14 March 2018
EMA/CAT/168481/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 14-16 March 2018

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

14 March 2018, 14:00 – 18:00, room 03-E

15 March 2018, 09:00 – 18:30, room 03-E

16 March 2018, 09:00 – 13:00, room 03-E

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 15-16 March 2018. See March 2018 CAT minutes (to be published post-April 2018 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 14-16 March 2018 meeting

1.3. Adoption of the minutes

CAT minutes for 14-16 February 2018 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

2.4.1. Tisagenlecleucel - Orphan - EMEA/H/C/004090

Novartis Europharm Limited; treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL)

Scope: Day 120 list of questions

Action: for adoption

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

2.6.1. Axicabtagene ciloleucel - Orphan - EMEA/H/C/004480

Kite Pharma EU B.V.; treatment of B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

Action: for discussion and adoption of the updated timetable

2.7. New applications

No items

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

No items

2.12. Other Post-Authorisation Activities

2.12.1. MACI - matrix applied characterised autologous cultured chondrocytes - EMEA/H/C/002522/R/0017

Vericel Denmark ApS

Rapporteur: Christiane Niederlaender, Co-Rapporteur: Hans Ovelgönne, CHMP, PRAC Rapporteur: Julie Williams

Scope: withdrawal of the 5 year Renewal of Marketing Authorisation

Action: for information

Request for Supplementary Information adopted on 19.01.2018.

2.12.2. Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - Orphan - EMEA/H/C/002801/IB/008

MolMed SpA

Rapporteur: Hans Ovelgönne, CHMP Coordinator: Paula Boudewina Van Hennik

Scope: Type IB: to extend the due date for the Specific Obligation (SOB) to the Conditional Marketing Authorisation (CMA) in the Annex II and RMP from Q1 2021 to Q1 2023.

Action: for discussion

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

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. Allogeneic foetal neural stem cells (ALS) – H0005022

Intended for the treatment of *Amyotrophic Lateral Sclerosis*

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Allogeneic foetal neural stem cells (SCI) – H0005023

Intended for the treatment of spinal cord injury (SCI)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Fat graft - H00005024

Intended for lipofilling of anal fistula

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Pegylated exosomes carrying recombinant Cystic fibrosis transmembrane conductance regulator (CFTR) mRNA and microRNA-17 – H0005021

Intended for the treatment of cystic fibrosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Allogeneic umbilical cord derived mesenchymal stem cells – H0004999

Intended for the treatment of multiple sclerosis

Scope: scientific recommendation

Action: for adoption

4.2.2. Autologous bone marrow derived mesenchymal stem cells - H0004998

Intended for the treatment of multiple sclerosis

Scope: scientific recommendation

Action: for adoption

4.2.3. Allogeneic human neural stem cells - H0004995

Intended for the treatment of traumatic brain injuries (e.g. coma, minimally conscious state, persistent vegetative state) & stroke

Scope: scientific recommendation

Action: for adoption

4.2.4. Autologous bone marrow derived mesenchymal stem cells - H0004997

Intended for the treatment of articular cartilage damage and tendon injuries

Scope: scientific recommendation

Action: for adoption

4.2.5. *Ex vivo* fused autologous human bone marrow-derived mesenchymal stem cell with allogenic human myoblast - H0004994

Intended for the treatment of Duchenne muscular dystrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

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

4.3.1. Elastin recombinamer (ELR)-encapsulated allogeneic pancreatic islets - H0004980

Intended for treatment of severe forms of type 1 diabetes

Scope: scientific recommendation

Action: for adoption

4.3.2. Autologous CD31+ Cells - H0004981

Intended as adjunct therapy during primary care of proximal humeral fracture to decrease incidence of non-union and secondary displacement

Scope: scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Expanded autologous auricular chondrocytes - H0004979

Intended for the surgical implantation for the repair of microtia

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

Action: for information

5. Scientific Advice

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

5.1. New requests – appointment of CAT Rapporteurs

Timetable:
-Final Briefing Package: 04.04.2018
-Start of the procedure at SAWP: 12.04.2018
-CAT report due by: 13.04.2018
-CAT recommendation: 20.04.2018

5.2. CAT reports

5.3. List of Issues

5.4. Finalisation of SA procedures

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

No items

6.3.2. Month 1 – Discussion of eligibility

No items

6.3.3. Month 2 – Recommendation of eligibility

6.3.4. Month 3 – Nomination of Rapporteurs

No items

6.3.5. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Hungary: Katina Lengyel – nominated as the new member from 27 February 2018

Hungary: Kristian Fodor – membership ended on 17 February 2018

Luxembourg: Guy Berchem - nominated as the new member from 5 March 2018

Action: for information

7.1.2. Strategic Review & Learning meeting – Joint CHMP/PDCO/CAT, Oslo, Norway, 07-09 May 2018

CAT resources: Helga Olsen, Rune Kjeken

Scope: draft agenda

Action: for discussion

Note: Strategic Review & Learning meeting will be partnered with CAT/CHMP/PDCO.

7.1.3. Timing of scientific committees' chair elections

Scope: new practice in the timing of elections for scientific committees' chairs and vice-chairs

Action: for information

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 February 2018 meeting

Action: for information

7.2.2. Scientific Coordination Board (SciCoBo) – meeting on 12 March 2018

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting to take place on 12 March 2018

Action: for information

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

7.3.1. Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells

CAT Rapporteur: Marcos Timón

Scope: draft guideline

Action: for adoption

Note: the draft guideline was presented to the BWP and the CAT in February 2018 for a one-month reflection.

7.3.2. Guideline on quality of water for pharmaceutical use

Rapporteur/Coordinator: Eugenia Cogliandro (QWP)

Action: for information

Note: this guideline is currently being revised by QWP (with input from BWP and inspectors). It is planned to be adopted by QWP/CHMP/CVMP and released for public consultation in June 2018. The background to the revision is outlined in this Concept paper (EMA/CHMP/CVMP/QWP/BWP/428135/2016).

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

Scope:
-Draft PCWP and HCPWP joint meeting agenda – 17-18 April 2018
-Draft PCWP/HCPWP work plan for 2018-2019

Action: for information

7.4. Cooperation within the EU regulatory network

None

7.5. Cooperation with international regulators

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

CAT: Martina Schüßler-Lenz

Scope: draft agenda

Action: for discussion

7.6. CAT work plan

7.6.1. Expert meeting on adeno-associated viral vectors

CAT: Martina Schüßler-Lenz

Scope: report for publication

Action: for adoption

Note: comments from the experts have been incorporated.

7.7. Planning and reporting

None

7.8. Others

7.8.1. CAT regulatory session at the Annual Congress of the European Society of Gene and Cell Therapy (ESGCT)

Scope: feedback on a proposal for a CAT session at the ESGCT 2018 Congress (16-19 October 2018 in Lausanne, Switzerland)

Action: for information

8. Any other business

No items

Date of next CAT meeting:

18-20 April 2018

9. Explanatory notes

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

Abbreviations / Acronyms

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

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

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 Applicant

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

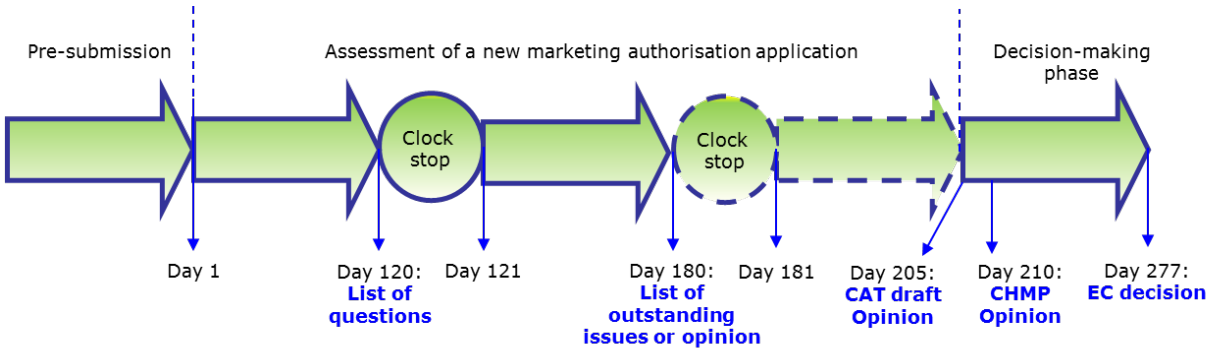
Evaluation of ATMPs (section 2)

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/