18 October 2019
EMA/CAT/14825/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 11-13 September 2019

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. 22 or more members were present in the room. No new or additional interests or restrictions were declared.

The CAT chair welcomed the new member representing the clinicians (Alessandro Aiuti), who attended the CAT for the first time.

1.2. Adoption of agenda

The CAT agenda for 11-13 September 2019 meeting was adopted

1.3. Adoption of the minutes

The CAT minutes for 17-19 July 2019 meeting were adopted

1.4. August 2018 Written Procedure

The CAT minutes of the August 2019 Written Procedure 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. Viable T-cells - Orphan - EMEA/H/C/002397

Kiadis Pharma Netherlands B.V.; indicated as an adjunctive treatment to a haploidentical, T-cell depleted haematopoietic stem cell transplantation (HSCT) in adult patients with high-risk haematological malignancies in complete remission.

Scope: feedback from the ad-hoc expert group meeting that took place on 3 September 2019.

Action: for information

The CAT chair (who co-chaired the ad-hoc expert group meeting) provided feedback from the ad-hoc expert group meeting.

CAT noted the feedback and the report of the ad-hoc expert group meeting. The Rapporteurs will take the feedback from the experts into consideration when finalising their assessment report in the next assessment round.

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

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

Scope: feedback from the scientific advisory group (SAG-Neurology) meeting that took place on 6 September 2019.

Action: for information

The chairperson of the SAG Neurology (Serge Bakchine) presented the responses from the SAG member and invited experts to the questions raised by CAT .

CAT noted the feedback and the report of the SAG meeting. The Rapporteurs will take the feedback from the SAG into consideration when finalising their assessment report.

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

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

Scope: letter from the applicant dated 23 August 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in June 2019

Action: for adoption

List of outstanding issues adopted on 21.06.2019. List of Questions adopted on 22.02.2019.

CAT discussed the company's justification for an extension of the timing to respond to the list of outstanding issues. The clock stop extension was agreed.

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

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

Scope: SmPC

Action: for discussion

The matter will be brought back to a next CAT meeting for discussion.

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

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

Scope: quality

Action: for information

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

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

Scope: quality

Action: for discussion

2.7. New applications

2.8. Withdrawal of initial marking 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. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0034

Amgen Europe B.V.

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

Scope: safety: to update the RMP for Imlygic to version 7.0 in order to add 2 category 3 studies (Studies 20180062 and 20180099), as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimization measures (aRMM). Opinion

Action: for adoption

Request for Supplementary Information adopted on 19.07.2019.

The opinion was adopted.

2.11.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0011

Novartis Europharm Limited

Rapporteur: Rune Kjeken; CHMP Coordinator: Bjorg Bolstad

Scope: quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.3. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0005/G

CO.DON AG

Rapporteur: Lisbeth Barkholt; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: safety: update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13[1] and the final study report with 60-month follow-up data for trial cod 16 HS 14[2]. Opinion

Action: for adoption

Request for Supplementary Information adopted on 21.06.2019, 24.05.2019.

The CAT Rapporteur informed the CAT of the responses to the RSI. The changes to the product information are acceptable. The opinion was adopted.

2.11.4. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0008

CO.DON AG

Rapporteur: Lisbeth Barkholt

Scope: quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 21.06.2019.

The opinion was adopted.

2.11.5. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0008

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 21.06.2019.

The opinion was adopted.

2.11.6. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0011

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality. RSI

Action: for adoption

The RSI was adopted.

[1] Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size between 1 and 4 cm2.
[2] Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 cm2) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee.

2.11.7. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0012

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.8. Zynteglo - autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - Orphan - EMEA/H/C/003691/II/0001/G

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts

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; CHMP Coordinator: Bjorg Bolstad

Scope: feedback

Action: for discussion

CAT endorsed the proposal from the Rapporteur .

2.12.2. Kymriah – tisagenleuleucel – Orphan – EMEA/H/C/004090/X/010

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: quality. List of questions

Action: for adoption

A list of question was presented and adopted.

2.12.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/003.1

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: MAH Response to ANX-003 [Statistical Analysis Plan from CTL019B2401] as adopted in February 2019: in order to further characterise the safety - including long-term safety - of Kymriah, the applicant should conduct and submit a study based on data from disease registry CCTL019B2401 in ALL and DLBCL patients.

Action: for adoption

The Rapporteur presented the response from the MAH . CAT agreed with the position from the Rapporteur.

The post-authorisation measure is considered fulfilled.

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

CAT: Martina Schüßler-Lenz

Scope: CAR-T cell-imposed PASS studies: issues with implementation and current status; feedback from PRAC discussion.

Action: for discussion

The CAT chair provided feedback from the discussions at the September PRAC meeting on the imposed PASS for Kymriah and Yescarta.

CAT acknowledged the approach agreed at the level of PRAC.

2.12.5. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/REC/004

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Scope: quality .

Action: for adoption

The RSI was adopted.

2.12.6. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480

CAT: Martina Schüßler-Lenz

Scope: CAR-T cell-imposed PASS studies: issues with implementation and current status; feedback from PRAC discussion.

Action: for discussion

See 2.12.4

2.12.7. Zynteglo - autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - Orphan - EMEA/H/C/003691/REC/006

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik

Scope: quality

Action: for adoption

The RSI was adopted.

3. Certification of ATMPs

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

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

4. Scientific Recommendation on Classification of ATMPs

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

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Recombinant adeno-associated virus (AAV) vector based on the AAV serotype hu37 (AAVhu37) expressing human Factor VIII - H0005490

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. Adipose-derived mesenchymal stem cells - H0005458

Intended for the treatment of diabetic foot ulcers (DFU)

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 27 September 2019.

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. Human allogeneic melanoma cells Mich1H6 and Mich2H6 - H0005459

Intended for the treatment of advanced melanoma (stage IIB-IV)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 27 September 2019.

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. CD1c(BDCA-1)+/CD141(BDCA-3)+ myeloid dendritic cells - H0005460

Intended for the treatment of patients with advanced, pre-treated solid tumours with injectable metastases

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 27 September 2019.

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. Human autologous Adipose Tissue - derived Mesenchymal Stem / Stromal Cells (AT-MSCs) – H0005461

Intended for the treatment of bone and cartilage defects including osteoarthritis

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 27 September 2019.

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. Oncolytic adenovirus – H0005463

Intended for the treatment-naïve patients with localized prostate cancer

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 27 September 2019.

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. Platelet-Rich Stroma (PRS) - combination of platelet-rich plasma and stromal vascular fraction – H0005430

Intended for wound healing as additional therapy to fistula surgery in patients with complex and therapy refractory perianal fistula

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 27 September 2019.

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. *In vitro* transcribed mRNA encoding the human insulin-like growth factor 1 (IGF-1) – H0005462

Intended for the treatment of skeletal muscle injury

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 27 September 2019.

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)

4.4. Finalisation of procedure

4.4.1. Autologous, *ex vivo* expanded, clonal neoantigen specific tumour infiltrating lymphocytes – H0005417

Intended for the treatment of solid tumours

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

Action: for information

The information was noted

4.4.2. Autologous CD34+ cells transduced with lentiviral vector encoding human γ-globinG16D and short-hairpin RNA734 – H0005415

Intended for the treatment of moderate to severe Sickle Cell disease

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

Action: for information

The information was noted

4.4.3. Uncapped, non-coding ribonucleic acid – H0005400/0001

Intended for the treatment of adenoid cystic carcinoma, squamous cell carcinoma of the head and neck, melanoma and squamous cell carcinoma of the skin

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

Action: for information

The information was noted

4.4.4. Autologous tumour-infiltrating lymphocytes (TIL) – H0005414

Intended for the treatment of solid tumours

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

Action: for information

The information was noted

4.4.5. CD34+ haematopoietic stem/progenitor cells enriched with normal mitochondria derived from white blood cells from a related donor - H0005416

Intended for the treatment of non-inherited mtDNA deletion syndromes

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

Action: for information

The information was noted

4.4.6. Purified recombinant adeno-associated viral vector serotype 2 (AAV2) encoding the complementary DNA (cDNA) of human Rab escort protein type 1 (REP1) – H0005418

Intended for the treatment of choroideremia (CHM)

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

Action: for information

The information was noted

4.5. Follow-up and guidance

None

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

5.2. 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

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

No items

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

EMA: resignation on 02.09.19 of clinicians' representative Birgitte Klindt Poulsen – University Hospital of Aarhus and Aalborg (Denmark)

Action: for information

Note: the European Commission have been informed and they will refer to the reserve list to find a replacement

The information was noted.

7.1.2. Strategic Review & Learning meeting – Helsinki, Finland, 21 – 22 November 2019

CAT: Heli Suila

Scope: draft agenda

Action: for discussion

CAT made proposals for the agenda of the joint CAT-PDCO-COMP session and the joint CAT-COMP session. These proposals now will be discussed with COMP and PDCO. Agenda items for the CAT only session will be discussed at the October CAT meeting.

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 July 2019 meeting

Action: for information

The information was noted.

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

7.3.1. Patients and Consumers Working Party (PCWP) - Nomination of CAT representative(s)

Scope: nomination of a CAT representative(s) to the PCWP for a three-year mandate. Nominations received

Action: for nomination of a CAT member(s)

CAT nominated Kieran Breen as member and Roland Pochet as alternate member representing CAT in the PCWP.

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

Scope:

-HCPWP/PCWP workplan for 2019-2020

Action: for adoption

Scope:
-Agenda PCWP, HCPWP and Joint PCWP HCPWP meeting to take place on 25 September 2019

Action: for information

The HCPWP/PCWP workplan was adopted. The agenda of the meeting taking place on 25 September 2019 were noted.

7.3.3. Guideline on requirements for investigational ATMPs

Drafting group: Ilona Reischl (Rapporteur), Tiina Palomäki (Rapporteur), Martina Schüßler-Lenz, Simona Badoi, Violaine Closson-Carella, Paolo Gasparini, Carla Herberts, Metoda Lipnik-Stangelj, Margarida Menezes Ferreira, Maura O'Donovan, Olli Tenhunen, Heli Suila, Barbara Bonamassa, Giuseppa Pistritto, Marcel Hoefnagel

Scope: overview of comments

Action: for discussion

The overview of comments was presented and the next steps were agreed: the drafting groups will review all comments received and discuss them in virtual drafting group meetings. If needed, a face-to-face drafting group meeting will be organised to finalise the revision.

CAT members interested to join the drafting groups should inform the CAT Secretariat.

Post-meeting note: Ivana Haunerova will join the quality drafting group.

7.4. Cooperation within the EU regulatory network

7.4.1. Biosimilar ATMPs

CAT: Martina Schüßler-Lenz

Scope: CAT contribution to presentation on biosimilars at the upcoming CHMP SRLM

Action: for discussion

CAT discussed the question on biosimilar ATMPs.

7.4.2. European Ombudsman enquiry on EMA's pre-submission activities

Scope: proposal for implementation

Action: for information

Note: on 19/07/19 the European Ombudsman (EO) released the conclusions on their independent enquiry into how the EMA engages with medicine developers in the period leading up to applications for authorisations to market new medicines in the EU. The EO proposes 5 recommendations for improvement, and first actions have already been taken (see report and EMA responses below).

- Decision from the Ombudsman: https://www.ombudsman.europa.eu/en/decision/en/116683
- EMA press release: https://www.ema.europa.eu/en/news/ema-takes-note-european-ombudsmans-decision-pre-submission-activities
- Communication brochure: https://www.ema.europa.eu/en/documents/other/laboratory-patient-journey-centrally-authorised-medicine_en.pdf

EMA highlighted the recommendations for improvement and the impact on the appointment of Rapporteurs for new MAAs.

7.4.3. Interplay with GMO framework: new initiatives

Scope: environmental risk assessment of GTMPs in clinical trials

Action: for discussion

The European Commission representative presented the initiatives to optimise the interplay between the GMO and the pharmaceutical framework. The existing initiatives[3] (Q&A on medicinal product for human use containing or consisting of GMOs; Good practice on the assessment of genetically modified cells by means of retro/lentiviral vectors) and the new initiatives were highlighted.

Even though clinical trials are outside of the remit of the CAT (National authorities are responsible for the approval of clinical trials), the CAT members welcomed this detailed briefing. These initiatives will facilitate the conduct of clinical trials with GTMPs in the EU.

7.5. Cooperation with international regulators

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

The teleconference will take place

CAT: Martina Schüßler-Lenz

Scope: draft agenda

Action: for discussion

During the ATMP cluster, following agenda items were discussed.

7.6. CAT work plan

None

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q3/2019 update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

7.8. Others

7.8.1. Scientific opinions on the definitions of pharmacological, immunological, metabolic and medical diagnosis

Scope: reply from the EC Borderline and Classification group in response to the Article 57 opinions adopted by the CHMP and CAT in February 2019 on the definitions of Pharmacological, Immunological, Metabolic and Medical diagnosis

Action: for information

EMA presented the feedback from the EC Borderline and Classification group. If CAT members have any comment, please inform EMA.

[3] See: GMO requirements for investigational products https://ec.europa.eu/health/human-use/advanced-therapies_en

7.8.2. Curriculum on Advanced Therapies Medicinal Products (ATMPs) training

CAT: Ilona Reischl

Scope: priorities for ATMP training and timing

Action: for discussion

CAT agreed to restart the trainings of CAT members and NCA experts. These training will be organised in the margins of the CAT (Wednesday from 13.00-14.00) and will be broadcast to the NCAs .
A concrete plan of trainings for the end of 2019 and beginning of 2020 will be brought to the October CAT meeting for further discussion.

7.8.3. Harmonisation of communication subject naming convention received from NCAs

Scope:

Action: for information

A general presentation was given. This will be brought back to the October CAT meeting with more concrete (ATMP specific) examples.

8. Any other business

No items

Date of next CAT meeting:

09 – 11 October 2019

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

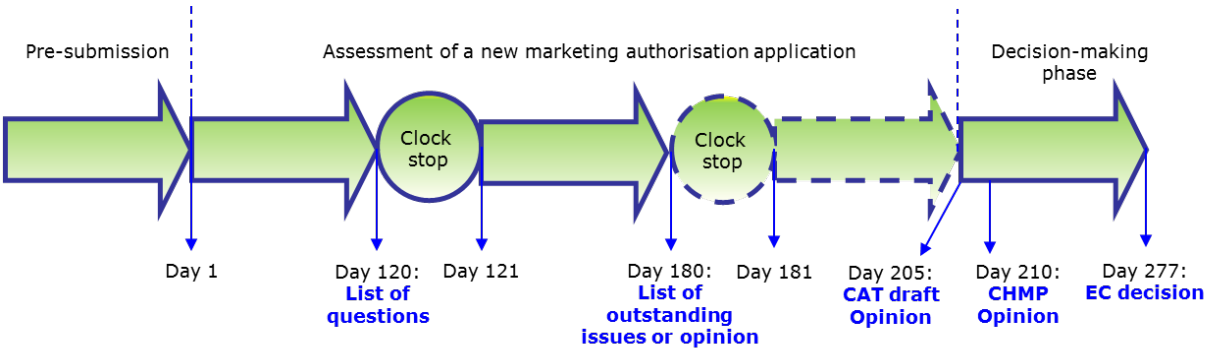
Evalua tion of ATMPs (section 2)

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 11-13 September 2019 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	
Belaïd Sekkali	Alternate	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Mirna Golemovic	Member	Croatia	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	
Nathalie Morgensztejn	Alternate	France	No interests declared	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Asterios Tsiftsoglou	Member	Greece	No interests declared	
Katalin Lengyel	Member	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Giulio Pompilio	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No interests declared	
John J. Borg	Member (CHMP member)		No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Johannes Hendrikus Ovelgonne	Alternate	Netherlands	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Margarida Menezes-Ferreira	Alternate (to CHMP representative)	Portugal	No interests declared	
Simona Badoi	Member	Romania	No interests declared	
Lukas Slovak	Member	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	
Björn Carlsson	Alternate	Sweden	No interests declared	
John Johnston	Member	United Kingdom	No interests declared	
Bernd Gänsbacher	Member	Healthcare Professionals' Representative	No interests declared	
Alessandro Aiuti	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Lydie Meheus	Alternate	Patients' Representative	No interests declared	
Kieran Breen	Member	Patients' Representative	No restrictions applicable to this meeting	
Roland Pochet	Alternate	Patients' Representative	No interests declared	
Catherine Milne	Observer/Alternate	European Directorate for the Quality of Medicine & HealthCare(EDQM)	No interests declared	
Barbara Bonamassa	Expert - in person*		No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Monique Wakelkamp	Expert - in person*	MPA-SE	No restrictions applicable to this meeting	
Marja van de Bovenkamp	Expert - in person*	CBG-MEB-NL	No interests declared	
Andreea Barbu	Expert - via telephone*		No restrictions applicable to this meeting	
Maren Hammann	Expert - via telephone*	PEI-DE		
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.