15 May 2023
EMA/CAT/198093/2023
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 15-17 May 2023

Chair: Ilona Reischl; Vice-Chair: Carla Herberts

15 May 2023, 14:00 – 18:30, room 1C

16 May 2023, 09:00 – 18:30, room 1C

17 May 2023, 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 15-17 May 2023. See May 2023 CAT minutes (to be published post June 2023 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 15-17 May 2023 meeting

1.3. Adoption of the minutes

CAT minutes for 19-22 April 2023 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. Exagamglogene autotemcel - PRIME - Orphan - EMEA/H/C/005763

Vertex Pharmaceuticals (Ireland) Limited; Treatment of transfusion-dependent β-thalassemia and sickle cell disease

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

2.8. 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

2.10.1.1. In vitro diagnostic medical device - EMEA/H/D/006255

Indicated as an aid in the selection of adult haemophilia A patients for whom valoctocogene roxaparvovec treatment is being considered

Scope: Opinion

Action: for adoption

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. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0032/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, Request for supplementary information

Action: for adoption

2.11.2. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/II/0044/G

Takeda Pharma A/S

Rapporteur: Lisbeth Barkholt

Scope: Safety, Request for supplementary information

Grouped application comprising one type II variation and two type IB as follows:
- Update of section 4.8 of the SmPC in order to update the Summary of the safety profile and to add anal abscess, proctalgia and anal fistula to the list of adverse drug reactions on post-marketing experience following the assessment of R/0036 based on a review of the MAH's Global Safety Database.
- Update of section 4.2 of the SmPC in order to add the term Perilesional as an EDQM term, following the assessment of R/0036.
- Update of sections 1, 2.2, 3, 4.2, 6.5 and 6.6 of the SmPC in order to replace the term 'suspension for injection' for 'dispersion for injection', following the assessment of R/0036. The Annex A, Package Leaflet and Labelling are updated in accordance.

Action: for adoption

2.11.3. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0062/G

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Quality

Action: for adoption

2.11.4. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0069

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality, Request for supplementary information

Action: for adoption

2.11.5. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0057

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, Opinion

Action: for adoption

Request for Supplementary Information adopted on 24.03.2023, 20.01.2023.

2.11.6. Tecartus; Yescarta - axicabtagene ciloleucel; brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2389/G

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, Opinion

Action: for adoption

Request for Supplementary Information adopted on 17.02.2023.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/REC/011.1

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

2.13.2. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/REC/012.1

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

2.13.3. Hemgenix - etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/REC/002

CSL Behring GmbH

Rapporteur: Silke Dorner

Scope: Quality

Action: for adoption

2.13.4. Hemgenix - etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/REC/003

CSL Behring GmbH

Rapporteur: Silke Dorner

Scope: Quality, Recommendation fulfilled

Action: for adoption

2.13.5. Hemgenix - etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/SOB/004

CSL Behring GmbH

Rapporteur: Silke Dorner

Scope: Clinical

Protocol and Statistical Analysis Plan of Study CSL222_4001: An observational post-authorisation long-term follow-up study to characterise the effectiveness and safety of Hemgenix (etranacogene dezaparvovec) in patients with haemophilia B.

Action: for adoption

2.13.6. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451/R/0040

Novartis Europharm Limited

Rapporteur: Sol Ruiz, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Gabriele Maurer

Scope: 5 year Renewal of Marketing Authorisation, Opinion

Action: for adoption

2.13.7. ROCTAVIAN - valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/R/0003

BioMarin International Limited

Rapporteur: Violaine Closson Carella, Co-Rapporteur: Silke Dorner, PRAC Rapporteur: Menno van der Elst

Scope: 1 year Renewal of Marketing Authorisation

Action: for adoption

Request for supplementary information adopted on 21.04.2023.

2.13.8. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/R/0056

Kite Pharma EU B.V.

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

Scope: 5 year Renewal of Marketing Authorisation, Opinion

Action: for adoption

Request for supplementary information adopted on 17.02.2023.

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

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

No items

4.2. Day 30 ATMP scientific recommendation

4.2.1. Living human adult allogeneic immunomodulatory progenitor (iMP) cells

Treatment of myocardial scarringScope: ATMP scientific recommendation

Action: for adoption

4.2.2. Allogeneic viable natural killer (NK) cells CD56+ CD3-

Treatment of patients with acute myeloid leukaemia (AML) who are in morphologic complete remission (CR) and for whom allogeneic haematopoietic stem cell transplantation (allo-HSCT) is not a suitable or preferred optionScope: ATMP scientific recommendation

Action: for adoption

4.2.3. Recombinant Adeno-associated virus serotype 9 vector containing the human-lysosome-associated membrane glycoprotein 2 isoform B transgene

Treatment of Danon diseaseScope: 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. Ixoberogene soroparvovec (Genetically engineered, replication-incompetent adeno-associated virus vector comprising the AAV.7m8 capsid proteins, carrying a version of complementary deoxyribonucleic acid for aflibercept)

Treatment of neovascular (wet) age-related macular degeneration

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.2. Ex vivo fused allogeneic human myoblasts (MB-N) with autologous human myoblast (MB-ALS)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.3. Ex vivo fused allogeneic human myoblasts (MB-N) with autologous human bone marrow derived mesenchymal stem cells (MSC-ALS)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.4. Ex vivo fused allogeneic human mesenchymal stem cell (MSC-N) with autologous human myoblast (MB-ALS)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.5. Ex vivo fused allogeneic human myoblasts (MB-N1) with allogeneic human myoblasts (MB-N2)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.6. Helper-dependent adenovirus vector coding for interleukin-1 receptor antagonist

Treatment of osteoarthritis of the knee

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.7. Autologous CD34+ cells from mobilised peripheral blood

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.8. Biotinylated cultured reticulocytes, cultured from haematopoietic stem cells

Treatment of red cell suppletion (e.g. trauma/anaemia)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.9. Autologous chondrocytes cultured in hyaluronan-derived scaffold

Repair of cartilage defects

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:	8-12.05.2023
- Appointment of CAT Peer Reviewers:	15-17.05.2023
- SAWP first reports:	30.05.2023
- CAT Peer Reviewer comments (NC/C):	02.06.2023
- CAT Peer Reviewer comments (Q):	07.06.2023
- Discussion at SAWP:	05.08.2023
- Discussion at CAT and feedback to SAWP:	14-16.06.2023

5.1.2. Scientific advice procedures starting at the next SAWP meeting

No items

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

No items

6.3.2. Month 1 – Discussion of eligibility

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. Vote by proxy

Action: for information

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Swedish presidency, 4 and 5 May 2023, Uppsala (Sweden)

CAT: Lisbeth Barkholt, Maria Lüttgen

Scope: Feedback from the SRLM

Action: for discussion

7.2. Coordination with EMA Scientific Committees

7.2.1. Co-rapporteur Day 95 Assessment

Scope: Application of the Co-Rapporteur Day 95 assessment to ATMP MAAs

Action: for discussion

7.2.2. Format of OEs during CAT meetings

Scope: New arrangement and format of the OEs during the CAT plenary meetings in order to enhance the experience for companies to be as close as possible to the face-to-face setting

Action: for information

7.2.3. Minutes and draft agenda - PCWP and HCPWP meetings

Scope: Minutes and draft agenda for the PCWP and HCPWP meetings

Action: for information

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. Workshop on ICH E6 R3 July 2023

Scope: Announcement of the public consultation of ACT EU PA04 - Multi-stakeholder Workshop on ICH E6 R3

Action: for information

7.6. CAT work plan

7.6.1. CAT stakeholders meeting 2023

CAT: Dariusz Sladowski, Ilona Reischl, Violaine Closson Carella, Carla Herberts

Scope: Agenda of the CAT stakeholders meeting taking place on 16.05.2023

Action: for information

7.7. Planning and reporting

7.7.1. Business Pipeline Report - 3 year Forecast report

Action: for information

7.8. Others

7.8.1. Onboarding Program for CAT members and alternates

CAT: Carla Herberts

Scope: To discuss the creation and further updating of an onboarding programme for CAT

members and alternates

Action: for discussion

8. Any other business

No items

Date of next CAT meeting:

14-16 June 2023

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

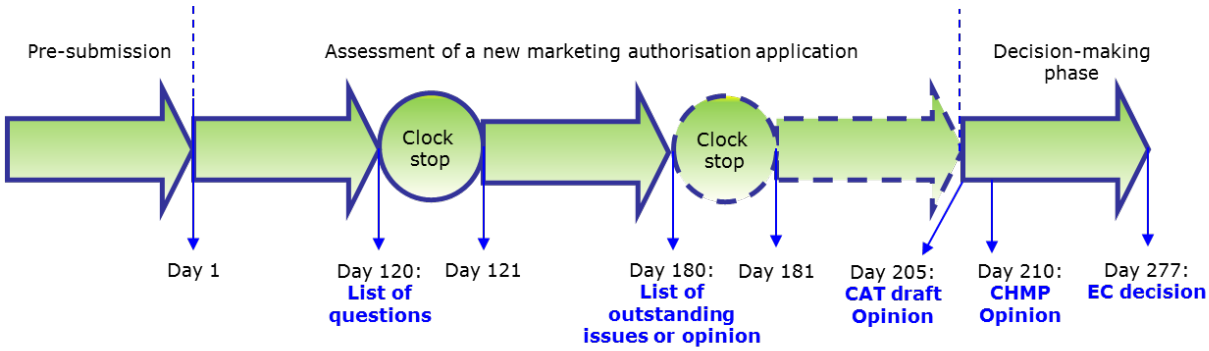
Evaluation of ATMPs (section 2)

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/