13 June 2016
EMA/CAT/489613/2016
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 13-15 July 2016

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

13 July 2016, 14:00 – 18:30, room 03-E
14 July 2016, 09:00 – 18:30, room 03-E
15 July 2016, 09:00 – 12:00, room 03-E

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CAT meeting reports once the procedures are finalised.

Of note, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CAT plenary session to be held on 13 - 15 July 2016. See July 2016 CAT minutes (to be published post-September 2016 CAT meeting).

1.2. Adoption of agenda

CAT agenda for the 13 - 15 July 2016 meeting

1.3. Adoption of the minutes

CAT minutes of the 16 - 17 June 2016 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 List of outstanding issues

No items

2.4. Day 120 Lists of questions

Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue; *Orphan*; EMA/H/C/0004258TiGenix S.A.U.; Treatment of complex perianal fistula(s)Scope: Day 120 list of questions

Action: for adoption

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

2.12.1. ChondroCelect - Characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins; EMEA/H/C/000878

MAH: TiGenix NV; Treatment of repair of single symptomatic cartilaginous defects

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

Action: for discussion

Document tabled:
MAH's Letter of withdrawal dated 05.07.16.

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

No items

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. Genetically-modified *Lactobacillus reuteri* bacteria, with a plasmid containing the gene for human CXCL12-1a with an inducible promoter

Intended for wound healing of chronic ulcers in patients with diabetes

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

Action: for nomination of CAT Coordinator

Document:
Request received

4.2. Day 30 Co-ordinators' first reports

4.2.1. RET activated human cord blood progenitor cells expanded *ex-vivo*; EMA/H0004545

Intended for the treatment of patients undergoing hematopoietic stem cell transplantion

Action: for adoption

Document:
ATMP classification report

4.2.2. Adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene; EMA/H0004544

Intended for the treatment of glycogen storage disease type Ia (GSDIa)

Action: for adoption

Document:
ATMP classification report

4.2.3. Recombinant adeno-associated virus 2 human aromatic L-amino acid decarboxylase gene; H0004546

Intended for the treatment of Parkinson's disease (PD)

Action: for adoption

Document:
ATMP classification report

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

4.3.1. Heterologous human adult liver-derived progenitor cells (HHALPC)

Intended for the treatment of liver diseases

Action: for adoption

Document:
Revised ATMP classification report
Applicant's responses to LoQ

4.4. Finalisation of procedures

4.4.1. Live attenuated *Listeria monocytogenes* transfected with plasmids encoding HPV-16E7 protein fused to a truncated fragment of the *Lm* protein listeriolysin O

Intended for the treatment of cervical cancer

Action: for information

Document:
ATMP classification report

The European Commission raised no comments

4.4.2. Autologous expanded human fibroblasts

Intended for the treatment of scar of different aetiology as post- traumatic, post-surgical or outcomes of acne scars

Action: for adoption

Document:
Revised ATMP classification report

Comments received from the European Commission

4.4.3. Autologous concentrated bone marrow

Intended for critical limb ischemia without surgical option

Action: for information

Document:
ATMP classification report

The European Commission raised no comments

4.4.4. Hepatitis B virus DNA vaccine delivered via electroporation

Intended for the treatment of chronic hepatitis B virus infection

Action: for adoption

Document:
Revised ATMP classification report

Comments received from the European Commission

4.4.5. Collagenase from *Clostridium histolyticum*; H0004547

Intended to be used for *ex-vivo* dissociation of adipose tissue

Action: for information

Document:
ATMP classification report

The European Commission raised no comments

4.5. Follow-ups and guidance

4.5.1. Informal classification discussion on request of a National Competent Authority

Procedure to treat cartilage defects **Action:** for discussion

Document**:** presentation

4.5.2. ATMP classification – revised template for request form and briefing information for applicants

Scope: improved revised template

Action: for information

Document:
-revised template
-revised template (annotated)

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. List of issues

5.4. Finalisation of Scientific Advice procedures

5.5. Follow-up of Scientific Advice procedures

No items

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

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation for eligibility

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Appointment members and alternates of the Committee for Advanced Therapies to represent clinicians and patients' associations

Scope: Commission decision dated 5th July 2016 (ref. C/2016 4160) on the new appointment of civil societies to CAT for a mandate of three years, from 1st July 2016 to 30th June 2019

Patients' associations:
-Member: Mariette H.E. Driesens representing the Patients Network for Medical Research and Health (EGAN)
-Alternate Erik Briers representing EUROPA UOMO – The European Prostate Cancer Coalition

-Member: Kieran Breen representing the European Parkinson's Disease Association
-Alternate: Michele Lipucci de Paola representing EURORDIS

Clinicians' organisations:
-Member: Bernd Gänsbacher representing the European Society of Gene and Cell Therapy (ESGCT)
-Member: Marc Turner representing the Scottish National Blood Transfusion Service

Action: for information

Note: the CAT Secretariat will organise an induction meeting for the new cohort of civil societies in the week of the next face-to-face CAT meeting (5th-8th October 2016)

7.1.2. Strategic Review & Learning meeting

CAT Strategic Review & Learning meeting will take place in Dublin, Ireland on 24-25 October 2016

CAT resources: Maura O'Donovan

Scope: initial discussion to agree on topics for the agenda

Action: for discussion

Document:
Draft agenda

Note: proposed topics so far: new medical device legislation, GMO issue including the wording for product information, use of real world data and registries.

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

7.1.3. Good manufacturing practice (GMP) requirements for ATMPs

CAT drafting group members: Ivana Haunerova, Margarida Menezes-Ferreira, Guido Panté, Ilona Reischl, Paula Salmikangas, Belaid Sekkali, Marcos Timón, Christiane Niederlaender, Jürgen Scherer, Marcel Hoefnagel

Action: for information

Documents:
-Letter dated 29 June 2016 from Robert Vanhoorde – DG for Health and Food Safety to CAT Chair and EMA (Compliance and Inspections Dept.) detailing next consultation steps following the drafting of the guideline
-European Commissions consultation document on good manufacturing practice for advanced therapy medicinal products

7.1.4. Survey to committee members on the service provided by the Scientific Committees Service

Action: for information

The link to the survey is: https://www.surveymonkey.co.uk/r/T98C8W7 The deadline for completion is July 29th 2016.

Note:
The purpose of the survey is to gather feedback on the service provided by the Committee Secretariats, as well as capturing information on the needs and expectations of those involved in Committee activities. The survey can, also, be completed by colleagues involved in supporting the work of members outside of the meeting and/or participation in person or by teleconference in committee and other associated meetings.

The Scientific Committees Service will share the outcome of the survey with the various committees and will also inform of any planned improvements or communication with respect to the support provided, further to analysis of the survey results.

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 2016 meeting

Action: for information

Documents:
-Summary of Outcomes

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

7.3.1. ATMP guideline on S&E follow-up and risk management

Scope: update on the revision

Action: for information

7.3.2. Review and update of EMA guidelines to implement best practice with regard to 3Rs (replacement, reduction and refinement of animal testing) in regulatory testing of medicinal products

Scope: report on actions taken

Action: for information

Documents:
-Review and update of EMA guidelines to implement best practice with regard to 3Rs - report on actions taken
-Background note on EMA guidelines to implement best practice with regard to 3Rs in regulatory testing of medicinal products

-Guideline on 'Potency testing of cell-based immunotherapy medicinal for the treatment of cancer': minor additions added in line with the 3R principles

Note:
-The document will be adopted by CHMP and CVMP in July 2016 for a three-month consultation.
-Agreement from CAT was sought on the part concerning guidelines for ATMPs. The final annex table contains information from all non-clinical guidelines. In May 2015 Tiina Palomäki presented to CAT the Annex table for cell and gene therapies.

7.4. Co-operation within the EU regulatory network

No items

7.5. Co-operation with international regulators

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

CAT resource: Paula Salmikangas

Scope: oral feedback from the teleconferences that took place on 14th June 2016

Action: for information

7.6. CAT Work Plan

7.6.1. Guideline on requirements for investigational ATMPs

CAT drafting groups: Tiina Palomäki (Rapporteur), Ilona Reischl (Rapp), Metoda Lipnik-Stangelj, Margarida Menezes Ferreira, Maura O'Donovan, Simona Badoi, Tomas Boráň, Christiane Niederlaender, Paolo Gasparini, Olli Tenhunen, Carla Herberts

Scope: initial draft of the guideline

Action: for discussion

Note: an outline of the structure of the guideline was provided in June 2016.

7.6.2. Questions and Answers on minimally manipulated ATMPs

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

Scope: initial draft of the Q&A document

Action: for discussion

Note:
The Questions-and-Answers will describe 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.

7.6.3. CAT workplan 2016

Scope: mid-year reporting

Action: for discussion

Document:
Workplan

7.6.4. CAT Workshop on cell-based cancer immunotherapies, 15-16 November 2016

CAT resource: Rune Kjeken, Björn Carlsson;

Scope: draft programme

Action: for discussion

7.7. Planning and reporting

7.7.1. ATMP Expert meeting, 27 May 2016

Action: for information

Documents:
-Regulators report and action plan

Link to the published stakeholders report:
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/06/WC500208080.pdf

7.8. Others

7.8.1. Gene therapy for Wiskott-Aldrich syndrome (WAS): long term efficacy and safety findings

CAT resource: Martina Schüßler-Lenz

Scope: finding of leukaemia cases in patients treated with retroviral vector containing the gene for WAS protein

Action: for information

8. Any other business

No items

Date of next CAT meeting:
Thursday 8th to Friday 9th September 2016 (virtual with Adobe Connect)

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

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

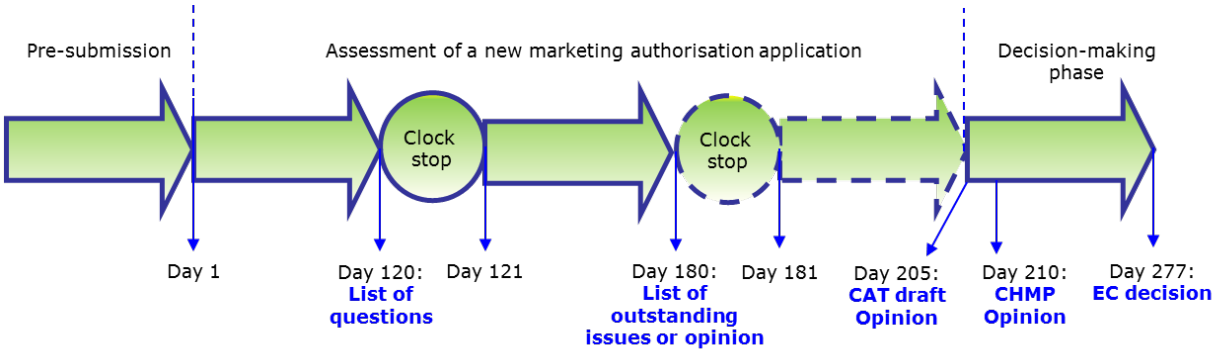
Evaluation of ATMPs (section 2)

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.

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/