10 May 2021
EMA/CAT/268790/2021
Human Medicines Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 10-12 May 2021

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

10 May 2021, 14:00 – 18:30, virtual

11 May 2021, 09:00 – 18:30, virtual

12 May 2021, 09:00 – 13:00, virtual

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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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 10-12 May 2021. See May 2021 CAT minutes (to be published post June 2021 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 10-12 May 2021 meeting

1.3. Adoption of the minutes

CAT minutes for 14-16 April 2021 meeting

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Elivaldogene autotemcel - Orphan - EMEA/H/C/003690

bluebird bio (Netherlands) B.V; treatment of ABCD1 genetic mutation and cerebral adrenoleukodystrophy

Scope: Opinion

Action: for adoption

List of Outstanding Issues adopted on 16.04.2021. List of Questions adopted on 22.01.2021.

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. Lenadogene nolparvovec - Orphan - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of vision loss due to Leber Hereditary Optic Neuropathy (LHON)

Scope: MAA's request (dated 22.04.2021) for a clock stop extension

Action: for adoption

D120 List of Questions adopted in February 2021

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. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0044

Amgen Europe B.V.

Rapporteur: Olli Tenhunen; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: submission of the final report from study 20180099 listed as a category 3 study in the RMP. This study consists of a cross-sectional survey to evaluate physician knowledge of safety messages included in the physician education booklet (PEB) for Imlygic. Request for supplementary information (RSI)

Action: for adoption

2.11.2. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0020

CO.DON AG

Rapporteur: Lisbeth Barkholt

Scope: extension of the indication for use in the paediatric population (15 to 18 years). Opinion

Action: for adoption

Request for Supplementary Information adopted on 19.03.2021.

2.11.3. Zynteglo - betibeglogene autotemcel - Orphan - EMEA/H/C/003691/II/0022

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts

Scope: quality Opinion

Action: for adoption

Request for Supplementary Information adopted on 16.04.2021.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - Orphan - EMEA/H/C/005102/ANX/002

Kite Pharma EU B.V.

Jan Mueller-Berghaus

Scope: clinical and pharmacovigilance
From Initial MAA: Study No. KTE-EU-472-6036: Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL); **Protocol**, [Due date: 31 March 2021] [future due date(s): - Annual report for first 5 years - first report by 31 December 2021 - Final study report by 30 June 2042]

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

4.1. New requests – Appointment of ITF Coordinator

4.1.1. Nanoparticle consisting of non-pseudotyped (bald) lentiviral vector encoding for a CD19 CAR , encapsulated

Intended for the treatment of CD19+ B-cell malignancy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Autologous T cells genetically modified ex vivo using a synthetic chromosome encoding CCR6, IL-2, a truncated version of CD34 and two independent inducible safety switches

Intended for treatment of patients with solid tumours for which a draining lymph node can be identified. Initially the product will be developed for colon cancer and urinary bladder cancer

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Live human mesenchymal stem cells derived from allogenic Wharton's jelly

Intended for treatment of atherosclerosis of the arteries of the lower extremities

Scope: appointment of CAT Coordinator and adoption of timetable

4.2. Day 30 ATMP scientific recommendation

4.2.1. *Ex-vivo* expanded autologous cryopreserved Wharton's Jelly derived mesenchymal stem cells

Intended for the treatment of Bronchopulmonary Dysplasia (BPD) for preterm infants

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Allogeneic corneal endothelial cells in a confluent monolayer adhering to a cornea-shaped sheet of cross-linked collagen

Intended for the treatment of corneal dysfunction

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Proliferation arrested myelomonocytic leukemic cell line-derived cells with a mature dendritic cell phenotype

Intended for the treatment of acute myeloid leukaemia

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Allogeneic human Wharton's jelly derived mesenchymal stem cells

Intended for the treatment of idiopathic pulmonary fibrosis (IPF), pulmonary fibrosis after COVID-19

Scope: ATMP scientific recommendation

Action: for adoption

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

4.3.1. Allogeneic, expanded, engineered E4ORF1+ human umbilical cord endothelial (CD31+) cells

Intended to treat organ vascular niche injuries caused by myeloablative, non-central nervous system penetrating high-dose chemotherapy (HDT) to prevent the development of severe regimen-related toxicities (SRRT) in patients diagnosed with aggressive systemic lymphoma

Scope: ATMP Scientific recommendation

Action: for adoption

CAT adopted the List of Questions in April 2021

4.4. Finalisation of procedure

4.4.1. Oncolytic adenovirus

Intended for the treatment of histologically and radiologically confirmed progressive neuroendocrine neoplasm (NEN) of gastrointestinal, pancreatic or bronchial origin with multiple liver metastases (liver-dominant disease)

Scope: the European Commission raised no comments. ATMP Scientific recommendation

Action: for information

4.4.2. Autologous antigen presenting cells loaded with SARS-CoV-2 antigen

Vaccine against SARS-CoV-2

Scope: the European Commission raised no comments. ATMP Scientific recommendation

Action: for information

4.4.3. Autologous mesenchymal stem cells combined with a matrix pre-loaded with BMP2

Intended to treat femoral osteochondral lesion (grade III to IV)

Scope: the European Commission raised minor comments. ATMP Scientific recommendation

Action: for information

4.4.4. DNA plasmid encoding several neoepitopes from the tumour of a patient, a live wild-type modified vaccinia strain Ankara (MVA) and a monoclonal antibody against Cytotoxic T-lymphocyte associated protein 4 (CTLA4)

Intended for the treatment of cancer

Scope: the European Commission raised no comments. ATMP Scientific recommendation

Action: for information

4.4.5. Autologous cultured chondrocytes

Intended for the treatment of filling of cartilage defectsScope: the European Commission raised no comments. ATMP Scientific recommendation

Action: for information

4.4.6. Recombinant adeno-associated virus encoding for the human α-sarcoglycan-protein

Intended for the treatment of patients with a confirmed diagnosis of Limb-Girdle muscular dystrophy Type 2D/R3 (LGMD2D/R3)

Scope: the European Commission raised minor comments. ATMP Scientific recommendation

Action: for information

4.5. Follow-up and guidance

No items

5. Scientific Advice

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

5.1. New requests – appointment of CAT Rapporteurs

5.1.1. Ongoing scientific advice procedures – Appointment of CAT Peer-Reviewers

Timetable:

-Start of the procedure at SAWP:	03-06.05.2021
-Appointment of CAT Peer-reviewers:	12.05.2021
-SAWP first reports:	31.05.2021
-CAT Peer-Reviewer's comments:	04.06.2021
-Discussion at SAWP:	07-10.06.2021
-Discussion at CAT and feedback to SAWP:	18.06.2021

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

-Start of procedure at SAWP:	07-10.06.2021
-Appointment of CAT Peer-Reviewers:	18.06.2021
-SAWP first reports:	28.06.2021
-CAT Peer-Reviewer's comments:	02.07.2021
-Discussion at SAWP:	05-08.07.2021
-Discussions at CAT and feedback to SAWP:	16.07.2021

5.2. Procedures with a discussion meeting with the applicant

5.3. Finalisation of SA procedures

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

No items

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting (SRLM) under the Portuguese presidency of the European Union – 27th May 2021, Lisbon, Portugal

CAT: Bruno Sepodes, Maria-Isabel Vieira

Scope: final agenda of the SRLM meeting scheduled to take place on 27th May 2021

Action: for information

Note: CAT adopted the agenda at its plenary in April 2021. The Portuguese organisers sent invitations to all CAT members on 17.04.2021

7.2. Coordination with EMA Scientific Committees

7.2.1. CHMP learnings that impact CAT decisions

CAT: Jan Mueller-Berghaus, Romaldas Mačiulaitis, John-Joseph Borg, Bruno Sepodes, Sol Ruíz

Scope: CHMP learnings with relevance to CAT

Action: for information

7.2.2. CAT-COMP Working Group

Scope: outcome of the working group meeting to take place on 7th May 2021

Action: for information

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

7.3.1. EMA – Review of Working Parties

CAT: Martina Schuessler-Lenz

Scope: feedback from the SciCoBo meeting that took place on 28 April 2021 on the review of activities of the working parties of the EMA

Action: for information

7.3.2. Scientific Advisory Group (SAG) – renomination of the inter-committee SAG oncology (SAG-O) – request for nominations

Action: for information

7.4. Cooperation within the EU regulatory network

7.4.1. Inspection of manufacturers of viral vectors used as starting materials for genetically modified cells

CAT drafting group members: Heli Suila, Ivana Haunerova, Marcos Timón, Violaine Closson Carella

Scope: Question and Answers on principles for GMP

Action: for information

Note: the Question and Answers have been published on the EMA website: https://www.ema.europa.eu/en/documents/other/questions-answers-principles-gmp-manufacturing-starting-materials-biological-origin-used-transfer_en.pdf

7.4.2. Planning estimates of forthcoming ATMP MAAs

Scope: MAAs 3-year forecast (March 2021 – December 2023) report: outlook of the initial MAAs planned for the next three years focusing on non-COVID-19 applications

Action: for information

7.4.3. Revision of the EU legislation on blood, tissues and cells (BTC)

Scope: exchange with the European Commission representative

Action: for discussion

7.4.4. Reduction of non-Covid-related workload

Action: for discussion

7.5. Cooperation with international regulators

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

CAT: Martina Schuessler-Lenz

Scope: agenda topic for the teleconference to take place on 20 May 2021

A**ction:** for discussion

7.5.2. Ad-hoc teleconference between CAT and US-FDA

CAT: Maura O'Donovan

Scope: teleconference to take place on 17 May 2021

Action: for information

Note: CAT discussed the scientific advice for this product during its January 2021 meeting

7.6. CAT work plan

7.6.1. DIA Europe 2021 meeting: 'Opportunities and challenges of real-world evidence (RWE) to support regulatory decision making'

CAT: Martina Schuessler-Lenz

Scope: CAT feedback from DIA Europe session

Action: for information

Note: this subject is linked to the work plan topic on RWE

7.7. Planning and reporting

None

7.8. Others

7.8.1. EMA's Research and Innovation (RNI) workstream

Scope: summary of recent activities in the workstream's areas of Innovation Task Force, Horizon Scanning and Business Pipeline / Forecasting

Action: for information

7.8.2. American Society of Gene + Cell Therapy (ASGCT) 24th Annual Meeting (virtual) – pre-meeting workshop, 10th May 2021

CAT: Martina Schuessler-Lenz, Alessandro Aiuti, Tomáš Boráň

Scope: pre-meeting workshops on *'Recent developments in global regulation of gene therapies'*. Session I: 'Regulatory Convergence in GMO Requirements and Environmental Risk Assessment' and Session II: 'Hot topics and emerging trends in the regulation of gene therapies', Monday 10th May 2021

Action: for information

8. Any other business

No items

Date of next CAT meeting:

16-18/06/2021

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

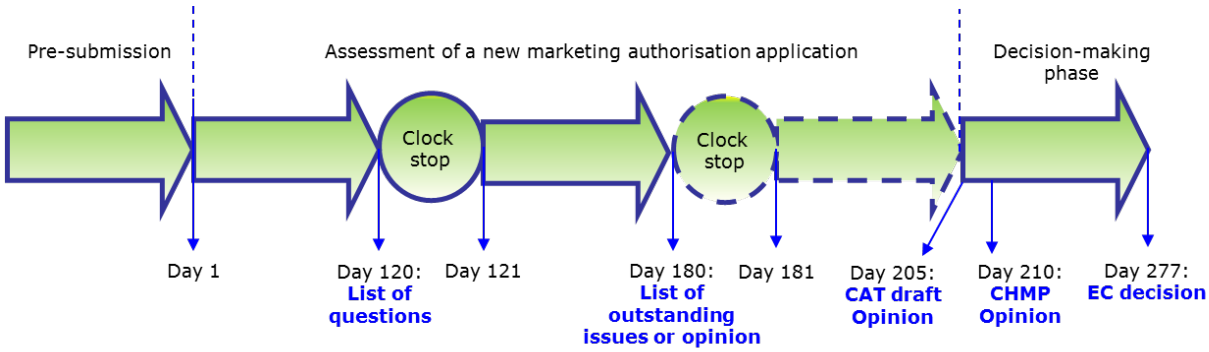
Evaluation of ATMPs (section 2)

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/