03 November 2016
EMA/CAT/707323/2016
Inspections, Human Medicines Pharmacovigilance & Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 03-04 November 2016

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

03 November 2016, 09:00 – 17:30, room 03-E
04 November 2016, 09:00 – 13:00, room 03-E

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 on 03 – 04 November 2016. See November 2016 CAT minutes (to be published post-December 2016 CAT meeting).

1.2. Adoption of agenda

CAT agenda for the 03 - 04 November 2016 meeting

1.3. Adoption of the minutes

CAT minutes of the 06 - 07 October 2016 meeting

1.4. Technical information

2. Evaluation of ATMPs

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No items

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No items

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No items

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2.5. Day 80 Assessment Reports

No items

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No items

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No items

2.8. Withdrawal of initial marketing authorisation application

No items

2.9. Re-examination of initial application procedure 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. Glybera - alipogene tiparvovec; Orphan; EMEA/H/C/002145 - SOB 002.5

UniQure Biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Greg Markey; PRAC Rapporteur: Julie Williams

Scope: an open label, multi-centre trial of Glybera (alipogene tiparvovec) for the treatment of lipoprotein lipase deficiency Patients – Protocol amendment. This is a phase III/IV prospective, interventional, randomised, open-label, parallel group study evaluating the clinical response as well as the dynamics of postprandial chylomicron metabolism in patients treated with Glybera with and without immunosuppressants.

Action: for adoption

Documents:
Assessment report
CAT opinion

2.12.2. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145 – S/57 Annual Re-Assessment (ANN 011)

UniQure Biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Greg Markey; PRAC Rapporteur: Julie Williams

Scope: Clinical and PhV: timetable for 4th Annual Reassessment

Action: 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. Opinions

No items

3.2. Day 60 Evaluation Reports

3.3. Ongoing initial application

No items

3.4. New applications

No items

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4.1. New Requests – Appointment of CAT Co-ordinators

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

Intended for the treatment of amyotrophic lateral sclerosis in adults

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

Action: for adoption

Documents:
Request received 24.10.16

4.1.2. Leukocytes with cancer killing activity; EMA/H0004704

Intended for the treatment of metastatic pancreatic ductal adeno carcinoma

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

Action: for adoption

Documents:
Request received 24.10.16

4.2. Day 30 Co-ordinators' First Reports

4.2.1. 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: Scientific Recommendation

Action: for adoption

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

No items

4.4. Finalisation of Procedure

4.4.1. Autologous bone marrow-derived non-haematopoietic stem cells; EMA/H004661/001

Intended for the treatment of multiple sclerosis

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.2. Anti-BCMA (B-cell Maturation Antigen) Chimeric Antigen Receptor T cells; EMA/H004662/001

Intended for the treatment of multiple myeloma and B cell lymphoma

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.3. Wharton's jelly derived mesenchymal stem cells; EMA/H004676/001

Intended for the treatment of acute myocardial infarction, chonic ishemic heart failure and no-option critical limb ischemia

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.4. Modified vaccinia virus Ankara encoding human mucin 1 and interleukin 2; EMA/H004658/001

Intended for the treatment of advanced non-squamous non-small cell lung cancer

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.5. Autologous human adipose mesenchymal stromal cells; EMA/H004677/001

Intended for the cardiac repair after myocardial infarction

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.6. Autologous skin cell suspension; EMA/H004679/001

Intended for the treatment of burns, donor sites and other wounds

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.7. Rilimogene galvacirepved and rilimogene glafolivec; EMA/H004657/001

Intended for the treatment of metastatic, castrate-resistant Prostate cancer

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.5. Follow-ups and Guidance

No items

5. Scientific Advice

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

5.1. New SAs – Appointment of CAT Rapporteur

5.2. CAT Rapporteurs' Reports

5.3. List of Issues

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 Plan (PIP)

No items

6.2. ITF Briefing Meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

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

6.3.1. Month 0 - Start of the procedure

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6.3.4. Month 3 – Nomination of Rapporteurs

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Scope: DK – Anne Pastoft - new alternate nominated on 12 October 2016

Action: for information

7.1.2. Strategic Review & Learning meeting

CAT Strategic Review & Learning meeting, Dublin, Ireland on 24-25 October 2016

CAT resources: Paula Salmikangas, Maura O'Donovan

Scope: oral report of the meeting

Action: for information

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 October 2016 meeting

Action: for information

Documents:
-Summary of Outcomes

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

7.3.1. Post-authorisation efficacy study (PAES) - scientific guidance

Scope: finalisation of the guidance document

Action: for silent adoption

Document:
-Scientific guidance on post-authorisation efficacy studies
-Overview of comments

Note: public consultation on the draft PAES scientific guidance ended on the 31 January 2016. Comments have been addressed and the guidance revised

7.4. Cooperation within the EU regulatory network

7.4.1. Guideline on Good Pharmacovigilance Practices (GVP) – Module V – Risk management systems (rev. 2)

Scope: two-week consultation with EMA committees. Comments to be sent by 4 November 2016

Action: For information

Note:
-the document was sent to all CAT members on 21.10.16.
-if no major changes are raised, the guidance will be considered endorsed by all committees and sent to the EC for review.
-Good Pharmacovigilance Practices (GVP) webpage (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c#section4)

7.5. Cooperation with international regulators

No items

7.6. CAT Work Plan

7.6.1. CAT 2017 Work Plan

Scope: draft Work Plan 2017

Action: for discussion

7.6.2. Guideline on requirements for investigational ATMPs

CAT drafting groups: Tiina Palomäki (Rapporteur), Ilona Reischl (Rapporteur), Metoda Lipnik-Stangelj, Margarida Menezes Ferreira, Maura O'Donovan, Simona Badoi, Tomáš Boráň, Christiane Niederlaender, Paolo Gasparini, Olli Tenhunen, Marit Hystad, Violaine Closson-Carella, Marcel Hoefnagel, Guido Pantè, Carla Herberts

Scope: draft guideline on the non-clinical and clinical parts

Action: for discussion

7.6.3. 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

Action: for discussion

Note:
The Questions-and-Answers document describes the quality, non-clinical and clinical requirements for the marketing authorisation for a 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 for the standard requirements for cell-based ATMPs as included in Annex I Part IV of Dir. 2001/83/EC.

7.7. Planning and reporting

7.7.1. Management Board data gathering exercise - CAT horizontal data collection

Scope: update on progress. The project started in March 2014 to gather evidence needed by the European Commission in drafting future legislative proposal on fees. The goal was to assemble evidence about the time spent on procedures at EMA and NCAs. The latest part of the projects relate to time spent by committee members/alternates when not acting in their principal role as centralised product rapporteurs/peer reviewers.

Action: For information

7.8. Others

7.8.1. EMA-EuropaBio Information Day 22 November 2016, Canary Wharf, London

Scope: EMA-EuropaBio Information Day, 22 November 2016

Action: for information

Document:
-Agenda

7.8.2. EMA-European Biopharmaceutical Enterprises (EBE). Annual regulatory conference, 16 December 2016, Canary Wharf, London

Scope: *'Optimising the development of ATMPs to meet patient needs'* - The fifth annual regulatory conference organised by the European Biopharmaceutical Enterprises (EBE) in collaboration with the European Medicines Agency (EMA)

Action: for information

Document:
-Agenda

Note: access to further information here:
http://www.ebe-biopharma.eu/calendar/136/46/Optimising-the-Development-of-ATMPs-to-Meet-Patient-Needs-The-fifth-annual-regulatory-conference-organised-by-the-European-Biopharmaceutical-Enterprises-EBE-in-collaboration-with-the-European-Medicines-Agency-EMA

8. Any other business

No items

Date of next CAT meeting:
Thursday 08 to Friday 09 December 2016 (virtual)

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

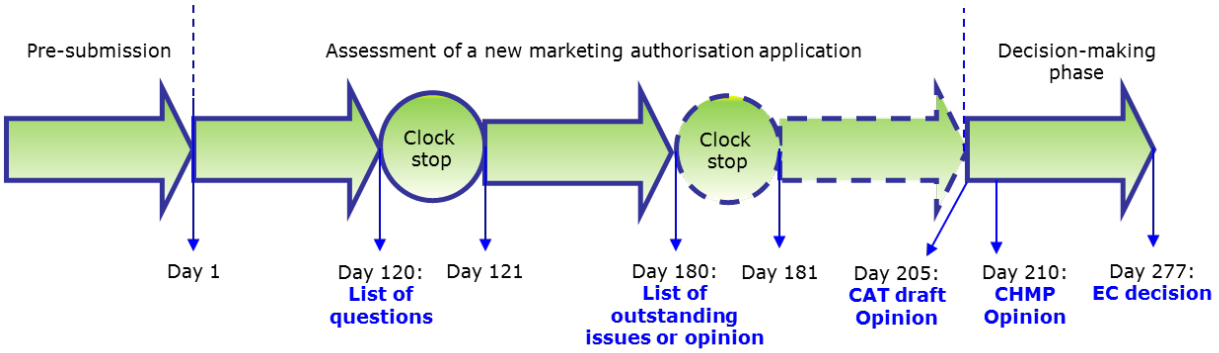
Evaluation of ATMPs (section 2)

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.

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/