5 October 2022
EMA/CAT/760739/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft minutes of the meeting on 07-09 September 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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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.

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.

1.2. Adoption of agenda

The CAT agenda for 07-09 September 2022 meeting was adopted with two additions:

- Strategic Review and Learning meeting under the Swedish Presidency of the European Union;

- EMA Regulatory & scientific conference on RNA based medicines.

1.3. Adoption of the minutes

The CAT minutes for 13-15 July 2022 meeting were adopted.

The CAT minutes of the 10-12 August 2022 written procedure 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. Tabelecleucel - PRIME - Orphan - EMEA/H/C/004577

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

Scope: Day 180 list of outstanding issues

Action: for adoption

List of Questions adopted on 18.03.2022.

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

CAT adopted the list of outstanding issues.

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

2.8. 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. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0004

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality. Request for Supplementary Information

Action: for adoption

The request for supplementary information was adopted.

2.11.2. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0005

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Clinical. Request for Supplementary Information

Extension of indication to include treatment of adult patients with Second-line (2L) Transplant Intended (TI) Large B-Cell Lymphoma (LBCL) for BREYANZI, based on interim analyses from pivotal study JCAR017-BCM-003; this is a global randomised multicentre Phase III Trial to compare the efficacy and safety of JCAR017 to standard of care in adult subjects with high-risk, transplant-eligible relapsed or refractory aggressive B-cell Non-Hodgkin Lymphomas (TRANSFORM); As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted.

Action: for adoption

The CAT Rapporteur presented the outcome of the assessment of the variation application.

The request for supplementary information was adopted.

2.11.3. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0054

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.4. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0056

Amgen Europe B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Pharmacovigilance. Request for Supplementary Information

Submission of the final report from study 20120139 listed as a category 3 study in the RMP in order to fulfil MEA/004. This is a multicentre, observational registry study to evaluate the survival and long-term safety of subjects who previously received talimogene laherparepvec in Amgen or BioVEX sponsored clinical trials.

Action: for adoption

The request for supplementary information was adopted.

2.11.5. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0055

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 17.06.2022.

The opinion was adopted.

2.11.6. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0056

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Safety and efficacy. Opinion

Update of sections 4.2 and 5.1 of the SmPC in order to update efficacy and safety information in paediatric population based on study CCTL019C2202 (BIANCA), a phase II, single arm, multicentre open label trial to determine the safety and efficacy of tisagenlecleucel in paediatric patients with relapsed or refractory mature B-cell non-Hodgkin lymphoma (NHL). The Package Leaflet is updated accordingly.

Action: for adoption

Request for Supplementary Information adopted on 17.06.2022.

The proposed changes of the product information were discussed. The opinion was adopted.

2.11.7. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0060

Novartis Europharm Limited

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

Scope: Safety. Opinion

Update of section 4.2 of the SmPC in order to update the paediatric statement for the B-cell acute lymphoblastic leukaemia (ALL) indication and section 4.4 to update the warning on

'prior treatment with anti-CD19 therapy' as well as sections 4.4 and 4.8 in order to update safety data to reflect the pool of the 3 studies B2202, B2205J and B2001X. The proposed changes are in line with the request of the CHMP following the assessment of P46/012. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct the Complete Response Rate (CRR) 95% confidence interval (CI) on enrolled set for E2202 study presented in table 8 in section 5.1 of the SmPC. The RMP version 5.0 has also been submitted.

Action: for adoption

Request for Supplementary Information adopted on 15.07.2022.

The proposed changes of the product information were discussed. The opinion was adopted.

2.11.8. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0061/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 15.07.2022.

The opinion was adopted.

2.11.9. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0062

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Clinical. Opinion

Submission of the final report from study CCTL019B2401 listed as a category 1 study in the Annex II of the Product Information in order to fulfil ANX/007.3. This is a post authorisation efficacy studies (PAES) sub-analysis to assess efficacy in patients with relapsed or refractory diffuse large B-cell lymphoma based on data from the registry study to assess the long-term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel. The Annex II is updated accordingly.

Action: for adoption

The opinion was adopted.

2.11.10. Yescarta - axicabtagene ciloleucel - 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: Safety and efficacy. Opinion

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) 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

Request for Supplementary Information adopted on 15.07.2022, 13.05.2022 and 18.02.2022.

The Rapporteur presented the outcome of the assessment of the responses to the list of outstanding issues. The changes to the product information were discussed.

The opinion was adopted.

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

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Quality. Request for Supplementary Information

Action: for adoption

The request for supplementary information was adopted.

2.11.12. Tecartus; Yescarta - axicabtagene ciloleucel; brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2247

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 15.07.2022 and 13.05.2022.

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/010

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The Rapporteur's assessment of the recommendation was agreed.

2.13.2. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/011

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality

Action: for adoption

The Rapporteur's assessment of the recommendation was agreed.

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

Takeda Pharma A/S

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

Scope: 5-year Renewal of Marketing Authorisation

Action: for adoption

The Rapporteur presented the outcome of the assessment of the 5-year renewal application. No new safety signals were identified, and the benefit-risk profile is unchanged.

Some clarifications and additional information are requested from the applicant: a request for additional information was adopted.

2.13.4. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/ANX/001

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: In order to further assess the consistency of product quality and clinical outcomes, the MAH shall submit batch analysis and corresponding clinical safety and effectiveness data from a minimum of thirty (30) lots of Breyanzi finished product used to treat patients included in a non-interventional study based on secondary use of data from existing registries, according to an agreed protocol. Based on these data the MAH should also provide an evaluation on the need for a revision of the finished product specifications. Interim reports should be provided after approximately 15 lots and any significant out of trend results should be reported immediately.
Action: for adoption

The Rapporteur presented the outcome of the assessment of report on the fulfilment of the Annex II condition.

Some clarifications and additional information are requested from the applicant: a request

for additional information was adopted.

2.13.5. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/010

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality
Action: for adoption

The Rapporteur's assessment of the recommendation was agreed.

2.13.6. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/P46/017

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Clinical study report (Study No. CCTL019BUS03): a phase II, open label, multi-centre trial to determine the efficacy and safety of tisagenlecleucel re-infusion in Paediatric and Adolescent Young Adult (AYA) patients with acute lymphoblastic leukaemia (ALL) experiencing loss of B cell aplasia.

Action: for adoption

Request for Supplementary Information adopted on 17.06.2022.

The Rapporteur's assessment of the responses to the request for additional information was discussed. The outcome was agreed.

2.13.7. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/REC/019

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality
Action: for adoption

The Rapporteur's assessment of the recommendation was agreed.

2.13.8. Libmeldy - atidarsagene autotemcel - Orphan - EMEA/H/C/005321/ANX/003.1

Orchard Therapeutics (Netherlands) B.V.

Rapporteur: Carla Herberts

Scope: Second Progress Report: Measures proposed to reduce the overall time from patient screening to treatment to within the ranges observed during clinical development (median 8.2 weeks; range 6-12.4 weeks). Reduction of the time needed for product testing and release should be part of these measures.

Action: for adoption

The Rapporteur's assessment of the of progress report on the Annex II condition was agreed.

2.13.9. Tecartus - brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/MEA/005.3

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Protocol, study no. KT-EU-472-5966: Prescriber Survey: Assess the prescribers' understanding of the risks of KTE-X19. Evaluate the effectiveness of risk minimisation activities: Health Care Professionals' educational materials, and Patient Alert Card. Further alignment of the questionnaire with other approved product is requested. Updated protocol expected within 60 days. 60 days assessment procedure.
[MAH Response to MEA-0005.2 as adopted in May 2022]

Action: for adoption

The Rapporteur's assessment of the recommendation was agreed.

2.13.10. Tecartus - brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/R/0025

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Rune Kjeken, PRAC Rapporteur: Menno van der Elst

Scope: 1-year Renewal of Marketing Authorisation

Action: for adoption

The Rapporteur presented the outcome of the assessment of the 1-year renewal application. The specific obligation related to the submission of the results of the Zuma-2 trial is fulfilled (variation II/19, adopted in May 2022). No new safety signals have been identified and the benefit-risk profile is unchanged.

The 1-year renewal of the conditional marketing authorisation 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:	09.09.2022
-EMA Coordinator's draft report:	23.09.2022
-CAT Coordinator's comments:	28.09.2022
-Revised scientific recommendation:	30.08.2022
-CAT's discussion of scientific recommendation:	07.10.2022

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic adipose derived mesenchymal stem cells

Intended for the treatment of Crohn-related perianal fistula

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Autologous adipose derived mesenchymal stem cells

Intended for the treatment of Crohn-related perianal fistula

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Autologous anti-BCMA CAR-T cells

Intended for the treatment of multiple myeloma

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

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

Intended for the treatment of multiple sclerosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.5. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.6. 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: 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. Autologous cultured limbal epithelial and limbal epithelial stem cells growing on fibrin scaffold

Intended for the treatment of moderate to severe limbal stem cell deficiency (LSCD) caused by burns, including chemical burns to the eyes

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 22 September 2022.

4.2.2. Human allogeneic cardiac progenitor cell subpopulation selected for the absence of the surface marker CD90

Intended to improve cardiac perfusion and function in patients with refractory angina

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 22 September 2022.

4.2.3. Allogeneic CD33-directed genetically modified T-cell immunotherapy

Intended for the treatment of patients with CD33-positive acute myeloid leukaemia (AML) who are at a high risk of relapse

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 22 September 2022.

4.2.4. Allogeneic CRISPR/Cas9-edited hematopoietic stem and progenitor cells (HSPCs) lacking CD33 protein expression

Intended for the treatment of patients with CD33-positive acute myeloid leukaemia (AML) who are at a high risk of relapse

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 22 September 2022.

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

No items

4.4. Finalisation of procedure

No items

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:	29.08–01.09.2022
- Appointment of CAT Peer Reviewers:	07–09.09.2022
- SAWP first reports:	19.09.2022
- CAT Peer Reviewer comments (NC,C):	23.09.2022
- CAT Peer reviewer comments (Q):	28.09.2022
- Discussion at SAWP:	26–29.09.2022
- Discussion at CAT and feedback to SAWP:	07.10.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	26-29 September 2022
- Appointment of CAT Peer Reviewers:	05-07.10.2022
- SAWP first reports:	17.10.2022
- CAT Peer Reviewer comments (NC,C):	21.10.2022
- CAT Peer reviewer comments (Q):	26.10.2022
- Discussion at SAWP:	24-27.10.2022
- Discussion at CAT and feedback to SAWP:	04.11.2022

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

No items

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. Rules of procedure

Scope: Following the entry into force of Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (IVDR) certain changes in the CAT Rules of Procedure (RoP) are required so that the relevant legislative provisions related to EMA work in the area of medical devices are fully reflected in the CAT mandate and RoP.

Action: for adoption

The changes to the CAT rules of procedure were presented. CAT adopted the revised RoP.

7.1.4. Update on procedure for Chair election

Action: for information

Postponed to the October CAT meeting.

CAT members were informed that the election of the chair will take place during the January 2023 CAT meeting, and the election of the vice-chair during the February 2023 CAT meeting.

7.1.5. Strategic Review and Learning meeting (SRLM) under the Swedish Presidency of the European Union

CAT: Lisbeth Barkholt

Scope: Proposed date of the SRLM under the Swedish Presidency

Action: For information

CAT was informed that the SRLM under the Swedish Presidency is planned to take place on 4 – 5 May 2023 in Upsala, Sweden. There will be joint sessions with the COMP.

7.2. Coordination with EMA Scientific Committees

7.2.1. PRIME implementation of 5-year review recommendations

Scope: Presentation of the proposals for implementation of the recommendations arising from the first 5 years' experience with the scheme (see also prime-analysis-first-5-years-experience_en.pdf (europa.eu) as discussed and agreed by the PRIME oversight group.

Action: for adoption

Further feedback was provided from the discussion with the concerned committees and working parties.

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

No items

7.4. Cooperation with the EU regulatory network

7.4.1. European Institute of Innovation and Technology (EIT) Health / European Medicines Agencies Regulatory Network (EMRN) joint workshop on genome editing

Scope: Agenda of this genome editing expert workshop.

Action: for adoption

The workshop aims to close knowledge gaps relating to the regulation of future genome editing products. The draft agenda was presented. The agenda was endorsed.

Alessandro Aiuti and Ilona Reischl are supporting EMA in organising the workshop. CAT members were asked to propose name of suitable speakers for the different sessions.

7.4.2. The European Pharmacopoeia Commission texts amendment in the area of cell and gene therapy

CAT: Barbara Bonamassa

Scope: All new European Pharmacopoeia (Ph. Eur.) texts and texts that have undergone technical revisions are published in Pharmeuropa for public consultation https://www.edqm.eu/en/-/pharmeuropa-34.3-just-released. The deadline for comments on Pharmeuropa 34.3 is 30 September 2022.

Action: for information

CAT members were informed of the new Ph.Eur. monograph / general chapters in the area of cell and gene therapies. It is important that regulatory authorities provided comments on the draft texts, to ensure that these are not in contradiction with the established EU guidelines and are not restricting the flexibilities that are needed for (novel) ATMPs. The binding character of monograph raised concerns.

CAT members are asked to circulate the draft monograph and general chapters within their national agencies and provide comments directly to the EDQM/European Pharmacopoeia. BWP members were also alerted.

7.4.3. Regulatory & scientific conference on RNA-based medicines

Scope: Background, objectives and content of the conference that is scheduled to take place on 2 February 2023.

Action: for information

The objectives and draft programme of the conference was presented. Volunteers are sought to work together with EMA to prepare the agenda and identify speakers.

7.5. Cooperation with international regulators

No items

7.6. CAT work plan

No items

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q3/2022 update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

7.8. Others

7.8.1. Pilot on formal expert elicitation in the context of benefit-risk assessment

Scope: Project proposal on systematic approaches in expert groups on benefit risk

Action: for discussion

Feedback was provided on the scope and objectives of this project. Following CAT members will take part in this activity: Alessandro Aiuti, Maura O'Donovan and Maria Gazouli.

7.8.2. Adeno-associated viral (AAV) vector toxicities: regulatory considerations

CAT: Carla Herberts, Egbert Flory

Scope: Discussion paper on insertional mutagenesis and follow-up for AAV gene therapy

Action: for discussion

CAT discussed the updated discussion paper. The main discussion focussed on the duration of follow-up.

CAT members were asked to review the current version of the document and finalise the discussion paper at the October CAT meeting.

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

CAT: Martina Schüssler-Lenz

Scope: Agenda of the CAT regulatory session at the ESGCT annual meeting that will take place in Edinburgh on 14 October 2022.

Action: for discussion

The final agenda of the CAT regulatory session was presented. The duration of this session has been extended to 2 hours.

CAT was informed that a separate session on enhanced support from EMA to academic developers has been included in the ESGCT annual meeting. This will be a one-hour session with presentation by EMA and Alessandro Aiuti.

7.8.4. CAT Learnings

Action: for adoption

The CHMP learning was presented as part of the discussions on tabelecleucel. The CHMP learning was endorsed.

8. Any other business

No items

Date of next CAT meeting:

05-07/10/2022

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

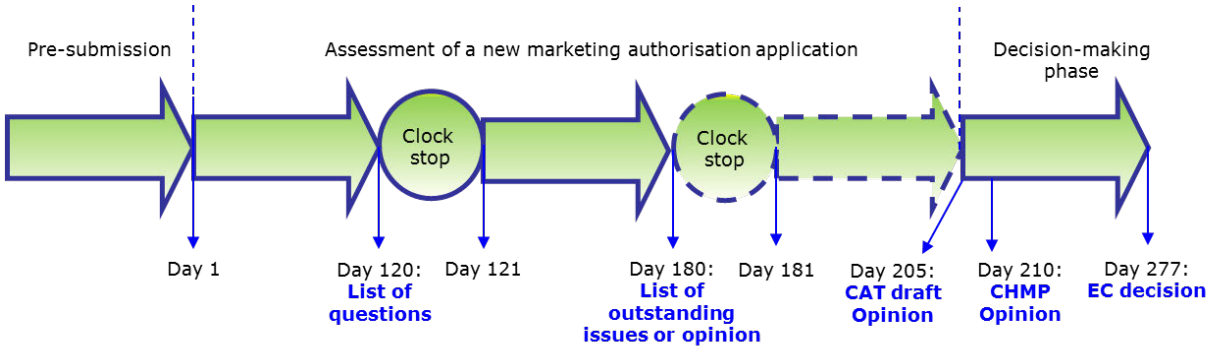
Evaluation of ATMPs (section 2)

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 07-09 September 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	
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	
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 participation in discussions, final deliberations and voting:	4.2.2.
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No restrictions applicable to this meeting	
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:	
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
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	Cannot act as rapporteur, other leading/co-ordinating role or peer reviewer for: No participation in final deliberations and voting on:	 2.11.5., 2.11.6., 2.11.7., 2.11.8., 2.11.9., 2.11.11., 2.13.6 & 2.13.7.
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	Cannot act as rapporteur, other leading/co-ordinating role	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			or peer reviewer for: No participation in final deliberations and voting on:	
Bernd Gänsbacher	Alternate	Clinicians' Representative	No interests declared	
Paolo Gasparini	Member	Clinicians' Representative	No interests declared	
Alessandro Aiuti	Member	Clinicians' Representative	No participation in discussions, final deliberations and voting on:	2.13.8.
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
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	
Catherine Milne	Observer/Alternate	EDQM	No interests declared	
Hans Hillege	Expert - via Webex	CBG/MEB (NL)	No interests declared	
Hans Ovelgonne	Expert - via Webex	CBG/MEB (NL)	No interests declared	
Amelia Cupelli	Expert - via Webex	AIFA (IT)	No interests declared	
Filip Van Nuffel	Expert - via Webex	FAGG-AFMPS(BE)	No interests declared	
Olga Kholmanskikh	Expert - via Webex	FAGG-AFMPS(BE)	No interests declared	
Thomas Hinz	Expert - via Webex	PEI (DE)	No interests declared	
Verena Scheer	Expert - via Webex	PEI (DE)	No interests declared	
Zuzana Jedlicková	Expert - via Webex	PEI (DE)	No interests declared	
Attila Sebe	Expert - via Webex	PEI (DE)	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Armando Genazzani	Expert - via Webex	AIFA (IT)	No interests declared	
Maria Grazia Evandri	Expert - via Webex	AIFA (IT)	No interests declared	
Graziella Curtale	Expert - via Webex	AIFA (IT)	No interests declared	
Filomena Nappi	Expert - via Webex	AIFA (IT)	No interests declared	
Francesca Tittone	Expert - via Webex	AIFA (IT)	No restrictions applicable to this meeting	
Odoardo Olimpieri	Expert - via Webex	AIFA (IT)	No interests declared	
Antonella Isgrò	Expert - via Webex	AIFA (IT)	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				