18 February 2023
EMA/CAT/36517/2023
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 18-19 January 2023

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

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 these minutes are considered commercially confidential or sensitive and therefore not disclosed. Regarding 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

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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

The Chairperson opened the meeting by welcoming all participants.

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants for agenda topics was identified.

Participants were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The chair welcomed the new alternate from Denmark, who attended CAT for the first time.

1.2. Adoption of agenda

The CAT agenda for 18-20 January 2023 meeting was adopted.

1.3. Adoption of the minutes

The CAT minutes for 07-10 December 2022 meeting were adopted.

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

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/0059

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Pharmacovigilance, request for supplementary information

Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies in the Annex II.

Action: for adoption

The request for supplementary information was adopted.

2.11.2. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0005/G

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Quality, request for supplementary information

Action: for adoption

The request for supplementary information was adopted.

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

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus;

PL: Pascal Venneugues

Scope: Quality, request for supplementary information

Action: for adoption

The request for supplementary information was adopted.

2.11.4. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0033/G

Novartis Europharm Limited

Rapporteur: Carla Herberts, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Clinical safety, opinion

Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce additional guidance on liver function laboratory tests and monitoring before and after infusion and update information based on new safety information on the topic of acute liver failure (ALF) following two reports of fatal ALF.

Update of sections 4.2 and 4.4 of the SmPC in order to provide additional guidance relevant to patient's overall health status prior to dosing and to strengthen the existing description and guidance on systemic immune response.

Update of the section 4.4 of the SmPC in order to indicate prompt attention to thrombotic microangiopathy and to reflect the risk of life-threatening or fatal outcomes.

The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update the Annex II.

Action: for adoption

Request for Supplementary Information adopted on 04.11.2022.

The Rapporteur presented the outcome of the assessment of this variation and the responses to the request for supplementary information. Feedback was provided from the discussion at the PRAC (agreement of the key messages in the Dear Healthcare Professional (DHCP) letter and RMP update). CAT discussed the wording of the SmPC changes. The SmPC changes, the key messages for the DHCP letter and the RMP update were adopted.

The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/ANX/001.1

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Clinical

Protocol follow up (protocol version identifier CA082-1105): in order to further assess the consistency of product quality and clinical outcomes, the MAH shall submit batch analysis and corresponding clinical safety and effectiveness data from a minimum of thirty (30) lots of Breyanzi finished product used to treat patients included in a non-interventional study based on secondary use of data from existing registries, according to an agreed protocol. Based on this data the MAH should also provide an evaluation on the need for a revision of the finished product specifications. Interim reports should be provided after approximately 15 lots and any significant out of trend results should be reported immediately.

Action: for adoption

Request for supplementary information adopted on 9 September 2022

The Rapporteur informed the CAT that the MAH answered satisfactorily to the request for supplementary information. The protocol for the follow-up study was agreed.

2.13.2. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/R/0008

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Marcos Timón, PRAC Rapporteur: Jo Robays

Scope: 1-year Renewal of Marketing Authorisation

Action: for adoption

The Rapporteur presented the outcome of the assessment of the 1-year renewal. The benefit risk remains favourable. The changes to the SmPC were highlighted.

The opinion was adopted.

2.13.3. ROCTAVIAN - valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/ANX/002

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Clinical

Protocol (Study 270-601): a non-interventional, multi-national, longitudinal study of patients treated with Roctavian (valoctocogene roxaparvovec)

Action: for adoption

The Rapporteur presented the outcome of the assessment of the protocol for the post authorisation study. CAT agreed that additional information is needed. A request for supplementary information was adopted.

2.13.4. ROCTAVIAN - valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/ANX/004

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Clinical

Protocol (Study 270-801): a retrospective cohort study of patients treated with Roctavian (valoctocogene roxaparvovec): an analysis of patient registries

Action: for adoption

The Rapporteur presented the outcome of the assessment of the protocol for the post authorisation study. CAT agreed that additional information is needed on the proposed registries. A request for supplementary information was adopted.

2.13.5. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/SOB/002.1

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Clinical

MAH's response to SOB 002 [Study PTC-AADC-MA-406]: a real-world, multicentre, observational and longitudinal study of patients with aromatic L amino acid decarboxylase (AADC) deficiency and with a severe phenotype treated with Upstaza globally, based on data from a registry, according to an agreed protocol.

Action: for adoption

Request for supplementary information adopted on 7 October 2022.

The Rapporteur presented the outcome of the assessment of the response to the specific obligation (registry study). There was a discussion on the age range of the patients included in the study protocol: this range was agreed by CAT. The protocol was agreed.

2.13.6. ROCTAVIAN - valoctocogene roxaparvovec – Orphan - EMEA/H/C/005830

BioMarin International Limited.

Rapporteur: Violaine Closson Carella

PRAC Rapporteur: Menno van der Elst

Scope: Reproductive toxicity testing

Action: for discussion

Carla Herberts (on behalf of the PRAC Rapporteur) introduced the issue that arose during the assessment of the protocols for reproductive toxicity studies for Roctavian: the RMP asks for such a study to improve the recommendation of use in women of childbearing potential and inform on the contraception recommendation in the SmPC. The PRAC Rapporteur considers that the proposed study will not provide useful information to address the contraception question and sought (informal) feedback from CAT on the best approach to study this. CAT provided feedback.

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:	23 January 2023
EMA Coordinator's draft report:	03 February 2023
CAT Coordinator's comments:	08 February 2023
Revised scientific recommendation:	10 February 2023
CAT's discussion of scientific recommendation:	17 February 2023

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Umbilical Cord Wharton Jelly-derived mesenchymal stem cells (MSCs) cells

Treatment of spinal cord injury; drug resistant epilepsy; hypoxia ischemia encephalopathy

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Bladder acellular matrix (BAM) based scaffold seeded with allogenic or autologous adipose-derived stromal cells

Treatment of urinary bladder wall augmentation in patients with small capacity high pressure urinary bladder

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Fibrin gel containing autologous leucocyte- and platelet-rich plasma, autologous thrombin, and ascorbic acid

Treatment of wounds

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. Ex-vivo expanded allogeneic human corneal endothelial cells

Treatment of diseases of the corneal endothelium

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.5. Recombinant Adeno-Associated Viral Vector expressing a codon optimised human RPGR gene (rAAV2tYF-GRK1-RPGR)

Treatment of X-linked retinitis pigmentosa (XLRP) caused by mutations in the RPGR gene

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous platelet concentrate, consisting of a fibrin matrix enriched with platelets, leukocytes and of cytokines and growth factors

Treatment of patients with critical limb ischaemia, in combination with mechanical lower limb revascularization (angioplasty)

Scope: ATMP scientific recommendation

Action: for adoption

This is a resubmission of an ATMP classification request that was submitted in February 2022 that was closed without conclusion in June 2022 due to lack of response by the applicant. The applicant has now resubmitted the request with information.

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.2.2. Autologous adipose tissue derived progenitor cells in biodegradable chemically crosslinked hydrogel

Treatment of subacute spinal cord injury in adults with a complete lesion (ASIA A score)

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.2.3. Genetically engineered *Escherichia coli* train containing a plasmid expressing CRISPR-Cas against clbA, clbB and clbC

Prevention of disease progression in Familial Adenomatous Polyposis (FAP)

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.2.4. Mitochondria isolated from allogeneic umbilical-cord mesenchymal stem cells

Treatment of Polymyositis/Dermatomyositis

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.2.5. Macrophage-Drug Conjugate (MDC) composed of allogenic human monocyte-derived macrophages loaded with a protein-drug conjugate

Treatment of solid tumours

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.2.6. DNA plasmid vector encoding human insulin like growth factor binding protein 2

Treatment of newly diagnosed advanced ovarian cancer after debulking surgery

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.2.7. Autologous muscle precursor cells (MPCs)

Treatment of female stress urinary incontinence

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

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

4.3.1. Adult autologous regenerative cells

Indicated for regeneration, repair, or replacement of weakened or injured subcutaneous tissue

Scope: ATMP scientific recommendation

Action: for adoption

The applicant provided responses to the questions from CAT. The updated classification report was discussed. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 3 February 2023.

4.4. Finalisation of procedure

4.4.1. Autologous adipose-derived stromal vascular fraction cells (ADSVFCs)

Indicated for the treatment of haemophilic arthropathy

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definitions of a somatic cell therapy medicinal product and a tissue engineered product and based on that is considered as tissue engineered product as provided in Article 2(4) of Regulation (EC) No 1394/2007.

4.4.2. Allogeneic Natural Killer cells armed with anti-EGFR monoclonal antibody

Indicated for the treatment of epidermal growth factor receptor (EGFR) positive cancers

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of a somatic cell therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.3. Allogeneic natural killer cells armed with anti-HER2 monoclonal antibody

Indicated for the treatment of human epidermal growth factor receptor 2 (HER2) positive cancers

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of a somatic cell therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.4. Ex-vivo expanded allogeneic neural crest-like stem cells

Indicated for the treatment of diabetic foot ulcer

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of a tissue engineered product as provided in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.5. Allogeneic Wharton's jelly mesenchymal stem cells (WJ-MSCs)

Indicated for the treatment of stress incontinence

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of an advanced therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 1394/2007. CAT considered that the applicant has not provided sufficient information on the claimed mode of action of the product in the indication sought and therefore CAT concluded that the product is an ATMP, but did not decide yet if it is a tissue engineered product or a somatic cell therapy medicinal product.

4.4.6. Autologous monocyte-derived dendritic cells electroporated with mRNAs encoding for immunostimulatory proteins caTLR4, CD40L and CD70 combined with one of the tumour-associated antigens (TAA) MAGE-C2, MAGE-A3, WT1 and NY-ESO-1

Indicated for the treatment of gastric cancer

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of a gene therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.7. Autologous human tumour infiltrating lymphocytes

Indicated for the treatment of locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of a somatic cell therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 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

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

Timetable:

Start of procedure at SAWP:	9-12.01.2023
Appointment of CAT Peer Reviewers:	18-20.01.2023
SAWP first reports:	30.01.2023
CAT Peer Reviewer comments (NC,C):	03.02.2023
CAT Peer Reviewer comments (Q):	08.02.2023
Discussion at SAWP:	6-9.02.2023
Discussion at CAT and feedback to SAWP:	15-17.02.2023

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

Start of procedure at SAWP:	6-9.02.2023
Appointment of CAT Peer Reviewers:	15-17.02.2023
SAWP first reports:	6.03.2023
CAT Peer Reviewer comments (NC,C):	10.03.2023
CAT Peer Reviewer comments (Q):	15.03.2023
Discussion at SAWP:	13-16.03.2023
Discussion at CAT and feedback to SAWP:	22-24.03.2023

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:	04 January 2023
SAWP recommendation:	09 February 2023
CAT recommendation:	17 February 2023
CHMP adoption of report and final recommendation:	23 February 2023

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. Election of CAT Chairperson

Action: For adoption

The election of the Chairperson took place on 19 January at 13.30hrs. EMA reminded the CAT members of the Rule of Procedure pertaining to the election of the chairperson.

The candidate addressed the CAT.

The election took place in the presence of 31 CAT members that were eligible to vote. Ilona Reischl was elected as CAT chair for a period of 3 years. Her mandate will start on 15 February 2023.

The CAT members and EMA thanked Martina Schüssler-Lenz for her contributions to CAT and skilful chairwomanship over the last 6 years.

7.1.2. CAT membership

No items

7.1.3. Vote by proxy

No items

7.1.4. CAT Strategic Review & Learning meeting (SRLM) under the Sweden presidency, 4-5 May 2023, Upsala (Sweden)

CAT: Lisbeth Barkholt, Maria Luttgen

Scope: topics for discussion at the upcoming SRLM

Action: for discussion

Lisbeth Barkholt presented the upcoming SRLM: a joint session with COMP will take place on 4 May 2023 in the morning, CAT only sessions on 4 May 2023 in the afternoon and on 5 May 2023. The draft agenda of the CAT-COMP and CAT sessions was presented and discussed. Additional topics were suggested for the CAT session.

7.1.5. Policy 44 on handling of competing interests for scientific committees' members and experts (revision)

Scope: To inform the committee of the new changes implemented to Policy 044 and the further action needed to be taken by the members

Action: for information

EMA presented the updated Policy 044. CAT members were informed that they will be asked to update their declaration of interest by 17 February 2023.

7.1.6. Report from the CAT chair to EMA management board

CAT: Martina Schüssler-Lenz

Scope: Presentation to the management board on 14 December 2022

Action: for information

The CAT chair informed the Committee of her presentation to the EMA management board.

7.2. Coordination with EMA Scientific Committees

7.2.1. CHMP Scientific Advice Working Party (SAWP): CAT–SAWP joint members

Scope: renomination or nomination of new joint CAT-SAWP members

Action: for discussion

EMA presented the procedure for the (re)nomination of joint CAT-SAWP members. Different from previous nomination procedure, full coordinator responsibilities are expected from the joint members.

Expression of interest to become a joint CAT-SAWP member should be sent to the CAT secretariat by 15 February 2023.

7.2.2. Regulatory and scientific virtual conference on RNA-based medicines - Agenda (europa.eu)

Scope: Draft agenda of the virtual conference on 2 February 2022

Action: for information

The information was noted.

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

No items

7.4. Cooperation with the EU regulatory network

No items

7.5. Cooperation with international regulators

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

CAT: Martina Schuessler-Lenz

Scope: Feedback from the teleconference of 15 December 2022

Action: for information

A short feedback was provided from the discussions at the ATMP cluster teleconference that took place on 15 December 2022. The next ATMP cluster teleconference is scheduled to take place on 23 February 2023.

7.5.2. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH): ICH S12 on non-clinical biodistribution studies for gene therapy products

CAT members: Rune Kjeken, Claire Beuneu - EU Rapporteurs

Scope: feedback on the ICH S12 guideline: non-clinical biodistribution studies for gene therapy products

Action: for information

Rune Kjeken (EU Rapporteur) presented to CAT the content of the ICH S12 guideline. Some points were put to CAT for their consideration.

The guideline is nearing completion (internal regulatory review ongoing). CAT members were asked to review of final ICH proposal and to provide any additional comments directly to the EU Rapporteurs.

7.6. CAT work plan

7.6.1. CAT Workplan for 2023

CAT: Martina Schuessler-Lenz

Scope: draft CAT workplan for 2023

Action: for adoption

CAT discussed the latest version of the CAT work plan and agreed with the minor amendments proposed. Additional Topic Leads were proposed. The CAT work plan for 2023 was adopted.

7.7. Planning and reporting

No items

7.8. Others

7.8.1. CAT Stakeholder meeting 2023

Scope: Proposals for topics to be included in the agenda of the CAT stakeholder meeting that will be organised on 16 May 2023.

Action: for discussion

CAT discussed the proposal received from the European Commission Representative and suggested some additional proposals. The CAT proposal will now be shared with the CAT stakeholders. The CAT stakeholders can also propose their own topics for discussion at the

stakeholder meeting. In a subsequent step, a limited number of agenda items will be selected and presenters (from CAT and from the stakeholders) will be identified.

7.8.2. Update on IRIS for core regulatory procedures

Scope: Update on how core regulatory procedures will be further implemented in IRIS and highlight open opportunities for national competent authorities (NCAs) experts to contribute to ongoing work

Action: for information

EMA presented an update on IRIS and how that will incorporate the regulatory procedures. A call for interest for experts from the NCAs was launched: ideally procedure managers at the NCA could contribute to the IRIS project.

8. Any other business

8.1. Reminder of EMA's reimbursement rules

Scope: Reminder of the reimbursement rules for members and alternates

EMA presented the reimbursement rule of members and alternates. No specific rules are established for hybrid meetings (meetings where part of the members is attending in person and part remotely).

Date of next CAT meeting:

15-17 February 2023

9. Explanatory notes

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

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

EU NTC: European Union Network Training Centre

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Application

MAH: Marketing Authorisation Holder

MNAT: Multinational assessment team

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

QRD: Quality review of documents

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

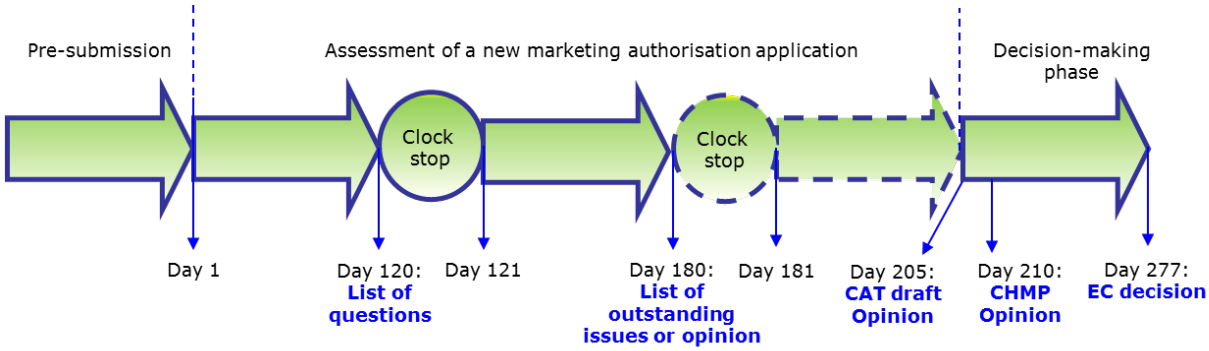
Evaluation of ATMPs (section 2)

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/

10. List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 18-19 January 2023 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martina Schüssler-Lenz	Chair	Germany	No interests declared	
Ilona Reischl	Member (Vice-Chair)	Austria	No interests declared	
Silke Dorner	Alternate	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Azra Selimovic	Member	Croatia	No interests declared	
Isavella Kyriakidou	Alternate	Cyprus	No interests declared	
Kristyna Rehorova Hradilkova	Alternate	Czechia	No interests declared	
Ebru Karakoc Madsen	Member	Denmark	No interests declared	
Bibi Fatima Syed Shah	Alternate	Denmark	No interests declared	
Toivo Maimets	Member	Estonia	No interests declared	
Pille Saalik	Alternate	Estonia	No interests declared	
Heli Suila	Member	Finland	No interests declared	
Violaine Closson	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Egbert Flory	Alternate (to CHMP representative)	Germany	No interests declared	
Maria Gazouli	Member	Greece	No interests declared	
Katalin Lengyel	Member	Hungary	No interests declared	
Balázs Sarkadi	Alternate	Hungary	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Maura O'Donovan	Member	Ireland	No interests declared	
Concetta Quintarelli	Member	Italy	No interests declared	
Barbara Bonamassa	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	
Nancy De Bremaeker	Member	Luxembourg	No interests declared	
John J. Borg	Member (CHMP member)	Malta	No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Babs Fabriek	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Silviu Istrate	Member	Romania	No interests declared	
Katarina Vavrová	Member	Slovakia	No interests declared	
Margareta Fogelová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Suzana Vidic	Alternate	Slovenia	No restrictions applicable to this meeting	
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Lisbeth Barkholt	Member	Sweden	No interests declared	
Maria Luttgen	Alternate	Sweden	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Paolo Gasparini	Member	Clinicians' Representative	No interests declared	
Alessandro Aiuti	Member	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Mencia de Lemus Belmonte	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member	Patients' Representative	No interests declared	
Federica Chiara	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Helena Fonseca	Expert - via telephone*	Portugal	No interests declared	
Attila Sebe	Expert - via telephone*	Germany	No interests declared	
Juliane Rau	Expert - via telephone*	Germany	No interests declared	
Torbjorn Callreus	Expert - in person*	Malta	No interests declared	
Marianne Klanker	Expert - in person*	Netherlands	No interests declared	
Ulla Wändel Liminga	Expert - in person*	Sweden	No interests declared	
A representative from the European Commission attended the meeting Meeting run with support from relevant EMA staff				