15 February 2017
EMA/CAT/126633/2017
Inspections, Human Medicines Pharmacovigilance & Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 15 – 17 February 2017

Chair: vacant; Vice-chair: Martina Schüßler-Lenz

15 February 2017, 15:00 – 19:00, room 03-F
16 February 2017, 09:00 – 18:30, room 03-F
17 February 2017, 09:00 – 12:00, room 03-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

Table of contents

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 15-17 February 2017. See February 2017 CAT minutes (to be published post-March 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for the 15-17 February 2017 meeting

1.3. Adoption of the minutes

CAT minutes for the 18-20 January 2017 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

2.3.1. 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: Day 180 list of outstanding issues

Action: for adoption

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

Intended for the repair of symptomatic articular cartilage defects of the knee and hip (International Cartilage Repair Society [ICRS] grade III or IV) with defect sizes up to 10 cm2 in skeletally mature patients. Treatment is eligible for single as well as multiple adjacent defects. The medicinal product is indicated for adults and adolescents (12-18 years of age) with closed epiphyseal growth plate in the affected joint.

Scope: Day 180 list of outstanding issues

Action: for adoption

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

No items

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

2.11.1. Imlygic – Talimogene laherparepvec; EMA/H/C/002771/II/0008

Amgen Europe B.V.

Rapporteur: Olli Tenhunen; CHMP Coordinator: Tuomo Lapveteläinen

Scope: quality RSI

Action: for adoption

Note: the CAT adopted the evaluation timetable by written procedure in January 2017.

2.12. Other Post-Authorisation Activities

2.12.1. 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

Scope: Opinion

Action: for adoption

Note: opinion on the 4th Annual Reassessment.

2.12.2. Glybera – Alipogene tiparvovec; *Orphan*; EMA/H/C/002145 SOB002.6

UniQure Biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Greg Markey

Scope: second RSI. Clinical and PhV: SOB002.6 (assessment of postprandial chylomicron metabolism in at least 12 patients before 12 months and 24 months after treatment with Glybera to be chosen in addition to the patients included in study CT-AMT.011.02 and eight healthy subjects in the second study)

Action: for adoption

2.12.3. Glybera – Alipogene tiparvovec; *Orphan*; EMA/H/C/002145 SOB002.7

UniQure Biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Greg Markey

Scope: Clinical. Assessment of MAH's response to SOB-002.5: open label, multi-centre trial of Glybera (alipogene tiparvovec) for the treatment of LPLD Patients, as adopted in November 2016. Protocol amendment to phase IV clinical trial.

Action: for adoption of an RSI

2.12.4. Strimvelis - Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence; EMEA/H/C/003854 REC/007

UniQure Biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Greg Markey

Scope: Quality

Action: timetable for adoption

2.12.5. Strimvelis - Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence; EMEA/H/C/003854 -008

UniQure Biopharma B.V.

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

Scope: Quality

Action: timetable for adoption

3. Certification of ATMPs

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

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

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. Implantable continuous glucose monitoring system; EMA/H0004762

Intended for glucose monitoring in diabetes patients

Scope: appointment of CAT Coordinator

Action: for initial discussion

Note: involvement of the EU-Innovation Network / HMA Borderline group on the borderline discussion.

4.1.2. Autologous bone marrow derived mesenchymal stems cells (MSC); EMA/H0004766

Intended for the treatment of coma (brain injury, stroke)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Allogeneic umbilical cord derived mesenchymal stems cells (MSC); EMA/H0004758

Intended for the intervertebral disc degeneration

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

Note: A similar product (MSCs form umbilical cord, adipose tissue or bone marrow) for treatment of amyotrophic lateral sclerosis was classified by CAT in November 2015 (CAT coordinator: Mikuláš Hrubiško).

4.1.4. Stimulated resistant cells suspension cancer vaccine; EMA/H0004763

Intended for the treatment of colorectal cancer

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. rAAV8-TBG-hUGT1A1; EMA/H0004757

Intended for the treatment of Crigler-Najjar (CN) syndrome

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Oncolytic adenovirus, named AdNuPARmE1A; EMA/H0004767

Intended for the treatment of pancreatic cancer

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous tumour-infiltrating lymphocytes (TIL); EMA/H0004741

Intended for the treatment of metastatic melanoma

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

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

Scope: no comments raised by the European Commission

Action: for information

4.4.2. Messenger ribonucleic acid (mRNA) components encoding six non-small cell lung cancer associated antigens; EMA/H0004716

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

Scope: no comments raised by the European Commission

Action: for information

4.4.3. Messenger ribonucleic acid (mRNA) construct encoding the wild type human OX40L protein; EMA/H0004726

Intended for the treatment of solid tumours

Scope: no comments raised by the European Commission

Action: for information

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

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

Scope: no comments raised by the European Commission

Action: for information

4.4.5. 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: no comments raised by the European Commission

Action: for information

4.5. Follow-up and guidance

4.5.1. Leukocytes with cancer killing activity; EMA/H0004704

Intended for the treatment of metastatic pancreatic ductal adeno carcinoma

Scope: comments received from applicant on classification

Action: for discussion

Note: the CAT classified this procedure as non-ATMP at its December 2016 plenary.

5. Scientific Advice (SA)

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

No items

6.2. ITF briefing meetings in the field of ATMPs

No items

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 of eligibility

6.3.4. Month 3 – Nomination of Rapporteurs

6.3.5. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Election for Chairperson to CAT

Scope: election of Chair to take place on 15 February 2017 at 15.00.

Action: election of CAT chair

Candidatures received:

7.1.2. Organisational change in the Scientific Committees Secretariat Service (SCS)

Action: for information

7.1.3. Strategic Review & Learning meeting

CAT Strategic Review & Learning meeting will take place in Gozo, Malta on 1-2 June 2017 under the auspices of the Maltese Presidency of the Council of the European Union

Scope: draft programme

Action: for discussion

7.1.4. 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

7.1.5. Combination packs requirements for ATMPs

CAT resources: Claire Beuneu, Ilona Reischl and Violaine Closson; EMA: Laura Liebers – Regulatory Affairs

Scope: draft eligibility criteria for combination packs, updated to reflect the specificities of ATMPs.

Action: for discussion

7.1.6. Good manufacturing practice (GMP) requirements for ATMPs

Scope: feedback from the European Commission

Action: for information

7.1.7. Good laboratory practice (GLP) requirements for ATMPs

Scope: feedback from the European Commission

Action: for information

7.1.8. Similarity for ATMPs

Scope: feedback from the European Commission

Action: for information

7.1.9. CAT meeting dates 2019 - 2021

Scope: final meeting dates for 2019 – 2021

Action: for adoption

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 January 2017 meeting

Action: for information

7.2.2. Scientific Co-ordination Board (SciCoBo) – meeting of 31 January 2017

CAT: Paula Salmikangas

Action: for information

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

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

Scope: discussion of the comments received.

Action: for discussion

7.4. Cooperation within the EU regulatory network

7.4.1. EDQM/Council of Europe – 3rd edition of the guide to the quality and safety of tissues and cells for human application

CAT: Paula Salmikangas

Scope: invitation to participate in the consultation of the 3rd edition of the Guide to the Quality and Safety of Tissues and Cells for Human Application. Deadline: 20 February 2017.

Action: for discussion

Note: weblink to the consultation:

http://extranet.edqm.eu/dropboxout/0409nKR1KjbrCl40aFo8VdZtzEozYcHdpwkIdtCRPFu/TO%2016%2042-Draft%20TC%20Guide%203rd%20edition.zip

7.4.2. Evaluation of the EU blood and tissue and cells legislation

CAT: Paula Salmikangas

Scope: public consultation on the evaluation of the legislation for blood and tissues and cells. Deadline: 15 February 2017.

Action: for information

Note: weblink to the consultation: https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en

7.4.3. EU regulatory network

Scope: regulatory affairs awareness sessions for 2017

Action: for information

7.5. Cooperation with international regulators

7.5.1. IPRF gene therapy discussion group

Feedback from recent international teleconference calls of the International Pharmaceutical Regulators Forum (IPRF) Gene therapy group

CAT: Paula Salmikangas

Action: for information

7.6. CAT work plan

7.6.1. Questions and Answers document on minimally manipulated ATMPs

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

Scope: draft Questions & Answers

Action: for final 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 on 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 Directive 2001/83/EC.

7.7. Planning and reporting

7.7.1. Issues identified by stakeholders: follow-up from EMA's ATMP workshop, May 2016

Scope: published document

Action: for information

Note: EMA presented the report to the CAT at their December 2016 and January 2017 meetings.

7.8. Others

7.8.1. Sterility testing requirement for cell-based ATMPs

European Directorate for the Quality of Medicines (EDQM): Emmanuelle Charton, Giovanni Migliaccio, Sébastien Jouette

Scope: further to discussions at the January 2017 CAT meeting, a follow-up discussion in the presence of representatives of the EDQM/European Pharmacopoeia on alternative sterility assays will take place

Action: for discussion

8. Any other business

8.1.1. EMA's operation and relocation preparedness - Workstream 2

Scope: operational preparedness

Action: For information

Date of next CAT meeting:
Wednesday 15 to Friday 17 March 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

DNA: Deoxyribonucleic Acid

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

HMA: Heads of Human Agencies

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

MNAT: Multinational Assessment Team

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

RNA: Ribonucleic acid

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

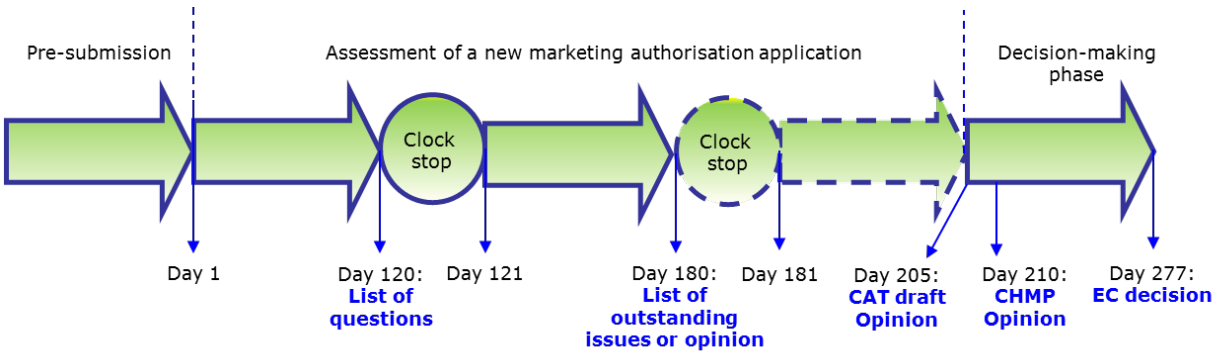
Evaluation of ATMPs (section 2)

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/