30 October 2023
EMA/CAT/462463/2023
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 30-31 October 2023

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

30 October 2023, 13:00 – 18:30

31 October 2023, 09:00 – 18:00

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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Table of contents

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 28-31 October 2023. See November 2023 CAT minutes (to be published post December 2023 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 28-31 October 2023 meeting

1.3. Adoption of the minutes

CAT minutes for 04-07 October 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

2.3.1. Exagamglogene autotemcel - PRIME - Orphan - EMEA/H/C/005763

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

Scope: Opinion

Action: for adoption

List of questions adopted on 17.05.2023; list of outstanding issues adopted on 08.09.2023.

2.4. Day 120 list of questions

No items

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

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. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0031

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Clinical and Quality, request for supplementary information

Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least two prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD-38 antibody and have demonstrated disease progression on the last therapy for Abecma (idecabtagene vicleucel, ide-cel), based on results from study BB2121-MM-003 (MM-003, KarMMa-3). This is a Phase 3, multicentre, randomised, open-label study to compare the efficacy and safety of ide-cel

versus standard regimens in subjects with RRMM. As a consequence, sections 2.1, 2.2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.3, 6.4 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 3.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the Guideline on core SmPC, Labelling and Package Leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells.

Action: for adoption

Request for Supplementary Information adopted on 16.06.2023.

2.11.2. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0018

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, opinion

Action: for adoption

Request for Supplementary Information adopted on 14.07.2023.

2.11.3. Hemgenix - etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/II/0009/G

CSL Behring GmbH

Rapporteur: Silke Dorner

Scope: Quality, request for supplementary information

Action: for adoption

2.11.4. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0071

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Clinical, request for supplementary information

Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on final results from study CCTL019B2202 (a phase II, single arm, multicentre trial to determine the efficacy and safety of CTL019 in paediatric patients with relapsed and refractory B-cell acute lymphoblastic leukaemia). Submission of cellular kinetic report for the B-cell acute lymphoblastic leukaemia (ALL) indication based on data from pivotal study CCTL019B2202 and the supportive study CCTL019B2205J involving paediatric ALL patients (partially fulfil REC). In addition, the MAH took this opportunity to introduce editorial changes.

Action: for adoption

2.11.5. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0075

Novartis Europharm Limited

Rapporteur: Rune Kjeken, PRAC Rapporteur: Gabriele Maurer

Scope: Clinical, request for supplementary information

Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on final results from study CCTL019C2201 post authorisation efficacy study (PAES) in the Annex II (ANX008): this is a Phase II, single arm, multicentre trial to determine the efficacy and safety of Kymriah in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). The RMP version 6 has also been submitted. In addition, the MAH took the opportunity to update Annex II.D of the product information (PI).

Action: for adoption

2.11.6. ROCTAVIAN - valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/II/0008/G

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Clinical, opinion

Grouped application comprising two variations as follows: 1) Update of section 4.5 of the SmPC in order to add drug-drug interaction information with isotretinoin and efavirenz based on results from study '*in vitro* drug-drug interaction study: effects of concomitant administration of isotretinoin, amphetamine, omeprazole, celecoxib and selected HAART medications with AAV5-FVIII-SQ on cytotoxicity and AAV5-FVIII-SQ DNA and RNA expression in primary human hepatocytes" and 2) To change the ATC Code from B02BD1 to 'not yet assigned'.

Action: for adoption

2.11.7. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0063

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Clinical, opinion

Update of section 5.1 of the SmPC in order to include new clinical data based on overall survival (OS) primary analysis from study KTE-C19-107 (ZUMA-7): this is a phase 3, randomised, open-label study evaluating the efficacy of axicabtagene ciloleucel versus standard of care therapy in subjects with relapsed/refractory diffuse large B cell lymphoma (DLBCL) in the 2nd line setting. In addition, the MAH took the opportunity to submit a consolidated Environmental Risk Assessment (ERA) document.

Action: for adoption

Request for Supplementary Information adopted on 06.10.2023.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Hemgenix - etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/REC/008

CSL Behring GmbH

Rapporteur: Silke Dorner

Scope: Quality, REC considered fulfilled

Action: for adoption

2.13.2. Roctavian - valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/MEA/005.1

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Pharmacovigilance, opinion

MAH Response to MEA 005 [Haematologists survey] as adopted in June 2023
Title: Survey of haematologists to assess the effectiveness of the additional risk minimisation measures for Roctavian addressing the outstanding points in the MEA005 assessment report.

Action: for adoption

2.13.3. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/REC/010.1

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Quality

Action: for adoption

2.13.4. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/REC/011.1

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Quality

Action: for adoption

2.13.5. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/ANX/002.6

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Pharmacovigilance, opinion

Second annual interim report from PASS KT-EU-471-0117 [long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma. (EU PAS Register no.: EUPAS32539)] From initial MAA

Action: for adoption

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

Timetable:

-Start of the procedure:	20.11.2023
-EMA Coordinator's draft report:	24.11.2023
-CAT Coordinator's comments:	29.11.2023
-Revised scientific recommendation:	01.12.2023
-CAT's discussion of scientific recommendation:	08.12.2023

4.1. New requests – Appointment of CAT Coordinator

No items

4.2. Day 30 ATMP scientific recommendation

4.2.1. Allogeneic peripheral blood-derived HSPC, Treg cells and Tcon cells

Prevention of moderate to severe chronic graft-vs.-host disease and/or death in patients with acute leukaemias and in patients with myelodysplastic syndrome (MDS) undergoing

HLA-matched allogeneic hematopoietic stem cell transplant (alloHCT)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Spermatogonial stem cells, propagated *in vitro*

Male infertility due to gonadotoxic treatment

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Live, freeze-dried, genetically modified Lactococcus lactis strain, engineered to secrete human interleukin-10 (hIL-10) and a deamidated, human leukocyte antigen (HLA)-DQ2 restricted, 33-mer alpha-gliadin peptide (dDQ2)

Treatment of celiac disease

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Autologous lymphocytes enriched in activated natural killer cells

Cancer

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Umbilical cord blood leukocyte concentrate containing cord blood stem cells

Hypoxic-ischaemic encephalopathy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. Umbilical cord blood leukocyte concentrate containing cord blood stem cells

Cerebral palsy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.7. DNA plasmid expressing short hairpin RNA (shRNA) against lytic origin of DNA replication of Epstein Barr Virus (EBV) messenger RNA (mRNA)

Treatment of EBV infected patients

Scope: ATMP scientific recommendation

Action: for adoption

4.2.8. DNA plasmid expressing short hairpin RNA (shRNA) against BCL2 anti-apoptotic messenger RNA (mRNA)

Treatment of cancer patients

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. Devitalised cell-derived cartilaginous tissue

Bone substitute for maxillofacial and/or orthopaedic bone 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:	23-26.10.2023
- Appointment of CAT Peer Reviewers:	30-31.10.2023
- SAWP first reports:	20.11.2023
- CAT Peer Reviewer comments (NC/C)	24.11.2023
- CAT Peer Reviewer comments (Q)	29.11.2023
- Discussion at SAWP:	27-30.11.2023
- Discussion at CAT and feedback to SAWP:	06-08.12.2023

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	25-28.09.2023
- Appointment of CAT Peer Reviewers:	04-06.10.2023
- SAWP first reports:	16.10.2023
- CAT Peer Reviewer comments (NC/C)	20.10.2023
- CAT Peer Reviewer comments (Q)	25.10.2023
- Discussion at SAWP:	23-26.10.2023
- Discussion at CAT and feedback to SAWP:	30-31.10.2023

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:	23–26.10.2023
- SAWP recommendation:	30.11.2023
- CAT recommendation:	08.12.2023
- CHMP adoption of report and final recommendation:	14.12.2023

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. Vote by proxy

Action: for information

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Spanish presidency, 25-27 October 2023 Madrid (Spain)

CAT: Sol Ruiz, Marcos Timon

Scope: Feedback from the SRLM

Action: for information

7.2. Coordination with EMA Scientific Committees

7.2.1. 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

No items

7.6. CAT work plan

No items

7.7. Planning and reporting

No items

7.8. Others

7.8.1. Proposal to review the informal rules for granting companies extended clock-stops (Hudson's rules)

Call for expression of interest from the members of Committee. Expressions of interest to be sent by 7 November .

Action: for discussion

8. Any other business

Date of next CAT meeting:

06-08 December 2023

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

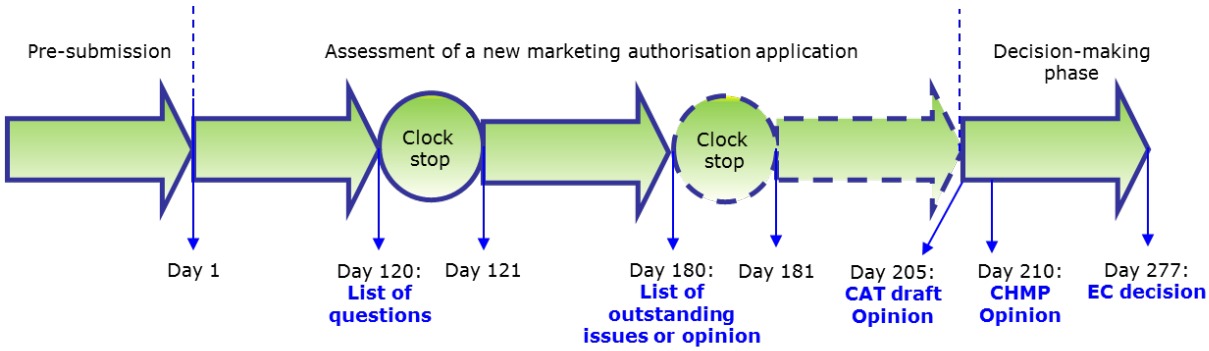
Evaluation of ATMPs (section 2)

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/