11 May 2022
EMA/CAT/184995/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 11-13 April 2022

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

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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

Table of contents

1. Introduction

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

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

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

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

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

1.2. Adoption of agenda

The CAT agenda for 11-13 April 2022 meeting was adopted with one addition under 8. AOB

1.3. Adoption of the minutes

The CAT minutes for 16-18 March 2022 meeting were adopted

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. Eladocagene exuparvovec - Orphan - EMEA/H/C/005352

PTC Therapeutics International Limited; treatment of aromatic L-amino acid decarboxylase (AADC) deficiency

Scope: oral explanation

Action: for adoption

List of Outstanding Issues adopted on 05.11.2021, 16.04.2021. List of Questions adopted on 20.05.2020.

The CAT Rapporteurs presented the assessment of the responses to the list of outstanding issues and provided feedback from the discussions in the BWP and in the Ad hoc Expert group (AHEG) meeting of 4 April 2022.

The CAT draft opinion will be adopted at the May CAT meeting.

2.2.2. Autologous glioma tumor cells, inactivated / autologous glioma tumor cell lysates, inactivated / allogeneic glioma tumor cells, inactivated / allogeneic glioma tumor cell lysates, inactivated - Orphan - EMEA/H/C/003693

Epitopoietic Research Corporation-Belgium (E.R.C.); treatment of glioma

Scope: oral explanation

Action: for information

List of Questions adopted on 22.01.2021. List of outstanding issues adopted on 16.07.2021

The Rapporteurs presented the assessment of the responses to the list of outstanding issues.

The CAT draft opinion will be adopted at the May CAT meeting.

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

No items

2.6. Update on ongoing initial applications

2.6.1. Autologous CD34+ haematopoietic stem cells transduced ex vivo with a lentiviral vector encoding for the human Wiskott-Aldrich syndrome gene – Orphan - EMEA/H/C/0005677

Orchard Therapeutics; treatment of Wiskott-Aldrich syndrome

Scope: Notification of cancellation of the MAA submission

Action: for information

The information was noted.

2.6.2. Lenadogene nolparvovec - Orphan - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of vision loss due to Leber hereditary optic neuropathy (LHON)

Scope: MAA's request for additional clock stop extension

Action: for adoption

D120 List of Questions adopted in February 2021

CAT discussed the request of clock stop extension. The revised timetable was adopted.

2.7. New applications

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

Accelerated assessment

CSL Behring GmbH; treatment of adults with Haemophilia B (congenital Factor IX deficiency) and with a pre-existing neutralising anti-AAV5 antibody titre below 1:700 to reduce the frequency of bleeding episodes and the need for Factor IX replacement therapy

Scope: Timetable for assessment

Action: for adoption

The assessment timetable was adopted.

2.8. Withdrawal of initial marketing authorisation application

No items

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

No items

2.10. GMP and GCP inspections requests

No items

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

2.11.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0050

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Request for Supplementary Information

Action: for adoption

The request for supplementary information was adopted.

2.11.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0052

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.3. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451/II/0026/G

Novartis Europharm Limited

Rapporteur: Sol Ruiz

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 21.01.2022.

The opinion was adopted.

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

Kite Pharma EU B.V.

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

Scope: Clinical. Opinion

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

Action: for adoption

Request for Supplementary Information adopted on 18.02.2022, 05.11.2021.

The Rapporteur presented the outcome of the assessment. CAT discussed the product information and the assessment of the orphan similarity. An amendment for the orphan similarity report was proposed.

CAT adopted a positive opinion of the extension of indication of Yescarta.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/R/0014

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Annika Folin

Scope: 1-year Renewal of Marketing Authorisation

Action: for adoption

The Rapporteur presented the outcome of the assessment. The status of the specific obligations (SO) was presented: the change in timing of the interim analysis of the second SO was agreed.

The renewal of the conditional marketing authorisation of Abecma was adopted.

2.13.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/003.7

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Study CCTL019B2401: non-interventional post-authorisation safety study (PASS): 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 ALL and DLBCL patients. Fourth semi-annual report (EBMT data only)

Action: for adoption

The Rapporteur provided feedback from the PRAC discussion on the semi-annual report of the PASS study. The PRAC outcome was agreed.

2.13.3. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/P46/018

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.
FINAL STUDY REPORT, Study AVXS-101-CL-306 (CL-306): a Phase 3, Open-Label, Single Arm, Single-dose Gene Replacement Therapy Clinical Trial for Patients with Spinal Muscular Atrophy Type 1 with One or Two SMN2 Copies Delivering AVXS-101.

Action: for adoption

Request for Supplementary Information adopted on 18.02.2022.

As per the requirements of the paediatric legislation, the MAHs are obliged to report on the

outcome of paediatric studies. In the application, Novartis provided the final report of study CL-306. The results of this study do not result in changes to the product information.

The outcome of the assessment was agreed.

2.13.4. CAT recommendation to MAHs of CAR-T cell-based therapies with regards to long-term safety and efficacy follow-up studies using EBMT as a data source

Scope: draft recommendation

Action: for discussion

Following the trilateral with EBMT and MAHs and following consultation with CAT and PRAC Rapporteurs of affected products, EMA is presenting two proposals for recommendation for approved ATMPs using EBMT as a data source for PAES/PASS studies. Following discussion, CAT agreed that the second option is the most appropriate. The recommendation will be updated to incorporate the comments made by CAT and sent to CAT for adoption via a written procedure. Thereafter, the CAT recommendation will be discussed at PRAC.

3. Certification of ATMPs

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

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

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

Intended for the treatment of autism spectrum disorder

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Ultra-purified adipose tissue-derived product devoid of mature adipocytes

Intended for fat grafting, augmenting and managing soft tissue defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Cultured human adipose derived stromal cells

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. Human autologous tumour and hypoxia educated macrophages

Intended for the treatment of spinal cord injury

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 transduced CD8+ T cells expressing the melanoma associated antigen 1-(MAGE-A1)-specific T cell receptor TCR 8001

Intended for the treatment of patients with MAGE-A1 expressing solid tumours

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 2 May 2022.

4.2.2. Suspension of VST cells

Intended for the treatment of adults and children with therapy-resistant viral infection after allogeneic hematopoietic stem cell transplantation

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 2 May 2022.

4.2.3. Adipose-derived stem cells

Intended for the treatment of type 2 diabetes mellitus, Treatment of cardiac and pulmonary complications after Covid-19

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 2 May 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: ATMP scientific recommendation

Action: for adoption

Awaiting responses from the applicant. Postponed until the May CAT meeting.

4.4. Finalisation of procedure

4.4.1. Gingival fibroblast

Intended for the treatment of gonarthrosis

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definitions of a cell therapy medicinal product and a tissue engineered product and is therefore classified as tissue engineered product as defined in Article 2(4) of Regulation (EC) No 1394/2007.

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

Intended for the treatment of advanced solid tumours

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medicinal product as defined in Article 2(1) of Regulation (EC) No 1394/2007.

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

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

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medicinal product as defined in Article 2(1) of Regulation (EC) No 1394/2007.

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

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

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a somatic cell therapy medicinal product as defined in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.5. Plasmid expressing variant of human interleukin-10

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

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medicinal product as defined in Article 2(1) of Regulation (EC) No 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:	04-07.04.2022
- Appointment of CAT Peer Reviewers:	11-13.04.2022
- SAWP first reports:	25.04.2022
- CAT Peer Reviewer comments (NC/C):	29.04.2022
- CAT Peer Reviewer comments (Q):	04.05.2022
- Discussion at SAWP:	02-05.2022
- Discussion at CAT and feedback to SAWP:	13.05.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	02-05.05.2022
- Appointment of CAT Peer Reviewers:	11-13.05.2022
- SAWP first reports:	30.05.2022
- CAT Peer Reviewer comments (NC/C):	03.06.2022

- CAT Peer Review comments (Q):	08.06.2022
- Discussion at SAWP:	07-10.06.2022
- Discussion at CAT and feedback to SAWP:	16.06.2022

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

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

5.4. Final Advice Letters for procedures finalised the previous month

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:	
Procedure start:	04-07.04.2022
SAWP recommendation:	05.05.2022
CAT recommendation:	13.05.2022
CHMP adoption of report and final recommendation:	19.05.2022

No items

6.3.2. Month 1 – Discussion of eligibility

No items

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 welcomed Kristyna Rehorova Hradilkova as the new alternate member for Czech Republic, replacing Petr Soukup, who took over the role of member. The Chair thanked Tomáš Boráň for his contribution as a member for Czech Republic.

Action: for information

7.1.2. Vote by proxy

No items

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 review - nomination of ESEC members

CAT: Martina Schüssler-Lenz

Action: for information

EMA provided information on the Working Party implementation project, including the European Specialist Expert Community (ESEC) and the Quality Innovation Group (QIG). CAT was also informed when the call for expression of interest for the ESEC and QIG will be launched. These calls of expression of interest will be circulated to CAT. The mandate of the QIC will be presented to CAT in May.

Further feedback will be provided to CAT in May on how the new working party organisation will impact on the development of multi-disciplinary guidelines for ATMPs (at present, dedicated CAT drafting groups are set for ATMP guidelines).

7.3.2. Core SmPC for genetically modified cells

CAT drafting group: Martina Schüssler-Lenz, Ilona Reischl, Violaine Closson Carella, Isabel Vieira, Metoda Lipnik-Stangelj, Carla Herberts, Alessandro Aiuti

Scope: Core SmPC for genetically modified cells

Action: for adoption

EMA Secretariat on behalf of the CAT drafting group presented the final Core SmPC for genetically modified cells. The main changes from the version that went out for public consultation were highlighted. CAT agreed that immunogenicity statement should be included in section 4.8 of the SmPC.

The Core SmPC for genetically modified cells was adopted.

7.3.3. EC/EMA/CTCG (ACT-EU) Complex Clinical trials Q&A – Final Draft

CAT: Ilona Reischl, Alessandra Renieri

Action: for adoption

EMA Secretariat presented the Q&A on complex clinical trials. There was a short discussion on the relevance of the concept to ATMPs and if CAT members have encountered ATMP clinical trials with such complex trial designs.

The Q&A was adopted.

7.3.4. Procedure on ATMP scientific advice and BWP interaction

Scope: procedure for interactions with BWP on scientific advices and timing/role of CAT peer review

Action: for discussion

EMA Secretariat presented the revised procedure for interactions with BWP on scientific advice for ATMPs. Some practical observations were made by CAT members. Further comments from CAT members are awaited. The procedure will be adopted at the May CAT meeting.

7.4. Cooperation with the EU regulatory network

7.4.1. Revision of the EU pharmaceutical legislation (Directive 2001/83/EC and Regulation (EC) No 726/2004): revised gene therapy definition

Action: for discussion

7.4.2. Revision of the EU pharmaceutical legislation: specific objectives for ATMPs

Action: for information

The Commission representative introduced herself and provided an overview of the ATMP specific objectives that will be taken forward in the revision of the pharmaceutical legislation.

7.5. Cooperation with international regulators

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

CAT: Martina Schuessler-Lenz

Scope: Agenda of the teleconference that will take place on 21 April 2022

Action: for information

CAT was informed that the next ATMP cluster meeting is postponed and is now scheduled to take place on 24 May 2022.

7.6. CAT work plan

No items

7.7. Planning and reporting

7.7.1. Marketing authorisation applications: 3-year forecast report

Scope: Update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

7.8. Others

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

CAT: Carla Herberts, Egbert Flory

Scope: CAT discussion paper: follow-up of patients treated with AAV-based gene therapies

Action: for discussion

Carla Herberts presented the draft discussion paper. CAT discussed the duration of follow-up (FU) of patient treated with AAV-based gene therapies. Carla Herberts will update the discussion paper with the comments made by CAT and present it again at the May CAT meeting.

7.8.2. DIA Europe

CAT: Ilona Reischl

Scope: Feedback from the panel session: 'A future vision for cell & gene therapies in Europe' and from the session: 'The future of Drug-Device combination product registries'

Action: for information

A short feedback from the ATMP related session in DIA Europe was provided.

8. Any other business

8.1.1. Position from the Supreme Medical Council (Poland) on the commercialisation of stem cell treatments

CAT: Dariusz Sladowski

Scope: Feedback from the meeting the of Supreme Medical Council (NRL) of 8 April 2022

Action: for information

Dariusz Sladowski provided feedback from the meeting. The NRL endorsed the EMA/CAT statement of 28 April 2022 warning against unproven cell-based therapies[1] and issued

[1] https://www.ema.europa.eu/documents/public-statement/ema-warns-against-using-unproven-cell-based-therapies_en.pdf

information for patients and recommendation to Bioethical Committees (describing the principles of using ATMPs under exception / hospital exemption).

Date of next CAT meeting:

11-13/05/2022

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

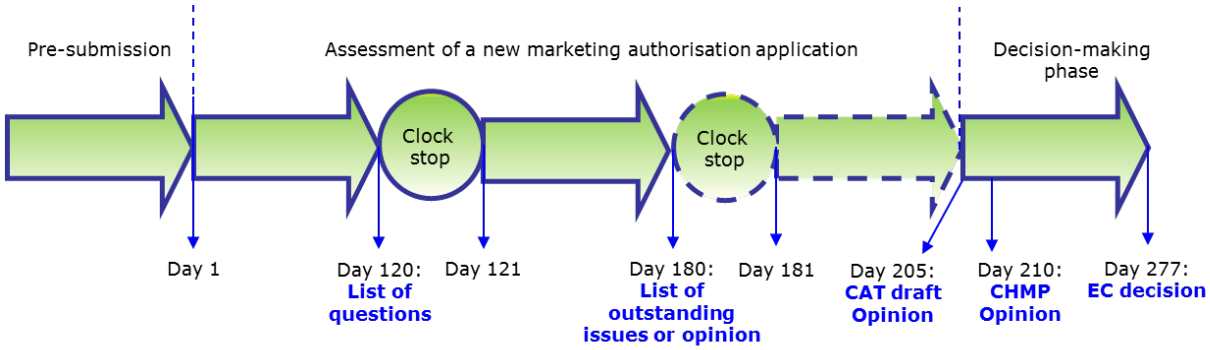
Evaluation of ATMPs (section 2)

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 11-13 April 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	Cannot act as rapporteur, other leading/co-ordinating role or peer reviewer for:	5.1.1.3.
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	
Marcin Kolakowski	Alternate	Poland	No interests declared	
Bruno Sepodes	Member (CHMP member)	Portugal	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Silviu Istrate	Member	Romania	No interests declared	
Alexandrina Preda	Alternate	Romania	No interests declared	
Lukas Slovak	Member	Slovakia	No interests declared	
Katarina Vavrová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Suzana Vidic	Alternate	Slovenia	No participation in final deliberations and voting on: Cannot act as rapporteur, other leading/co-ordinating role or peer reviewer for:	2.11.1., 2.11.2., 2.11.3., 2.13.2. & 2.13.3. 5.1.1.7.
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	No restrictions applicable to this meeting	
Bernd Gänsbacher	Member	Clinicians' Representative	No interests declared	
Frederic Bernard	Alternate	Clinicians' Representative	No interests declared	
Alessandro Aiuti	Member	Clinicians' Representative	No participation in discussions, final deliberations and voting on:	2.6.1.
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Lydie Meheus	Alternate	Patients' Representative	No interests declared	
Kieran Breen	Member	Patients' Representative	No interests declared	
Roland Pochet	Alternate	Patients' Representative	No interests declared	
	Observer	EDQM		
Catherine Milne	Observer/Alternate	EDQM	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	
Blanca García-Ochoa	Expert - via Webex	AEMPS ES	No interests declared	
Susana Rojo	Expert - via Webex	AEMPS ES	No interests declared	
Milena Peralta	Expert - via Webex	AEMPS ES	No interests declared	
Manuel Schiff	Expert - via Webex	France	No restrictions applicable to this meeting	
Paula van Hennik	Expert - via Webex	CBG/MEB NL	No interests declared	
Anneruth Huttinga	Expert - via Webex	CBG/MEB NL	No interests declared	
Peter Kiely	Expert - via Webex	CHMP IE	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

11. CAT quarterly statistics[2]

This report provides the statistical data on authorisation of ATMPs, type II variations, CAT scientific recommendations on Advanced Therapy Medicinal Product (ATMP) classification, certifications, and on CAT contributions to Scientific Advice, Paediatric Investigation Plans and PRIME (priority of medicines) eligibity requests.

The period covered by this report is: January – April 2022.

[2] The CAT quarterly statistics replaces the CAT monthly report.

Advanced therapy medicinal products approvals

During its plenary meeting of January 2022, CAT adopted a positive draft opinion for **Breyanzi** (lisocabtagene maraleucel) for the following indication: treatment of adult with relapsed or refractory diffuse large B cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), after at least two previous lines of treatments. Based on the assessment of the CAT, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Breyanzi. More information on Breyanzi can be found in the EPAR.

During its plenary meeting of March 2022, CAT adopted a positive draft opinion for **Carvykti** (ciltacabtagene autoleucel) for the following indication: treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy. Based on the assessment of the CAT, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Carvykti. More information on Carvykti can be found in the Summary of opinion.

Extension of indication of authorised ATMPs

During its plenary meeting of March 2022, CAT adopted an extension of indication for **Kymriah** to include the treatment of adult patients with follicular lymphoma after two or more lines of therapy who are refractory or relapsed during or within 6 months after completion of anti-CD20 antibody maintenance or relapsed after autologous haematopoietic stem cell transplantation.

During its plenary meeting of April 2022, CAT adopted an extension of indication for **Yescarta** to include the treatment of adult patients with relapsed or refractory follicular lymphoma after three or more lines of systemic therapy.

Overview of product-related activities

The Committee discussed ongoing evaluation procedures for ATMPs and other related procedures as summarised in the following tables:

Initial Evaluation of Marketing Authorisation Applications (MAA) for ATMP				
	2009-2020	**2021**	**2022**	**Total**
Submitted MAAs	32	3	1	36
Positive draft Opinion	18 [i]	2	2	22*
Negative draft opinions	4 [i,ii,iii]	0	0	4
Withdrawals	8 [ii, iv]	0	0	8
Ongoing MAAs				6

*** Corresponding to 21 ATMPs (see List of authorised ATMPs)**
[i] One negative draft opinion and two positive draft opinions for the Glybera
[ii] Negative draft opinion and withdrawal for the Cerepro
[iii] Two negative draft opinions for Heparesc
[iv] Luxceptar, Roctavian, Artobend

Variations (Type II) for authorised ATMP				
	2009-2020	**2021**	**2022**	**Total**
Positive opinion	78	32	14	124

Scientific recommendation on advanced therapy classification[3]				
	2009-2020	**2021**	**2022**	**Total**
Submitted	489	66	13	568
Adopted	483	61	16	560

Certification of quality and non-clinical data for small and medium-sized enterprises developing ATMPs[4]				
	2009-2020	**2021**	**2022**	**Total**
Adopted	14	0	0	14

Scientific advice procedure for ATMPs				
	2009-2020	**2021**	**2022**	**Total**
Number of procedures	442	64	16	522

Paediatric Investigation Plans (PIP) for ATMPs				
	2009-2020	**2021**	**2022**	**Total**
Number of procedures	45	0	0	45

PRIME[5] Eligibility for ATMPs				
	2016-2020	**2021**	**2022**	**Total**
Discussed	91	14	1	106
Granted	39	7	0	46

[3] More information on the scientific recommendation on advanced therapy classification and the summaries of ATMP classification can be found on the ATMP classification webpage.
It is stressed that the scientific recommendation on advanced therapy classification does not amount to any endorsement of the plausibility of the product, including the mode of action or therapeutic indication(s) claimed by the applicant.
[4] More information on the ATMP certification procedure can be found ATMP certification webpage.
[5] PRIority MEdicines (PRIME) scheme. More information can be found at the PRIME webpage.

List of authorised ATMPs

NAME	Type of ATMP	Authorisation Date	Orphan	PRIME[6]	Comment
Chondrocelect	TEP	5/10/2009	No	No	MA withdrawn July 2016
Glybera	GTMP	25/10/2012	Yes	No	MA not renewed (MA ended Oct. 2017)
MACI	TEP, combined ATMP	27/06/2013	No	No	MA not renewed (MA ended June 2018)
Provenge	CTMP	6/09/2013	No	No	MA withdrawn May 2015
Holoclar	TEP	17/02/2015	Yes	No	
Imlygic	GTMP	16/12/2015	No	No	
Strimvelis	GTMP	26/05/2016	Yes	No	
Zalmoxis	CTMP	18/08/2016	Yes	No	MA withdrawn Oct. 2019
Spherox	TEP	10/07/2017	No	No	
Alofisel	CTMP	23/03/2018	Yes	No	
Yescarta	GTMP	23/08/2018	Yes	Yes	
Kymriah	GTMP	23/08/2018	Yes	Yes	
Luxturna	GTMP	22/11/2018	Yes	No	
Zynteglo	GTMP	29/05/2019	Yes	Yes	MA withdrawn March 2022
Zolgensma	GTMP	18/05/2020	Yes	Yes	
Libmeldy	GTMP	17/12/2020	Yes	No	
Tecartus	GTMP	14/12/2020	Yes	Yes	
Skysona	GTMP	16/07/2021	Yes	Yes	MA withdrawn Nov. 2021
Abecma	GTMP	18/08/2021	Yes	Yes	
Breyanzi	GTMP	4/04/2022	No	Yes	
Carvykti	GTMP	Positive opinion March 2022	Yes	Yes	Commission decision pending

More information on authorised products can be found on: www.ema.europa.eu (type in the product name in the search box)

[6] PRIME (PRIority MEdicines scheme) was set up in March 2016 to provide early and enhanced scientific and regulatory support to medicines that have the potential to significantly address patients' unmet medical needs.

Abbreviations: ATMP: advanced therapy medicinal product; GTMP: gene therapy medicinal product; CTMP: cell therapy medicinal product; TEP: tissue engineered product; MA: Marketing authorisation