17 July 2019
EMA/CAT/408363/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 17-19 July 2019

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

17 July 2019, 14:00 – 18:30, room 0-C

18 July 2019, 09:00 – 18:30, room 0-C

19 July 2019, 09:00 – 12:00, room 0-C

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 this agenda 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, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the agenda 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

Pre-meeting list of participants and restrictions in relation to declarations of interests, applicable to the items of the agenda for the CAT plenary session to be held 17-19 July 2019. See July 2019 CAT minutes (to be published post-September 2019 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 17-19 July 2019 meeting

1.3. Adoption of the minutes

CAT minutes for 19-21 June 2019 meeting

1.4. Technical information

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.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: ad-hoc expert group meeting to take place on 3 September 2019. Update on the draft list of experts.

Action: for information

List of Outstanding Issues adopted on 21.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

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

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

Scope: scientific advisory group (SAG-Neurology) meeting to take place on 6 September 2019. Update on the draft list of experts

Action: for adoption

List of Outstanding Issues adopted on 21.06.2019. List of Questions adopted on 22.02.2019.

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). Request for Supplementary Information (RSI)

Action: for adoption

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

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Request for Supplementary Information (RSI)

Action: for adoption

2.11.3. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0007

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 24.05.2019.

2.11.4. Zalmoxis - nalotimagene carmaleucel - Orphan - EMEA/H/C/002801/II/0016

MolMed S.p.A

Rapporteur: Carla Herberts; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: proposal to terminate the study TK008 (specific obligation for the Conditional MA) and replace it with study TK013: request by the MAH for an extension of the clock stop to respond to the RSI

Action: for adoption

Request for Supplementary Information adopted on 24.05.2019.

2.11.5. Zalmoxis - nalotimagene carmaleucel - Orphan - EMEA/H/C/002801/R/0015

MolMed S.p.A

Rapporteur: Carla Herberts; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: update on annual renewal

Action: for discussion

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: Quality

Action: for discussion

2.12.2. Luxturna – voretigene neparvovec – Orphan - EMEA/H/C/004451

Novartis Europharm Ltd.

Rapporteur: Sol Ruiz, Co-Rapporteur: Jan Mueller-Berghaus

Scope: query on the scope of a future variation application

Action: for discussion

2.12.3. Chimeric antigen receptor T-cell (CAR-T cell) products

CAT: Martina Schüßler-Lenz

Scope: feedback

Action: for information

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

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. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

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

Intended for the treatment of solid tumours

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. 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: ATMP scientific recommendation

Action: for adoption

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

Intended for the treatment of solid tumours

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. 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: ATMP scientific recommendation

Action: for adoption

4.2.5. 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: ATMP scientific recommendation

Action: for adoption

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

4.3.1. 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: assessment of the responses from the applicant. Revised ATMP scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Modified Vaccinia Ankara-Bavarian Nordic- Brachyury (MVA-BN-Brachyury) and recombinant fowlpox virus (FPV-Brachyury) encoding the human brachyury gene and three human costimulatory molecules known as TRICOM (triad of costimulatory molecules): B7.1, intercellular adhesion molecule-1 (ICAM-1), and leukocyte function-associated antigen-3 (LFA-3) – H0005394/0001

Scope: editorial comments from European Commission. Final ATMP scientific recommendation

Action: for information

4.4.2. Autologous $CD34^+$ cells – H0005399/0001

No-option critical limb ischemia

Scope: editorial comments from European Commission. Final ATMP scientific recommendation

Action: for information

4.4.3. Messenger ribonucleic acid (mRNA) coding for coiled-coil domain-containing protein 40 (CCDC40) protein – H0005395/0001

Intended for the treatment of primary ciliary dyskinesia (PCD) caused by biallelic mutation in the CCDC40 gene

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

Action: for information

4.4.4. Autologous peripheral blood T cells CD4 and CD8 selected, and CD3 and CD28 activated transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - H0005396/0001

Intended for the treatment of various types of cancer

Scope: editorial comments from European Commission. Final ATMP scientific recommendation

Action: for information

4.5. Follow-up and guidance

4.5.1. Allogeneic human enucleated red cell therapy expressing Anabaena variabilis (Av) phenylalanine ammonia lyase (AvPAL) – H0005355

Intended for the treatment of phenylketonuria (PKU)

Scope: request for clarification

Action: for discussion

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

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

6.3.2. Month 1 – Discussion of eligibility

No items

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

United Kingdom: John Johnston – becomes member (swap of roles) from 03 July 2019

United Kingdom: Louise Bisset – new alternate. Membership mandate from 03 July 2019
United Kingdom: Christiane Niederlaender – membership ended on 30 June 2019

Action: for information

7.1.2. Strategic Review & Learning meeting – joint CAT/Clinical trial facilitation group (CTFG), Bucharest, Romania, 13-14 June 2019

CAT: Simona Badoi

Scope: feedback from the SRLM meeting

Action: for discussion

NB: a half day of this SRLM was held jointly with the CTFG.

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 June 2019 meeting

Action: for information

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

No items

7.4. Cooperation within the EU regulatory network

7.4.1. Questions and Answers on the exemption from EU batch release testing for imported ATMPs

Scope: Questions and answers document

Action: for discussion

7.4.2. Environmental risk assessment of medicinal products containing /consisting of genetically modified organisms through the centralised procedure

Scope: Revised procedure for consultation

Action: for discussion

Note: the revised consultation procedure of GMO competent authorities was developed during the drafting groups on 4, 8 and 12 July. Following CAT members were involved: Margarida Menezes Ferreira, Carla Herberts, Rune Kjeken, Violaine Closson Carella, Jan Mueller-Berghaus

7.4.3. Handling of competing interests within the EU network

Scope: training session on handling of competing interests held by delegates

Action: for information

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

7.6. CAT work plan

None

7.7. Planning and reporting

None

7.8. Others

7.8.1. CAT regulatory session at the 2019 Annual Congress of the European Society of Gene and Cell Therapy (ESGCT), 25 October 2019, Barcelona (Spain)

CAT: Martina Schüssler-Lenz

Scope: proposal for the contents of the CAT session

Action: for discussion

Link to the ESCGT annual congress: https://www.esgct.eu/Congress/Barcelona-2019.aspx

8. Any other business

8.1. EMA's move to the permanent building

Scope: update

Action: For information

Date of next CAT meeting:

11-13/09/2019

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

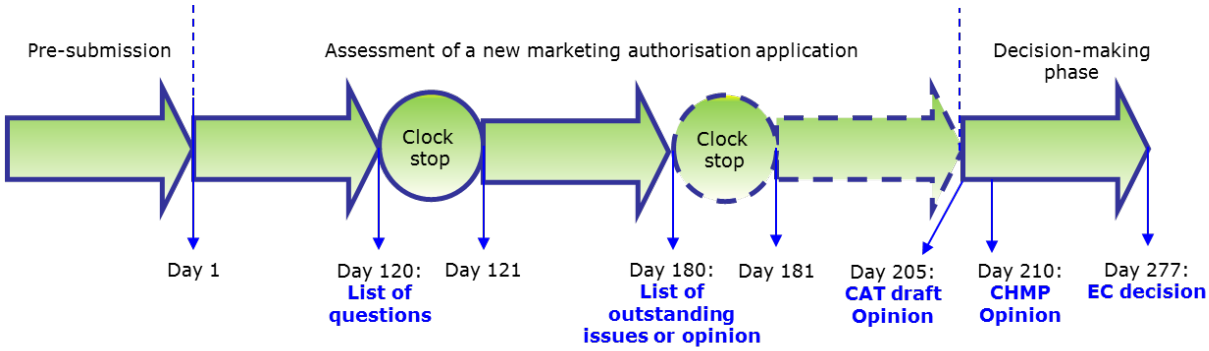
Evaluation of ATMPs (section 2)

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/