14 July 2017
EMA/CAT/451773/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 12-14 July 2017

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

12 July 2017, 14:00 – 18:30, room 02-A

13 July 2017, 09:00 – 18:30, room 02-A

14 July 2017, 09:00 – 12:00, room 02-A

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 13-14 July 2017. See July 2017 CAT minutes (to be published post September 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 12-14 July 2017 meeting

1.3. Adoption of the minutes

CAT minutes for 15-16 June 2017 meeting

1.4. Technical information

1.4.1. Templates for MAA and Certification

URL address in the EMA website:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000337.jsp&mid=WC0b01ac0580022719

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

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. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human adenosine deaminase cDNA sequence - Orphan - EMEA/H/C/003854/II/0006

GlaxoSmithKline Trading Services

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Robert J. Hemmings; PRAC Rapporteur: Sabine Straus

Scope: Quality. section 4.3 and 4.4 of the SmPC are updated. RMP version 1.6 is submitted. The MAH took the opportunity to introduce editorial changes in Annex II and IIIB of the PI. Opinion (including the PRAC's risk management plan assessment overview and advice)**Action:** for adoption

2.12. Other Post-Authorisation Activities

2.12.1. Zalmoxis – Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔIngfr) and the herpes simplex I virus thymidine kinase (hsv-tk mut2) – Orphan - EMEA/H/C/PSP/S/0055

MolMed SpA; indicated for the treatment of adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies

Rapporteur: Hans Ovelgönne; CHMP Coordinator: Paula Boudewina van Hennik; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: submission of a PASS protocol for study TK011: a prospective, non-interventional PASS on Zalmoxis prescribed in patients undergoing haploidentical hematopoietic stem cell transplantation for high-risk hematological malignancies. PRAC has endorsed the protocol

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

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. Allogeneic human glial-restricted precursors - H0004887/0001

Intended for the treatment of amyotrophic lateral sclerosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous adipose tissue-derived mesenchymal stem cells - H0004813/0001

Intended for the treatment of chronic wound

Scope: 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. Autologous uncultured cells of stromal vascular fraction - H0004838/0001

Intended for the relief of symptoms of osteoarthritis

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

Action: for information

4.4.2. Autologous keratinocyte suspension - H0004841/0001

Intended for the treatment of burns and chronic, severe wounds

Scope: minor comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.3. Autologous chondrocyte suspension - H0004840/0001

Intended for the repair of single symptomatic cartilage defect of the knee or ankle

Scope: minor comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.4. Human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs) - H0004839/0001

Intended for the treatment of atopic dermatitis

Scope: minor comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

See also 5.1.3.

4.5. Follow-up and guidance

4.5.1. Resorbable, viscoelastic matrix for use with autologous stromal vascular fraction (SVF) - H0004819/0001

A resorbable matrix to be used for the delivery of autologous SVF adipose derived cells for the treatment of HIV-related facial lipoatrophy

Scope: publication of the summary report

Action: for discussion

Note: CAT considered in May 2017 this product not to be an ATMP

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 Coordinators

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

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Scope: membership changes

Czech Republic: Ivana Haunerová becomes the member and Tomáš Boráň becomes the alternate from 16 June 2017
Estonia: Tarmo Tiido – member's membership ended on 08 June 2017
Finland: Paula Salmikangas – member's membership ended on 26 June 2017

Action: for information

7.1.2. Strategic Review & Learning meeting – Malta, June 2017

Scope: feedback from the meeting that took place in Gozo, Malta on 1-2 June 2017 under the auspices of the Maltese Presidency of the Council of the European Union

Action: for information

7.1.3. Training on best use of EMA's business software for delegates

Scope: training session on best use of technical tools

Action: for information

See also 7.1.4.

7.1.4. CAT's good practice guide

CAT: Martina Schüßler-Lenz, Ilona Reischl

Scope: follow-up on discussion in April 2017 on best practice guide: focus on science-based discussion

Action: for discussion

See also 7.1.3.

7.1.5. CAT August 2017 – Written procedure

Scope: timelines and topics

Action: for information

7.1.6. GMP requirements for ATMPs

Scope: final wording

Action: for information

Note: the version of the GMP for ATMPs was presented at CAT in June. The Guideline will be published by the European Commission

7.1.7. CAT Rapporteurs' D80 assessment report for MAAs: timelines

Scope: proposal and rationale to move Rapporteurs' ARs from D80 to D82

Action: for adoption

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 2017 meeting

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

Drafting group: Marcos Timón (Rapporteur), Ilona Reischl, Christiane Niederlaender, Belaïd Sekkali, Margarida Menezes Ferreira, Tiina Palomäki, Guido Pantè, Matthias Renner, Brigitte Anliker, Nicoloas Anagnou

Scope: concept paper for the revision of the guideline

Action: for adoption

7.3.2. Guideline on requirements for investigational ATMPs

Drafting group: Ilona Reischl (Rapporteur), Tiina Palomäki (Rapporteur), Simona Badoi, Tomáš Boráň, Violaine Closson-Carella, Paolo Gasparini, Carla Herberts, Metoda Lipnik-Stangelj, Margarida Menezes Ferreira, Christiane Niederlaender, Maura O'Donovan, Olli Tenhunen, Guido Pantè, Marcel Hoefnagel

Scope: progress on the development of the guideline

Action: for discussion

7.3.3. Guideline on quality, non-clinical and clinical aspects of gene therapy medicinal products

Drafting group members: Quality: Margarida Menezes-Ferreira, Christiane Niederlaender, Sol Ruiz; Non-clinical: Kieran Breen, Balazs Sarkadi, Matthias Renner, Tiina Palomäki; Clinical: Paolo Gasparini, Bettina Klug, Olli Tenhunen, Bernd Gänsbacher

Scope: presentation of pre-final version of the guideline

Action: for discussion

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

Scope: minutes of PCWP/HCPWP joint meeting that took place on 15 March 2017

Action: for information

7.3.5. QWP multidisciplinary guideline on manufacture of the finished dosage form.

Scope: final guideline

Action: for information

Note: the principle of the guideline also applies to ATMPs (see Scope of the guideline).

7.4. Cooperation within the EU regulatory network

None

7.5. Cooperation with international regulators

7.5.1. ICH Q12 guideline - Lifecycle management and ATMPs

CAT: Jean-Louis Robert, Nanna Aaby Kruse

Scope: update by the EU team on the outcome of the experts working group meeting in Montreal (Canada) with regards to the exclusion of ATMP from the scope of ICH Q12

Action: for information

7.6. CAT work plan

7.6.1. Expert meeting on adeno-associated viral vectors, 6 September 2017, EMA, London

CAT: Martina Schüßler-Lenz

Scope: agenda of the expert meeting to take place on 6 September 2017

Action: for adoption

Note: the CAT adopted the list of questions in July 2017, which had been updated following the focus group in the margins of the Strategic & Review meeting that took place in May - June 2017.

7.6.2. Expert meeting on Genome Editing, EMA, 18 October 2017

CAT: Paolo Gasparini

Scope: expert meeting organised jointly by CAT and CHMP Pharmacogenomics Working Party (PgWP): draft agenda and proposed experts

Action: for discussion

7.7. Planning and reporting

7.7.1. ATMP action plan

Scope: update on ongoing ATMP-related activities

Action: for discussion

Note: Following the EMA's ATMP workshop of May 2016, a report was discussed at the CAT in December 2016 – January 2017 on issues identified by stakeholders. This report was published on the EMA website in February 2017. The document 'Update on ongoing ATMP-related activities' contains an update on concrete activities by EMA and CAT that are ongoing or will start in the course of 2017.

7.8. Others

7.8.1. Health and Environmental Sciences Institute (ILSI-HESI) annual meeting, May 2017

CAT: Carla Herberts

Scope: feedback from participating CAT member Carla Herberts on the initiation and subsequent activities of the ILSI-Health and Environmental Sciences Institute emerging issue committee on Cell Therapy - TRAcking, Circulation, & Safety (CT-TRACS)

Action: for information

8. Any other business

No items

Date of next CAT meeting:

06-08 September 2017

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

ICH: International Conference on Harmonisation

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

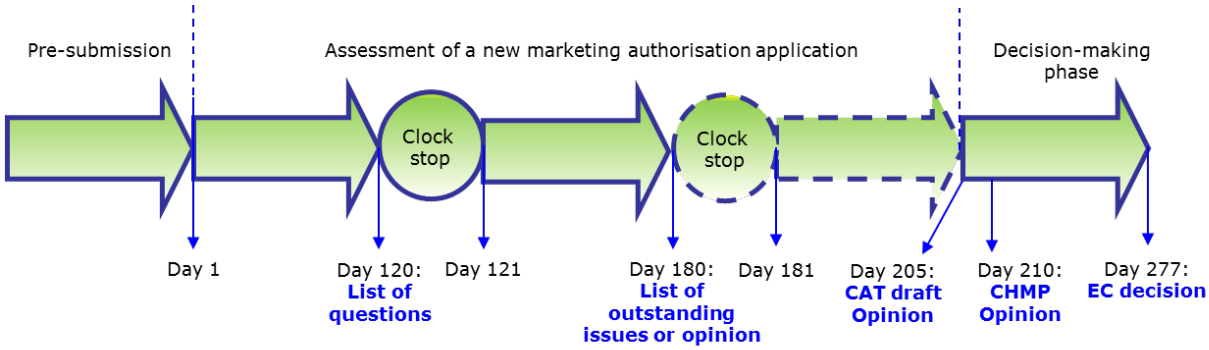
Evaluation of ATMPs (section 2)

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/