21 January 2022
EMA/CAT/752469/2021
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 08-10 December 2021

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

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).

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.

1.2. Adoption of agenda

The CAT agenda for 08-10 December 2021 meeting was adopted with following additions: SRLM in Paris in March 2022; Update on the NAS reflection paper; Report of the CAT stakeholders meeting of 26 October 2021.

1.3. Adoption of the minutes

The CAT minutes for 03-06 November 2021 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

2.3.1. Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095

Janssen-Cilag International NV; treatment of multiple myeloma

Scope: Day 180 list of outstanding issues

Action: for adoption

List of Questions adopted on 10.09.2021.

The Rapporteurs presented the outcome of the assessment of the responses to the list of questions.

The list of outstanding issues was adopted. The response timetable was adopted.

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

No items

2.7. New applications

2.7.1. Tabelecleucel - Orphan - EMEA/H/C/004577

Accelerated assessment

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

Scope: Timetable for assessment

Action: for adoption

The assessment timetable was adopted.

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. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0005/G

Celgene Europe B.V.

Rapporteur: Rune Kjeken;

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.2. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0009

Celgene Europe B.V.

Rapporteur: Rune Kjeken; PRAC Rapporteur: Annika Folin

Scope: Clinical. Opinion

Update of sections 4.2 and 4.4 of the SmPC, Annex IID and package information leaflet (PIL) in order to add statements for the use of Abecma exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab"

Action: for adoption

The opinion was adopted.

2.11.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0044

Novartis Europharm Limited

Rapporteur: Rune Kjeken; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Quality and clinical. Request for supplementary information

Extension of indication to include treatment of adult patients with follicular lymphoma (FL) after two or more lines of therapy who are refractory or relapsed during or within 6 months after completion of anti-CD20 antibody maintenance or relapsed after autologous haematopoietic stem cell transplantation (HSCT) for Kymriah. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and corresponding sections in the package leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, minor editorial corrections are made throughout the SmPC and package leaflet to align with the current QRD template version 10.2.

Action: for adoption

The Rapporteur presented his assessment of the variation to extend the indication of Kymriah.

The Request for supplementary information was adopted on 13 December following a written procedure.

2.11.4. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0047

Novartis Europharm Limited

Rapporteur: Rune Kjeken; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Safety. Opinion

Update of sections 4.2 and 4.4 of the SmPC, Annex IID and PIL (information intended for healthcare professionals) in order to add statements for the use of Kymriah exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab".

Action: for adoption

The opinion was adopted.

2.11.5. Libmeldy - atidarsagene autotemcel - Orphan - EMEA/H/C/005321/II/0004

Orchard Therapeutics (Netherlands) BV

Rapporteur: Carla Herberts

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information was adopted on 08.10.2021.

The opinion was adopted.

2.11.6. 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 - Orphan - EMEA/H/C/005102/II/0012

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 08.10.2021.

The opinion was adopted.

2.11.7. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0020/G

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Quality. Request for supplementary information

Action: for adoption

The Rapporteur presented the assessment of this quality variation and provided feedback from the BWP discussion. The request for supplementary information was adopted.

2.11.8. Tecartus; Yescarta - axicabtagene ciloleucel; 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 - Orphan - EMEA/H/C/WS2206

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus; PRAC Rapporteur: Menno van der Elst

Scope: Safety. Opinion

Update of sections 4.2 and 4.4 of the SmPC and Annex IID in order to add statements for the use of Tecartus and Yescarta exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab". The RMPs for both products are updated accordingly (version 1.2 for Tecartus and version 5.2 for Yescarta).

Action: for adoption

The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. 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

The Rapporteur presented the assessment of the renewal application of Spherox.

The request for supplementary information was adopted.

2.13.2. 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 - Orphan - EMEA/H/C/005102/MEA/005.1

Kite Pharma EU B.V.

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

Scope: MAH Response to MEA-005 [Protocol, study no. KT-EU-472-5966] as adopted in July 2021: Prescriber Survey: Assess the prescribers' understanding of the risks of KTE-X19. Evaluate the effectiveness of risk minimization activities: Healthcare Professionals (HCP) educational materials and Patient Alert Card.

Action: for adoption

The outcome of the post-marketing measure was adopted

2.13.3. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/ANX/002.2

Kite Pharma EU B.V.

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

Scope: First 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 feedback on the assessment of the first annual interim report of the non-interventional study. PRAC concluded that the benefit risk is unchanged. The outcome of the annex II obligation was adopted.

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

Timetable:

-Start of the procedure:	20.12.2021
-EMA Coordinator's draft report:	07.01.2022
-CAT Coordinator's comments:	12.01.2022
-Revised scientific recommendation:	14.01.2022
-CAT's discussion of scientific recommendation:	21.01.2022

4.1. New requests – Appointment of CAT Coordinator

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

Intended for the kidney transplantation

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Expanded mesenchymal stem cells (MSCs) cells isolated from umbilical cord Wharton jelly

Intended for the treatment of dilative cardiomyopathy (DCM)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

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

Intended for the treatment of advanced Parkinson's disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.6. Stem cells isolated from dental pulp, cultured

Intended for the treatment of surgical bone defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.7. Modulated immune cells

Intended for solid organ transplantation / Treatment of autoimmune disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.8. Autologous bone marrow concentrate

Intended for the treatment of bone fractures

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. Non-replicating recombinant adeno-associated virus serotype 2 (rAAV2) encoding a soluble form of human CD59 (sCD59)

Intended for the treatment of geographic atrophy (via targeting the complement pathway)

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 4 January 2022.

4.2.2. VTXM01 messenger RNA (mRNA) encoding for an adenine base editor (ABE) and VTXG01 guide RNA (gRNA) targeting the proprotein convertase subtilisin/kexin type 9 (PCSK9) serine protease gene

Intended for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of low-density lipoprotein cholesterol (LDL-C) despite maximally tolerated lipid-lowering therapy

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 4 January 2022.

4.2.3. Autologous anti-CD19 chimeric antigen receptor T-cells

Intended for the treatment of CD19-expressing B-cell malignancies

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 4 January 2022.

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

No items

4.4. Finalisation of procedure

4.4.1. CD 19 CAR T-cells transduced with lentiviral vector

Intended for the treatment of adults and children with B-cell non-Hodgkin's lymphoma and acute lymphoblastic leukemia.

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

Action: for information

The information was noted.

4.4.2. Allogeneic adipose-derived mesenchymal stromal cells, ex-vivo expanded

Intended for the treatment of osteoarthritis, knee

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

Action: for information

The information was noted.

4.4.3. Recombinant adeno-associated virus, serotype 2, containing human ND4 codon-optimised gene (rAAV2-ND4) - EMA/PRIME/21/039

Treatment of Leber’s hereditary optic neuropathy (LHON) associated with ND4 G11778A mutation

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

Action: for information

The information was noted.

4.4.4. Allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured

Intended for the treatment of paediatric and adult patients undergoing partially human leucocyte antigen (HLA) compatible allogeneic haematopoietic stem cell transplantation to accelerate adaptive immunological reconstitution

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

Action: for information

The information was noted.

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:	29.11 – 02.12.2021
- Appointment of CAT Peer Reviewers:	08-10.12.2021
- SAWP first reports:	03.01.2022
- CAT Peer Reviewer comments:	07.01.2022
- Discussion at SAWP:	10-13.01.2022
- Discussion at CAT and feedback to SAWP:	15.01.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	10–13.01.2022
- Appointment of CAT Peer Reviewers:	19-21.01.2022
- SAWP first reports:	31.01.2022
- CAT Peer Reviewer comments:	04.02.2022
- Discussion at SAWP:	07-10.02.2022
- Discussion at CAT and feedback to SAWP:	18.02.2022

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

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:	02.12.2021
SAWP recommendation:	13.01.2022
CAT recommendation:	21.01.2022
CHMP adoption of report and final recommendation:	27.01.2022

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

No items

6.3.4. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

No items

7.1.2. Vote by proxy

No items

7.1.3. Strategic Review & Learning meeting (SRLM) under the French presidency, 3 March 2021, Paris (France)

CAT: Violaine Closson-Carella

Scope: feedback on the next SRLM meeting

Action: for information

Violaine Closson-Carella informed the CAT that due to ongoing COVID-19 pandemic, the French Authorities have decided to conduct the upcoming SRLM virtually.

7.2. Coordination with EMA Scientific Committees

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

Scope: Presentation on the regulatory aspects

Action: for information

Topic postponed until the January 2022 meeting.

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 on the 21-22 September 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 - Annual PCWP-HCPWP joint meeting with all Eligible Organisations on 24 November

Action: for information

The information was noted.

7.3.3. Reflection paper on criteria to be considered for the evaluation of new active substance (NAS) status of biological substances

EMA: Veronika Jekerle (on behalf of the drafting group)

Scope: feedback on the status of the NAS reflection paper

Action: for information

EMA provided detailed information on status of the reflection since it was discussed at the CAT in July 2021. The document underwent regulatory and legal scrutiny by both EMA regulatory and legal affairs offices, and by the Commission. This was a necessary step with regards to the regulatory nature of the NAS status. EMA informed CAT members that the European Commission shared EMA's view that this is an important document in view of its regulatory implications, which go beyond purely scientific assessment. All documents and comments received are made available to the BWP-CAT drafting group and to all CAT and BWP members.

This topic was included in the agenda on specific request from CAT members to be informed on the grounds for delays in the finalisation of this CAT 2021 work plan topic. During the preparation of the December CAT agenda, EMA considered that this topic was not mature enough to bring back to the CAT: the BWP-CAT drafting group has to review all the comments and finalise the draft reflection paper. It was considered more

appropriate to present the revised draft reflection paper to CAT for discussion and adoption early 2022, once finalised by the drafting Group.

The European Commission representative summarised the legal issues that they have identified during the review.

The CAT chair thanked EMA for the information provided and asked for a more proactive communication to CAT on CAT work plan topics and legal/regulatory considerations relevant to ATMPs.

As the comments from the external consultation will have to be reviewed in 2022, it was agreed to include the NAS reflection paper in the CAT work plan for 2022 (see 7.6.2).

7.4. Cooperation with the EU regulatory network

7.4.1. Revision of the Pharmaceutical legislation

CAT: Martina Schüssler-Lenz

Action: for discussion

CAT raised and discussed comments.

7.4.2. Update on the Companion Diagnostics (CDx) consultation procedure

Scope: Revised EMA guidance on CDx consultation and CHMP/CAT AR CDx template

Action: For adoption

EMA presented the revised documents, in which have been incorporated.

The EMA guidance on CDx consultation and CHMP/CAT AR CDx template will be published for external consultation in January 2022.

7.4.3. Revision of the EU legislation on blood, tissues and cells (BTC)

CAT: Martina Schüssler-Lenz

Action: for discussion

CAT discussed additional feedback related to the classification of borderline products and the perception of the negative impact of the ATMP Regulation on BTC innovation and patient access.

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 that took place on 14 October 2021

Action: for information

EMA provided a short feedback from the discussions at the last ATMP cluster teleconference.

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 16 December 2021

Action: for information

Note: the meeting has been cancelled

The information was noted.

7.5.3. WHO consultation on cell and gene therapy products

CAT: Ilona Reischl

Action: for information

The information was noted.

7.6. CAT work plan

7.6.1. Real World Data (RWD) in regulatory decision making of ATMPs

CAT: Martina Schuessler-Lenz

Scope: Feedback from the meeting with registry holders

Action: for information

The CAT chair provided an oral feedback. Registry holders have been contacted to explain the EMA pilot project: a tender has been sent to them for participation in an EMA funded project.

This topic will be included in the CAT work plan 2022.

7.6.2. CAT work plan 2022

CAT: Martina Schüssler-Lenz

Scope: draft work plan for 2022

Action: for discussion and identification of CAT contributors

The draft work plan was presented. CAT agreed with the proposed topics, and additional CAT collaborators for proposed work plan topics were identified. A work plan topic on NAS (see 7.3.3) will be added to the work plan, which will be scheduled for adoption in January 2022.

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q4/2021 update of the business pipeline report for the human scientific committees

Action: for information

Note: confidential document, not for public release

The information was noted.

7.8. Others

7.8.1. European Society of Gene and Cell Therapy (ESGCT)

CAT: Alessandro Aiuti

Scope: feedback from the meeting that took place on the 19-22 October 2021.

Action: for information

Alessandro Aiuti provided a detailed updated on the selected scientific topics presented during the October ESGCT meeting.

7.8.2. Lifecycle Regulatory Submissions Metadata project (LRSM)

Action: for information

Topic postponed until the January 2022 meeting.

7.8.3. Duration of follow-up of patients treated with AAV-based GTMPs

CAT: Martina Schüssler-Lenz

Scope: duration of follow-up of patients treated with AAV-based GTMPs

Action: for discussion

It was agreed to have a reflection on this in the frame of the CAT Learnings (see 8.1).

7.8.4. International Society for Extracellular Vesicles

Scope: Letter from the International Society for Extracellular Vesicles (ISEV) Task Force on Regulatory Affairs and Clinical Use of Extracellular Vesicle-based Therapeutics

Action: for information

The letter was noted.

7.8.5. CAT stakeholder meeting on 26 October 2021

CAT: Martina Schuesser-Lenz

Scope: Minutes of the stakeholder meeting

Action: for adoption

EMA presented the draft minutes. The minutes were adopted and will now be sent to the industry stakeholders for their comments. Afterwards the minutes will be published on the EMA website.

8. Any other business

8.1.1. CAT Learnings

CAT: Martina Schüssler-Lenz

Scope: CAT learnings on Insertional mutagenesis and germline transmission risk analysis in the context of genome editing

Action: for discussion

CAT discussed following topics: Duration of follow-up (see 7.8.3), insertional mutagenesis, germline integration for genome editing (GE) products.

On the need to include genome editing in the ICH S12 Biodistribution guideline, CAT agreed with the position from the EU Rapporteurs (Rune Kjeken, Claire Beuneu) that germline integration for GE should not be specifically mentioned: the general principle apply also for GE products.

On the topics: duration of follow-up and insertional mutagenesis, CAT members will develop a discussion paper to facilitate the CAT discussions.

Date of next CAT meeting:

19 – 21/01/2022

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

HCP: Healthcare Professionals

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

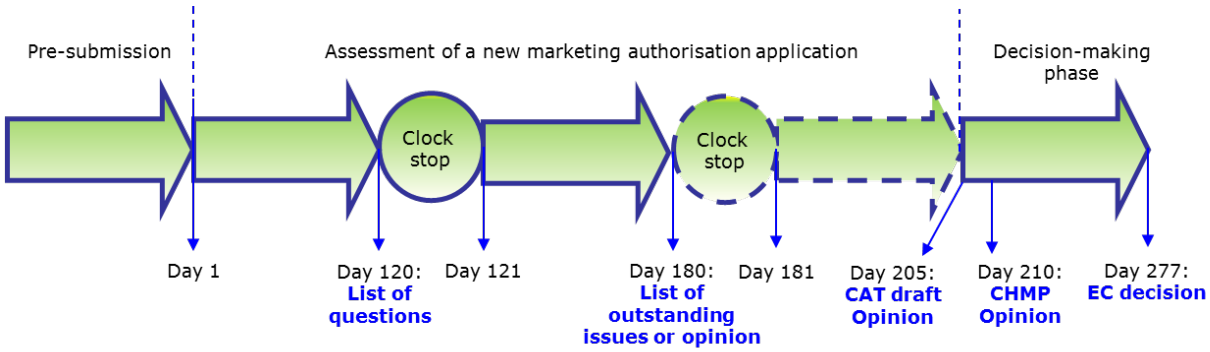
Evaluation of ATMPs (section 2)

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 08-10 December 2021 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	
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	
Maria Gazouli	Member	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Angeliki Rompoti	Alternate	Greece	No interests declared	
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	Restrictions applicable to this meeting:	5.1.2.2. & 5.4.5.
Nancy De Bremaeker	Member	Luxembourg	No interests declared	
John J. Borg	Member (CHMP member)	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 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
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Marcin Kolakowski	Alternate	Poland	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	
Alexandra Padova	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Suzana Vidic	Alternate	Slovenia	Restrictions applicable to this meeting:	2.11.3., 2.11.4. & 2.11.7.
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	Restrictions applicable to this meeting:	5.4.1., 5.1.2.2. & 5.1.1.7.
Bernd Gänsbacher	Member	Healthcare Professionals' Representative	No interests declared	
Alessandro Aiuti	Member	Healthcare Professionals' Representative	Restrictions applicable to this meeting:	2.11.5. & 5.4.6.
Alessandra Renieri	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Lydie Meheus	Alternate	Patients' Representative	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Jessica Harskamp	Expert - via Webex*	Netherlands	No interests declared	
Johannes Hendrikus Ovelgonne	Expert - via Webex*	Netherlands	No interests declared	
Jörg Engelbergs	Expert - via Webex*	Germany	No interests declared	
Hilke Zander	Expert - via Webex*	Germany	No interests declared	
Jürgen Scherer	Expert - via Webex*	Germany	No interests declared	
Matthias Renner	Expert - via Webex*	Germany	No restrictions applicable to this meeting	
Ann Mari Lone	Expert - via Webex*	Norway	No restrictions applicable to this meeting	
Ingebjorg Buajordet	Expert - via Webex*	Norway	No interests declared	
Marianne Dalhus	Expert - via Webex*	Norway	No interests declared	
Mats Okvist	Expert - via Webex*	Norway	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				