7 December 2022
EMA/CAT/867072/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 03-04 November 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).

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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 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 on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda points.

Participants 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. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The chair welcomed the new member and alternate from Slovakia and thanked the departing member for his contributions to the Committee.

1.2. Adoption of agenda

The CAT agenda for 02-04 November 2022 meeting was adopted with one addition:

- 2.13.16: Zolgensma – onasemnogene abeparvovec - EMEA/H/C/004750/P46/020.

1.3. Adoption of the minutes

The CAT minutes for 05-07 October 2022 meeting were adopted.

2. Evaluation of ATMPs

2.1. Opinions

2.2. Oral explanations

2.3. Day 180 list of outstanding issues

2.4. Day 120 list of questions

2.5. Day 80 assessment reports

2.6. Update on ongoing initial applications

2.7. New applications

2.8. Withdrawal of initial marketing authorisation application

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

2.10. GMP and GCP inspections requests

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

2.11.1. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0002

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

The opinion was adopted.

2.11.2. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0031

Novartis Europharm Limited

Rapporteur: Carla Herberts

Scope: Quality

Action: for adoption

Request for Supplementary Information adopted on 09.09.2022.

The opinion was adopted.

2.11.3. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0033/G

Novartis Europharm Limited

Rapporteur: Carla Herberts, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Clinical. Request for supplementary information

Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce additional guidance on liver function laboratory tests and monitoring before and after infusion and update information based on new safety information on the topic of acute liver failure (ALF) following two reports of fatal ALF.
Update of sections 4.2 and 4.4 of the SmPC in order to provide additional guidance relevant to patient's overall health status prior to dosing and to strengthen the existing description and guidance on systemic immune response.
Update of the section 4.4 of the SmPC in order to indicate prompt attention to thrombotic microangiopathy (TMA) and to reflect the risk of life-threatening or fatal outcomes.
The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted.
In addition, the MAH took the opportunity to update the Annex II.

Action: for adoption

The request for supplementary information was adopted.

2.11.4. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0034/G

Novartis Europharm Limited

Rapporteur: Carla Herberts

Scope: Quality

Action: for adoption

The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/013

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.2. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/014

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.3. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/015

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.4. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/016

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.5. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/017

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.6. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/018

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.7. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/019

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.8. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/R/0036

Takeda Pharma A/S

Rapporteur: Lisbeth Barkholt, Co-Rapporteur: Isabel Vieira; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year Renewal of Marketing Authorisation, opinion

Action: for adoption

Request for Supplementary Information (RSI) adopted on 09.09.2022.

The Rapporteur presented the outcome of the assessment of the responses to the RSI. The changes to the SmPC were presented. The renewal was adopted with unlimited duration. CAT noted the new commitment from the MAH .

2.13.9. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/013

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.10. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/REC/008

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.11. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/P46/011

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Clinical study report of Study No. 20110261: A Phase 1, Multi-centre, Open-label, Dose De-escalation Study to Evaluate the Safety and Efficacy of Talimogene Laherparepvec in Paediatric Subjects with Advanced Noncentral Nervous System Tumours that are amenable to direct injection.

Action: for adoption

The Rapporteur presented the outcome of the assessment of the interim report of the paediatric study No. 20110261. The safety profile is consistent with the known safety profile. No changes to the product information are proposed. This will be re-discussed when the final report of this study is available. The conclusion of the assessment of the application was adopted.

2.13.12. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/REC/003

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.13. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/REC/004

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Quality

Action: for adoption

The assessment of this recommendation was adopted.

2.13.14. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/ANX/002.4

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Second Annual Interim Report / No.: KT-EU-471-0117
Title: Long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma (EU PAS Register no.: EUPAS32539).

Action: for adoption

The Rapporteur presented the conclusion of the PRAC assessment of the second annual interim report of the post-authorisation safety study KT-EU-471-0117. The safety and effectiveness of the Yescarta in the post authorisation setting are similar to that at the time of the approval; the incidence of cytokine release syndrome is lower than in the pivotal clinical trial. No change to the product information is proposed. A short discussion took place on the secondary malignancies after Yescarta treatment: it was agreed that these are rather linked to prior chemotherapy treatments, irradiation and the underlying genetics.

2.13.15. Holocar - Ex vivo expanded autologous human corneal - Orphan - EMEA/H/C/002450/R/0048

Holostem Terapie Avanzate s.r.l.

Rapporteur: Egbert Flory

Scope: Annual renewal

Action: for adoption

The Rapporteur presented the outcome of the assessment. No new findings or new safety signals were reported. CAT adopted the annual renewal of Holocar.

2.13.16. Zolgensma – onasemnogene abeparvovec - EMEA/H/C/004750/P46/020

Novartis Europharm Limited

Rapporteur: Carla Herberts

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Final study report of study No. AVXS-101-CL-102 (COAV101A12102): Phase 1, Open-Label, Dose Comparison Study of AVXS-101 for Sitting but Non-Ambulatory Patients with Spinal Muscular Atrophy.

Action: for adoption

The Rapporteur presented the outcome of the assessment of the report of the paediatric study AVXS-101-CL-102. The study did not show efficacy after intrathecal administration. No changes to the SmPC are proposed.

2.14. Feedback from CHMP discussions on ATMP applications

2.14.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0053; EMEA/H/C/004090/II/0059

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Outcome of CHMP discussion

Action: for information

The Rapporteur provide feedback from the CHMP discussion on the two Kymriah variations, and the difference in views from the CHMP on the fulfilment of the Annex II condition (variation II/53) and on the inclusion of the results of the study B2401 (overall survival) in the SmPC for Kymriah, section 5.1 (variation II/59).

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

3.2. Day 60 Evaluation Reports

3.3. New Applications

4. Scientific Recommendation on Classification of ATMPs

Timetable:

-Start of the procedure:	20.11.2022
-EMA Coordinator's draft report:	25.11.2022
-CAT Coordinator's comments:	30.11.2022
-Revised scientific recommendation:	02.12.2022
-CAT's discussion of scientific recommendation:	09.12.2022

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Adult autologous regenerative cells

Indicated for regeneration, repair, or replacement of weakened or injured subcutaneous tissue

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Autologous adipose-derived stromal vascular fraction cells (ADSVFCs)

Indicated for the treatment of haemophilic arthropathy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Allogeneic Natural Killer cells armed with anti-EGFR monoclonal antibody

Indicated for the treatment of epidermal growth factor receptor (EGFR) positive cancers

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. Allogeneic natural killer cells armed with anti-HER2 monoclonal antibody

Indicated for the treatment of human epidermal growth factor receptor 2 (HER2) positive cancers

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.5. Ex-vivo expanded allogeneic neural crest-like stem cells

Indicated for the treatment of diabetic foot ulcer

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.6. Allogeneic Wharton's jelly mesenchymal stem cells (WJ-MSCs)

Indicated for the treatment of stress incontinence

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.7. Autologous monocyte-derived dendritic cells electroporated with mRNAs encoding for immunostimulatory proteins caTLR4, CD40L and CD70 combined with one of the tumour-associated antigens (TAA) MAGE-C2, MAGE-A3, WT1 and NY-ESO-1

Indicated for the treatment of gastric cancer

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.8. Autologous human tumour infiltrating lymphocytes

Indicated for the treatment of locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.2. Day 30 ATMP scientific recommendation

4.2.1. Allogeneic adipose-derived mesenchymal stem cells (ADMSCs)

Intended for the treatment of osteoarthritis of the knee and hip

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 18 November 2022.

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

No items

4.4. Finalisation of procedure

4.4.1. Allogeneic adipose derived mesenchymal stem cells

Intended for the treatment of Crohn-related perianal fistula

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of an advanced therapy medicinal product as defined in Article 2(1) of Regulation (EC)

1394/2007. CAT considered that the applicant did not provide sufficient information to support the claimed mechanism of action of the product in the indication sought and therefore CAT concluded that the product is an ATMP, but did not decide if it is a tissue engineered product or a somatic cell therapy medicinal product.

4.4.2. Autologous adipose derived mesenchymal stem cells

Intended for the treatment of Crohn-related perianal fistula

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of an advanced therapy medicinal product as defined in Article 2(1) of Regulation (EC) 1394/2007. CAT considered that the applicant did not provide sufficient information to support the claimed mechanism of action of the product in the indication sought and therefore CAT concluded that the product is an ATMP, but did not decide if it is a tissue engineered product or a somatic cell therapy medicinal product.

4.4.3. Autologous anti-BCMA CAR-T cells

Intended for the treatment of multiple myeloma

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definitions of a somatic cell therapy medicinal product and a gene therapy medicinal product, and based on that it is considered as gene therapy medicinal product as provided in Article 2(5) of Regulation (EC) No 1394/2007.

4.4.4. Allogeneic latency-2 Epstein-Barr virus-targeted cytotoxic T lymphocytes

Intended for the treatment of multiple sclerosis

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a somatic cell therapy medicinal product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.5. E1-deleted (replication defective) recombinant human adenovirus serotype 5 expressing TIMP3 (tissue inhibitor of metalloproteinases-3) under the control of the cytomegalovirus immediate early promoter

Intended for the treatment of coronary artery disease requiring artery bypass grafting (CABG)

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medicinal product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.6. Autologous CD34+ cells transfected with a lentiviral vector containing codon-optimised RPS19 gene

Intended for the treatment of transfusion-dependent, steroid-resistant paediatric patients with Diamond-Blackfan anaemia, who have a mutation in the RPS19 gene

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medicinal product as defined in Article 2(1) of Regulation (EC) 1394/2007.

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:	24-27.10.2022
- Appointment of CAT Peer Reviewers:	03-04.11.2022
- SAWP first reports:	21.11.2022
- CAT Peer Reviewer comments (NC/C):	25.11.2022
- CAT Peer Reviewer comments (Q):	30.11.2022
- Discussion at SAWP:	28.11.2022 – 01.12.2022
- Discussion at CAT and feedback to SAWP:	07-09.12.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	28.11–01.12 2022
- Appointment of CAT Peer Reviewers:	07-09.12.2022
- SAWP first reports:	02.01.2023
- CAT Peer Reviewer comments (NC,C):	06.01.2023
- CAT Peer reviewer comments (Q):	11.01.2023
- Discussion at SAWP:	09-12.01.2023
- Discussion at CAT and feedback to SAWP:	18-20.01.2023

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

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

No items

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

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:	24-27.10.2022
SAWP recommendation:	01.12.2022
CAT recommendation:	09.12.2022
CHMP adoption of report and final recommendation:	15.12.2022

6.3.2. Month 1 – Discussion of eligibility

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

End of membership: Lucas Slovak (Slovakia) on 11-10-2022

Change of role: Katarina Vavrova: member for Slovakia since 11-10-2022

New alternate member for Slovakia since 11-10-2022: Margaréta Fogelová

Action: for information

7.1.2. Vote by proxy

No items

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Czechia presidency, 17 – 18 November 2022 in Paris

CAT: Petr Soukup, Martina Schuessler-Lenz

Scope: final agenda content

Action: for discussion

The final agenda of the upcoming SRLM was presented and discussed. It was proposed to add a chair and a moderator to each of the sessions.

7.1.4. CAT meeting dates 2023

Scope: Face-to-face CAT meetings in 2023

Action: for information

The information was noted.

7.2. Coordination with EMA Scientific Committees

7.2.1. COMP project on conditions for orphan designation in inherited retinal diseases

Scope: conclusions of the COMP project

Action: for information

CAT noted the outcome of the COMP project on conditions for orphan designation in inherited retinal diseases. CAT was informed that COMP agreed to go ahead with this proposal.

7.2.2. Focus group on submission predictability

Scope: invite nominations to participate in this focus group which aims to carry out analysis of the root causes of the delays and poor predictability in submissions of initial marketing

authorisation applications; identify potential solutions to promote better submission planning by applicants, avoid delays and allow better resources planning at NCA level

Action: for discussion

The following CAT members will take part in this focus group: Carla Herberts and Maura O'Donovan.

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

No items

7.4. Cooperation with the EU regulatory network

No items

7.5. Cooperation with international regulators

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

CAT: Martina Schuessler-Lenz

Scope: Feedback from the teleconference of 20 October 2022

Action: for information

A short feedback from the discussions in the ATMP cluster was provided.

7.5.2. International Pharmaceutical Regulators Programme (IPRP) – Gene therapy and cell therapy working groups

CAT: Pille Säälik, Ivana Haunerova

Scope: Feedback from the international teleconference that took place on 25 October 2022.

Action: for information

A short feedback from the discussions in the teleconference of IPRP gene therapy and cell therapy working groups was provided.

7.5.3. Real World Evidence (RWE) cluster teleconference with US-FDA and Health Canada

CAT: Jan Mueller-Berghaus, Marcos Timon

Scope: Feedback from the teleconference of 24 October 2022 (discussion on the authorisation of Carvykti)

Action: for information

The CAT CoRapporteur of Carvykti provided a short feedback from the discussion in the RWE cluster. EMA will define the scope of the meeting, and streamline the process for selection of products and identification of experts.

7.6. CAT work plan

7.6.1. CAT Workplan for 2023

CAT: Martina Schüssler-Lenz

Scope: draft CAT workplan for 2023

Action: for discussion

The first draft of the work plan for 2023 was discussed. CAT members were asked to review and comment in advance of the next discussion that is planned during the upcoming SRLM (see 7.1.3).

7.7. Planning and reporting

No items

7.8. Others

7.8.1. Good Practice Guide for the use of the EU metadata catalogue and Data Quality Framework

Scope: Presentation of the following documents for public consultation: a. Good Practice Guide for the use of the EU metadata catalogue, and b. Data Quality Framework

Action: for information

Agenda item postponed until the December CAT meeting.

7.8.2. European Society for Gene and cell therapy (ESGCT) annual meeting

CAT: Martina Schüssler-Lenz

Scope: Feedback from the CAT session at the ESGCT conference that took place in Edinburgh on 14 October 2022

Action: for discussion

A short feedback was provided from the CAT regulatory session at the ESGCT annual meeting. The CAT presentations are available in the MMD folder of this month.

7.8.3. Blood/tissue establishment in third countries providing starting materials for ATMPs

CAT: Barbara Bonamassa

Scope: Inspection of leukapheresis centres in third countries

Action: for discussion

Barbara Bonamassa presented the issue, highlighting the 3 possible scenarios: 1) the blood/tissue establishment is located in the EU; 2) the blood/tissue establishment and the ATMP manufacturing site are located outside of the EU; 3) the blood/tissue establishment is located outside of the EU and the ATMP manufacturing takes place in the EU. Depending on

the scenario, different possibilities for inspection of the blood/tissue establishment or verification of compliance with EU standards are possible. Further to the discussion in CAT, Barbara Bonamassa with the input from Silke Dorner and Marja van de Bovenkamp (expert) will finalise the considerations. The finalised document will then be sent to the European Commission and brought back to the December CAT for adoption.

8. Any other business

No items

Date of next CAT meeting:

07-09/12/2022

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

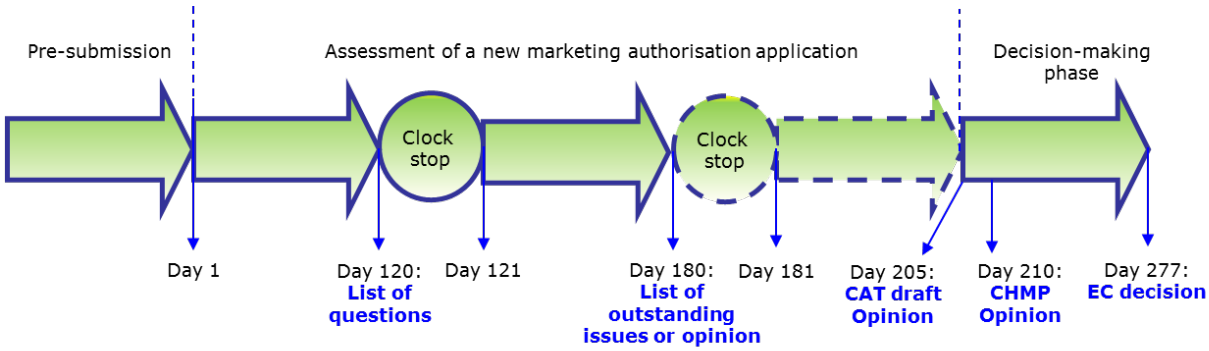
Evaluation of ATMPs (section 2)

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 03-04 November 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	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Petra Sokol	Alternate	Croatia	No interests declared	
Rafaella Pontou	Member	Cyprus	No interests declared	
Isavella Kyriakidou	Alternate	Cyprus	No interests declared	
Petr Soukup	Member	Czechia	No interests declared	
Kristyna Rehorova Hradilkova	Alternate	Czechia	No interests declared	
Ebru Karakoc Madsen	Member	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	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Egbert Flory	Alternate (to CHMP representative)	Germany	No interests declared	
Angeliki Rompoti	Alternate	Greece	No interests declared	
Katalin Lengyel	Member	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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Barbara Bonamassa	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
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	
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Silviu Istrate	Member	Romania	No interests declared	
Katarina Vavrová	Member	Slovakia	No interests declared	
Margareta Fogelová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Lisbeth Barkholt	Member	Sweden	No interests declared	
Maria Luttgen	Alternate	Sweden	No restrictions applicable to this meeting	
Alessandro Aiuti	Member	Clinicians' Representative	No participation in discussions, final deliberations and voting on:	
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Mencia de Lemus Belmonte	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member	Patients' Representative	No interests declared	
Federica Chiara	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Marja van de Bovenkamp	Expert - via telephone*	Netherlands	No interests declared	
Johannes Hendrikus Ovelgonne	Expert - via telephone*	Netherlands	No interests declared	
Meeting run with support from relevant EMA staff				