/R/0021

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts, Co-Rapporteur: Egbert Flory, PRAC Rapporteur: Ulla Wändel Liminga

Scope: 1-year Renewal of Marketing Authorisation. Request for supplementary information

Action: for adoption

The Rapporteur presented the outcome of the evaluation of the second renewal of the marketing authorisation of Zolgensma. Provided that the MAH response satisfactorily to a number of minor questions, all specific obligations for this product are fulfilled. CAT agreed that at the time of the adoption of this renewal the marketing authorisation can be switched from conditional to full. The request for supplementary information was adopted.

2.13.7. Zynteglo - betibeglogene autotemcel - PRIME - Orphan - EMEA/H/C/003691/SOB/003

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik

Scope: From Initial MAA:
Study HGB-207: in order to confirm the efficacy and safety of Zynteglo in patients 12 years and older with transfusion-dependent β thalassaemia (TDT) who do not have a β0/β0 genotype, the MAH should submit interim and final data.

Action: for adoption

The Rapporteur presented the outcome of the assessment of the specific obligations (SOBs) 03 and 04. The SOBs are considered fulfilled. CAT adopted the outcome of the assessment.

CAT also noted the upcoming withdrawal by the MAH of the marketing authorisation of this product for commercial reasons.

2.13.8. Zynteglo - betibeglogene autotemcel - PRIME - Orphan - EMEA/H/C/003691/SOB/004

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik

Scope: From Initial MAA:
Study HGB-212: in order to confirm the efficacy and safety of Zynteglo in patients 12 years and older with transfusion-dependent β thalassaemia (TDT) who do not have a β0/β0 genotype, the MAH should submit interim and final data from patients with a severe non β0/β0 genotype such as IVS I 110.

Action: for adoption

CAT adopted the outcome of the assessment.

See 2.13.8

2.13.9. Interactions with the European Society for Blood and Marrow Transplantation (EBMT) and marketing authorisation holders of CAR-Ts on the use of data from the EBMT registry for the imposed PASS

Scope: feedback from the meeting on 26.01.2022

Action: for discussion

EMA provided feedback from the discussion with EBMT and the MAHs of CAR-T products. A meeting will be set up with the CAT Rapporteurs of CAR-T products to discuss possible follow-up steps.

3. Certification of ATMPs

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Gingival fibroblast

Intended for the treatment of gonarthrosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. (AAV2.hIL-12) Recombinant serotype 2 adeno-associated virus (AAV2) carrying a single-stranded expression cassette for human Interleukin 12 (IL-12)

Intended for the treatment of advanced solid tumours

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Leukocyte and platelet rich plasma, autologous

Intended for the treatment of critical limb ischemia

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. Messenger RNA (mRNA) containing a bicistronic coding sequence that upon translation produces two independent proteins, ZF-DNMT and ZF-KRAB

Intended for the treatment of adult patients with intermediate (stage B) or advanced (stage C) MYC-associated hepatocellular carcinoma (HCC)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.5. Stimulated anti-viral T-lymphocytes with specific anti-viral activity

Intended for the treatment of resistant viral infections in patients after allo-HSCT

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.6. Plasmid expressing variant of human interleukin-10

Intended for the treatment of osteoarthritis, neuropathic pain, amyotrophic lateral sclerosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.2. Day 30 ATMP scientific recommendation

No items

4.3. Day 60 revised scientific recommendation (following list of questions)

No items

4.4. Finalisation of procedure

4.4.1. Kidney progenitor cells isolated from the urine of preterm neonates

Intended for the kidney transplantation

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.2. Expanded mesenchymal stem cells (MSCs) cells isolated from umbilical cord Wharton jelly dilative cardiomyopathy (DCM)

Intended for the treatment of dilative cardiomyopathy (DCM)

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.3. Recombinant serotype 9 adeno-associated virus (rAAV9) encoding a wild-type human MECP2 (methyl cytosine binding protein 2) transgene (AAV9-hMECP2)

Intended for the treatment of Rett syndrome

Scope: Minor comments were made by the European Commission. Revised ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.4. Recombinant adeno-associated virus (rAAV) containing human homology arms, expressing codon-optimised human phenylalanine hydroxylase (hPAH)

Intended for the treatment of phenylalanine hydroxylase (PAH) deficiency

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.5. Human embryonic stem cell (hESC)-derived midbrain dopaminergic (mDA) neuron cells

Intended for the treatment of advanced Parkinson's disease

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.6. Stem cells isolated from dental pulp, cultured

Intended for the treatment of surgical bone defects

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.7. Modulated immune cells

Intended for solid organ transplantation / Treatment of autoimmune disease

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.4.8. Autologous bone marrow concentrate

Intended for the treatment of bone fractures

Scope: Minor comments were made by the European Commission. Revised ATMP scientific recommendation

Action: for information

The information was noted. The finalised classification report will be sent to the applicant.

4.5. Follow-up and guidance

No items

5. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.1. New requests - appointment of CAT Rapporteurs

5.1.1. Ongoing scientific advice procedures - Appointment of CAT Peer Reviewers

Timetable:

- Start of procedure at SAWP:	07-10.02.2022
- Appointment of CAT Peer Reviewers:	16-18.02.2022
- SAWP first reports:	28.02.2022
- CAT Peer Reviewer comments:	04.03.2022
- Discussion at SAWP:	07-10.03.2022
- Discussion at CAT and feedback to SAWP:	18.03.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	07-10.03.2022
- Appointment of CAT Peer Reviewers:	16-18.03.2022
- SAWP first reports:	28.03.2022
- CAT Peer Reviewer comments:	01.04.2022
- Discussion at SAWP:	04-07.04.2022
- Discussion at CAT and feedback to SAWP:	13.04.2022

5.2. Procedures discussed at SAWP – 1st reports, D40 JRs, LoIs

5.3. Finalisation of D70 procedures – feedback from the discussion meeting

5.4. Final Advice Letters for procedures finalised the previous month

6. Pre-Authorisation Activities

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	07-10.02.2022
SAWP recommendation:	10/03/2022
CAT recommendation:	18/03/2022
CHMP adoption of report and final recommendation:	24/03/2022

No items

6.3.2. Month 1 – Discussion of eligibility

No items

6.3.3. Month 2 – Recommendation of eligibility

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

The Chair welcomed Katarina Vavrova as the new alternate member for Slovak Republic.

Action: for information

7.1.2. Joint CAT-CHMP Strategic Review & Learning meeting (SRLM) under the Slovenian presidency, 21 October 2021 (virtual)

CAT: Metoda Lipnik-Štangelj, Martina Schuessler-Lenz

Scope: Minutes of the meeting

Action: for information

CAT noted the minutes of the SRLM of 21 October 2021.

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the French presidency, 3 March 2022 (virtual)

CAT: Violaine Closson-Carella, Martina Schuessler-Lenz

Scope: Review and adoption of the agenda content

Action: for discussion

The final agenda of the upcoming SRLM was presented. CAT members were reminded to register for the meeting and to inform the organisers of any additional expert / assessor from the NCA that plans to attend the meeting.

7.2. Coordination with EMA Scientific Committees

7.2.1. Classification of Post-Authorisation Studies (CPAS)

Scope: Presentation of the mandate of the CPAS

Action: For discussion

CAT noted the presentation on the role and mandate of the CPAS.

7.2.2. CHMP learnings with relevance to CAT: Revision to the Appendix 3 of the anticancer guideline

Scope: Revision to the Appendix 3 of the anticancer guideline related to section 4.8 of the Summary Products Characteristics (SmPC) for the anticancer medicinal products.

Action: for discussion

EMA and the Rapporteur of the guideline, Sigrid Klaar, presented the revised Appendix 3. Guidance is provided in this document on how to present safety data in section 4.8 of the SmPC, especially safety data from related indications. It is part of the assessment to determine if the population in related indications are similar enough for the safety data to be presented in a single safety table in the SmPC.

7.2.3. CHMP learnings with relevance to CAT: Topics discussed at February CHMP PROM[1]

CAT: Martina Schüssler-Lenz

Scope: Summary of topics of interest that were discussed at the last CHMP PROM meeting

Action: for information

Following topics are of relevance for CAT:

- Oncology working party: selection of candidates has taken place;

- Call for nominations for candidates for clinical working parties (with the exception of the oncology working party), non-clinical and methodology working parties: CAT members interested should contact their national authorities; CAT members representing the doctors and patient organisations can also be proposed by one of the national authorities;

- Classification of post-authorisation studies: presentation of mandate (see 7.2.1);

- Extrapolation: assessor guidance template;

- Proof of concept raw data pilot.

CAT asked for the last two topics to be presented at the March CAT meeting.

7.2.4. Extension of indication of approved ATMPs: additional 1-year protection period

Scope: Presentation on the regulatory aspects

Action: for information

[1] The CHMP PROM is a meeting to discuss CHMP organisational matters and other topics in preparation for the CHMP Plenary meeting.

EMA presented the regulatory aspects related to the additional 1-year protection period when the indication of an approved ATMP is extended. As part of the assessment of a variation for extension of indication, clinical superiority have to be assessed.

7.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

7.3.1. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope: Meeting summary of the PCWP/HCPWP joint meeting with all eligible organisations on the 24 November 2021

Action: for information

The information was noted.

7.3.2. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope: Draft agenda - PCWP-HCPWP joint meeting on 02-03 March 2022

Action: for information

The information was noted.

7.3.3. BWP/QWP/IWG Toolbox guidance on scientific elements and regulatory tools to support quality data packages for PRIME and certain marketing authorisation applications targeting an unmet medical need

DG members: Mats Welin, Sean Barry, Marcel Hoefnagel, Tone Agasoster, Kristofer Olofsson, Jobst Limberg, Giampiero Lorenti

Action: for adoption

EMA and Marcel Hoefnagel presented the final Toolbox and highlighted the main changes that were implemented following the external consultation: the scope has been extended to cover not only PRIME designated products but also other medicinal products targeting an unmet medical need.

The document is now presented to BWP, QWP, IWG and CAT: comments are awaited within the next 2 weeks. The Toolbox will be considered adopted if no major comments are received (minor comments will be reviewed and if needed implemented by the drafting group).

7.3.4. EMA Working Parties Implementation Plan Review – (H+V)

Scope: Information on creation of the Quality Innovation Group (QIG) within the Quality Domain

Action: For discussion

EMA presented the creation of the QIG and how this group fits within the new working party organisation model. The QIG will specifically look at the translation of innovation, trying to find solutions for innovative developments, set priorities and develop strategies towards the needs of the network. A call for nomination will be initiated in April 2022.

7.4. Cooperation with the EU regulatory network

7.4.1. Accelerating Clinical Trials in the EU (ACT EU)

Scope: This business-change programme aims to strengthen the European environment for clinical trials and was recently endorsed at both HMA November 2021 and EMA Management Board December 2021 meetings, including the accompanying paper outlining the objectives and priority actions for the ACT EU.

Action: for information

EMA presented the topic. The main objective of ACT EU is to optimise the environment for clinical trials in the EU. The ACT-EU steering group will be looking for CAT experts to lead and participate in different actions.

CAT members mentioned the implementation of the clinical trial information system (CTIS) is causing problems with clinical trials of products containing or consisting of GMOs and also with the interoperability of trials with medicinal products and medical devices. It is clear that these issues have to be tackled in order to make EU attractive for clinical trials with ATMPs.

7.5. Cooperation with international regulators

7.5.1. Joint EMA-FDA Q&As on PRIME/Breakthrough applications (control strategy, process validation, stability, GMP)

DG members: Mats Welin, Sean Barry, Marcel Hoefnagel, Tone Agasoster, Kristofer Olofsson, Jobst Limberg, Giampiero Lorenti

Scope: Joint EMA-FDA Q&As on PRIME/Breakthrough applications

Action: for adoption

Marcel Hoefnagel presented the content of the Q&A related to: control strategy, process validation, stability and GMP considerations.

The document is now presented to BWP, QWP, IWG and CAT: comments are awaited within the next 2 weeks. The Q&A document will be considered adopted if no major comments are received (minor comments will be reviewed and if needed implemented by the drafting group).

7.5.2. ATMP cluster teleconference with US-FDA, Health Canada and PMDA (Japan)

CAT: Martina Schuessler-Lenz

Scope: Agenda of the teleconference that will take place on 24 February 2022

Action: for information

The agenda for the upcoming ATMP cluster was presented.

CAT members interested to join this ATMP cluster should inform CAT Secretariat.

7.5.3. WHO consultation on cell and gene therapy products

CAT: Ilona Reischl

Scope: Presentations from WHO consultation meeting that took place on 07-09 February 2022.

Action: for information

CAT noted the information

7.6. CAT work plan

7.6.1. ATMP training for 2022

CAT: Ilona Reischl

Scope: Identification of ATMP training for assessors and experts

Action: for discussion

The plan for training for the network (ATMP assessors in the NCAs and CAT members) was discussed. Friday (13.30 – 14.30) after the virtual CAT plenary meeting was identified as a suitable time. Following training topics will be developed first: guideline for genetically modified cells, Q&A for comparability, comprehensiveness criteria, marketing authorisation procedure for ATMPs. CAT secretariat will contact the CAT members to identify speakers.

7.6.2. Implementation of the medical device and in-vitro diagnostics Regulations

CAT: Ilona Reischl

Scope: Status update

Action: for discussion

A detailed update on this topic was provided.

7.7. Planning and reporting

No items

7.8. Others

No items

8. Any other business

No items

Date of next CAT meeting:

16-18/03/2022

9. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

EU NTC: European Union Network Training Centre

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Application

MAH: Marketing Authorisation Holder

MNAT: Multinational assessment team

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

QRD: Quality review of documents

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

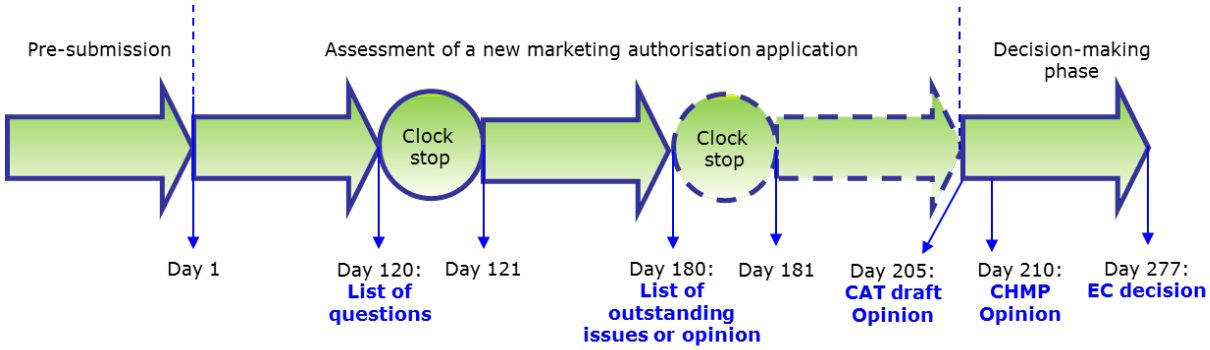
Evaluation of ATMPs (section 2)

This section lists applications for marketing authorisations of new Advanced Therapy Medicinal Products (ATMPs) that are to be discussed by the Committee. It also lists any ATMP related inspection requests (section 2.9) and Post-authorisation activities (section 2.10).

New applications (sections 2.1. to 2.12.)

Section 2.1 is for ATMPs nearing the end of the evaluation and for which the CAT is expected to adopt a draft **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CAT opinion is transmitted to the CHMP for final adoption. The CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU. More information on the evaluation of ATMPs can be found here.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CAT. The clock stop happens after day 120 and may also happen after day 180, when the CAT has adopted respectively a **Day 120 list of questions** (section 2.3) or a List of outstanding issues to be addressed by the company, which is listed in the agenda under sections 2.7 (**Ongoing evaluation procedures**). Section 2.7 also includes the CAT discussions at any other timepoint of the evaluation procedure of new applications.

Oral explanation (section 2.2.)

Prior to adoption of the CAT opinion, marketing authorisation applicants are normally invited to the CAT plenary meeting to address questions raised by the Committee.

Oral explanations normally relate to ongoing applications, but they can also relate to any other issue for which the CAT would like to discuss with company representatives in person.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.6.)

This section lists applications for new marketing authorisation for ATMPs for which the applicant has requested a re-examination of the opinion previously issued by the CHMP. Similar to the initial evaluation of a marketing authorisation of an ATMP, CAT will adopt a draft re-examination opinion, which is transmitted to the CHMP for final adoption.

Withdrawal of applications (section 2.7.)

This section includes information on marketing authorisation applications that are withdrawn by the applicant. Applicants may decide to withdraw applications at any stage during the assessment and a CAT opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

New applications (section 2.9.)

In this section, information is included on upcoming marketing authorisation applications for ATMPs, as well as information on appointment of Rapporteurs for new ATMP applications.

GMP and GCP Inspections Issues (section 2.10.)

This section lists inspections that are undertaken for ATMPs. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Post-authorisation activities (section 2.12.)

This section lists type II variations, extension application according to Annex I of Reg. 1234/2008, re-examination procedures for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP and other issues concerning authorised medicines that are not covered elsewhere in the agenda such as annual reassessments, 5-year renewals, supply shortages, qualify defects. Issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines, will also be included here.

Certification of ATMPs (section 3)

This section includes the scientific evaluation by the CAT of quality and non-clinical data that small and medium-sized enterprises have generated at any stage of the ATMP development process. More information on the ATMP certification procedure can be found here.

Scientific Recommendation on Classification of ATMPs (Section 4)

This section includes the scientific recommendation by the CAT on whether medicines based on genes, cells or tissues meet the scientific criteria that define ATMPs. More information on the ATMP classification procedure, including the outcomes of finalised classifications, can be found here.

Scientific Advice (section 5)

This section includes all scientific advice given to companies during the development of an ATMP. Information related to the number of ATMP related scientific advices discussed by CAT can be found in the CAT Monthly reports. Further information on SAWP can be found here.

Pre-Authorisation (section 6)

Paediatric Investigation Plan (PIP)

This section includes the discussion of an ATMP before a formal application for marketing authorisation is submitted. These cases refer for example to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation: in case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

CAT contributes to the evaluation of a Paediatric Investigation Plan (PIPs) for ATMPs by the Paediatric Committee. These PIPs are included in this section of the Agenda.

ITF Briefing meeting in the field of ATMPs

This section refers to briefing meetings of the Innovation Task Force and International co-operations activities of the CAT

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes of meetings with applicants developing ATMPs and of other ITF meetings of interest to the CAT are included in this section of the agenda. Further information on the ITF can be found here.

Priority Medicines (PRIME)

This section includes the new requests for eligibility to PRIME for ATMPs under development, the discussions in CAT of these eligibility requests and the final recommendations for eligibility of ATMPs adopted by CHMP.

CAT will appoint one of its members as the CAT sponsor for each new ATMP eligibility request who will lead the CAT discussion based on the recommendation from the SAWP.

Organisational, regulatory and methodological matters (section 7)

This section includes topics related to regulatory and procedural guidance, CAT workplan, CAT meeting organisation (including CAT membership), planning and reporting, co-ordination with other committees, working parties and scientific advisory groups.

Furthermore, this section refers to the activities of the CAT drafting groups developing scientific guidelines for gene therapy medicinal products and for cell-based medicinal products, cooperation within the EU regulatory network and international regulators as well as direct interaction with interested parties. It also includes topics of scientific interest for the Committee that are not directly related to the work of the CAT drafting groups or CAT associated working parties.

Any other business (section 8)

This section is populated with miscellaneous topics not suitable under the previous headings.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/

10. List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 16-17 February 2022 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martina Schüssler-Lenz	Chair	Germany	No interests declared	
Ilona Reischl	Member (Vice-Chair)	Austria	No interests declared	
Silke Dorner	Alternate	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Belaïd Sekkali	Alternate	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Evelina Shumkova	Alternate	Bulgaria	No interests declared	
Azra Selimovic	Member	Croatia	No interests declared	
Petra Sokol	Alternate	Croatia	No interests declared	
Rafaella Pontou	Member	Cyprus	No interests declared	
Isavella Kyriakidou	Alternate	Cyprus	No interests declared	
Tomas Boran	Member	Czechia	No interests declared	
Petr Soukup	Alternate	Czechia	No interests declared	
Ebru Karakoc Madsen	Alternate	Denmark	No restrictions applicable to this meeting	
Toivo Maimets	Member	Estonia	No interests declared	
Pille Saalik	Alternate	Estonia	No interests declared	
Heli Suila	Member	Finland	No interests declared	
Maija Tarkkanen	Alternate	Finland	No interests declared	
Violaine Closson	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Egbert Flory	Alternate (to CHMP representative)	Germany	No interests declared	
Maria Gazouli	Member	Greece	No interests declared	
Angeliki Rompoti	Alternate	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Katalin Lengyel	Member	Hungary	No interests declared	
Balázs Sarkadi	Alternate	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Niamh Curran	Alternate	Ireland	No restrictions applicable to this meeting	
Concetta Quintarelli	Member	Italy	No interests declared	
Barbara Bonamassa	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No interests declared	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	
Vlasta Zavadova	Member	Liechtenstein	No interests declared	
Guy Berchem	Alternate	Luxembourg	Cannot act as rapporteur, other leading/co-ordinating role or peer reviewer for:	5.1.1.4.
Nancy De Bremaeker	Member	Luxembourg	No interests declared	
John J. Borg	Member (CHMP member)	Malta	No interests declared	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Babs Fabriek	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Maja Sommerfelt Grønvold	Alternate	Norway	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Marcin Kolakowski	Alternate	Poland	No interests declared	
Bruno Sepodes	Member (CHMP member)	Portugal	No interests declared	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Silviu Istrate	Member	Romania	No interests declared	
Alexandrina Preda	Alternate	Romania	No interests declared	
Lukas Slovak	Member	Slovakia	No interests declared	
Katarina Vavrová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Suzana Vidic	Alternate	Slovenia	No participation in final deliberations and voting on:	2.11.1., 2.13.1., 2.13.2. & 2.13.6.
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Lisbeth Barkholt	Member	Sweden	No interests declared	
Maria Luttgen	Alternate	Sweden	Cannot act as rapporteur, other leading/co-ordinating role or peer reviewer for: No participation in final deliberations and voting on:	5.1.1.4. 5.4.5.
Bernd Gänsbacher	Member	Clinicians' Representative	No interests declared	
Frederic Bernard	Alternate	Clinicians' Representative	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Alessandro Aiuti	Member	Clinicians' Representative	No participation in discussions, final deliberations and voting on:	2.13.3.
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Lydie Meheus	Alternate	Patients' Representative	No interests declared	
Kieran Breen	Member	Patients' Representative	No restrictions applicable to this meeting	
Roland Pochet	Alternate	Patients' Representative	No interests declared	
Catherine Milne	Observer/Alternate	EDQM	No interests declared	
Sofie Peirs Peirs	Expert - via Webex	FAGG AFMPS (BE)	No restrictions applicable to this meeting	
Marcel H.N. Hoefnagel	Expert - via Webex	CBG/MEB (NL)	No interests declared	
Sigrid Klaar	Expert - via Webex	MPA (SE)	No restrictions applicable to this meeting	
Matthias Renner	Expert - via Webex	PEI	No restrictions applicable to this meeting	
Attilla Sebe	Expert - via Webex	PEI	No interests declared	
Beate Mosl	Expert - via Webex	PEI	No restrictions applicable to this meeting	
Olga Kholmanskikh	Expert - via Webex	FAGG AFMPS (BE)	No interests declared	
Filip Van Nuffel	Expert - via Webex	FAGG AFMPS (BE)	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				