08 December 2016
EMA/CAT/847259/2016
Inspections, Human Medicines Pharmacovigilance & Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 08-09 December 2016

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

08 December 2016, 09:00 – 13:30
09 December 2016, 09:00 – 13:00

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 08 – 09 December 2016. See December 2016 CAT minutes (to be published post-January 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for the 08-09 December 2016 meeting

1.3. Adoption of the minutes

CAT minutes for the 03-04 November 2016 meeting

1.4. Technical information

2. Evaluation of ATMPs

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No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

2.6.1. Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue; Orphan; EMA/H/C/0004258

TiGenix S.A.U.; Treatment of complex perianal fistula(s)

Scope: restart of procedure

Action: for information

2.6.2. Human autologous spheroids of matrix– associated chondrocytes for transplantation; EMA/H/C/0002736

Treatment is eligible for single as well as multiple adjacent defects. Cartilage defects of the knee, hip, elbow, shoulder and ankle joints were treated successfully. In a few cases, defect sizes between 11 and 23 cm^2 were treated successfully. The product is indicated for adults and adolescents with a closed epiphyseal growth plate

Scope: restart of the procedure

Action: for information

2.7. New applications

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

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

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

2.11. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

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. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

4. Scientific Recommendation on Classification 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.

4.1. New requests – Appointment of CAT Coordinators

4.1.1. Adeno-associated virus type 8 encoding the human myotubularin (MTM1) gene; EMA/H0004719

Intended for the treatment of X-linked myotubular myopathy (XLMTM)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Messenger RNA components encoding six non-small cell lung cancer associated antigens; EMA/H0004716

Intended for the treatment of non-small cell lung cancer (NSCLC)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. mRNA construct encoding the wild type human OX40L protein; EMA/H0004726

Intended for the treatment of solid tumours

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Bone marrow derived mesenchymal cells (MSCs); EMA/H0004718

Intended for the treatment of acute graft *versus* host disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Allogeneic Cytomegalovirus-specific cytotoxic T lymphocytes (CMV-CTLs) - Orphan; EMA/H0004717

Intended for the treatment of cytomegalovirus-associated viraemia or disease after allogeneic haematopoietic cell transplant or solid organ transplant

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Bone marrow-derived lineage-negative heterogenic stem and progenitor cells; EMA/H0004703

Intended for the treatment of amyotrophic lateral sclerosis in adults

Scope: adoption of scientific recommendation

Action: for adoption

4.2.2. Leukocytes with cancer killing activity; EMA/H0004704

Intended for the treatment of metastatic pancreatic ductal adeno carcinoma

Scope: adoption of scientific recommendation

Action: for adoption

4.3. Day 60 revised ATMP scientific recommendation (following list of questions)

No items

4.4. Finalisation of procedure

4.4.1. Bone marrow derived mesenchymal cells (MSCs); EMA/H004688

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

Scope: no comments from the European Commission

Action: for information

4.5. Follow-up 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 Coordinators

5.2. CAT Rapporteurs' reports

5.3. List of Issues

5.4. Finalisation of SA 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

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 1 – Discussion of eligibility

6.3.2. Month 2 – Recommendation of eligibility

6.3.3. Month 3 – Nomination of Rapporteurs

No items

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Forthcoming elections for Chair and Vice-Chair

Scope: election of Chair to take place in February 2017; election of Vice-Chair to take in March 2017

Action: for information

7.1.2. Survey to committees members on the service provided by the Scientific Committees Service

Scope: findings of the survey that was conducted in July 2016

Action: for information

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

Scope: Summary of Outcomes (SoO) for the November 2016 meeting

Action: for information

7.1.4. Conditional marketing authorisation for medicinal products for human use

Scope: EMA report on ten years of experience with the regulatory tool of conditional marketing authorisations

Action: for information

Note:
-the CAT was consulted on draft guideline in 2015 and introduced to the final guideline in March 2016
-the CHMP adopted the guideline in February 2016

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

7.2.1. ATMP guideline on safety and efficacy follow-up and risk management

Scope: presentation on the guideline. Comments should be provided by 05 January 2017

Action: for discussion

7.2.2. Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope: HCPWP work plan 2017

Action: for adoption

7.2.3. Working Party with Patients' and Consumers' Organisations (PCWP)

Scope: agenda of the training session for patients and consumers interested in EMA activities (29 November 2016); agenda of the PCWP meeting with all eligible organisations (30 November 2016)

Action: for information

Scope: PCWP work plan 2017

Action: for adoption

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

Scope: report of the PCPWP/HCPWP workshop on social media (19 September 2016)

Action: for information

7.3. Cooperation within the EU regulatory network

7.3.1. Environmental assessment for gene therapy products

Scope: nomination of CAT members/representatives from NCAs to take part in a group of national experts of medicines and from the environmental authorities to discuss genetically modified organism (GMO) related issues during clinical trials, marketing authorisation and post approval

Action: for information

Note: in October 2016, CAT members were asked to provide names of assessors/experts with experience in reviewing GMO/GTMP clinical trials. CAT members will also be involved.

7.4. Cooperation with international regulators

No items

7.5. CAT work plan

7.5.1. CAT 2017 work plan

Scope: appointment of CAT topic leaders and participants. Deadline for receipt of comments and interest to participate: 1 December 2016

Action: for adoption of nominations

Note: the CAT work plan will be adopted at is plenary in January 2017

7.5.2. CAT workshop: scientific and regulatory challenges of genetically modified cell-based cancer immunotherapy products that took place on 15-16 November 2016, EMA, London

CAT members: Rune Kjeken, Björn Carlsson

Scope: feedback on the workshop

Action: for information

All presentations and video recordings are published on the EMA website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2016/08/event_detail_001318.jsp&mid=WC0b01ac058004d5c3

7.5.3. Questions and Answers document on minimally manipulated ATMPs

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

Scope: draft Questions & Answers. Comments by CAT member until 01 January 2016

Action: for discussion

Note:
The Questions-and-Answers document describes the application of the risk-based approach for minimally manipulated ATMP (e.g. 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 from the standard requirements for cell-based ATMPs as included in Annex I Part IV of Dir. 2001/83/EC.

7.6. Planning and reporting

7.6.1. 2017 forecast of the business pipeline report for the human scientific committees

Scope: fourth quarterly update on the planning estimates of forthcoming marketing authorisation applications for human medicinal products (including advanced therapies)

Action: for information

7.6.2. Action plan following ATMP multi-stakeholder workshop that took place on 27 May 2016

Action: for information

Note: EMA presented to the CAT at its July 2016 meeting both the stakeholders and the regulators reports together with the action plan.

7.7. Others

7.7.1. Policy on handling competing interests for scientific committees members and experts - update

Action: for information

8. Any other business

Date of next CAT meeting:

Wednesday 18 to Friday 20 January 2017

9. Explanatory notes

The notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Abbreviations / Acronyms

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Applicant

MAH: Marketing Authorisation Holder

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

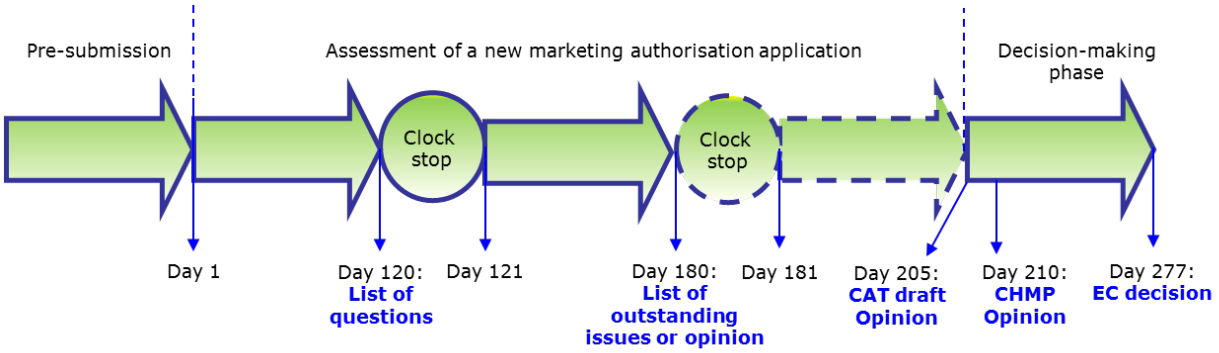
Evaluation of ATMPs (section 2)

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

New applications (sections 2.1. to 2.12.)

Section 2.1 is for ATMPs nearing the end of the evaluation and for which the CAT is expected to adopt a draft **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CAT opinion is transmitted to the CHMP for final adoption. The CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU. More information on the evaluation of ATMPs can be found here.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CAT. The clock stop happens after day 120 and may also happen after day 180, when the CAT has adopted respectively a **Day 120 list of questions** (section 2.3) or a List of outstanding issues to be addressed by the company, which is listed in the agenda under sections 2.7 (**Ongoing evaluation procedures**). Section 2.7 also includes the CAT discussions at any other timepoint of the evaluation procedure of new applications.

Oral explanation (section 2.2.)

Prior to adoption of the CAT opinion, marketing authorisation applicants are normally invited to the CAT plenary meeting to address questions raised by the Committee.

Oral explanations normally relate to ongoing applications, but they can also relate to any other issue for which the CAT would like to discuss with company representatives in person.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.6.)

This section lists applications for new marketing authorisation for ATMPs for which the applicant has requested a re-examination of the opinion previously issued by the CHMP. Similar to the initial evaluation of a marketing authorisation of an ATMP, CAT will adopt a draft re-examination opinion, which is transmitted to the CHMP for final adoption.

Withdrawal of applications (section 2.7.)

This section includes information on marketing authorisation applications that are withdrawn by the applicant. Applicants may decide to withdraw applications at any stage during the assessment and a CAT opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

New applications (section 2.9.)

In this section, information is included on upcoming marketing authorisation applications for ATMPs, as well as information on appointment of Rapporteurs for new ATMP applications.

GMP and GCP Inspections Issues (section 2.10.)

This section lists inspections that are undertaken for ATMPs. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Post-authorisation activities (section 2.12.)

This section lists type II variations, extension application according to Annex I of Reg. 1234/2008, re-examination procedures for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP and other issues concerning authorised medicines that are not covered elsewhere in the agenda such as annual reassessments, 5-year renewals, supply shortages, qualify defects. Issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines, will also be included here.

Certification of ATMPs (section 3)

This section includes the scientific evaluation by the CAT of quality and non-clinical data that small and medium-sized enterprises have generated at any stage of the ATMP development process. More information on the ATMP certification procedure can be found here.

Scientific Recommendation on Classification of ATMPs (section 4)

This section includes the scientific recommendation by the CAT on whether medicines based on genes, cells or tissues meet the scientific criteria that define ATMPs. More information on the ATMP classification procedure, including the outcomes of finalised classifications, can be found here.

Scientific Advice (section 5)

This section includes all scientific advice given to companies during the development of an ATMP. Information related to the number of ATMP related scientific advices discussed by CAT can be found in the CAT Monthly reports. Further information on SAWP can be found here.

Pre-Authorisation (section 6)

Paediatric Investigation Plan (PIP)

This section includes the discussion of an ATMP before a formal application for marketing authorisation is submitted. These cases refer for example to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation: in case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

CAT contributes to the evaluation of a Paediatric Investigation Plan (PIPs) for ATMPs by the Paediatric Committee. These PIPs are included in this section of the Agenda.

ITF Briefing meeting in the field of ATMPs

This section refers to briefing meetings of the Innovation Task Force and International co-operations activities of the CAT

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes of meetings with applicants developing ATMPs and of other ITF meetings of interest to the CAT are included in this section of the agenda. Further information on the ITF can be found here.

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/