17 April 2024
EMA/CAT/162597/2024
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 17-19 April 2024

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

17 April 2024, 14:00 – 18:30, room 1C

18 April 2024, 09:00 – 18:30, room 1C

19 April 2024, 09:00 – 13:00, room 1C

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 17-19 April 2024. See April 2024 CAT minutes (to be published post May 2024 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 17-19 April 2024 meeting

1.3. Adoption of the minutes

CAT minutes for 13-16 March 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

No items

2.4. Day 120 list of questions

2.4.1. Autologous cartilage-derived articular chondrocytes, in-vitro expanded - EMEA/H/C/004594

Repair of symptomatic, localised, full-thickness cartilage defects of the knee joint grade III or IV

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

2.7.1. Mozafancogene autotemcel - PRIME - Orphan - EMEA/H/C/005537

Rocket Pharmaceuticals B.V.; Treatment of paediatric patients with Fanconi Anaemia Type A

Scope: Timetable for assessment

Action: for adoption

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. Companion diagnostics

2.10.1. Initial consultation

No items

2.10.2. Follow-up consultation

No items

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

2.11.1. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0023

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, Opinion

Action: for adoption

Request for supplementary information adopted on 19.01.2024, 06.10.2023.

2.11.2. ROCTAVIAN - Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/II/0010

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Safety

Submission of the final report from study BMN270-302 listed as a category 3 study in the RMP. This is a phase 3 open-label, single-arm study to evaluate the efficacy and safety of BMN 270, an adeno-associated virus vector–mediated gene transfer of human factor VIII at a dose of 4E13 vg/kg in hemophilia A patients with residual FVIII levels ≤ 1 IU/dL receiving prophylactic FVIII infusions.

Action: for adoption

2.11.3. Tecartus; Yescarta - Axicabtagene ciloleucel; Brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2607

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, opinion

Action: for adoption

Request for supplementary information adopted on 19.01.2024.

2.11.4. Tecartus; Yescarta - Axicabtagene ciloleucel; Brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2632

Kite Pharma EU B.V.

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

Scope: Safety & Clinical, opinion

Update of sections 4.2 and 5.1 of the SmPC in order to update the safety monitoring timelines based on data from clinical studies, post-marketing studies, and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to sections 2.2, 6.3 and 6.6 and to update sections 4.4 and 4.5 of the SmPC to align the language across both products.

Action: for adoption

2.11.5. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0072

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality

Action: for information

Note: Withdrawal request received on 14 March 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/REC/020

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, Request for supplementary information, fulfilled

Action: for adoption

2.13.2. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/REC/014.1

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

2.13.3. Ebvallo - Tabelecleucel - Orphan - EMEA/H/C/004577/REC/007

Pierre Fabre Medicament

Rapporteur: Egbert Flory

Scope: Quality, opinion

Action: for adoption

2.13.4. ROCTAVIAN - Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/SOB/006.1

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Clinical & Pharmacovigilance, opinion

MAH Response to SOB 006 as adopted in January 2024: Study 270-303 1-Year CSR - A Phase 3b, Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of BMN 270, an

Adeno-Associated Virus Vector–Mediated Gene Transfer of Human Factor VIII, with Prophylactic Corticosteroids in Hemophilia A Patients.

Action: for adoption

2.13.5. Tecartus - Brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/ANX/002.3

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Clinical & Pharmacovigilance

From initial MAA:

PAES Study No. KTE-EU-472-6036: First Annual Report - Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)

Action: for adoption

2.13.6. Zolgensma - Onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/P46/022

Novartis Europharm Limited

Rapporteur: Emmely de Vries

Scope: Clinical

Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Final study report COAV101A12306: Phase IIIb, open-label, single-arm, single-dose, multicenter study evaluating the safety, tolerability, and efficacy of gene replacement therapy with intravenous OAV101 (AVXS-101) in paediatric patients with spinal muscular atrophy (SMA)

Action: for adoption

Request for supplementary information adopted on 16.02.2024.

2.13.7. Abecma - idecabtagene vicleucel; Breyanzi - lisocabtagene maraleucel; Carvykti - ciltabtagene autoleucel; Kymriah - tisagenlecleucel; Tecartus - brexucabtagene autoleucel; Yescarta - axicabtagene ciloleucel

Bristol-Myers Squibb Pharma EEIG (Abecma, Breyanzi), Janssen-Cilag International NV (Carvykti), Novartis Europharm Limited (Kymriah), Kite Pharma EU B.V. (Tecartus, Yescarta)

CAT Rapporteurs: Rune Kjeken (Kymriah, Abecma), Jan Mueller-Berghaus (Carvykti, Tecartus, Yescarta), Concetta Quintarelli (Breyanzi)

PRAC Rapporteur (for the signal): Ulla Wändel Liminga

Scope: Feedback from PRAC discussion on signal of secondary malignancies of T-cell origin (EPITT 20040)

Action: for discussion

2.14. GMP and GCP inspections requests

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

4. Scientific Recommendation on Classification of ATMPs

Timetable:

-Start of the procedure:	22.04.2024
-EMA Coordinator's draft report:	08.05.2024
-CAT Coordinator's comments:	15.05.2024
-Revised scientific recommendation:	17.05.2024
-CAT's discussion of scientific recommendation:	24.05.2024

4.1. New requests – Appointment of CAT Coordinator

4.1.1. MicroRNA against BCL2 anti-apoptotic messenger RNA

For treatment of cancer patients

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Allogeneic natural killer cells expanded in vitro and transfected to express modified Fas ligand

For treatment of hematological malignancies and glioblastoma

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Stromal vascular fraction

For treatment of osteoarthritis

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Implantable device 3D bioprinted with autologous microfat and hydrogel bioink

For treatment of Breast reconstruction, soft tissue repair

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. mRNA encoding ARCUS nuclease

For treatment of chronic hepatitis B (CHB) virus infection

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Allogeneic human corneal endothelial cells (neltependocel) and a low molecular weight Rho kinase inhibitor (Y-27632)

For treatment of corneal oedema due to corneal endothelial dysfunction

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Lymphocyte concentrate

For improvement of the pregnancy outcomes among women with unexplained repeated pregnancy loss and HLA sharing among partners

Scope: ATMP scientific recommendation

Action: for adoption

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

No items

4.4. Finalisation of procedure

4.4.1. Allogeneic human induced pluripotent stem cells-derived corneal limbal stem cells

For treatment of limbal stem cell deficiency

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.2. Olfactory glial cells isolated from autologous human olfactory bulb, expanded in culture

For treatment of complete spinal cord injuries

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.3. Circular RNA capable to bind to mutated regions of the messenger RNA from the DMPK gene

For treatment of myotonic dystrophy type 1

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

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:	08-11.04.2024
- Appointment of CAT Peer Reviewers:	17-19.04.2024
- SAWP first reports:	06.05.2024
- CAT Peer Reviewer comments (NC/C):	10.05.2024
- CAT Peer Reviewer comments (Q):	15.05.2024
- Discussion at SAWP:	13-16.05.2024
- Discussion at CAT and feedback to SAWP:	22-24.05.2024

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	13-16.05.2024
- Appointment of CAT Peer Reviewers:	22-24.05.2024
- SAWP first reports:	03.06.2024
- CAT Peer Reviewer comments (NC/C):	07.06.2024
- CAT Peer Reiveiwer comments (Q):	12.06.2024
- Discussion at SAWP:	10-13.06.2024
- Discussion at CAT and feedback to SAWP:	19-21.06.2024

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

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

No items

5.4. Final Advice Letters for procedures finalised the previous month

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	08-11.04.2024
SAWP recommendation:	16.05.2024
CAT recommendation:	24.05.2024
CHMP adoption of report and final recommendation:	30.05.2024

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

Action: for information

7.1.2. Vote by proxy

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Belgian presidency – 15-17 May 2024

CAT: Claire Beuneu

Scope: Draft agenda of the upcoming SRLM

Action: for discussion

7.2. Coordination with EMA Scientific Committees

7.2.1. Paediatric procedures on IRIS platform

Scope: Inform the Committee about the progress on paediatric procedures that will be onboarded on IRIS on 4th June 2024

Action: for information

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

7.3.1. Question and Answer on decentralised manufacturing

Scope: Presentation of the draft Question and Answers (prepared by Quality Innovation Group)

Action: for discussion

7.3.2. Joint CAT-SAWP membership

Scope: Appointment of joint CAT-SAWP member.

Action: for agreement

Note: further to the call for interest, a CAT member has put forward its candidature

7.3.3. BWP/CAT training on Quality aspects of AAV based gene therapy medicinal products (ATMPs)

Scope: Agenda of the training to take place on 31 May 2024

Action: for awareness

7.4. Cooperation with the EU regulatory network

7.4.1. European Pharmacopoeia text on cell-based preparations for human use

CAT: Violaine Closson Carella

Scope: To inform the committee of the public consultation in Pharmeuropa on the European Pharmacopoeia text (5.32) on cell-based preparations for human use

Action: for information

7.4.2. European Pharmacopoeia texts on gene therapy adopted at the European Pharmacopoeia Commission session in March 2024

CAT: Catherine Milne

Scope: Adopted European Pharmacopoeia texts on gene therapy

Action: for information

7.5. Cooperation with international regulators

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

CAT: Ilona Reischl

Scope: Agenda of the teleconference of 25.04.2024

Action: for information

7.6. CAT work plan

7.6.1. Questions and Answers on gene therapy: revision

CAT: Ilona Reischl

Scope : Feedback from the first drafting group meeting; plan of actions to identify additional questions

Action: for discussion

7.7. Planning and reporting

No items

7.8. Others

7.8.1. EMA lecture on 'Gene editing and its relevance for innovative treatments'

Scope: Lecture by Lluis Montoliu Ph.D., a CSIC Research Scientist and Deputy Director at the National Centre for Biotechnology in Madrid

Action: for information

7.8.2. Real World Evidence, including DARWIN EU®

Scope: Quarterly update on Real World Evidence (RWE), including DARWIN EU

Action: For information

8. Any other business

Date of next CAT meeting:

22-24 May 2024

9. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

For a list of acronyms and abbreviations, see:

List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in relation to EMA's regulatory activities

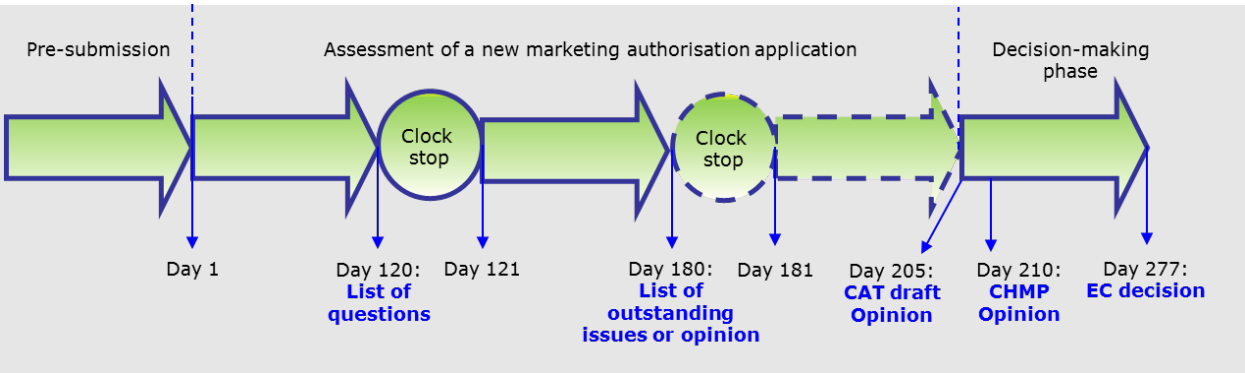
Evaluation of ATMPs (section 2)

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/