7 September 2022
EMA/CAT/691207/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of CAT written procedure 10-12 August 2022

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

Disclaimers

Some of the information contained in these minutes 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, these minutes are a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes 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. Adoption of agenda

The CAT agenda for 10-12 August 2022 meeting was adopted.

1.2. Adoption of the minutes

The CAT minutes for 13-15 July 2022 meeting will be adopted at the September CAT plenary on 07–09 September 2022.

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

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

No items

2.7. New applications

No items

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

No items

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/010

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani

Scope: Quality

Action: for adoption

The conclusion of the quality recommendation was adopted.

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:	12.08.2022
-EMA Coordinator's draft report:	26.08.2022
-CAT Coordinator's comments:	31.08.2022
-Revised scientific recommendation:	02.09.2022
-CAT's discussion of scientific recommendation:	09.09.2022

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous cultured limbal epithelial and limbal epithelial stem cells growing on fibrin scaffold

Intended for the treatment of moderate to severe limbal stem cell deficiency (LSCD) caused by burns, including chemical burns to the eyes

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.2. Human allogeneic cardiac progenitor cell subpopulation selected for the absence of the surface marker CD90

Intended to improve cardiac perfusion and function in patients with refractory angina

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.3. Allogeneic CD33-directed genetically modified T-cell immunotherapy

Intended for the treatment of patients with CD33-positive acute myeloid leukaemia (AML) who are at a high risk of relapse

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.4. Allogeneic CRISPR/Cas9-edited hematopoietic stem and progenitor cells (HSPCs) lacking CD33 protein expression

Intended for the treatment of patients with CD33-positive acute myeloid leukaemia (AML) who are at a high risk of relapse

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.2. Day 30 ATMP scientific recommendation

No items

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

No items

4.4. Finalisation of procedure

4.4.1. Adeno-associated viral vector serotype 2 encoding glial cell line-derived neurotrophic factor

Intended for the treatment of Parkinson's disease (PD)

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medical product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.2. Ex-vivo expanded allogeneic human corneal epithelial cells containing P63 positively expressing cells

Intended for the treatment of persistent corneal epithelial defects

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a tissue engineered product and combined ATMP as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.3. Allogeneic adipose-derived mesenchymal stem cells

Intended for the treatment of arthritis and diabetes type I and II

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of an advanced therapy medicinal product as defined in Article 2(1) of Regulation (EC) 1394/2007. CAT considered that the applicant did not provide sufficient information to support the claimed mechanism of action of the product in the indication sought and therefore CAT concluded that the product is an ATMP, but did not decide if it is a tissue engineered product or a somatic cell therapy medicinal product.

4.4.4. Acellular tubular graft composed of human collagen types I and III and other extracellular matrix proteins, including fibronectin and vitronectin

Intended for replacement or repair of injured blood vessels in cases of vascular trauma; for replacement or repair of diseased vessels as an arterial bypass conduit for peripheral

arterial disease (PAD); and as an implanted vascular access conduit for haemodialysis in patients with end-stage renal disease (ESRD)

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

Action: for adoption

The ATMP classification report was adopted. The product does not fulfil the definition of an advanced therapy medicinal product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.5. A heterologous vaccine regimen composed of 2 components: replication incompetent gorilla adenovirus serotype 20 (GAd20) and modified vaccinia ankara (MVA) vectors encoding tumor-specific antigens mutant calreticulin (mutCALR) and Janus kinase 2 (mutJAK2)

Intended for the treatment of patients with myeloproliferative neoplasms (MPNs)

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medical product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.6. Recombinant adeno-associated virus vector containing the human aspartoacylase complementary DNA (ASPA cDNA) with an optimized expression cassette and constitutive promoter

Intended for the treatment of Canavan disease

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medical product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.7. Adeno-associated virus serotype hu68 vector encoding human GLB1 gene

Intended for the treatment of GM1 gangliosidosis

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a gene therapy medical product as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.8. Autologous human bone marrow derived mesenchymal stromal cells (MSCs)

Intended for the treatment of pathologies affecting the oesophageal tract in which total or partial organ replacement is required

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a tissue engineered product and combined ATMP as defined in Article 2(1) of Regulation (EC) 1394/2007.

4.4.9. Skin cell suspension obtained with the help of recombinant non-animal trypsin

Intended for skin regeneration after burns, skin trauma, invasive surgery

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

Action: for adoption

The ATMP classification report was adopted. The product does fulfil the definition of a tissue engineered product as defined in Article 2(1) of Regulation (EC) 1394/2007.

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

No items

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

No items

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

No items

5.4. Final Advice Letters for procedures finalised the previous month

No items

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:	07/07/2022
SAWP recommendation:	01/09/2022
CAT recommendation:	09/09/2022
CHMP adoption of report and final recommendation:	15/09/2022

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

no items

7.2. Coordination with EMA Scientific Committees

No items

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

No items

8. Any other business

No items

Date of next CAT meeting:

07-09/09/2022

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

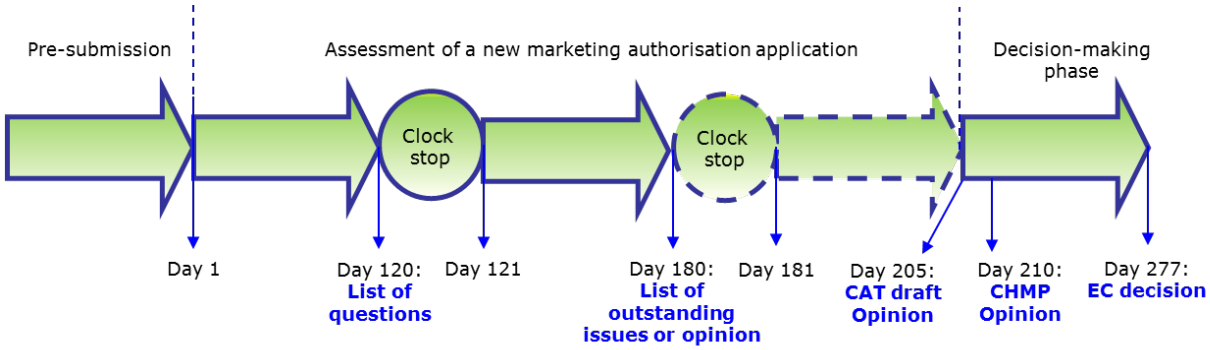
Evaluation of ATMPs (section 2)

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/