EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 March 2020
EMA/CAT/266752/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 19-21 February 2020

Chair: Martina Schüßler-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 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, the 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).

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1. Introduction

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

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 based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

Participants in this meeting 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.

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 and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 21 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The CAT chair welcomed the new alternate member representing clinicians (Frederic Bernard), who attended the CAT for the first time, and thanked the alternate from Austria (Corina Spreitzer), who is attending the CAT for the last time, for her active contribution to the work of the CAT.

In view of the UK's withdrawal from the European Union on 1 February 2020, persons representing, appointed by, or nominated by the UK can no longer participate in EMA meetings. The EMA secretariat would like to thank the member and alternate from the UK (John Johnston and Louise Bisset) for their involvement in the Agency's scientific and regulatory activities and for their contributions to the Committee.

1.2. Adoption of agenda

The CAT agenda for 19-21 February 2020 meeting was adopted

1.3. Adoption of the minutes

The CAT minutes for 22-24 January 2020 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

2.6.1. Onasemnogene abeparvovec - Orphan - EMEA/H/C/004750

AveXis Netherlands B.V.; treatment of spinal muscular atrophy (SMA)

Scope: notification on the start of a compassionate use programme by member states

Action: for information

The information was noted

2.7. New applications

2.7.1. 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

Accelerated assessment

Kite Pharma EU B.V.; treatment of adult patients with relapsed or refractory Mantle cell lymphoma (MCL).

Scope: Timetable for assessment

Action: for adoption

The timetable for assessment was adopted.

2.7.2. Eladocagene exuparvovec - Orphan - EMEA/H/C/005352

PTC Therapeutics International Limited; treatment of aromatic L-amino acid decarboxylase (AADC) deficiency

Scope: Timetable for assessment

Action: for adoption

The timetable for assessment was adopted.

2.7.3. 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

Accelerated assessment

Kite Pharma EU B.V.; treatment of adult patients with relapsed or refractory Mantle cell lymphoma (MCL)

Scope: draft minutes from TC

Action: for discussion

CAT noted the feedback from the TC . No further discussion took place.

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 - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/II/0009

Takeda Pharma A/S

Rapporteur: Lisbeth Barkholt

Scope: quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 08.11.2019.

The opinion was adopted.

2.11.2. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/II/0010/G

Takeda Pharma A/S

Rapporteur: Lisbeth Barkholt

Scope: quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 06.12.2019.

The opinion was adopted.

2.11.3. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0036

Amgen Europe B.V.

Rapporteur: Olli Tenhunen

Scope: quality. RSI

Action: for adoption

The RSI was adopted.

2.11.4. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0037

Amgen Europe B.V.

Rapporteur: Olli Tenhunen

Scope: quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.5. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0013/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: safety. Opinion

Submission of a group of 3 type II variations (C.I.4) to include:
- Long-term efficacy and safety of Kymriah in relapsed/refractory DLBCL based on the 24 months follow-up results from study CCTL019C2201 (update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC)
- Interim results from study CCTL019B2202 (update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC)
- Interim results from study CCTL019B2205J (update section 5.2 of the SmPC)

The Marketing authorisation holder (MAH) took the opportunity to clarify the wording of the indication to include patients over 25 years of age and to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet.

In addition, the MAH requested updates to sections 2.2 and 6.5 of the SmPC, the labelling and to the package leaflet to accommodate the administration of additional infusion bags, when applicable.

The requested group of variations proposed amendments to the Summary of Product Characteristics, Annex II, Annex IIIA and Package Leaflet and to the Risk Management Plan (RMP). The RMP version 2.0 has been submitted.

Action: for adoption

Request for Supplementary Information adopted on 06.12.2019.

The changes made to the product information were presented. The opinion was adopted.

Post-meeting note:

Further changes to the SmPC were introduced . The revised opinion was adopted via written procedure

2.11.6. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0015

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality. RSI

Action: for adoption

The RSI was adopted.

2.12. Other Post-Authorisation Activities

2.12.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090

Novartis Europharm Limited

Rapporteur: Rune Kjeken, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Letter from Novartis

Action: for discussion

CAT discussed the query from the MAH. It was felt it was not possible to conclude on the basis of the letter alone, and it was agreed to organise a teleconference with the MAH to better understand the issue .

2.12.2. Zynteglo - betibeglogene autotemcel - Orphan - EMEA/H/C/003691/R/0005

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, Co-Rapporteur: Violaine Closson Carella, CHMP Coordinator: Paula Van Hennink, Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 1-year Renewal of Marketing Authorisation

Action: for adoption

Request for Supplementary Information adopted on 24.01.2020.

The renewal opinion 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

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

Timetable:
-Start of the procedure: 24.02.2020
-Draft CAT co-ordinator's report: 06.03.2020

-ITF peer-review comments: 11.03.2020
-Revised scientific recommendation: 13.03.2020
-Adoption of scientific recommendation by CAT: 20.03.2020

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Recombinant chimeric vesicular stomatitis virus carrying the envelope glycoprotein (GP) of the visceral non-neurotropic strain of the lymphocytic choriomeningitis virus

Intended for the treatment of solid tumours, including non-small cell lung carcinoma.

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Autologous CD34+ cells transduced with CL20-4i-EF1α-hγc-OPT lentiviral vector – H0005602

Intended for the treatment of X-linked severe combined immunodeficiency (XSCID)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Wharton's jelly derived mesenchymal stem cells, AMN – H0005623

Intended for the treatment of adrenomyeloneuropathy (AMN)

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, *ex vivo* expanded, clonal neoantigen specific tumour infiltrating lymphocytes – H0005575

Intended for the treatment of solid tumours

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.2. Autologous adipose derived mesenchymal stem cells, ALS – H0005580

Intended for the treatment of Amyotrophic Lateral Sclerosis (ALS)

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.3. Wharton jelly derived mesenchymal stem cells – H0005608

Intended for the treatment of spinal cord injury, drug resistant epilepsy and hypoxia ischemia encephalopathy

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.4. Allogeneic CRISPR/Cas9-mediated genetically modified CAR T cells targeting CD19 antigen – H0005581

Intended for the treatment of CD19+ haematological malignancies

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.5. Allogeneic CRISPR/Cas9-mediated genetically modified CAR T cells targeting B-cell maturation antigen (BCMA) – H0005582

Intended for the treatment of relapsed or refractory multiple myeloma

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.6. Micronized autologous adipose tissue particles and costal cartilage powder – H0005607

Intended for the treatment of cartilage defects

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT noted the additional information provided by the applicant on the viable cell count and the proposed mechanism of action. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.7. Human embryonic stem cell-derived otic neural progenitor cells – H0005583

Intended for the treatment of sensorineural hearing loss

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.8. Wharton's jelly derived mesenchymal stem cells, ALS – H0005619

Intended for the treatment of Amyotrophic Lateral Sclerosis (ALS)

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.9. Wharton's jelly derived mesenchymal stem cell, Huntington's disease - H0005571

Intended for the treatment of Huntington's disease

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.10. Wharton's jelly derived mesenchymal stem cell, Lewy body dementia (LBD) - H0005572

Intended for the treatment of Lewy body dementia (LBD)Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.2.11. Wharton's jelly derived mesenchymal stem cell, secondary progressive multiple sclerosis (SPMS) - H0005573

Intended for the treatment of secondary progressive multiple sclerosis (SPMS)

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

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

4.3.1. Autologous adipose-derived mesenchymal stem cells ex-vivo expanded, alopecia - H0005567

Intended for the treatment of alopecia

Scope: Responses received by the applicant. Revised ATMP scientific recommendation

Action: for adoption

Request for LoQs adopted on 24 January 2020

CAT discussed the ATMP classification report, which was revised based on the additional information provided. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.3.2. Autologous adipose-derived mesenchymal stem cells ex-vivo expanded, hypertrophic scars - H0005568

Intended for the treatment of hypertrophic scars

Scope: Responses received by the applicant. Revised ATMP scientific recommendation

Action: for adoption

Request for LoQs adopted on 24 January 2020

CAT discussed the ATMP classification report, which was revised based on the additional information provided. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 6 March 2020.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

4.4. Finalisation of procedure

4.4.1. Adeno-associated viral vector serotype 5 containing the human RPGR gene - Orphan - H0005544

Intended for the treatment of X-linked Retinitis Pigmentosa owing to defects in Retinitis Pigmentosa GTPase Regulator (RPGR)

Scope: no comments raised by the European Commission. ATMP scientific recommendation

Action: for adoption

The information was noted.

4.4.2. Wharton's jelly derived mesenchymal stem cell , age-related macular degeneration (AMD) - H0005562

Intended for the treatment of age-related macular degeneration

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation.

Action: for adoption

The information was noted.

4.4.3. Wharton's jelly derived mesenchymal stem cell , bone non-union - H0005563

Intended for the treatment of bone non-union

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for adoption

The information was noted.

4.4.4. Wharton's jelly derived mesenchymal stem cell , chorioretinal disorders - H0005564

Intended for the treatment of other retinal and choroid diseases

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for adoption

The information was noted.

4.4.5. Wharton's jelly derived mesenchymal stem cell , epidermolysis bullosa - H0005565

Intended for the treatment of epidermolysis bullosa

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for adoption

The information was noted.

4.4.6. Wharton's jelly derived mesenchymal stem cell , hypoxic-ischemic encephalopathy (HIE) - H0005566

Intended for the treatment of hypoxic-ischemic encephalopathy

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for adoption

The information was noted.

4.4.7. Adeno-associated viral vector serotype 9 encoding a codon-optimised human AGA transgene - H0005560

Intended for the treatment of treatment of aspartylglucosaminuria, a recessively inherited lysosomal storage disease caused by loss-of-function mutations in the AGA gene.

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation.

Action: for adoption

The information was noted.

4.5. Follow-up and guidance

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

Timetable:

-Final Briefing Package:	06.03.2020
-Start of the procedure at SAWP:	12.03.2020
-CAT report due by:	13.03.2020
-CAT recommendation:	20.03.2020

5.2. CAT reports

5.3. List of Issues

5.4. 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

Timetable for assessment:
Procedure start: 13.02.2020
SAWP recommendation: 12.03.2020
CAT recommendation: 20.03.2020
CHMP adoption of report and final recommendation: 26.03.3030

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. CAT Vice-Chairperson - election

Scope: election of Vice-Chairperson .

Action: for election

The mandate of the current vice-chair (Ilona Reischl) will finish on 14 March 2020.

Prior to the election process, EMA reminded the CAT members of the rule of procedure pertaining to the election of the vice-chairperson.

The candidate addressed the CAT.

The election took place in the presence of 26 CAT members that were eligible to vote. . Ilona Reischl was elected as CAT vice-chair for a second mandate of 3 years.

7.1.2. CAT membership

Members representing clinicians: Frederic Bernard – new alternate. Membership mandate started on 7 January 2020

Action: for information

The CAT chair welcomed the new alternate.

7.1.3. Procedural advice on the CHMP/CAT/PRAC (Co-)Rapporteur appointment

Scope: Rapporteur appointment procedure

Action: for information

CAT was informed of the suggested amendment to the (Co)-Rapporteur appointment procedure

7.2. Coordination with EMA Scientific Committees

7.2.1. Committee for Medicinal Products for Human Use (CHMP)

Scope: Summary of Outcomes (SoO) for the January 2020 meeting

Action: for information

The information was noted.

7.2.2. CHMP paper on single-arm trials

CAT: Jan Mueller-Berghaus

Scope: presentation of the CHMP paper on single-arm trials

Action: for information

CAT noted the content of the CHMP paper on single-arm trials. The presentation covered 3 topics: Single arm trials as pivotal evidence? Conditional marketing authorisation vs. Full marketing authorisation; What is a comprehensive dossier?

7.2.3. CAT-COMP Working Group

CAT core members: Kieran Breen, Carla Herbert, Maura O'Donovan, Maja Sommerfelt and Martina Schüßler-Lenz

Scope: feedback on the kick-off meeting - COMP-CAT Working Group to take place on 19 February from 18:30-19:30hrs

Action: for information

Feedback was provided from the discussions in the kick-off meeting. CAT noted the proposal to meet on a monthly basis (in the evening of the first day CAT plenary) to discuss the orphan ATMPs under evaluation.

The first meeting will take place on 18 March 2020. The CAT core-members and the Rapporteur/CoRapporteur of the ATMP identified for discussion will be invited.

7.2.4. Scientific Coordination Board (SciCoBo) – meeting of 5 February 2020

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting that took place on 5 February 2020.

Action: for information

The CAT chair gave an oral feedback from the SciCoBo meeting.

7.2.5. Scientific Coordination Board (SciCoBo) - EMA Regulatory Science Strategy to 2025

CAT: Martina Schüßler-Lenz

Scope: draft final RSS to 2025 Reflection for CAT members' review and comments by Friday 21st February 2020

Action: for information

Note: this document has also been sent to all Committee Chairs and Working Party Chairs with same timeframe for review following which it will be circulated for endorsement by the Management Board of the EMA at its March 2020 plenary meeting.

The information was noted.

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

7.3.1. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope:
- Meeting Summary from the Annual PCWP/HCPWP meeting with all eligible organisations, 20 November 2019
-Agenda for the PCWP/HCPWP joint meeting, 3-4 March 2020

Action: for information

The information was noted.

7.4. Cooperation within the EU regulatory network

7.4.1. Concerns over the use of unregulated/unproven ATMPs

CAT: Rune Kjeken, Dariusz Sladowski, Claire Beuneu, Egbert Flory

Scope: revision of the EMA public statement on concerns over unregulated medicinal products containing stem cells

Action: for discussion

CAT discussed the public statement related to unproven cell-based therapies: the risk to public health and the development of advanced therapies.

7.5. Cooperation with international regulators

7.5.1. ICH S12 - guideline on biodistribution of gene therapy medicinal products

CAT: Claire Beuneu, Rune Kjeken

Scope: preparation of the ICH S12 concept paper: feedback from the drafting groups at the ICH meeting in Singapore (November 2019)

Action: for information

Feedback was provided by Claire Beuneu and Rune Kjeken, who are appointed as EU representatives for the drafting of the ICHS12 guideline. Following non-clinical experts from CAT will support them (consultation on an ad-hoc basis): Egbert Flory, Bjorn Carlsson, Anne Pastoft, Brigitte Anliker (DE-PEI) and Tineke van den Hoorn (NL).

7.5.2. ATMP cluster teleconference with FDA-USA, Health Canada and PMDA-Japan

Scope: draft agenda for the teleconference

Action: for discussion

The agenda topics were presented and CAT speakers for the topics were identified.

7.6. CAT work plan

None

7.7. Planning and reporting

None

7.8. Others

7.8.1. EU NTC proposal for training on pharmacoepidemiology

Action: For information

CAT noted the proposal for training on pharmacoepidemiology. Following CAT members are interested to contribute to the development of this training: Alessandro Aiuti, Isabel Vieira, Angeliki Roboti.

7.8.2. Presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients

MAHs: various

Scope: presentation of the issue and steps taken

Action: for information

CAT noted the presentation on nitrosamine impurities in medicines.

8. Any other business

8.1. EMA's new Human Division

Scope: presentation of the new Human Division after the update on EMA organisation aspects

Action: for information

CAT noted the information on the new human division. CAT welcomed the establishment of a therapeutic office specific for ATMPs.

8.2. UK withdrawal from the EU

Scope: update

Action: for discussion

The EMA secretariat updated the Committee on the practical aspects of the UK's withdrawal from the EU.

8.3. 5th International alliance for biological standardization (IABS), 2-4- February 2020, Tokyo (Japan)

CAT: Marcos Timón

Scope: feedback on session: *'Global regulatory landscape of cell therapy products meting'*

Action: for information

M Timon provided a short feedback from the discussion at the session of the Global regulatory landscape.

8.3. American Society of Gene & Cell Therapy (ASGCT)'s annual meeting, 11th May 2020, Boston MS (USA)

Scope: nomination of Jan Mueller-Berghaus to present at the ASGCT pre-meeting workshop: 'Commercialization I Workshop'

Action: for agreement

CAT agreed with the representation of CAT by Jan Mueller-Berghaus at the AGSCT pre-meeting workshop.

Date of next CAT meeting:

18-20/03/2020

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

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

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

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: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

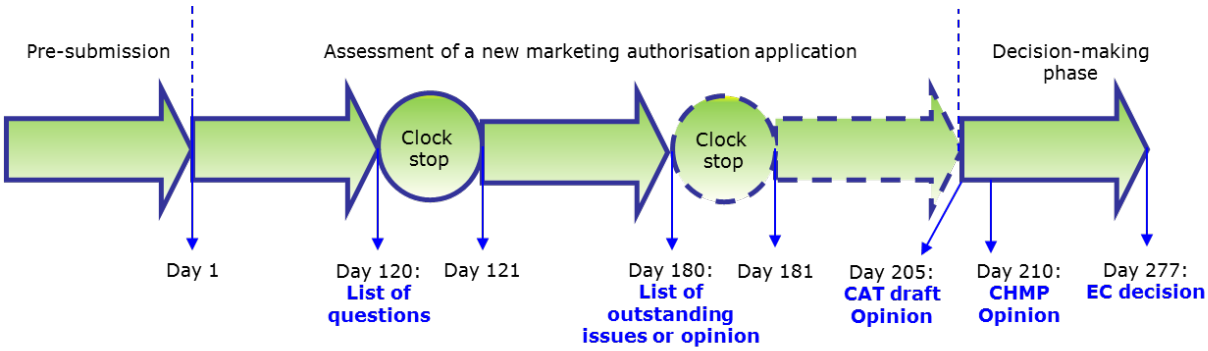
Evaluation of ATMPs (section 2)

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 19-21 February 2020 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	Austria	No interests declared	
Corina Spreitzer	Alternate	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Belaïd Sekkali	Alternate	Belgium	No interests declared	
Petra Sokol	Alternate	Croatia	No interests declared	
Rafaella Pontou	Member	Cyprus	No interests declared	
Ivana Haunerova	Member	Czech Republic	No interests declared	
Anne Pastoft	Member	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	
Olli Tenhunen	Alternate	Finland	No interests declared	
Violaine Closson	Member	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	
Angeliki Rompoti	Alternate	Greece	No interests declared	
Katalin Lengyel	Member	Hungary	No interests declared	
Niamh Curran	Alternate	Ireland	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	Italy	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No interests declared	
John J. Borg	Member (CHMP member)		No interests declared	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Johannes Hendrikus Ovelgonne	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Maja Sommerfelt Grønvold	Alternate	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	
Alina Musetescu	Member	Romania	No restrictions applicable to this meeting	
Lukas Slovak	Member	Slovakia	No interests declared	
Alexandra Padova	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Carlsson	Alternate	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bernd Gänsbacher	Member	Healthcare Professionals' Representative	No interests declared	
Frederic Bernard	Alternate	Healthcare Professionals' Representative	No interests declared	
Alessandro Aiuti	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Alessandra Renieri	Alternate	Healthcare Professionals' Representative	No interests declared	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Lydie Meheus	Alternate	Patients' Representative	No interests declared	
Kieran Breen	Member	Patients' Representative	No restrictions applicable to this meeting	
Monique Wakelkamp	Expert - in person*	MPA-SE	No restrictions applicable to this meeting	
Reet Rumvolt	Expert - in person*	RAVIMIAMET-EE		
Barbara Bonamassa	Expert - in person*	AIFA-IT	No interests declared	
Peter Lönn	Expert - via telephone*	MPA-SE	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the agenda topics or activities they participated in.