14 April 2021
EMA/CAT/172956/2021
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 17-18 March 2021

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

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).

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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. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

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. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The CAT chair welcomed Azra Semilovic, Concetta Quintarelli and Nancy de Bremaecker, the new members for Croatia, Italy and Luxembourg respectively and thanked the departing members for their contributions to the CAT over the last years.

1.2. Adoption of agenda

The CAT agenda for 17-19 March 2021 meeting was adopted with two additions that were included under AOB.

1.3. Adoption of the minutes

The CAT minutes for the 17-19 February 2021 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. Idecabtagene vicleucel - Orphan - EMEA/H/C/004662

Celgene Europe BV; treatment of multiple myeloma

Scope: letter from the applicant dated 08.03.2021 requesting an extension of the clock stop

Action: for adoption

List of Questions adopted on 11.09.2020. List of outstanding issues adopted on 04.12.2020. List of outstanding issues adopted on 19.02.2021

CAT agreed with the clock stop extension. The new evaluation timetable was adopted.

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

CO.DON AG

Rapporteur: Lisbeth Barkholt

Scope: Clinical. RSI

Extension of the indication for use in the paediatric population (15 to 18 years).

Action: for adoption

The Rapporteurs presented the assessment of this variation to extend the indication of Spherox to younger patients. The request for supplementary information (RSI) was adopted.

2.11.2. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0022

CO.DON AG

Rapporteur: Lisbeth Barkholt

Scope: Clinical. RSI

Update of section 5.1 of the SmPC with the final results of study cod 16 HS 13, a 60-month follow up data assessing long-term efficacy and safety of Spherox.
Annex II has also been updated to reflect the completion of the study.

Action: for adoption

The Rapporteurs presented the assessment of this variation. A request for supplementary information (RSI) was adopted.

2.11.3. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0030

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 22.01.2021.

The opinion was adopted.

2.11.4. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0031

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 22.01.2021.

The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Glybera – Alipogene tiparvovec – EMA/H/C/0002145/SOB/001.10

UniQure biopharma B.V.; treatment lipoprotein lipase deficiency (LPLD)

Rapporteur: Egbert Flory; CHMP Coordinator: Jan Mueller-Berghaus

Scope: Clinical. Annual safety update report

Long term surveillance programme/ disease registry to collect information on the epidemiology of the disease and the demographics, safety, and the effectiveness outcomes of patients treated with Glybera. The patients enrolled in clinical studies (CT-AMT-010 -10, CT-AMT 011-01, CT-AMT 011-02) should be followed up in the LPLD registry.

Action: for adoption

The Annual safety update report was adopted.

2.13.2. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/R/0012

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts, Co-Rapporteur: Egbert Flory; PRAC Rapporteur: Ulla Wändel Liminga

Scope: 1-year renewal of Marketing Authorisation

Action: for adoption

Request for Supplementary Information adopted on 22.01.2021.

The renewal was adopted.

2.13.3. Zynteglo - betibeglogene autotemcel - Orphan - EMEA/H/A-20/1504

bluebird bio (Netherlands) B.V

CAT-PRAC working group: CAT: Carla Herberts (Rapporteurs) and Violaine Closson-Carella (Co-Rapporteur), Alessandro Aiuti; PRAC: Brigitte Keller-Stanislawski, Menno van der Elst

Scope: Referral procedure under Article 20 PhV. List of Questions to the MAH

Action: for information

The information on the ongoing Zynteglo referral procedure and the list of questions that was sent to the MAH were noted.

2.13.4. Tecartus – Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured – EMEA/H/C/005102

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

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Rune Kjeken; PRAC Rapporteur: Menno van der Elst, PRAC Co-Rapporteur: Brigitte Keller-Stanislawski

Scope: question from the MAH.

Action: for discussion

The MAH will be informed of the conclusion of the CAT.

2.13.5. Committees discussion and outcome on milestones and performance indicators for the deadline for improvement for imposed PASS using the European Society for Blood and Marrow Transplantation (EBMT) as data source

Scope: draft proposal

The proposal was agreed

3. Certification of ATMPs

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

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of ITF Coordinator

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

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.2. Oncolytic adenovirus

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

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

Vaccine against SARS-CoV-2Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

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

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

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

Intented for the treatment of cancer

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

4.1.6. Autologous cultured chondrocytes

Intended for the treatment of filling of cartilage defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Coordinator was appointed.

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

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

Scope: 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 antigen specific Cytotoxic T Lymphocytes

Intended for the treatment of cancer patients that are over expressing the specific antigen

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 31 March 2021

4.2.2. Autologous dendritic cells activated against tumour peptides

Intended for the treatment of cancer patients; *in vivo* immune stimulation against specific cancer overexpressing the tumour antigen

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 31 March 2021

4.2.3. Autologous M1-polarized macrophages

Intended for the treatment of cancer patients

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 31 March 2021

4.2.4. Autologous Cytotoxic Natural Killer (NK) cells

Intended for the treatment of cancer patients

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 31 March 2021

4.2.5. Autologous plasma cells producing monoclonal antibodies against specific tumor antigen, for treatment of cancer patients

Intended for the treatment of cancer patients

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 31 March 2021

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

No items

4.4. Finalisation of procedure

4.4.1. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, muscle and tendons disease

Intended for diseases of muscles and tendons

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.2. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, anal fistula

Intended for the treatment of anal fistula

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.3. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, androgenic alopecia

Intended for the treatment of androgenic alopecia, unspecified

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.4. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, diabetic foot syndrome

Intended for the treatment of diabetic foot syndrome (DFS)

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.5. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, Parkinson's disease

Intended for the treatment of Parkinson's disease

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.6. Allogeneic human mesenchymal stem cells derived from Wharton's jelly seeded on the dermal scaffold, skin ulcers

Intended for the treatment of skin ulcers

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.7. Autologous human mesenchymal stem cells derived from adipose tissue, anal fistula

Intended for the treatment of anal fistula

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.8. Autologous human mesenchymal stem cells derived from adipose tissue, androgenic alopecia

Intended for the treatment of androgenic alopecia, unspecified

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.9. Autologous human mesenchymal stem cells derived from adipose tissue, muscle and tendons disease

Intended for diseases of muscles and tendons

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.10. Two mRNA active substances, encoding separately for Human Papilloma Virus type (HPV) 16 E6 and HPV16 E7 protein

Intended for the treatment of recurrent/metastatic HPV16-positive carcinoma

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.11. Human amniotic membrane, allogeneic, sterile, cryomilled and lyophilized

Intended for the treatment of symptoms of osteoarthritis

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.12. Autologous dendritic cells activated against SARS-COV-2 peptides

Intended for the prevention of SARS-COV-2 infection

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.13. Human umbilical cord MSC derived exosomes carrying recombinant hTERT mRNA and protein, hsa-miR-125b-5p, hsa-miR-125b-1-3p, AntimiR-21-5p

Intended for the treatment of Acute Respiratory Distress Syndrome and Chronic Obstructive

Respiratory Disease

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.14. DNA plasmid encoding human transferring gene

Intended for the treatment of retinitis pigmentosa

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.15. Bacteriophage cocktail consisting of four CRISPR-armed phages

Intended for the treatment of prophylaxis of bloodstream *E. coli* infection in neutropenic patients with haematological malignancy

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

Action: for information

The information was noted. The classification report will be sent to the applicant.

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

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

Timetable:

-Start of procedure at SAWP:	08-11.03.2021
-Appointment of CAT Peer Reviewers:	19.03.2021
-SAWP first reports:	29.03.2021
-CAT Peer reviewer comments:	02.04.2021
-Discussion at SAWP:	06-09.04.2021
-Discussions at CAT and feedback to SAWP:	15.04.2021

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

-Start of procedure at SAWP:	06-09.04.2021
-Appointment of CAT Peer Reviewers:	16.04.2021
-SAWP First Reports:	26.04.2021
-CAT Peer reviewer comments:	30.04.2021
-Discussion at SAWP:	03-06.05.2021
-Discussions at CAT and feedback to SAWP:	11.05.2021

5.2. CAT discussion

5.3. Finalisation of SA procedures

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

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:	11.03.2021
SAWP recommendation:	09.04.2021
CAT recommendation:	16.04.2021
CHMP adoption of report and final recommendation:	22.04.2121

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 membership

Croatia – Azra Semilovic – membership mandate (member) started 21.02.2021
Italy - Concetta Quintarelli - membership mandate (member) started on 22.02.2021
Italy – Paolo Gasparini – membership mandate (member) ended 21.02.2021

Latvia – Liga Kunrade - membership mandate (alternate) ended 03.09.2021

Luxembourg – Nancy de Bremaeker – membership mandate (member) started 06.03.2021

Luxembourg – Guy Berchem – swap of role from member to alternate started 06.03.2021

Luxembourg – Anne-Cecile Vuillemin – membership mandate (member) ended 05.03.2021

Action: for information

The CAT chair welcomed the new members and new alternate. She thanked the departing members for their contributions to the CAT.

7.1.2. Strategic Review & Learning meeting (SRLM) under the Portuguese presidency of the European Union - Lisbon, Portugal

CAT: Bruno Sepodes, Maria-Isabel Vieira

Scope: draft agenda of the joint CAT-CHMP meeting that is scheduled to take place at the SRLM on 27th May 2021

Action: for discussion

The updated agenda of the CAT-only session was presented. The agenda for the joint CAT-CHMP session need to be further developed. CAT proposed to include the topic on comprehensiveness of clinical trial data on the agenda, however more topics need to be added. This will be further discussed in the April CAT meeting.

7.2. Coordination with EMA Scientific Committees

7.2.1. CHMP learnings that impact CAT decisions

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

Scope: procedure to identify CHMP learnings that are relevant to CAT

Action: for information

The following proposal was agreed: the excel sheet with the new CHMP learnings will be put on screen during the CAT meeting and the CHMP-CAT double members will be asked to provide input, especially in relation to their relevance to CAT. This will be a pilot for the upcoming 6 months.

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

7.3.1. Inter-Committee Scientific Advisory Group (SAG) Oncology

Scope: request for nominations

Action: for information

This topic was postponed to a future CAT meeting.

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

CAT: Martina Schüßler-Lenz, Kieran Breen

Scope: feedback on the PCWP/HCPWP joint meeting that took place on 3-4 March 2021

Action: for information

Note: the CAT Chair - Martina Schüßler-Lenz - took part on the topic of: *'Timely patients' access to advanced therapy medicinal products in the EU'*

A short feedback was provided from the PCWP/HCPWP meeting.

7.3.3. CAT-COMP Working Group

CAT: Martina Schüßler-Lenz

Scope: feedback from the CAT-COMP working group meeting that took place on 15 March 2021

Action: for information

A short feedback was provided from the CAT-COMP meeting.

7.3.4. New active substance (NAS) status of ATMPs

CAT topic lead: Rocío Salvador Roldán; BWP Rapporteur: Martijn van der Plas

Scope: development of the BWP guidance on the structure and properties for the determination of new active substance (NAS) status of biological substances: timeline and plan of actions

Action: for discussion

The BWP Rapporteur presented the plan of action to restart the development of Reflection paper on the biological structure and properties criteria to be considered for the evaluation of new active substance (NAS) status of biological substances. The development of this reflection paper has been on hold since 2019 due to business continuity restrictions.

The considerations on NAS for ATMPs need to be developed. Following CAT members and experts will contribute to this activity: Ilona Reischl, Heli Suila, Niamh Curran, Marja van der Bovenkamp, Barbara Bonamassa, Jürgen Scherer and Rocío Salvador Roldán.

7.4. Cooperation within the EU regulatory network

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

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

Scope: draft Q&A on principles for GMP

Action: for discussion

Note: CAT members are requested to send comments by 17 March 2021

The Q&A on principles of GMP was presented. Final comments were made related to the scope (indication that the document is mainly focused on viral vectors used for commercial product manufacture, change to footnote 3 on the GMP requirements for induced pluripotent stem cell), introduction of some flexibility for starting materials used to manufacture clinical trial material and clarifying the requirement for a supplier qualification programme.

The document was subsequently endorsed by CAT.

7.4.2. Product information for medicinal products that contain or consist of modified viruses

Scope: Product information for medicinal products that contain or consist of modified viruses: learning from recent cases.

Action: for discussion

In the light of the current experience with GMO-based vaccines, it was proposed to enlarge the group involved in the interplay between the Pharma and GMO authorities to discuss GMO topics for all medicines (so far the focus was mainly on GTMPs).

7.4.3. Questions and Answers related to the assessment of similarity for ATMPs in the context of the orphan legislation

CAT members and experts: Claire Beuneu, Barbara Bonamassa, Violaine Closson-Carella, Niamh Curran, Rune Kjeken, Ilona Reischl, Heli Suila, Marja van der Bovenkamp

Scope: revised Questions and Answers

Action: for discussion

The European Commission Representative presented the final version of the Q&A on orphan similarity for ATMPs. Some additional comments were discussed. The document was subsequently adopted by CAT.

Legal clarifications were provided on the differences between orphan similarity and significant benefit demonstration and orphan similarity vs. new active substance status.

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

CAT: Martina Schüßler-Lenz

Scope: Appointment of CAT members to be involved in workshops organised by the Commission on the revision of the BTC legislation

Action: for discussion

Note:

-The European Commission is hosting different workshops on the revision of the BTC legislation. For some of them, EMA / CAT will be consulted.

-The proposal is to appoint approx. 5 CAT members that will form the CAT expert group to join these workshops. The CAT experts will provide feedback to the CAT plenary.

The following CAT members expressed interest to take part in this interaction: Ilona Reischl, Violaine Closson-Carella, Marcos Timon, Maura O'Donovan, Egbert Flory, Claire Beuneu, Rune Kjeken, Dariusz Sladowski, Maria Gazouli. The CAT chair and CAT secretariat will identify 5 to 6 members to participate in the discussions with the European Commission on the revision of the BTC legislation.

7.5. Cooperation with international regulators

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

CAT: Martina Schüßler-Lenz

Scope: draft agenda of the teleconference to take place on 25 March 2021

Action: for discussion

The topics on the agenda were presented.

7.5.2. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) – ICH-S12 guideline

CAT: Rune Kjeken, Claire Beuneu

Scope: feedback on the development of the ICH-S12 guideline: nonclinical biodistribution studies for gene therapy products

Action: for discussion

The EU Rapporteur (Claire Beuneu) provided feedback on the development of the ICH S12 guideline. The next steps were presented.

7.5.3. International Pharmaceutical Regulators Programme (IPRP) – Gene therapy and cell therapy working group

CAT: Pille Säälik, Ivana Haunerova

Scope: feedback from the joint gene and cell therapy working groups teleconference that took place on 4 March 2021

Action: for discussion

A short feedback from the IPRP meeting was provided.

7.6. CAT work plan

None

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q1/2021 update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

7.8. Others

7.8.1. Quality Review of Document (QRD) – core SmPC for genetically modified cells of ATMPs

CAT Ad Hoc labelling group: Martina Schüßler-Lenz, Alessandro Aiuti, Violaine Closson-Carella, Metoda Lipnik-Stangelj, Ilona Reischl, Isabel Vieira, Carla Herberts

Scope: presentation of the new core SmPC for consultation with CAT

Action: for discussion

A detailed presentation of the core SmPC for genetically modified cells was given. It was agreed that this core SmPC should be applicable to all genetically modified cells: genetically modified CD34+ cells and CAR-T cells are mentioned as relevant examples.

A 4-week consultation period by CAT members was agreed. CAT members were asked also to consult their quality colleagues and provide feedback by 16 April 2021. Thereafter, the QRD consultation and adoption will take place, followed by an external consultation over summer.

7.8.2. Curriculum on Advanced Therapies Medicinal Products (ATMPs)

CAT: Ilona Reischl

Scope: plan of trainings for 2021

Action: for discussion

It was agreed to develop a simple system to provide training to CAT. In the meanwhile, it was proposed to put trainings on hold until after the Corona pandemic.

8. Any other business

8.1.1. Selection of CAR-T treatment centres

CAT: Claire Beuneu

Scope: Informal question to CAT

Action: for discussion

Claire Beuneu informed CAT that the Belgian authorities received a letter from one of the large hospitals in which they question why the selection of CAR-T treatment centres (for Kymriah and Yescarta) is done by the MAHs and not by, or with the involvement of, the NCAs.

CAT members provided input from the situation in their country. In most countries, the national authorities are not involved in the selection of treatment centres, but regulatory authorities or reimbursement bodies have defined criteria for CAR-T treatment centres thus restricting the number of treatment centres per country; qualification of the centres is the responsibility of the company.

8.1.2. Companion diagnostics: consultation process for Notified Bodies (NBs)

CAT: Ilona Reischl

Scope: Call for interest of CAT member/assessor to participate in dialogue with NBs

Action: for discussion

The topic was introduced: in accordance with the In vitro diagnostic Regulation (Regulation (EU) 2017/746), the Notified body (NB) will have to consult a medicines national competent authority (NCA) regarding the suitability of the companion diagnostic (CDx) before issuing an EU technical documentation assessment certificate for the CDx.

EMA is developing a procedure for this consultation between NB and EMA/NCA. A call for CAT members/experts to participate in dialogue with the NBs was launched; this discussion would be focused mainly on data requirements for CDx conformity assessment and scientific evidence for CDx (scientific validity, analytical and clinical performance): 2-3 workshops (via TC) will be organised for this interaction.

Ilona Reischl and Alessandro Aiuti will be involved in this activity.

Date of next CAT meeting: 14-16 April 2021

9. Explanatory notes

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

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

EU NTC: European Union Network Training Centre

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Application

MAH: Marketing Authorisation Holder

MNAT: Multinational assessment team

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

QRD: Quality review of documents

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

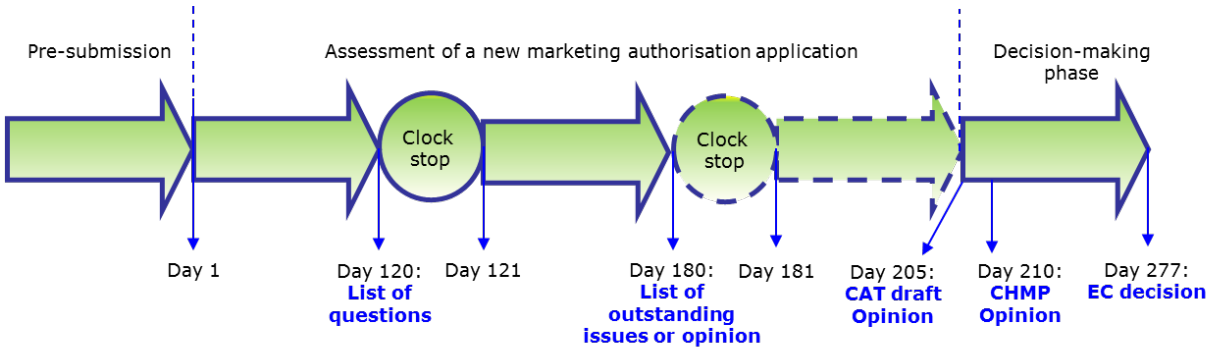
Evaluation of ATMPs (section 2)

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

New applications (sections 2.1. to 2.12.)

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

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



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

Oral explanation (section 2.2.)

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

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

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

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

Withdrawal of applications (section 2.7.)

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

New applications (section 2.9.)

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

GMP and GCP Inspections Issues (section 2.10.)

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

Post-authorisation activities (section 2.12.)

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

Certification of ATMPs (section 3)

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

Scientific Recommendation on Classification of ATMPs (Section 4)

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

Scientific Advice (section 5)

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

Pre-Authorisation (section 6)

Paediatric Investigation Plan (PIP)

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

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

ITF Briefing meeting in the field of ATMPs

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

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

Priority Medicines (PRIME)

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

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

Organisational, regulatory and methodological matters (section 7)

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

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

Any other business (section 8)

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

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

10. List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 17-18 March 2021 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	
Belaïd Sekkali	Alternate	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Azra Selimovic	Member	Croatia	No interests declared	
Petra Sokol	Alternate	Croatia	No interests declared	
Isavella Kyriakidou	Alternate	Cyprus	No interests declared	
Ivana Haunerova	Member	Czechia	No interests declared	
Tomas Boran	Alternate	Czechia	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	
Maria Gazouli	Member	Greece	No interests declared	
Angeliki Rompoti	Alternate	Greece	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Katalin Lengyel	Member	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Niamh Curran	Alternate	Ireland	No restrictions applicable to this meeting	
Concetta Quintarelli	Member	Italy	No interests declared	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No interests declared	
Guy Berchem	Alternate	Luxembourg	No restrictions applicable to this meeting	
Nancy De Bremaeker	Member	Luxembourg	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	
Babs Fabriek	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	
Silviu Istrate	Member	Romania	No interests declared	
Lukas Slovak	Member	Slovakia	No interests declared	
Alexandra Padova	Alternate	Slovakia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Lisbeth Barkholt	Member	Sweden	No interests declared	
Bernd Gänsbacher	Member	Healthcare Professionals' Representative	No interests declared	
Alessandro Aiuti	Member	Healthcare Professionals' Representative	Restrictions applicable to this meeting	
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	
Christophe Genisset	Expert	ANSM - France	Direct Interests declared	7.4.1
Martijn Van der Plas	Expert	Netherlands - CBG/MEB	No interests declared	
Barbara Bonamassa	Expert	Italy - AIFA	Direct interests declared	7.4.3
Jürgen Scherer	Expert	Germany - PEI	No interests declared	
Monique Wakelkamp	Expert	Sweden - MPA	Indirect Interests declared	2.11
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.