19 June 2019
EMA/CAT/ 350204/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 19-21 June 2019

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

19 June 2019, 14:00 – 18:30, room 0-H

20 June 2019, 09:00 – 18:30, room 0-H

21 June 2019, 09:00 – 12:00, room 0-H

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 19-21 June 2019. See June 2019 CAT minutes (to be published post July 2019 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 19-21 June 2019 meeting

1.3. Adoption of the minutes

CAT minutes for 22-24 May 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

2.3.1. 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: List of Outstanding Issues (LoOIs)

Action: for adoption

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

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

Accelerated assessment

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

Scope: List of Outstanding Issues (LoOIs)

Action: for adoption

List of Questions adopted on 22.02.2019.

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

No items

2.7. New applications

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

CO.DON AG

Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

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 24.05.2019.

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

CO.DON AG

Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

Scope: quality Request for supplementary information (RSI).

Action: for adoption

[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 cm^2

[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 cm^2) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee.

2.11.3. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0006

Kite Pharma EU B.V.

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

Scope: quality Opinion

Action: for adoption

Request for Supplementary Information adopted on 17.04.2019.

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

Kite Pharma EU B.V.

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

Scope: quality Request for supplementary information (RSI).

Action: for adoption

2.12. Other Post-Authorisation Activities

2.12.1. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854/ANX/004.1

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruiz; PRAC Rapporteur: Menno van der Elst

Scope: clinical and PhV. From initial MAA: non-interventional PASS: In order to investigate the long term safety and efficacy of Strimvelis gene therapy, the MAH should conduct and submit the results of a long term prospective, non-interventional follow up study using data from a registry of patients with adenosine deaminase severe combined immunodeficiency (ADA-SCID) treated with Strimvelis. The MAH will follow up on the risk of immunogenicity, insertional mutagenesis and oncogenesis as well as hepatic toxicity. The MAH will review the occurrence of angioedema, anaphylactic reactions, systemic allergic events and severe cutaneous adverse reactions during the FU period, particularly in those patients who had unsuccessful response and received ERT or SCT. The MAH will also evaluate intervention-free survival.
Due date: The MAH shall plan to include regular progress reports of the registry in the PSUR and provide interim study reports every 2 years until the registry finishes. Interim registry reports to be submitted every 2 years. Final CSR - to be submitted after the 50th patient has 15 year follow-up visit; Q4 2037.

Action: for adoption

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

MolMed S.p.A

Rapporteur: Carla Herberts, Co-Rapporteur: Sol Ruiz, CHMP Coordinator: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 1 year renewal of Marketing Authorisation

Action: for adoption

Request for Supplementary Information adopted on 24.05.2019.

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 CAT Coordinator

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

Intended for the treatment of solid tumours

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. 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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

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

Intended for the treatment of solid tumours

Scope: appointment of CAT Coordinator and adoption of timetableAction: for adoption

4.1.4. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. 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

Intended for the treatment of chordoma

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Autologous $CD34^+$ cells – H0005399

Intended for the treatment of no-option critical limb ischemia

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Uncapped, non-coding ribonucleic acid – H0005400

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: ATMP scientific recommendation

Action: for adoption

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

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

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. 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 – H0005396

Intended for the treatment of various types of cancer

Scope: ATMP scientific recommendation

Action: for adoption

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

No items

4.4. Finalisation of procedure

4.4.1. Human embryonic stem cell-derived Müller cells – H0005356

Intended for the treatment of primary open angle glaucoma

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

Action: for information

4.4.2. Allogeneic neonatal human cardiac progenitor cells – H0005357

Intended for the treatment of cardiac failure

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

Action: for information

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

Intended for the treatment of phenylketonuria (PKU)

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

Action: for information

4.5. Follow-up and guidance

No items

5. Scientific Advice

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

5.1. New requests – appointment of CAT Rapporteurs

5.2. 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

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

Cyprus: Rafaella Pontou – new member. New membership mandate from 16 May 2019

Cyprus: Isavella Kyriakidou – new alternate. New membership mandate from 16 May 2019

Cyprus: Marina Ieridi – membership ended on 15 May 2019

Cyprus: Maria Vassiliou - membership ended on 15 May 2019

France: Nathalie Morgensztejn – new alternate. New membership started on 03 June 2019

Action: for information

7.1.2. Appointed members and alternates to represent clinicians and patients' associations to Committee for Advanced Therapies (CAT), July 2019 to June 2022

Scope: Commission decision dated 28 May 2019 (ref. C(2019) 3919) on the new appointment of civil societies to CAT for a mandate of three years, from 1 July 2019 to 30 June 2022

Patients' associations:
-Member: Kerstin Sollerbrant affiliated to the Swedish Childhood Cancer Fund;
-Alternate: Lydie Meheus affiliated to The Anticancer Fund.

-Member: Kieran Breen affiliated to the European Parkinson's Disease Association;
-Alternate: Roland Pochet affiliated to the Belgian Brain Council.

Clinicians:
-Member: Bernd Gänsbacher from the European Society of Gene and Cell Therapy (ESGCT);
-Alternate: Birgitte Klindt Poulsen from University Hospital of Aarhus and Aalborg.

-Member: Alessandro Aiuti from Vita Salute Raffaele University;
-Alternate: Alessandra Renieri from University of Siena.

Action: for information

Note: the CAT Secretariat will organise an induction meeting for the new cohort of civil societies.

7.1.3. 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

Note: 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 May 2019 meeting

Action: for information

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

7.3.1. Meeting report from workshop with stakeholders on support to quality development in early access approaches (i.e. PRIME, breakthrough therapies), 26 November 2018

CAT experts: Matthias Renner, Marcel Hoefnagel

Scope: presentation on the draft revised workshop report following industry comments. Compiled industry comments and responses

Action: for discussion

7.4. Cooperation within the EU regulatory network

7.4.1. Environmental risk assessments of medicinal products containing/consisting of genetically modified organisms (GMOs) through the centralised procedure

Scope: presentation of the procedure

Action: for information

7.4.2. European Commission's pharmaceutical committee on hospital exemption: upcoming discussions

Scope: Update on upcoming discussions in the pharmaceutical commmittee

Action: for information

7.4.3. Principles for good manufacturing practice/viral vectors for genetically modified cells/advance therapy medicinal products

Scope: presentation of the outcome of the survey for viral vector inspections

Action: for information

7.5. Cooperation with international regulators

None

7.6. CAT work plan

None

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q2/2019 update of the business pipeline report for the human scientific committees

Action: for information

7.8. Others

7.8.1. Global consultation on the review and update of the Changsha Communique on Xenotranplantation, 12 – 14 December 2018, Changsha, China

CAT: Ralf Tönjes, PEI-DE

Scope: feedback from the meeting

Action: for information

8. Any other business

No items

Date of next CAT meeting:

17-19 July 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

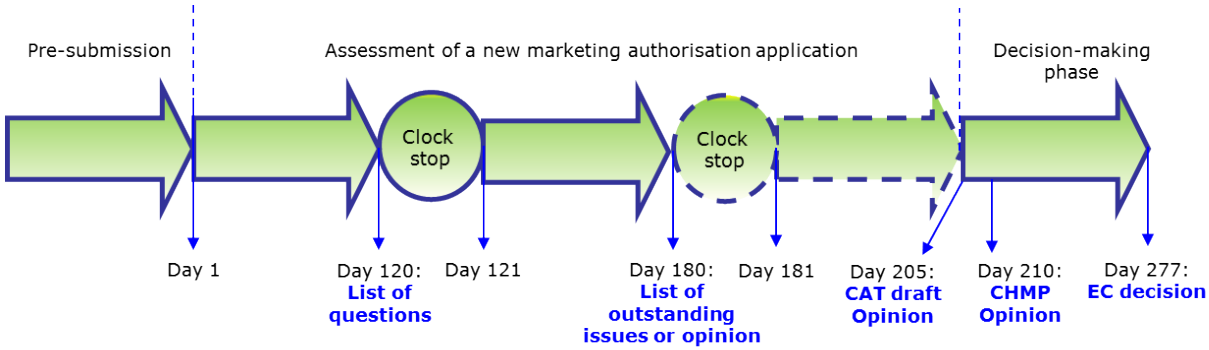
Evaluation of ATMPs (section 2)

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/