13 July 2022
EMA/CAT/600000/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 15-17 June 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.

The chairperson thanked the departing members/alternates for their contributions to the Committee.

1.2. Adoption of agenda

The CAT agenda for 15-17 June 2022 meeting was adopted with following additions:

- 2.11.5. YESCARTA - axicabtagene ciloleucel

- 7.1.4. CAT Strategic Review and Learning meeting under the presidency of the Czech Republic

- 7.5.3. AMP cluster teleconference to take place on 23 June 2022.

1.3. Adoption of the minutes

The CAT minutes for 11-13 May 2022 meeting were adopted.

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830

BioMarin International Limited; treatment of severe haemophilia A

Scope: Opinion

Action: for adoption

List of Outstanding Issues adopted on 18.03.2022. List of Questions adopted on 05.11.2021. Ad-hoc expert group (AHEG) meeting taking place on 09.06.2022

The Rapporteurs presented the assessment of the response to the list of outstanding issue. The outcome of the discussion in the AHEG meeting was presented by EMA on behalf of the AHEG Rapporteur.

CAT noted the outcome of the assessment and the input from the AHEG. CAT agreed with the Rapporteurs' position that the benefit risk is positive. Specific obligations for a conditional marketing authorisation were discussed.

CAT discussed in detail the product information. CAT also reviewed the Annex II.D which include the key messages that will have to be incorporated in the education material.

CAT agreed by consensus that the benefit-risk in the indication as in the SmPC (heading 4.1) is positive and that a conditional marketing authorisation can be recommended. Norway and Lichtenstein were in agreement with the CAT draft opinion. The CAT draft opinion will be forwarded to CHMP for adoption.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

2.5.1. Etranacogene dezaparvovec - PRIME - Orphan - EMEA/H/C/004827

Accelerated assessment

CSL Behring GmbH; treatment of adults with Haemophilia B

Scope: Day 80 assessment report

Action: for information

The information was noted. CAT members were asked to provide comments to the Day 80 assessment reports.

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. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0052/G

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 13.05.2022.

The opinion was adopted.

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

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Request for Supplementary Information

Action: for adoption

The request for additional information was adopted.

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

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Clinical. Request for Supplementary Information

Update of sections 4.2 and 5.1 of the SmPC in order to update efficacy and safety information in the paediatric population based on data from study CCTL019C2202, a phase

2, 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) (BIANCA). The package leaflet is updated accordingly.

Action: for adoption

The Rapporteur presented the outcome of the assessment of this variation. Some outstanding issues were identified. The request for additional information was adopted.

2.11.4. Tecartus - brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/II/0019

Kite Pharma EU B.V.

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

Scope: Safety. Opinion

Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information based on 24-month follow-up data from all treated patients in cohort 1 of the pivotal clinical study, KTE-C19-102 (ZUMA-2), a Phase 2, multicentre, open-label study evaluating the safety and efficacy of KTE-X19 in subjects with relapsed or refractory (r/r) mantle cell lymphoma (MCL). This submission is in fulfilment of the specific obligation (SOB 004) to confirm the long-term efficacy and safety of Tecartus in adult patients with relapsed/refractory (r/r) MCL. In addition, the MAH has taken the opportunity to make minor editorial changes in the SmPC. The RMP version 2.1 has also been submitted.

Action: for adoption

The Rapporteur presented the outcome of the assessment of this variation. The changes to the product information were accepted. The opinion was adopted. The specific obligation (SOB 004) is fulfilled.

2.11.5. Yescarta- axicabtagene ciloleucel – Orphan – EMEA/H/C/004480/PSUSA/0010703/202110/0049

Kite Pharma EU B.V.

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

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

Scope: ATMP PSUSA variation: Update of section 4.8 of the SmPC to add the adverse reaction status epilepticus with a frequency of 'common'. The Package leaflet is updated accordingly.

Action: for adoption

The opinion was adopted via a written procedure.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/003.8

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Non-interventional post-authorisation safety study (Study CCTL019B2401): in order to further characterise the safety – including long-term safety – of Kymriah, the applicant should conduct and submit a study based on data from a disease registry in acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL) patients. Fifth semi-annual report (EBMT data only).

Action: for information

The information was noted.

2.13.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/LEG/018

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: From II/0044: to provide the final investigator site inspection report from study site #1700 (Spain, Hospital Virgen del Rocio) that participates in the study CCTL019E2202/ELARA.

Action: for adoption

The Rapporteur presented the conclusion of the assessment of this post-authorisation measure. The GCP findings do not impact on the benefit risk or the validity of the data of variation II/44 (extension of indication follicular lymphoma). The Rapporteur's conclusion was adopted.

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

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No 1901/2006, as amended. Clinical study report / Study No. CCTL019BUS03: a phase 2, open label, multicentre trial to determine the efficacy and safety of tisagenlecleucel re-infusion in Pediatric and Adolescent Young Adult (AYA) patients with acute lymphoblastic leukaemia (ALL) experiencing loss of B cell aplasia.

Action: for adoption

The Rapporteur presented the conclusion of the assessment of this post-authorisation measure. The study reported related to the retreatment of paediatric ALL patients with Kymriah. Limited information was obtained from this study; no new safety signals were reported. A request for supplementary information was adopted.

2.13.4. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451/REC/008.1

Novartis Europharm Limited

Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro

Scope: Quality: MAH's response to questions on REC 008 as adopted in January 2022

Action: for adoption

The quality follow-up measure was adopted.

2.13.5. Strimvelis – Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/PSUSA/00010505/202111

Orchard Therapeuthics

PRAC Rapporteur: Menno van der Elst

Scope: Periodic safety update report (PSUR): The eighth periodic benefit-risk evaluation report with reporting period 26 November 2020 up to 25 November 2021 for autologous $CD34^+$ enriched cell fraction that contains human haematopoietic stem/progenitor ($CD34^+$) cells transduced with retroviral vector that encodes for the human adenosine deaminase complementary deoxyribonucleic acid sequence.

Action: for information

The outcome of the PSUR assessment was noted.

2.13.6. Tecartus - brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/REC/009

MAH: Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

The quality follow-up measure was adopted.

2.13.7. Tecartus - brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/REC/010

MAH: Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

The quality follow-up measure 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:	17.06.2022
-EMA Coordinator's draft report:	01.07.2022
-CAT Coordinator's comments:	06.07.2022
-Revised scientific recommendation:	08.07.2022
-CAT's discussion of scientific recommendation:	15.07.2022

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Adeno-associated viral vector serotype 2 encoding glial cell line-derived neurotrophic factor

Intended for the treatment of Parkinson's disease (PD)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.2. Ex-vivo expanded allogeneic human corneal epithelial cells containing P63 positively expressing cells

Intended for the treatment of persistent corneal epithelial defects

Scope: appointment of CAT Coordinator

Action: for adoption

The CAT Coordinator was appointed.

4.1.3. Allogeneic adiposed-derived mesenchymal stem cells

Intended for the treatment of arthritis and diabetes type I and II

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.4. Acellular tubular graft composed of human collagen types I and III and other extracellular matrix proteins, including fibronectin and vitronectin

Intended for replacement or repair of injured blood vessels in cases of vascular trauma; for replacement or repair of diseased vessels as an arterial bypass conduit for peripheral arterial disease (PAD); and as an implanted vascular access conduit for hemodialysis in patients with end-stage renal disease (ESRD)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.5. A heterologous vaccine regimen composed of 2 vaccine components: replication incompetent gorilla adenovirus serotype 20 (GAd20) and modified vaccinia ankara (MVA) vectors encoding tumor-specific antigens mutant calreticulin (mutCALR) and Janus kinase 2 (mutJAK2)

Intended for the treatment of patients with myeloproliferative neoplasms (MPNs)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.6. Recombinant adeno-associated virus vector containing the human aspartoacylase complementary DNA (ASPA cDNA) with an optimized expression cassette and constitutive promoter

Intended for the treatment of Canavan disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.7. Adeno-associated virus serotype hu68 vector encoding human GLB1 gene

Intended for the treatment of GM1 gangliosidosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.8. Autologous human bone marrow derived mesenchymal stromal cells (MSCs)

Intended for the treatment of pathologies affecting the oesophageal tract in which total or partial organ replacement is required

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.9. Skin cell suspension obtained with the help of recombinant non-animal trypsin

Intended for skin regeneration after burns, skin trauma, invasive surgery

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. Jelly Derived Mesenchymal Stem Cells – allogeneic

Intended for the treatment of other specified inflammatory spondylopathies (non-radiographic axial spondyloarthritis, M46.8)

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 27 June 2022.

4.2.2. Autologus keratinocytes, fibroblasts

Intended for the treatment of partial deep dermal and full thickness burn wounds and reconstructive surgery

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 27 June 2022.

4.2.3. Dopaminergic neuronal microtissues containing A9 TH+ (Tyrosine hydroxylase) dopaminergic mature neuron

Intended for the treatment of Parkinson's disease

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 27 June 2022.

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

4.3.1. Leukocyte and platelet rich plasma, autologous

Intended for the treatment of critical limb ischemia

Scope: Closure of this procedure without conclusion due to lack of response by the applicant

Action: for adoption

CAT closed this applicant without conclusion.

4.4. Finalisation of procedure

4.4.1. Ex-vivo expanded autologous Wharton's Jelly derived mesenchymal stem cells (WJ-MSCs)

Intended for the treatment of autism spectrum disorder

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

Action: for adoption

The ATMP classification report was reported. 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 tissue-derived stromal cell fraction devoid of mature adipocytes

Intended for the treatment of temporomandibular disorders

Scope: Comments raised by the European Commission. ATMP scientific recommendation

Action: for adoption

The comments from the European Commission did not require a revision of the ATMP classification report. The ATMP classification report was adopted. The product does fulfil the definition of a tissue engineered product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.3. Cultured human adipose derived stromal cells

Intended for the treatment of stress urinary incontinence in men after radical prostatectomy

Scope: Comments raised by the European Commission. ATMP scientific recommendation

Action: for adoption

The comments from the European Commission did not require a revision of the ATMP classification report. The ATMP classification report was adopted. The product does fulfil the definitions of a somatic cell therapy product and a tissue engineered product and is therefore classified as a tissue engineered product as defined in Article 2(4) of Regulation (EC) 1394/2007.

4.4.4. Human autologous tumour and hypoxia educated macrophages

Intended for the treatment of spinal cord injury

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 tissue engineered 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:	07-10.06.2022
- Appointment of CAT Peer Reviewers:	15-17.06.2022
- SAWP first reports:	27.06.2022
- CAT Peer Reviewer comments (NC,C):	01.07.2022
- CAT Peer reviewer comments (Q):	06.07.2022
- Discussion at SAWP:	04-07.07.2022
- Discussion at CAT and feedback to SAWP:	14.07.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	04-07.07.2022
- Appointment of CAT Peer Reviewers:	13-15.07.2022
- SAWP first reports:	22.08.2022
- CAT Peer Reviewer comments (NC,C):	26.08.2022
- CAT Peer reviewer comments (Q):	31.08.2022
- Discussion at SAWP:	29.08-01.09.2022
- Discussion at CAT and feedback to SAWP:	09.09.2022

No items

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

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

5.4. Final Advice Letters for procedures finalised the previous month

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	10/06/2022
SAWP recommendation:	07/07/2022
CAT recommendation:	15/07/2022
CHMP adoption of report and final recommendation:	21/07/2022

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

The chair thanked Maja Sommerfelt Gronvold for her contribution as alternate member for Norway.

The chair also thanked the members and alternates representing the clinicians and patient organisations at the CAT for their contributions as members and alternate members over the last 3 years.

7.1.2. Vote by proxy

No items

7.1.3. Publication of CAT regulatory outcomes on the EMA webpage

CAT: Martina Schüssler-Lenz

Scope: Presentation of current situation and proposed changes

Action: for information

The CAT chair presented the topic and introduced some suggestions for improvement. EMA noted that it will not be possible to make reference of CAT in CHMP highlights on ATMP approvals, but that CAT's work is clearly acknowledged in the press releases. The process for the timely publication of CAT minutes is being improved.

CAT suggested to rename the CAT quarterly statistics to better cover its content and to publish these statistics as a separate document: attaching this document to the CAT minutes (as was done for the April CAT minutes) does not make it possible to find them when doing an internet search.

7.1.4. CAT strategic Review and Learning Meeting (SRLM), under the presidency of the Czech Republic

CAT: Kristyna Rehorova Hradikova

Scope: update on the upcoming SRLM meeting that will take place in Paris on 17-18 November 2022.

Action: for information

The date of the upcoming SRLM meeting was noted. CAT will have a discussion on the topic for agenda of this SRLM in the July CAT meeting.

7.2. Coordination with EMA Scientific Committees

No items

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 2-3 March 2022

Action: for information

The information was noted.

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

Scope: Draft Agenda - PCWP-HCPWP joint meeting on 1-2 June 2022

Action: for information

The information was noted.

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

Scope: PCWP-HCPWP Draft Workplan 2022-2025

Action: for information

The information was noted.

7.3.4. CAT - ITF interactions

Scope: CAT-ITF annual report 2021

Action: for information

CAT noted the presentation on the CAT-ITF interactions during 2021.

7.3.5. Diffuse large B-cell lymphoma (DLBCL) indication wording and inclusion of high-grade B-cell lymphoma (HGBL)

Scope: key points from the discussion with haematologists that took place on the 31 May 2022

Action: for information

Topic postponed until the July CAT meeting.

7.3.6. Q&A on the interface between Regulation (EU) 536/2014 on clinical trials for medicinal products for human use (CTR) and Regulation (EU) 2017/746

CAT: Ilona Reischl

Scope: link to download the updated document EudraLex - Volume 10 (europa.eu) or Guidance - MDCG endorsed documents and other guidance (europa.eu)

Action: for information

The information was noted.

7.3.7. Q&A on complex clinical trials

CAT: Ilona Reischl, Alessandra Renieri

Scope: The Q&A has been publicly released and is available at EudraLex – Volume 10 (europa.eu) or medicinal_qa_complex_clinical-trials_en.pdf (europa.eu)

Action: for information

The information was noted.

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: Draft agenda of the joint EIT Health/EMRN workshop

Action: for discussion

The outline of the multi-stakeholder workshop on genome editing (GE) was presented. The aim of the meeting is to discuss knowledge gaps and to allow for networking between developers and regulators. The aim and expected outcome of this workshop need to be well-defined, as GE is discussed at almost all scientific meetings / conferences. There were some questions on the discussion on ethical issues.

Following CAT members agreed to be involved in the further development of the agenda: Alessandro Aiuti, Ilona Reischl. It was suggested also to involve the chair of the Clinical Trials Coordination Group (CTCG): Marianne Lunzer.

7.4.2. Companion Diagnostics (CDx) consultation procedure

Scope: Finalisation of the CDx consultation procedure

Action: for adoption

Further to public consultation on the draft version published in December 2021, the EMA guidance on the CDx consultation has been updated and is now final. The CHMP/CAT AR CDx template as well as the application forms for both initial and follow-up procedures have also been updated.

CAT adopted the CDx consultation procedure.

7.5. Cooperation with international regulators

7.5.1. ATMP cluster teleconference with US-FDA, Health Canada and PMDA (Japan), May 2022

CAT: Martina Schuessler-Lenz

Scope: Feedback from the teleconference that took place on 24 May 2022

Action: for information

Short feedback was provided of the discussion at the ATMP cluster of 24 May 2022.

7.5.2. EDQM Stakeholder consultation 5th edition Tissue and Cells Guide

CAT: Ilona Reischl

Scope: CAT feedback on the consultation for the 5th edition of the Guide to the quality and safety of tissues and cells for human application

Action: for information

The CAT feedback on the EDQM consultation was noted. The CAT chair thanked the members that provided comments.

7.5.3. ATMP cluster teleconference with US-FDA, Health Canada and PMDA (Japan), June 2022

CAT: Martina Schuessler-Lenz

Scope: Agenda of the teleconference that will take place on 23 June 2022

Action: for information

CAT noted the agenda of the upcoming ATMP cluster teleconference.

7.6. CAT work plan

7.6.1. ATMP curriculum

CAT: Ilona Reischl, Martina Schüssler-Lenz, Concetta Quintarelli, Una Riekstina, Dariusz Sladowski, Alessandro Aiuti, Isabel Vieira, Roland Pochet

Scope: ATMP trainings for 2022

Action: for discussion

EMA provided feedback from the discussion at the breakout meeting that took place on 15 June 2022. An overview of the planned training for 2022 was provided.

On Friday 15 July, a webinar will be organised on the ATMP authorisation procedure (training by Ilona Reisch): this webinar is open to all CAT members and experts/assessors in the NCAs.

It was suggested to make a compilation of websites providing useful ATMP training material. This can then be used by new ATMP assessors for training purposes. CAT members were asked to send (to CAT Secretariat) any links to such training websites.

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q2/2022 update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

7.8. Others

7.8.1. American Society for Gene and Cell Therapy (ASGCT) Annual meeting

CAT: Alessandro Aiuti

Scope: Oral feedback from the ASGCT annual meeting that was held in Washington DC from 16-19 May 2022

Action: for information

EMA and Alessandro Aiuti provided feedback from the ASGCT meeting.

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

CAT: Martina Schüssler-Lenz

Scope: Invitation to organise a CAT regulatory session at the ESGCT annual meeting that will take place in Edinburgh from 11-14 October 2022

Action: for discussion

The invitation to organise a CAT regulatory session at ESGCT was presented and agreed.

Alessandro Aiuti and Martina Schüssler-Lenz will develop a draft programme, and this will be presented at CAT in July for discussion and identification of CAT speakers.

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

CAT: Carla Herberts, Egbert Flory

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

Action: for discussion

Carla Herberts presented the discussion paper, and more specifically the section on the follow-up (FU) of patients treated with AAV based gene therapies. The duration of FU was discussed. It was agreed to set up a small drafting group before the July CAT to discuss the topic on FU of patients further.

There was feedback on discussion on this topic in a non-clinical expert group. As the expertise is mainly present in CAT, it was suggested to inform the Non-clinical working party /Peer-clinical assessor meeting (PAM) of the CAT scientific views. CAT members can already share the draft document with the PAM members.

8. Any other business

No items

Date of next CAT meeting:

13-15/07/2022

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

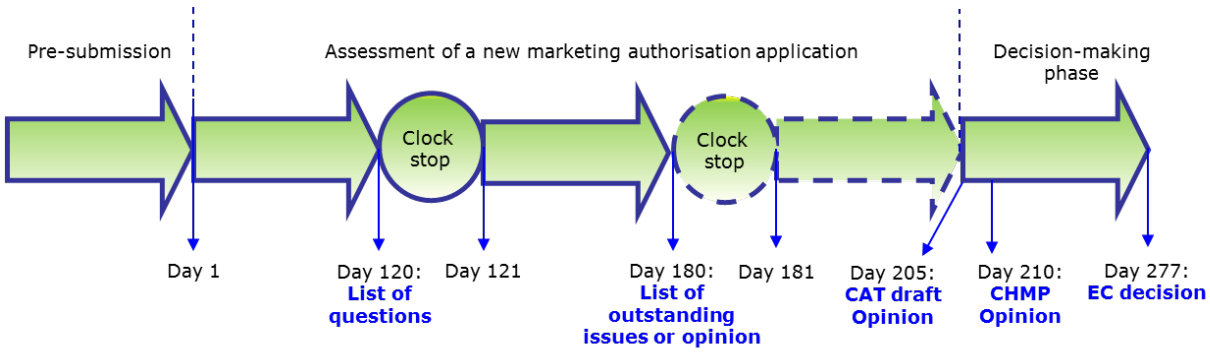
Evaluation of ATMPs (section 2)

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 15-17 June 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	Alternate	Denmark	No restrictions applicable to this meeting	
Toivo Maimets	Member	Estonia	No interests declared	
Pille Saalik	Alternate	Estonia	No interests declared	
Heli Suila	Member	Finland	No interests declared	
Maija Tarkkanen	Alternate	Finland	No interests declared	
Violaine Closson	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Egbert Flory	Alternate (to CHMP representative)	Germany	No interests declared	
Maria Gazouli	Member	Greece	No interests declared	
Angeliki Rompoti	Alternate	Greece	No interests declared	
Katalin Lengyel	Member	Hungary	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	No participation in discussions, final deliberations and voting on:	4.1.3.
Nancy De Bremaeker	Member	Luxembourg	No interests declared	
John J. Borg	Member (CHMP member)	Malta	No interests declared	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Babs Fabriek	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Maja Sommerfelt Grønvold	Alternate	Norway	No interests declared	
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	
Alexandrina Preda	Alternate	Romania	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Katarina Vavrová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Suzana Vidic	Alternate	Slovenia	No participation in final deliberations and voting on:	2.11.2., 2.11.3., 2.13.1. 2.13.2., 2.13.3., & 2.13.4.
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	No restrictions applicable to this meeting	
Bernd Gänsbacher	Member	Clinicians' Representative	No interests declared	
Alessandro Aiuti	Member	Clinicians' Representative	No participation in discussions, final deliberations and voting on:	2.13.5.
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Lydie Meheus	Alternate	Patients' Representative	No interests declared	
Kieran Breen	Member	Patients' Representative	No interests declared	
Roland Pochet	Alternate	Patients' Representative	No interests declared	
Catherine Milne	Observer/Alternate	EDQM	No interests declared	
Johannes Ovelgonne	Expert - via Webex	SAWP (NL)	No interests declared	
Paula van Hennik	Expert - via Webex	CBG-MEB (NL)	No interests declared	
Marja van de Bovenkamp	Expert - via Webex	CBG-MEB (NL)	No interests declared	
Gabriela Ullio-Gamboa	Expert - via Webex	ANSM (FR)	No interests declared	
Stéphanie Jambon	Expert - via Webex	ANSM (FR)	No interests declared	
Norontsoa Rasolondramanitra	Expert - via Webex	ANSM (FR)	No interests declared	
Caroline Matko	Expert - via Webex	ANSM (FR)	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Sylvie Benchetrit	Expert - via Webex	ANSM (FR)	No interests declared	
Nathalie Morgensztejn	Expert - via Webex	ANSM (FR)	No interests declared	
Bruno Delafont	Expert - via Webex	ANSM (FR)	No restrictions applicable to this meeting	
Paolo Petracci	Expert - via Webex	ANSM (FR)	No interests declared	
Yseult Brun	Expert - via Webex	ANSM (FR)	No interests declared	
Andrea Laslop	Expert - via Webex	AGES (AT)	No interests declared	
Brigitte Mueller	Expert - via Webex	AGES (AT)	No interests declared	
Rene Anour	Expert - via Webex	AGES (AT)	No interests declared	
Florian Klinglmueller	Expert - via Webex	AGES (AT)	No interests declared	
Philipp Janesch	Expert - via Webex	AGES (AT)	No interests declared	
Christine Vaculik	Expert - via Webex	AGES (AT)	No interests declared	
Martin Walter	Expert - via Webex	AGES (AT)	No interests declared	
Tjerk Feenstra	Expert - via Webex	AGES (AT)	No interests declared	
Susanne Wolf	Expert - via Webex	AGES (AT)	No interests declared	
Christoph Mück	Expert - via Webex	AGES (AT)	No interests declared	
Attila Sebe	Expert - via Webex	PEI (DE)	No interests declared	
Beate Mosl	Expert - via Webex	PEI (DE)	No restrictions applicable to this meeting	
Matthias Renner	Expert - via Webex	PEI (DE)	No restrictions applicable to this meeting	
Hilke Zander	Expert - via Webex	PEI (DE)	No interests declared	
Joerg Engelbergs	Expert - via Webex	PEI (DE)	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				