9 October 2024
EMA/CAT/471065/2024
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 09 & 11 October 2024

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

09 October 2024, 14:00 – 18:30, room 1D

11 October 2024, 09:00 – 13:00, room 1D

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 this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to 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, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CAT plenary session to be held 09-11 October 2024. See October 2024 CAT minutes (to be published post November 2024 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 09-11 October 2024 meeting

1.3. Adoption of the minutes

CAT minutes for 11-14 September 2024 meeting

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

2.3.1. Beremagene geperpavec - PRIME - Orphan - EMEA/H/C/006330

Krystal Biotech Netherlands B.V.; Treatment of patients from birth with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene

Scope: Day 180 list of outstanding issues

Action: for adoption

List of Questions adopted on 15.03.2024.

2.4. Day 120 list of questions

2.4.1. Delandistrogene moxeparvovec - Orphan - EMEA/H/C/005293

Roche Registration GmbH; Treatment of ambulatory patients aged 3 to 7 years old with Duchenne muscular dystrophy

Scope: Day 120 list of questions

Action: for adoption

2.4.2. Dorocubicel / Allogeneic umbilical cord-derived CD34- cells, non-expanded - PRIME - Orphan - EMEA/H/C/005772

Accelerated assessment

Cordex Biologics International Limited; Treatment of adult patients with haematological malignancies

Scope: Day 120 list of questions

Action: for adoption

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

No items

2.7. New applications

No items

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/0086/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Safety, Opinion

A grouped application consisting of:

C.I.4: Update of section 4.4 of the SmPC in order to amend existing warnings on cytokine release syndrome based on literature.

C.I.4: Update of section 4.4 of the SmPC in order to amend existing warnings on neurological adverse reaction based on literature. The Package Leaflet is updated accordingly.

C.I.4: Update of section 4.4 of the SmPC in order to amend existing warnings on hypersensitivity reactions based on post marketing data and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to implement editorial changes to the PI.

Action: for adoption

2.11.2. Upstaza - Eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0023/G

PTC Therapeutics International Limited

Rapporteur: Joseph DeCourcey

Scope: Quality, request for supplementary information

Action: for adoption

2.11.3. Yescarta - Axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0075/G

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Karin Erneholm

Scope: Clinical, opinion

Grouped application comprising two type II variations as follows:

C.I.13 - Submission of the final report from study KTE-C19-101 (ZUMA-1) listed as a category 3 study in the RMP. This is a Phase 1/2 Multicenter Study Evaluating The Safety And Efficacy Of Kte-C19 In Subjects With Refractory Aggressive Non-Hodgkin Lymphoma.

C.I.13 - Submission of the final report from study KTE-C19-106 (ZUMA-6) listed as a category 3 study in the RMP. This is a Phase 1-2 Multi-Center Study Evaluating The Safety And Efficacy Of Kte-C19 In Combination With Atezolizumab In Subjects With Refractory Diffuse Large B-Cell Lymphoma (Dlbcl).

The RMP version 9.2 has also been submitted.

Action: for adoption

Request for Supplementary Information adopted on 21.06.2024.

2.11.4. Zolgensma - Onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0052

Novartis Europharm Limited

Rapporteur: Emmely de Vries

Scope: Clinical, request for supplementary information

Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and vector shedding data following request in procedure EMA/H/C/004750/P46/022 and based on data from study COAV101A12306. In addition, a reference to section 5.2 is added to section 4.4, as requested in final Assessment report of procedure EMA/H/C/004750/P46/022.

Action: for adoption

2.11.5. Tecartus; Yescarta - Axicabtagene ciloleucel; Brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2500

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, request for supplementary information

Action: for adoption

Request for Supplementary Information adopted on 24.05.2024, 16.02.2024.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Breyanzi - Lisocabtagene maraleucel / Lisocabtagene maraleucel - EMEA/H/C/004731/P46/023

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Clinical, opinion

Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

CLINICAL STUDY REPORT / Study No. JCAR017-BCM-004

Title: A Phase 1/2, Open-label, Single Arm, Multicohort, Multicentre Trial to Evaluate the

Safety and Efficacy of JCAR017 in Paediatric Subjects with Relapsed/Refractory B-cell acute lymphoblastic leukaemia (B-ALL) and B-cell non-Hodgkin lymphoma (B-NHL) (TRANSCEND PEDALL; hereafter referred to as BCM-004).

Action: for adoption

2.13.2. Casgevy - Exagamglogene autotemcel - Orphan - EMEA/H/C/005763/R/0006

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Bianca Mulder

Scope: 1 year Renewal of Marketing Authorisation

Action: for adoption

2.13.3. Hemgenix - Etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/R/0020

CSL Behring GmbH

Rapporteur: Silke Dorner, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Bianca Mulder

Scope: 1 year Renewal of Marketing Authorisation

Action: for adoption

2.14. Companion diagnostics - initial consultation

No items

2.15. Companion diagnostics – Follow-up consultation

No items

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:	11.10.2024
-EMA Coordinator's draft report:	22.10.2024
-CAT Coordinator's comments:	30.10.2024
-Revised scientific recommendation:	31.10.2024
-CAT's discussion of scientific recommendation:	08.11.2024

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic CD19(4G7)CAR+_TCRαβ−_CD52+/− cells

Treatment of CD19-expressing hematologic malignancies

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Autologous adult bone marrow-derived, non-expanded CD133+ haematopoietic stem cells

Treatment of Asherman's syndrome

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Chimeric group B adenovirus from parental wildtype viruses Ad3 and Ad7 with attenuation in E3 region and no inserted sequences

Treatment of ovarian cancer

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Human allogeneic cardiosphere-derived cells

Treatment of muscular dystrophy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Allogenic fibroblasts embedded in a scaffold of hyaluronic acid and fibrinogen

Treatment of chronic and refractory ulcers

Scope: ATMP scientific recommendation

Action: for adoption

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

4.3.1. hiPSC derived Ovarian Support Cells (OSCs)

For ex vivo maturation of human oocytes

Scope: Response to questions; revised ATMP scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Autologous cells mainly composed of CD45+CD3+ T cells and to minor extent of other cells like B cells and NK cells derived from the regional lymph node cells and enriched for neoantigen specific T cells

For the treatment of cancers in adults

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for information

4.4.2. In vitro transcribed mRNA encoding the peptide VMAPRTLFL, a ligand for the activating immune receptor CD94/NKG2C

For the treatment and / or prevention of leukaemia relapse, e.g. after haematopoietic stem cell transplant

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for information

4.4.3. Recombinant adeno-associated virus vector containing an expression cassette of Padua factor IX transgene

For the treatment of hemophilia B

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for information

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:	30.09-03.10.2024
- Appointment of CAT Peer Reviewers:	09.-11.10.2024
- SAWP first reports:	21.10.2024
- CAT Peer Reviewer comments (NC/C):	25.10.2024
- CAT Peer Reviewer comments (Q):	30.10.2024
- Discussion at SAWP:	28-31.11.2024
- Discussion at CAT and feedback to SAWP:	06-08.11.2024

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	28-31.10.2024
- Appointment of CAT Peer Reviewers:	06-08.11.2024
- SAWP first reports:	18.11.2024
- CAT Peer Reviewer comments (NC/C):	22.11.2024
- CAT Peer Reviewer comments (Q):	27.11.2024
- Discussion at SAWP:	25-28.11.2024
- Discussion at CAT and feedback to SAWP:	04-06.12.2024

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

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	30.09-03.10
SAWP recommendation:	31.10.2024
CAT recommendation:	08.11.2024
CHMP adoption of report and final recommendation:	14.11.2024

6.3.2. Month 1 – Discussion of eligibility

No items

6.3.3. Month 2 – Recommendation of eligibility

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

Action: for information

7.1.2. CAT Strategic Review & Learning meeting (SRLM) under the Hungarian presidency – 19-20 November 2024

CAT: Andras Donaszi-Ivanov, Viola Bardóczy

Scope: Draft agenda of the upcoming SRLM

Action: for discussion

7.2. Coordination with EMA Scientific Committees

No items

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

No items

7.4. Cooperation with the EU regulatory network

No items

7.5. Cooperation with international regulators

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

CAT: Ilona Reischl

Scope: Verbal report from the teleconference of 19.09.2024

Action: for information

7.6. CAT work plan

7.6.1. CAT symposium – 10.10.2024, Amsterdam, the Netherlands

Scope: Feedback from the symposium

Action: for information

7.7. Planning and reporting

7.7.1. Business Pipeline Report

Scope: Q3/2024 Update of the Business Pipeline report for the human scientific committees

Action: for information

7.8. Others

7.8.1. REVAMP overview template

Scope: To update members of the project on revising the template for the assessment report

Action: for information

7.8.2. Innovative features of developments

Scope: To highlight enabling technologies applying to their development from an established list. The current list of enabling technologies is outdated and we propose an updated list

Action: for discussion

7.8.3. 4th China Biologics CMC Conference

CAT: Ilona Reischl

Scope: Opportunity for remote presentation at the 4th China Biologics CMC Conference (26-27.12.2024)

Action: for information

Note: CAT members interested to give a remote or pre-recorded presentation on quality aspects of ATMP should inform CAT secretariat by 14.10.24.

8. Any other business

No items

Date of next CAT meeting:

06-08.11.2024

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

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

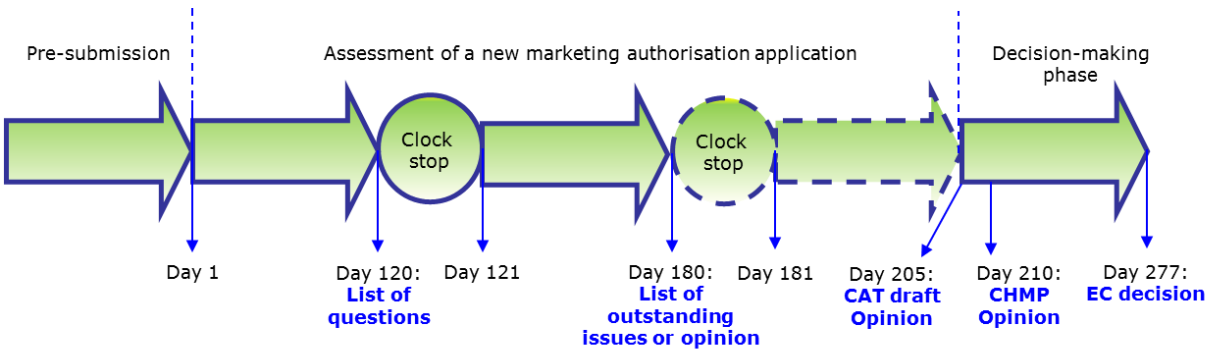
Evaluation of ATMPs (section 2)

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 Post-authorisation activities (section 2.11-2.13) and any ATMP related inspection requests (section 2.14).

New applications (sections 2.1. to 2.9.)

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 2.4) 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 2.3). Section 2.6 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.

New applications (section 2.7.)

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.

Withdrawal of applications (section 2.8.)

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.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.9.)

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.

Companion diagnostics (section 2.10)

This section lists applications for initial and follow-on consultation of companion diagnostics.

Post-authorisation activities (section 2.11-2.13.)

Section 2.11 lists type II variations, including extension of indication applications and re-examination procedures for type II variations for which the applicant has requested re-examination of the opinion previously issued by the CHMP. Section 2.12 list extension application according to Annex I of Reg. 1234/2008 and section 2.13 includes all other post-authorisation activities concerning authorised ATMPs that are not covered elsewhere in the agenda such as post-authorisation measures, 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.

GMP and GCP Inspections Issues (section 2.14.)

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).

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/