15 October 2015
EMA/CAT/691987/2015
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 15-16 October 2015

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

15 October 2015, 09:00 – 18:30, room 02-F
16 October 2015, 09:00 – 15:00, room 02-F

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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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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 October 2015. See October 2015 CAT minutes (to be published post November 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 15-16 October 2015

1.3. Adoption of the minutes

CAT minutes of 17-18 September 2015

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Talimogene laherparepvec; EMA/H/C/0002771

Treatment of adults with melanoma that is regionally or distantly metastatic

Scope: Opinion

Action: for adoption

Documents:
Scientific Advice Group (SAG) revised report
Draft CAT AR
Draft Opinion
Draft PI
Draft SmPC

Note:
Classification as a GTMP adopted in July 2012
SAs provided by SAWP in 2008 and 2013

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

2.6.1. Heparesc - allogeneic human heterologous liver cells; *Orphan;* EMA/H/C/003750

Cytonet GmbH & Co. KG; treatment of urea cycle disorders (UCD)Scope: Opinion and report from the ad-hoc expert group's Chais. Oral Explanation to take place on 15th October 2015

Action: for adoption

Documents:
Draft AR
Draft Opinion
Ad-hoc expert group report

The ad hoc expert group meeting took place on 6 October 2015.

Note:
The CHMP adopted in June 2015 a negative Opinion.
The CAT adopted in April 2015 a negative draft Opinion.

2.7. Withdrawal of initial full application

None

2.8. Ongoing initial full application

None

2.9. New applications

2.9.1. Expanded adipose-derived stem cells of allogeneic origin; *Orphan*; EMA/H/C/0004258

TiGenix S.A.U.; Treatment of complex perianal fistulas in adult patients with non-active / mildly active luminal Crohn's disease when fistulas are refractory to Crohn´s disease conventional therapy or biologic agents, or when patients are intolerant to such treatments

Scope: notification from the company dated 8 October 2015 informing of the delay in the intended submission of MAA by one month to 3 March 2016

Action: for information

Document:
Letter from the applicant

2.10. GMP and GCP inspections requests

None

2.11. Type II variations

2.11.1. Glybera – Alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/47

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinator: G. Markey

Scope: quality:

Action: for adoption

Document:
RSI

2.11.2. Glybera – Alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/48

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinator: G. Markey

Scope: quality:

Action: for adoption

Document:
RSI

2.12. Other post-authorisation activities

2.12.1. Holoclar – *Ex vivo* expanded autologous human corneal epithelial cells containing stem cells; *Orphan*; EMA/H/C/002450/R/0001

Chiesi Farmaceutici S.p.A.; Treatment of adult patients with moderate to severe limbal stem cell deficiency

Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini; CHMP Coordinator: Jan Müller-Berghaus

Scope: Conditional Renewal. Opinion

Action: for adoption

Documents:
CAT revised Assessment Report
CAT draft Opinion

Note: conditional MA adopted in December 2014

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

Oral Explanation to take place on 15th October 2015

Action: for adoption

Documents:
CAT draft Opinion

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

None

3.2. Day 60 evaluation reports

None

3.3. Opinions

None

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – appointment of CAT Co-ordinators

4.1.1. Allogeneic pro-inflammatory monocyte-derived dendritic cells

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

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

Action: for adoption

Document:
Request received 30th September 2015

4.1.2. Autologous peripheral blood-derived total nucleated cells

Intended for the treatment of critical limb ischemia

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

Action: for adoption

Document:
Request received 1st October 2015

4.1.3. 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.

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

Action: for adoption

Document:
Request received 01st October 2015

4.1.4. Autologous adipose derived regenerative cells encapsulated in hyaluronic acid

Intended for the treatment of articular cartilage and bone defects

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

Action: for adoption

Document:
Request received 01st October 2015

4.2. Day 30 Co-ordinators' first reports

4.2.1. Allogeneic mesenchymal precursor cells

Intended for the treatment of chronic lumbar back pain

Action: for adoption

Document:
Classification report

4.2.2. *In vitro* expanded autologous articular chondrocytes

Intended for the treatment of articular cartilage defect

Action: for adoption

Document:
Classification report

4.2.3. 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:
Classification report

4.2.4. 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 adoption

Document:
Classification report

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

Intended for the treatment of Amyotrophic Lateral Sclerosis

Action: for adoption

Document:
Classification report

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

4.3.1. hESC-derived hepatocyte like cells

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

Action: for adoption

Documents:
Revised ATMP Classification report
Response to the LoQs received on 29.09.15.

4.3.2. 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 adoption

Documents:
Revised classification report
Response to the LoQs received on 01.10.15.

4.4. Finalisation of procedures

4.4.1. Life-attenuated, double-delete Listeria monocytogenes expressing human mesothelin

Intended for the treatment of malignant pleural mesothelioma

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments.
See also 5.4.2.

4.4.2. Encapsulated allogeneic cells genetically modified to secrete GM-CSF and irradiated autologous tumour cells

Intended for the treatment of advanced solid tumours

Action: for information

Document:
ATMP classification report

Note:
The European Commission raised no comments.

4.5. Follow-ups and guidance

4.5.1. Functional apoptosis-based selection process to deplete haematopoietic cell transplants of GvHD effector T-cells

Intended for the reduction of GvHD during stem cell transplants.

Action: for discussion

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 scientific advices – appointment of CAT Rapporteur

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

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meetings

Scope: updated documents on organisational aspects

Action: for information

Documents:
Principles for organisation of NCA-hosted meetings
Responsibilities for confidentiality in NCA-hosted meetings

7.1.2. Call for Expression of Interest from Civil Societies for the position of Member of the Committee for Advanced Therapies (CAT)

Scope: the European Commission has extended the deadline by two weeks to 18 October 2015.

Action: for information

European Commission's website
link: http://ec.europa.eu/health/documents/public_call/call_index_en.htm#fragment2

Note:
-the term of office of the current members expires on 30 June 2016;
-the EC will appoint the new members after consultation with the European Parliament.

7.2. Coordination with EMA Scientific Committees

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

Summary of Outcomes (SoO) for the September 2015 meeting

Action: for information

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: U. Riekstina, T. Palomäki, E. Flory, C. Herberts (Netherlands), I. Vieira (Portugal)

Action: for discussion

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
15-16 October 2015: discussion of the observations made by the CAT drafting group members
November or December 2015 at CAT: joint discussion with the GLP IWP to agree on a common position

7.3.2. Good Pharmacovigilance Practices (GVP) - Module P.II Biological medicinal products

Action: for discussion

Document:
Written comments by CAT

Note: this module is presented to committees for discussion and comments before a public consultation

7.3.3. 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

7.3.4. Draft Scientific Guideline on Post-authorisation efficacy studies (PAES)

Scope: for public consultation

Action: for adoption

Document:
Guidance

Note:
-it was introduced to CAT in July 2015 for comments.
-the aim of this draft is to provide scientific guidance for MAHs and NCAs on the general need for such studies including within the scope of Delegated Regulation (EU) No 357/2014, on general methodological considerations, on specific situations and on study conduct. Following its adoption by the EMA Scientific Committees the draft guidance will be released for public consultation in Q4 2015.

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

Overview of comments received during the external consultation

Scope: Re-appointment of drafting group members

Action: for discussion

Note: The external consultation ended in July 2015.

7.3.6. PRIME - Enhanced early dialogue to foster development and facilitate accelerated assessment

Action: for information

Tabled document**:**
-Reflection paper

Note:
As a follow-up to EMA's presentation in July on PRIME (previously Pathfinder), it is now in the process of finalising the reflection paper which is planned to be adopted by the CHMP during its October meeting. After adoption, the reflection paper will be released for a 2-month public consultation, prior to a targeted launch in Q1 2016.

7.4. Co-operation within the EU regulatory network

7.4.1. Analysis of European Clinical Trials Database (EudraCT)

CAT drafting group: M. Menezes-Ferreira, I. Reischl, T. Boráň, P. Salmikangas, N. Ferry, R. Mačiulaitis, D. Śladowski, M. Lipucci di Paola, B. Gänsbacher

Scope: Analysis of EudraCT for trials with ATMPs

Action: for discussion

7.4.2. GMP requirements for ATMPs

CAT drafting group members: I. Haunerova, M. Menezes-Ferreira, G. Panté, I. Reischl, P. Salmikangas, B. Sekkali, M. Timón, Jürgen Scherer, Marcel Hoefnagel

Scope: feedback from the discussion at the GMP Inspectors Working Group

Action: for information

http://ec.europa.eu/health/files/advtherapies/2015_pc/publ_cons_doc_2015.pdf

Note:
CAT September 2015: feedback was provided by the European Commission on the consultation document that was released for external consultation over the summer of 2015. Similar feedback was provided to the GMP Inspectors Working Group. Both groups will be involved in the latter part of 2015 / early 2016 in the finalisation of the GMP document.

7.5. Co-operation with international regulators

7.5.1. ATMP cluster teleconference with FDA and Health Canada

The teleconference will take place during the plenary meeting on Thursday 15th October from 14.00hrs – 15.00hrs

CAT resources: P. Salmikangas

Action: for adoption

Document:
Agenda

7.6. CAT Work Plan

7.6.1. CAT Work Plan 2016

Scope: agreement of work plan topic, CAT lead /Rapporteurs and involved CAT members

Action: for discussion

Document**:**
Workplan

7.6.2. 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

7.7. Planning and reporting

None

7.8. Others

8. Any other business

Date of next CAT meeting:
Thursday 12th – Friday 13th November 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

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMP: Good Manufacturing Practice

ITF: Innovative Task Force

LoOI: List of outstanding issues

LoQ: List of questions

PDCO: Paediatric Committee

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee

RSI: Request for supplementary information

SA: Scientific Advice

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SmPC: Summary of Products Characteristics

TT: Timetable

Evaluation of ATMPs (section 2)

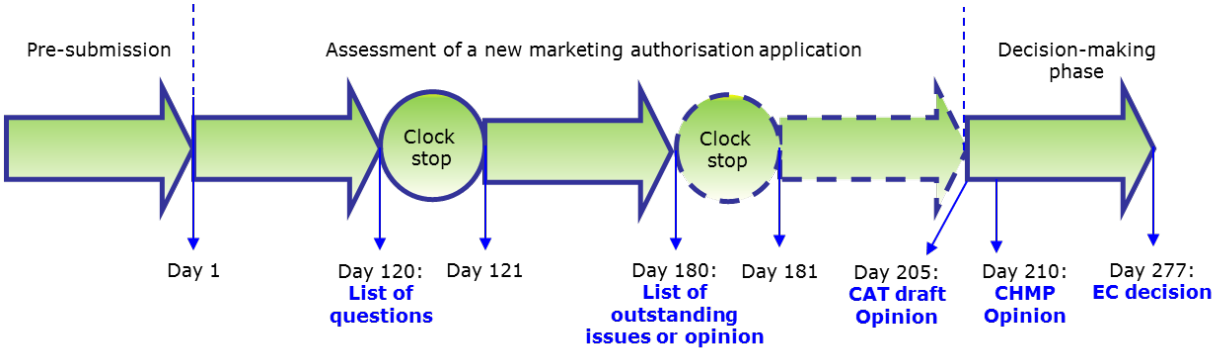
This section lists applications for marketing authorisations of new Advanced Therapy Medicinal Products (ATMPs) that are to be discussed by the Committee. It also lists any ATMP related inspection requests (*section 2.9*) and Post-authorisation activities (*section 2.10*).

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/