19 January 2022
EMA/CAT/778538/2021
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 19-21 January 2022

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

19 January 2022, 14:00 – 18:30, remote virtual meeting

20 January 2022, 09:00 – 18:30, remote virtual meeting

21 January 2022, 09:00 – 13:00, remote virtual meeting

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 19-21 January 2022. See January 2022 CAT minutes (to be published post February 2022 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 19-21 January 2022 meeting

1.3. Adoption of the minutes

CAT minutes for 08-11 December 2021 meeting

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Lisocabtagene maraleucel / lisocabtagene maraleucel - PRIME - Orphan - EMEA/H/C/004731

Bristol-Myers Squibb Pharma EEIG; treatment of large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B)

Scope: Opinion

Action: for adoption

List of Outstanding Issues adopted on 08.10.2021, 16.04.2021. List of Questions adopted on 06.11.2020.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

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

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

Scope: MAA's request (dated 10.01.2022) for a clock-stop extension

Action: for information

List of Questions adopted on 22.01.2021.

Note: the revised timetable was adopted via written procedure.

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. 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. Abecma - idecabtagene vicleucel - PRIME - Orphan - EMEA/H/C/004662/II/0002

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 05.11.2021.

2.11.2. Abecma - idecabtagene vicleucel - PRIME - Orphan - EMEA/H/C/004662/II/0010

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken, PRAC Rapporteur: Annika Folin

Scope: Clinical. Opinion

Update of section 5.1 of the SmPC in order to update efficacy information based on 24 month follow up data from the pivotal study submitted during initial (BB2121-MM-001: A Phase 2, Multicenter Study to determine the Efficacy and Safety of bb2121 in Subjects with Relapsed and Refractory Multiple Myeloma) listed as a specific obligation in the Annex II and in the RMP; The annex II is updated with the proposed deletion of the relevant SOB. The RMP version 1.1 has also been submitted.

Action: for adoption

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

Novartis Europharm Limited

Rapporteur: Sol Ruiz

Scope: Quality. Request for Supplementary Information

Action: for adoption

2.11.4. Tecartus - autologous anti-CD19-transduced CD3+ cells - PRIME - Orphan - EMEA/H/C/005102/II/0016

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Request for Supplementary Information

Action: for adoption

2.11.5. Zolgensma - onasemnogene abeparvovec - PRIME - Orphan - EMEA/H/C/004750/II/0019/G

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 05.11.2021.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Kymriah - tisagenlecleucel - PRIME - Orphan - EMEA/H/C/004090/ANX/007.1

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Statistical Analysis Plan (SAP) amendment 1 / (CCTL019B2401):
Sub-analysis to assess efficacy in patients with relapsed or refractory diffuse large B-cell

lymphoma based on data from the Registry study to assess the long-term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel.

Action: for adoption

2.13.2. Kymriah - tisagenlecleucel - PRIME - Orphan - EMEA/H/C/004090/P46/012.1

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Bioanalytical data reports and MAH's responses to P46 012 [Study no. CTL019B2001X, EudraCT no. 2016-001991-31] as adopted in June 2021.

Action: for adoption

2.13.3. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451/REC/008

Novartis Europharm Limited

Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro

Scope: From Letter of Recommendations:
MAH's response to questions on Quality Documentation

Action: for adoption

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:	21.01.2022
-EMA Coordinator's draft report:	04.02.2022
-CAT Coordinator's comments:	09.02.2022
-Revised scientific recommendation:	11.02.2022
-CAT's discussion of scientific recommendation:	18.02.2022

4.1. New requests – Appointment of CAT Coordinator

No items

4.2. Day 30 ATMP scientific recommendation

4.2.1. Kidney progenitor cells isolated from the urine of preterm neonates

Intended for the kidney transplantation

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Expanded mesenchymal stem cells (MSCs) cells isolated from umbilical cord Wharton jelly dilative cardiomyopathy (DCM)

Intended for the treatment of dilative cardiomyopathy (DCM)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Recombinant serotype 9 adeno-associated virus (rAAV9) encoding a wild-type human MECP2 (methyl cytosine binding protein 2) transgene (AAV9-hMECP2)

Intended for the treatment of Rett syndrome

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Recombinant adeno-associated virus (rAAV) containing human homology arms, expressing codon-optimised human phenylalanine hydroxylase (hPAH)

Intended for the treatment of phenylalanine hydroxylase (PAH) deficiency

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Human embryonic stem cell (hESC)-derived midbrain dopaminergic (mDA) neuron cells

Intended for the treatment of advanced Parkinson’s disease

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. Stem cells isolated from dental pulp, cultured

Intended for the treatment of surgical bone defects

Scope: ATMP scientific recommendation

Action: for adoption

4.2.7. Modulated immune cells

Intended for solid organ transplantation / Treatment of autoimmune disease

Scope: ATMP scientific recommendation

Action: for adoption

4.2.8. Autologous bone marrow concentrate

Intended for the treatment of bone fractures

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. Non-replicating recombinant adeno-associated virus serotype 2 (rAAV2) encoding a soluble form of human CD59 (sCD59)

Intended for the treatment of geographic atrophy (via targeting the complement pathway)

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

Action: for adoption

4.4.2. VTXM01 messenger RNA (mRNA) encoding for an adenine base editor (ABE) and VTXG01 guide RNA (gRNA) targeting the proprotein convertase subtilisin/kexin type 9 (PCSK9) serine protease gene

Intended for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of low-density lipoprotein cholesterol (LDL-C) despite maximally tolerated lipid-lowering therapy

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

Action: for adoption

4.4.3. Autologous anti-CD19 chimeric antigen receptor T-cells

Intended for the treatment of CD19-expressing B-cell malignancies

Scope: The European Commission raised minor 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:	10–13.01.2022
- Appointment of CAT Peer Reviewers:	19-21.01.2022
- SAWP first reports:	31.01.2022
- CAT Peer Reviewer comments:	04.02.2022
- Discussion at SAWP:	07-10.02.2022
- Discussion at CAT and feedback to SAWP:	18.02.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	07-10.02.2022
- Appointment of CAT Peer Reviewers:	16-18.02.2022
- SAWP first reports:	28.02.2022
- CAT Peer Reviewer comments:	04.03.2022
- Discussion at SAWP:	07-10.03.2022
- Discussion at CAT and feedback to SAWP:	18.03.2022

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

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

5.4. Final Advice Letters for procedures finalised the previous month

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	10-13.01.2022
SAWP recommendation:	10/02/2000
CAT recommendation:	18/02/2022
CHMP adoption of report and final recommendation:	24/02/2022

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

No items

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the French presidency, 3 March 2022 (virtual)

CAT: Violaine Closson-Carella, Martina Schuessler-Lenz

Scope: Practical information and agenda content

Action: for discussion

7.2. Coordination with EMA Scientific Committees

7.2.1. 5-year review of PRIME experience

Scope: Presentation of the main findings and recommendations of the experience with the PRIME scheme since its launch in March 2016

Action: for information

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

7.3.1. Call for nominations for Working Parties

CAT: Martina Schueslller-Lenz

Scope: Launch of call for nominations for the Oncology working parties

Action: for information

Note**:** In the context of the new operational model of working parties that was agreed at the EMA management Board April 2021, the call for nominations for Oncology Working Party has been launched with the aim to have the Working Party new members and Chair and Vice-chair appointed during February CHMP PROM meeting. CAT members are asked to liaise within their agency for possible nominations. Calls for nominations for other working parties will follow in the next months.

7.4. Cooperation with the EU regulatory network

None

7.5. Cooperation with international regulators

None

7.6. CAT work plan

7.6.1. CAT work plan 2022

CAT: Martina Schüssler-Lenz

Scope: final CAT work plan for 2022

Action: for adoption

7.6.2. Real World Data (RWD) in regulatory decision making of ATMPs

CAT: Martina Schuessler-Lenz

Scope: Technical specifications for an EMA funded study on spinal muscular atrophy (SMA) natural history and its clinical management

Action: for information

7.7. Planning and reporting

None

7.8. Others

7.8.1. Lifecycle Regulatory Submissions Metadata project (LRSM)

Action: for information

7.8.2. Speaker invitation to the International Society for Cellular Therapy (ISCT) 2022 Annual meeting

CAT: Martina Schuessler-Lenz

Scope: Opportunity to talk at the ISCT session (4 May 2022): "Shining a light on unlicensed CGTs: Where is the line between the right to care, ethics and patient safety?"

Action: identification of CAT speakers

8. Any other business

No items

Date of next CAT meeting:

16-18/02/2022

9. Explanatory notes

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

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

EU NTC: European Union Network Training Centre

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Application

MAH: Marketing Authorisation Holder

MNAT: Multinational assessment team

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

QRD: Quality review of documents

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

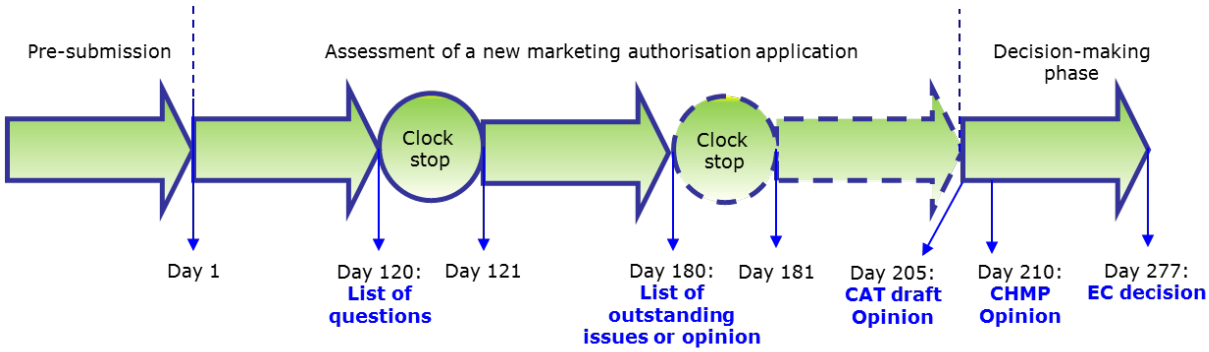
Evaluation of ATMPs (section 2)

This section lists applications for marketing authorisations of new Advanced Therapy Medicinal Products (ATMPs) that are to be discussed by the Committee. It also lists any ATMP related inspection requests (section 2.9) and Post-authorisation activities (section 2.10).

New applications (sections 2.1. to 2.12.)

Section 2.1 is for ATMPs nearing the end of the evaluation and for which the CAT is expected to adopt a draft **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CAT opinion is transmitted to the CHMP for final adoption. The CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU. More information on the evaluation of ATMPs can be found here.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CAT. The clock stop happens after day 120 and may also happen after day 180, when the CAT has adopted respectively a **Day 120 list of questions** (section 2.3) or a List of outstanding issues to be addressed by the company, which is listed in the agenda under sections 2.7 (**Ongoing evaluation procedures**). Section 2.7 also includes the CAT discussions at any other timepoint of the evaluation procedure of new applications.

Oral explanation (section 2.2.)

Prior to adoption of the CAT opinion, marketing authorisation applicants are normally invited to the CAT plenary meeting to address questions raised by the Committee.

Oral explanations normally relate to ongoing applications, but they can also relate to any other issue for which the CAT would like to discuss with company representatives in person.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.6.)

This section lists applications for new marketing authorisation for ATMPs for which the applicant has requested a re-examination of the opinion previously issued by the CHMP. Similar to the initial evaluation of a marketing authorisation of an ATMP, CAT will adopt a draft re-examination opinion, which is transmitted to the CHMP for final adoption.

Withdrawal of applications (section 2.7.)

This section includes information on marketing authorisation applications that are withdrawn by the applicant. Applicants may decide to withdraw applications at any stage during the assessment and a CAT opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

New applications (section 2.9.)

In this section, information is included on upcoming marketing authorisation applications for ATMPs, as well as information on appointment of Rapporteurs for new ATMP applications.

GMP and GCP Inspections Issues (section 2.10.)

This section lists inspections that are undertaken for ATMPs. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Post-authorisation activities (section 2.12.)

This section lists type II variations, extension application according to Annex I of Reg. 1234/2008, re-examination procedures for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP and other issues concerning authorised medicines that are not covered elsewhere in the agenda such as annual reassessments, 5-year renewals, supply shortages, qualify defects. Issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines, will also be included here.

Certification of ATMPs (section 3)

This section includes the scientific evaluation by the CAT of quality and non-clinical data that small and medium-sized enterprises have generated at any stage of the ATMP development process. More information on the ATMP certification procedure can be found here.

Scientific Recommendation on Classification of ATMPs (Section 4)

This section includes the scientific recommendation by the CAT on whether medicines based on genes, cells or tissues meet the scientific criteria that define ATMPs. More information on the ATMP classification procedure, including the outcomes of finalised classifications, can be found here.

Scientific Advice (section 5)

This section includes all scientific advice given to companies during the development of an ATMP. Information related to the number of ATMP related scientific advices discussed by CAT can be found in the CAT Monthly reports. Further information on SAWP can be found here.

Pre-Authorisation (section 6)

Paediatric Investigation Plan (PIP)

This section includes the discussion of an ATMP before a formal application for marketing authorisation is submitted. These cases refer for example to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation: in case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

CAT contributes to the evaluation of a Paediatric Investigation Plan (PIPs) for ATMPs by the Paediatric Committee. These PIPs are included in this section of the Agenda.

ITF Briefing meeting in the field of ATMPs

This section refers to briefing meetings of the Innovation Task Force and International co-operations activities of the CAT

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes of meetings with applicants developing ATMPs and of other ITF meetings of interest to the CAT are included in this section of the agenda. Further information on the ITF can be found here.

Priority Medicines (PRIME)

This section includes the new requests for eligibility to PRIME for ATMPs under development, the discussions in CAT of these eligibility requests and the final recommendations for eligibility of ATMPs adopted by CHMP.

CAT will appoint one of its members as the CAT sponsor for each new ATMP eligibility request who will lead the CAT discussion based on the recommendation from the SAWP.

Organisational, regulatory and methodological matters (section 7)

This section includes topics related to regulatory and procedural guidance, CAT workplan, CAT meeting organisation (including CAT membership), planning and reporting, co-ordination with other committees, working parties and scientific advisory groups.

Furthermore, this section refers to the activities of the CAT drafting groups developing scientific guidelines for gene therapy medicinal products and for cell-based medicinal products, cooperation within the EU regulatory network and international regulators as well as direct interaction with interested parties. It also includes topics of scientific interest for the Committee that are not directly related to the work of the CAT drafting groups or CAT associated working parties.

Any other business (section 8)

This section is populated with miscellaneous topics not suitable under the previous headings.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/