20 April 2016
EMA/CAT/286924/2016
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 20-21 April 2016

Chair: Paula Salmikangas - Vice-chair: Martina Schüßler-Lenz

20 April 2016, 14:00 – 18:30, room 03-E
21 April 2016, 09:00 – 18:30, 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 on 20 - 21 April 2016. See April 2016 CAT minutes (to be published post-May 2016 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 20 - 21 April 2016

1.3. Adoption of the minutes

CAT minutes of 22 - 23 March 2016

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 Lists of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Ongoing initial full application

No items

2.7. New applications

2.8. Withdrawal of initial marketing 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

No items

2.12. Other post-authorisation activities

No items

3. Certification of ATMPs

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

3.1. Opinions

3.2. Day 60 evaluation reports

No items

3.3. Ongoing initial application

No items

3.4. New applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – appointment of CAT Co-ordinators

4.1.1. DNA plasmid vector pGX1802

Intended for the treatment of chronic hepatitis B virus infection

Scope: appointment of CAT Co-ordinator and adoption of timetable

Action: for adoption

Document:
Request received 4 April 2016

4.1.2. Adeno-associated viral vector containing the ChrimsonR-td tomato gene

Intended for the treatment of retinitis pigmentosa

Scope: appointment of CAT Co-ordinator and adoption of timetable

Action: for adoption

Document:
Request received

4.1.3. Autologous regulatory T lymphocytes $CD3^+CD4^+CD25^+CD127^-FoxP3^+$

Intended for the treatment of, and prevention of progression of, recently diagnosed paediatric type I diabetes mellitus

Scope: appointment of CAT Co-ordinator and adoption of timetable

Action: for adoption

Document:
Request received

4.1.4. Allogeneic Epstein-Barr virus cytotoxic T lymphocytes

Intended for the treatment of Epstein-Barr virus-associated Post Transplant Lymphoproliferative disorder

Scope: appointment of CAT Co-ordinator and adoption of timetable

Action: for adoption

Document:
Request received

4.2. Day 30 Co-ordinators' first reports

4.2.1. Allogeneic bone marrow derived mesenchymal cells expanded *ex vivo* in synthetic media

Intended for the treatment of acute graft-versus-host disease grades III and IV resistant to first line treatment

Action: for adoption

Document:
ATMP classification report

4.2.2. Concentrate of autologous bone marrow-derived mononuclear cells (BM-MNC)

Intended for the improvement of heart function (left ventricular ejection fraction) and quality of life in patients with ischaemic post-acute myocardial infarction and in chronic heart disease

Action: for adoption

Document:
ATMP classification report

4.2.3. Live-attenuated, double-deleted *Listeria monocytogenes* (*Lm*) expressing human mesothelin

Intended for the treatment of non-small cell lung cancer

Action: for adoption

Document:
ATMP classification report

4.2.4. Live-attenuated, double-deleted *Listeria monocytogenes (Lm)* expressing prostate antigens

Intended for the treatment of prostate cancer

Action: for adoption

Document:
ATMP classification report

4.2.5. Autologous cultured fibroblasts

Intended for the indications of:
-Facial skin regeneration;
-Reducing facial wrinkles;
-Treatment of deep lines in the skin;
-Tissue loss and to heal chronic non-closing injuries;
-Treatment of acne scars

Action: for adoption

Document:
ATMP classification report

4.2.6. Extracellular matrix from adipose tissue

Intended for the treatment of non-healing wounds

Action: for adoption

Document:
ATMP classification report

4.2.7. Adipose derived MSC

Intended for the treatment of non-healing wounds

Action: for adoption

Document:
ATMP classification report

4.2.8. Bone marrow derived MSC

Intended for the treatment of children's encephalopathy, children's epilepsy, children's spinal cord injury

Action: for adoption

Document:
ATMP classification report

4.2.9. Autologous cultured chondrocytes

Intended for the treatment of filling of cartilage loss in knee-joint

Action: for adoption

Document:
ATMP classification report

4.2.10. Autologous cultured fibroblasts

Intended for the treatment of filling of skin connective tissue loss

Action: for adoption

Document:
ATMP classification report

4.2.11. Autologous cultured keratinocytes

Intended for the treatment of non-healing wounds, burns, trophic ulcers

Action: for adoption

Document:
ATMP classification report

4.2.12. Autologous cultured myoblasts

Intended for the treatment of faecal and urinary incontinence and of skeletal muscle injury

Action: for adoption

Document:
ATMP classification report

4.2.13. Autologous cultured melanocytes

Intended for the treatment of vitiligo

Action: for adoption

Document:
ATMP classification report

4.3. Day 60 Co-ordinators' revised reports following List of Questions

4.3.1. Hematopoietic stem and progenitor cells (HSPC) genetically modified with zinc finger nucleases (ZFNs) to disrupt the erythroid enhancer (ENH) of the gene encoding the human transcription factor BCL11A

Intended for the treatment of β-thalassemia

Action: for adoption

Documents:

Revised ATMP classification report
Applicant's responses to LoQ dated 06.04.16.

4.4. Finalisation of procedures

4.4.1. Autologous *ex vivo* expanded polyclonal $CD4^+CD25^+CD127^{lo/-}FOXP3^+$ regulatory T cells

Intended for the treatment of type 1 diabetes mellitus

Action: for information

Document:
ATMP classification report

Note: the European Commission raised no comments

4.4.2. DNA plasmid encoding a recombinant fusion protein consisting of the extracellular domain of human tumour necrosis factor alpha p55 receptor linked to the human immunoglobulin G1 Fc domain

Intended for the treatment of refractory chronic non-infectious uveitis

Action: for information

Document:
ATMP classification report

Note: the European Commission raised no comments

4.4.3. Autologous stromal vascular fraction

Intended as an autologous lipofiller

Action: for information

Document:
ATMP classification report

Note: the European Commission raised no comments

4.4.4. Autologous human bone marrow mononuclear cells

Intended for the treatment type 2 diabetes mellitus

Action: for information

Document:
ATMP classification report

Note: the European Commission raised no comments

4.4.5. Autologous adipose-derived regenerative cells encapsulated in carboxymethylcellulose

Intended for cosmetic dermal filling

Action: for information

Document:
ATMP classification report

Note: the European Commission raised no comments

4.5. Follow-ups and guidance

No items

5. Scientific Advice

Disclosure of 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 Co-ordinators

5.2. CAT Rapporteurs' reports

5.3. Lists of issues

5.4. Finalisation of Scientific Advice procedures

5.5. Follow-up of Scientific Advice procedures

6. -Pre-Authorisation Activities

Disclosure of 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 (PIP)

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. Strategic Review & Learning meeting

CAT-PDCO-CTFG joint Strategic Review & Learning meeting will take place in Utrecht, Netherlands on 1st-2nd June 2016 under the auspices of the Dutch Presidency of the Council of the European Union

CAT resources: Hans Ovelgönne

Scope: discussion to agree on topics for the agenda. The scientific focus will be on dose finding in the context of extrapolation to children

Action: for discussion

Document**:**
Draft agenda (CAT only session)

Note**:** CAT members are asked to send proposals for agenda topics

7.1.2. New CAT plenaries dates and times

EMA resources: Patrick Celis

Scope: Change in meeting times (from current timing of Thurs 09.00 – Fri 15.00 to new timing of Weds 14.00 - Fri 12.00, to accommodate CAT workload and needs)

Action: for adoption

Document:
-CAT plenary dates from April to December 2016

Note: at its plenaries in February and March 2016 the CAT discussed the new times and the rationale behind the changes.

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 March 2016 meeting

Action: for information

Documents:
-Summary of Outcomes

7.2.2. Scientific Co-ordination Board (SciCoBo) - meeting 18th March 2016

CAT resources: Paula Salmikangas

Action: for information

7.2.3. Benefit-risk assessment of the CHMP assessment report template

Scope: Revision of section 5, benefit-risk assessment template and guidance revision: second draft

Action: for information

Note: the CHMP adopted the template in February 2016

7.2.4. Letter from the European Commission on a definition for 'principal molecular structural features'

Letter from the European Commission, requesting that a definition for 'principal molecular structural features' as referred to in Art 3(3)c of Reg (EC) No 847/2000 on similar active substance is developed by end of March 2016

Action: For information

Document:
CHMP-CAT joint document containing a proposal for principal molecular structural features for chemical, biologicals and ATMPs.

Note: during its March 2016 meetings, CAT and CHMP adopted the proposal which has been sent to the European Commission

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

7.3.1. Guideline on Efficacy and Safety follow up - RMP

Scope: presentation on the action plan for revision

Action: for discussion

7.3.2. Questions and Answers on minimally manipulated ATMPs

CAT drafting group: Metoda Lipnik Stangelj, Paula Salmikangas, Tiina Palomäki, Egbert Flory, Margarida Menezes Ferreira, Pieter Doevendans, Mikuláš Hrubiško

Scope: creation of a Q&A document following the discussion that took place at the CAT-CHMP joint Strategic Review & Learning meeting in May 2015

Second drafting group meeting to take place on Wednesday 20th April 2016, from 18:30hrs to 20:00hrs, room 03-G

Action: feedback from drafting group meeting

Document:
First draft of Q&A document

Note:
First meeting took place on 21st January 2016

The proposal is to describe, in a Questions-and-Answers format, the quality, non-clinical and clinical requirements for the marketing authorisation for a minimally manipulated ATMP (CD34+ cells for cardiac repair). In the answers, a practical explanation will be provided how to use the risk based approach to identify and justify deviations for the standard requirements for cell-based ATMPs as included in Annex I Part IV of Dir. 2001/83/EC.

7.3.3. Accelerated assessment of priority medicines (PRIME)

Scope: procedure for the review of requests for PRIME eligibility for ATMPs in view of the first group of requests received by EMA with adoption of eligibility in May 2016

Action: for information

7.4. Co-operation within the EU regulatory network

7.4.1. GMO assessment of authorised ATMP used in a clinical trial

Action: for information

7.5. Co-operation with international regulators

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

The teleconference will take place during the plenary meeting on Thursday 21st April from 14.00hrs – 15.00hrs

CAT resources: Paula Salmikangas

Action: for adoption

Document table:
Agenda

7.5.2. International Pharmaceutical Regulators Forum (IPRF) Gene therapy group

CAT resource: Paula Salmikangas

Scope: oral feedback from the teleconference that took place on 7th January and 9th March 2016

Action: for information

Documents:
Agenda
Minutes

7.6. CAT Work Plan

7.6.1. CAT assessor training (23-24 June 2016)

Moderators: Quality session: Margarida Menezes-Ferreira and Ilona Reischl; Clinical session: Martina Schüßler-Lenz and Simona Badoi; Non-clinical session: Björn Carlsson and Egbert Flory

Action: for discussion

Document:
Preliminary programme

Note: EMA will reimburse one participant per member state. Also, the training will be streamed via Webinar

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming Advanced Therapies Medicinal Products (ATMP) MAAs

Action: for information

7.8. Others

No items

8. Any other business

8.1. Webinar - Advanced therapies in veterinary medicines: 25 – 27 April 2016

Scope: organised by AEMPS (Spain). Deadline for registration: 22th April 2016

Action: for information

Note: click here for full information

8.2. EMA workshop on Single Arm Trials - 30 June 2016

Scope:

Action: for information

Document: agenda

8.3. Procedure Management Department: update

Action: for information

Date of next CAT meeting:
Wednesday 18th to Friday 20th May 2016

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

DG: Drafting Group

EC: European Commission

FDA: Food and Drug Administration

FL: Final Letter

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Environmental Risk Assessment

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

SA: Scientific Advice

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

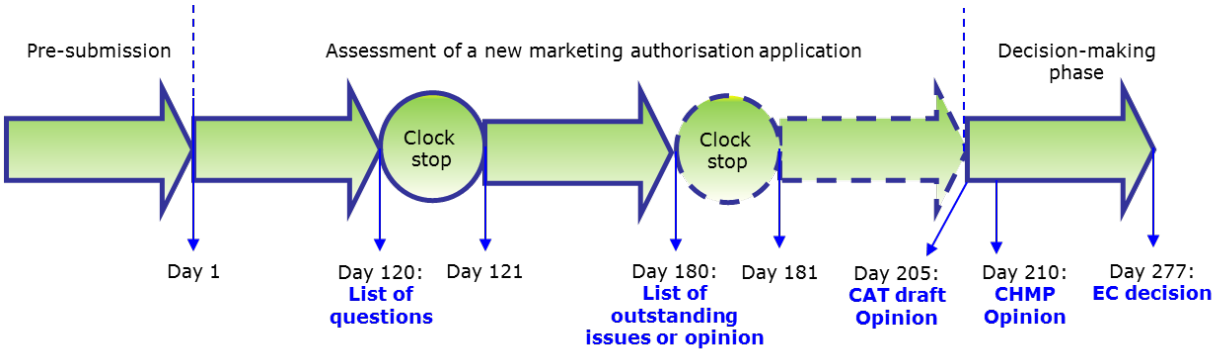
Evaluation of ATMPs (section 2)

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.

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/