12 November 2015
EMA/CAT/716666/2015
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 12-13 November 2015

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

12 November 2015, 09:00 – 13:30, virtual
13 November 2015, 09:00 – 13:30, virtual

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 12-13 November 2015. See November 2015 CAT minutes (to be published post December 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 12-13 November 2015

1.3. Adoption of the minutes

CAT minutes of 15-16 October 2015

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

None

2.2. Oral explanations

None

2.3. Day 180 List of outstanding issues (LoOIs)

None

2.4. Day 120 Lists of questions (LoQs)

None

2.5. Day 80 assessment reports

None

2.6. Re-examination procedure (new applications) under Article 9(2) of Regulation No. 726/2004

None

2.7. Withdrawal of initial full application

None

2.8. Ongoing initial full application

2.8.1. Characterised viable haploidentical Herpes Simplex Virus Thymidine Kinase (HSV-Tk) and Human Low Affinity Nerve Growth Factor Receptor (ΔLNGFR) transfected donor lymphocytes; *Orphan*; EMA/H/C/002801

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

Action: for adoption of the revised timetable

2.9. New applications

None

2.10. GMP and GCP inspections requests

None

2.11. Type II variations

None

2.12. Other post-authorisation activities

2.12.1. Glybera - Alipogene tiparvovec; Orphan; EMEA/H/C/002145/S/0051

UniQure biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinators: Greg Markey

Scope: 3rd annual reassessment

Action: timetable for adoption

2.12.2. ChondroCelect – Characterised viable autologous cartilage cells expanded *in vivo* expressing specific marker proteins; EMA/H/C/00878/MEA 16.4., 18.4

TiGenix N.V.

Rapporteur: Egbert Flory; Co-rapporteur: Tiina Palomäki; CHMP Coordinator: Jan Müller-Berghaus

Scope 16.4: Randomised control trial protocol TIG/ACT/04/2009
Scope 18.4: Non-interventional registry of ChondroCelect, study TGX001-2011 & randomised controlled study in small lesions using microfracture as comparator

Action: timetable for adoption

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. New applications

3.2. Day 60 evaluation reports

3.3. Opinions

None

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – appointment of CAT Co-ordinators

4.1.1. Autologous cells of SVF and autologous adipose derived stem cells

Intended for the treatment of treatment of (1) diabetic foot ulcer and (2) keloid scars and aging skin

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

Action: for adoption

Document:
Request received 29th October 2015

4.1.2. Autologous adipose-derived regenerative cells encapsulated in carboxymethylcellulose

Intended for the treatment of cosmetic dermal filling

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

Action: for adoption

Document:
Request received 29th October 2015

4.1.3. Human hepatoblastoma cells (HepG2) encapsulated in alginate, expanded in a fluidised bed bioreactor

Intended for the treatment of acute liver failure

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

Action: for adoption

Document:
Request received 23rd October 2015

4.1.4. Adeno-associated virus serotype 8 vector encoding human ornithine transcarbamylase

Intended for the treatment of ornithine transcarbamylase tl

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

Action: for adoption

Document:

Request received 29th October 2015

4.1.5. Fibroblasts and keratinocytes co-culture

Intended for the treatment of deep and extensive burns, chronic wounds, skin donor sites

Different product formulations:
-suspension of cell in platelet leukocyte rich gel
-in sheet
-seeded on acellular amniotic matrix
-seeded on acellular dermal matrix
-seeded on transgenic porcine acellular dermal matrix

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

Action: for adoption

Document:
Request received 2nd November 2015

4.1.6. Human acellular amniotic matrix

Intended for the treatment of deep and extensive burns, chronic wounds, skin donor sites

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

Action: for adoption

Document:

Request received 2nd November 2015

4.1.7. Human acellular dermal matrix

Intended for the treatment of deep and extensive burns, chronic wounds, skin donor sites

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

Action: for adoption

Document:

Request received 2nd November 2015

4.1.8. Allogeneic chondrocytes and irradiated genetically modified chondrocytes expressing human TGF-β1

Intended for the treatment of degenerative joint disease

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

Action: for adoption

Document:
Request received 16th October 2015

4.1.9. Allograft tendon combined with suture ready to use

Intended for the treatment of anterior cruciate ligament reconstruction

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

Action: for adoption

Document:
Request received 28th October 2015

4.1.10. Transgenic porcine acellular dermal matrix

Intended for the treatment of deep and extensive burns, chronic wounds, skin donor sites

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

Action: for adoption

Document:
Request received 2nd November 2015

4.2. Day 30 Co-ordinators' first reports

4.2.1. Autologous adipose derived regenerative cells encapsulated in hyaluronic acid

Intended for the treatment of articular cartilage and bone defects

Action: for adoption

Document:
ATMP classification report

4.2.2. Autologous bone marrow derived non-haematopoietic stem cells

Intended for the treatments of patients with rheumatoid arthritis; patients after ischemic stroke; patients after myocardial infarction; type I diabetes; type II diabetes

Action: for adoption

Document:
ATMP classification report

4.2.3. Autologous peripheral blood-derived total nucleated cells

Intended for the treatment of critical limb ischemia

Action: for adoption

Document:
ATMP classification report

4.2.4. Allogeneic pro-inflammatory monocyte-derived dendritic cells

Intended for the treatment of metastatic renal cell carcinoma (mRCC)

Action: for adoption

Document:
ATMP classification report

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

4.3.1. Autologous cells of stromal vascular fraction (SVF) of adipose tissue

Intended for (1) cosmetic lipofiling; (2) treatment for non-healing wounds and scared tissue; (3) treatment of osteoarthritis in the knee

Action: for adoption

Document:
Revised ATMP classification report
Response to the LoQs received 28th October 2015

4.4. Finalisation of procedures

4.4.1. Decellularised trachea seeded with autologous expanded MSCs

Intended for the treatment of reconstruction of trachea subsequent to damage or stenosis due to cancer, injury, infection or congenital deformities

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments

4.4.2. Autologous bone marrow - adipose tissue or allogeneic umbilical cord derived human mesenchymal stem cells

Intended for the treatment of Amyotrophic Lateral Sclerosis

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments

4.4.3. Allogeneic mesenchymal precursor cells

Intended for the treatment of chronic lumbar back pain

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments

4.4.4. *In vitro* expanded autologous articular chondrocytes

Intended for the treatment of articular cartilage defect

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments

4.4.5. hESC-derived hepatocyte like cells

Intended for the treatment of inborn errors of liver metabolism diseases and liver acute failure

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments

4.4.6. Allogeneic hematopoietic progenitor cells (HPC–CD34+) accompanied by facilitating cells (FC– CD8+/αβTCR-) and αβ T cells, prepared from mobilized peripheral blood mononuclear cells

Intended for the prophylaxis of organ rejection in adult patients receiving living donor kidney transplantation

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments

4.5. Follow-ups and guidance

None

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

None

5.4. Finalisation 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)

6.2. ITF briefing meetings in the field of ATMPs

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

None

7.2. Coordination with EMA Scientific Committees

7.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of Outcomes (SoO) for the October 2015 meeting

Action: for information

7.2.2. CAT – CHMP (SWP) cluster on tumourigenicity studies for ATMPs

CAT resources: Tiina Palomäki, Hans Ovelgönne, Björn Carlsson, Egbert Flory Scope: potential creation of a reflection paper

Action: for discussion

Document:
CAT – CHMP (SWP) Project plan

Note: first step in the exercise is to gather examples of NC study evaluation in the context of CTAs

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

7.3.1. Good Laboratory Practice (GLP) requirements of non-clinical studies for ATMPs

CAT drafting group: Una Riekstina, Tiina Palomäki, Egbert Flory, Ilona Reischl, Carla Herberts (NL), Isabel Vieira (PT)

Scope: Application of GLP principles on ATMPs

Action: for adoption

Document:
CAT's position

Note:
June 2015: presentation by the EMA GLP Inspections Working Party (IWP) on GLP requirements for ATMPs
July 2015: CAT agreed on the composition of a drafting group to draft a document summarising experiences and expectation in relation to the GLP requirements of non-clinical studies of ATMP
26 October 2015: teleconference of the DG drafting group to develop a draft CAT position

7.3.2. CHMP draft guideline on conditional marketing authorisation (CMA)

Scope: public consultation comments and corresponding amendments to the CHMP guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004

Action: for discussion

Documents**:**
CHMP guideline
Overview of comments

Note:
CAT was consulted on this update of the guideline in June 2015

7.3.3. CHMP draft guideline on the scientific application and the practical arrangements necessary to implement the procedure for accelerated assessment pursuant to article 14(9) of regulation (EC) No 726/2004

Scope: update on public consultation comments

Action: for appointment of CAT sponsors

Documents**:**
CHMP guideline
Note:
The guideline will be revised by the end 2015
Input of CAT on specific timetable

7.3.4. Adaptive pathway approach

CAT resources: Hans Ovelgönne;

Scope: presentation of the procedure and experience with ATMPs under discussion in the Adaptive Pathway pilot

Action: for information

Further information can be found here: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp&mid=WC0b01ac05807d58ce

7.3.5. Draft reflection on a proposal to enhance early dialogue to facilitate accelerated assessment of priority medicines (PRIME)

CAT resource: Paula Salmikangas

Scope: Reflection paper on enhanced early dialogue

Action: for discussion

Reflection paper: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/10/news_detail_002424.jsp&mid=WC0b01ac058004d5c1-

Note:
The CHMP adopted the RP at its October 2015 meeting and it has now been released for a two-month public consultation, prior to a targeted launch in Q1 2016

7.3.6. EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP)

Scope: Work plan 2016 for the PCWP
Scope: Work plan 2016 for the HCPWP
Scope: draft Agenda - training session for patients and consumers interested in EMA activities – 25 November 2015
Scope: draft Agenda - PCWP meeting with all eligible organisations – 26 November 2015

Action: for silent adoption

Documents:
Work plans
Agendas

7.4. Co-operation within the EU regulatory network

None

7.5. Co-operation with international regulators

None

7.6. CAT Work Plan

7.6.1. CAT- International Society for Cellular Therapy (ISCT) Joint Workshop: 'Challenges and Opportunities for the Successful Development and Approval of Advanced Therapy Medicinal Products', Seville (Spain), 25th September 2015

CAT resources: Paula Salmikangas

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/06/news_detail_002357.jsp&mid=WC0b01ac058004d5c1

Action: for information

Documents:
Presentations

7.6.2. CAT Workplan for 2015: Webinar on ATMP classification

Date: 11 December 2015, 13.00-14.00
Presenters: Nicolas Ferry, Belaid Sekalli, Paula Salmikangas, Patrick Celis
This Webinar is addressed to the National authorities who are conducting ATMP classifications in their member state
CAT members are asked to promote this Webinar at their Agency
CAT members can attend the Webinar in person

Action: for information

7.7. Planning and reporting

7.7.1. EMA's Management Board - extension to phase II

Scope: involvement of CAT members and assessment teams

Action: for information

7.8. Others

7.8.1. EMA website: upgrade of the ATMPs page

Action: for information

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000294.jsp&mid=WC0b01ac05800241e0

Note: the improvement of this web page results from a request from EC to clarify and map the requirements for ATMPs in order to help ATMP developers who are often SMEs.

8. Any other business

Date of next CAT meeting:
Thursday 10th – Friday 11th December 2015

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

FL: Final Letter

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMP: Good Manufacturing Practice

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

PDCO: Paediatric Committee

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee

RP: Reflection paper

RSI: Request for supplementary information

SA: Scientific Advice

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

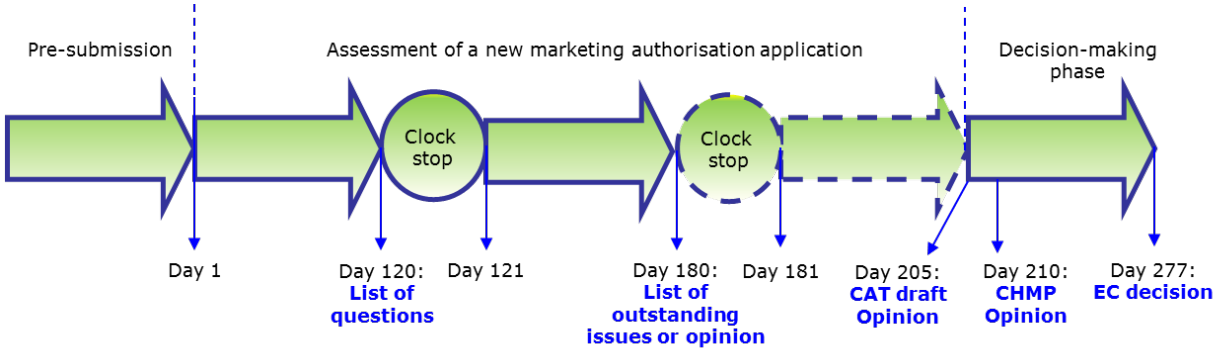
Evaluation of ATMPs (section 2)

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/