06 October 2016
EMA/CAT/662943/2016
Inspections, Human Medicines Pharmacovigilance & Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 06-07 October 2016

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

06 October 2016, 09:00 – 18:00, room 03-E
07 October 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).

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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 6 – 7 October 2016. See October 2016 CAT minutes (to be published post-November 2016 CAT meeting).

1.2. Adoption of agenda

CAT agenda for the 06 - 07 October 2016 meeting

1.3. Adoption of the minutes

CAT minutes of the 08 - 09 September 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 Lists of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Ongoing initial full application

No items

2.7. New applications

No items

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

2.11.1. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/56

UniQure Biopharma B.V.

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Greg Markey

Scope: quality: Opinion

Action: for adoption

2.11.2. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence; *Orphan*; EMA/H/C/003854/II/01/G

UniQure Biopharma B.V.;

Rapporteur: Christiane Niederlaender; CHMP Coordinator: Robert J. Hemmings

Scope: quality: Opinion

Action: for adoption

2.12. Other post-authorisation activities

2.12.1. Glybera - alipogene tiparvovec; Orphan; EMEA/H/C/002145 - SOB 001.6

UniQure Biopharma B.V.

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

Scope: Pharmacovigilance: long term surveillance programme/ disease registry to collect information on the epidemiology of the disease and the demographics, safety, and the effectiveness outcomes of patients treated with Glybera. The patients enrolled in clinical studies (CT-AMT-010 -10, CT-AMT 011-01, CT-AMT 011-02) should be followed up in the LPLD registry. All patients treated with Glybera should be enrolled in the registry and systematic data collection carried out to enrich the database: 1) on efficacy data such as biochemical markers as part of normal practice and frequency and severity of pancreatitis and 2) on safety including immunogenicity against Glybera and LPL. 3) Dietary diary and quality of life data should also be recorded. The diagnosis of LPLD has to be confirmed by genetic testing.

Action: for adoption of the timetable

2.12.2. Holoclar - *ex vivo* expanded autologous human corneal epithelial cells containing stem cells; *Orphan;* EMA/H/C/002450/R/0008

Rapporteur: Egbert Flory; CHMP Coordinator: Jan Mueller-Berghaus; PRAC Rapporteur: Julie Williams

Scope: one-year renewal. Opinion

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

No items

3.3. Ongoing initial application

No items

3.4. New applications

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – appointment of CAT Co-ordinators

4.1.1. 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: appointment of CAT Co-ordinator and adoption of timetable

Action: for adoption

Documents:
Document:
Request received 22.09.16

4.2. Day 30 Co-ordinators' first reports

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

Intended for the treatment of multiple sclerosis

Scope: Scientific Recommendation

Action: for adoption

4.2.2. 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: Scientific Recommendation

Action: for adoption

4.2.3. 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: Scientific Recommendation

Action: for adoption

4.2.4. 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: Scientific Recommendation

Action: for adoption

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

Intended for the cardiac repair after myocardial infarction

Scope: Scientific Recommendation

Action: for adoption

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

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

Scope: Scientific Recommendation

Action: for adoption

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

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

Scope: Scientific Recommendation

Action: for adoption

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

No items

4.4. Finalisation of procedures

4.4.1. Genetically-modified *Lactobacillus reuteri* bacteria, with a plasmid containing the gene for human CXCL12-1a with an inducible promoter; EMA/H004673/001

Intended for wound healing of chronic ulcers in patients with diabetes

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.2. Autologous cells of stromal vascular fraction (SVF) and autologous adipose derived stem cells; EMA/H004683/001

Intended for the treatment of treatment of cutis laxa senilis

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.3. Tumour selectively replicating oncolytic adenovirus expressing tumor necrosis factor alpha (TNFα) and interleukin 2 (IL2); EMA/H004684/001

Intended for the treatment of metastatic melanoma and other solid tumors

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.4. Natural killer group 2D autologous engineered T cells; EMA/H004680/001

Intended for the treatment of various tumour types (solid and liquid)

Scope: no comments from the EC

Action: for information

Document:
ATMP classification report

4.4.5. DNA plasmid vectors encoding for human papillomavirus type 16 consensus E6 and E7 antigens and HPV type 18 consensus E6 and E7 antigens; EMA/H004685/001

Intended for the treatment of HPV-16 and 18 related high-grade squamous intraepithelial lesions (HSIL) of the cervix and vulva

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 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

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. 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: agreement on topics for the agenda

Action: for discussion

Document:
Draft agenda

Note: preliminary agenda/proposed topics: new medical device legislation, genetically modified organism (GMO) issue including the wording for product information, use of real world data and registries.

Note: CAT members are asked to propose agenda topics:

7.1.2. Recommendation on criteria for competence and expertise of CAT members and alternates

Action: for discussion

Documents:
-Briefing note on competence and expertise of CAT members and alternates
-Annex B: CAT-EMA recommendation on criteria for competence and expertise of new CAT members. This annex will be added to nomination invitation letters to the Members State when a new member or alternate is to be appointed
-CAT Areas of Expertise
-CAT Criteria for Expertise and Experience

7.1.3. GMP requirements for ATMPs

Scope: Next steps

Action: for discussion

7.1.4. Combination packs requirements for ATMPs

Scope: in line with Notice to Applicants Chapter 1, 'combination packs' are to be understood as a combination of active substances, where the active substances are included in separate pharmaceutical forms which are included in the same package. The same document foresees that combination packs would be very exceptional and strictly related to public health, and not be for convenience or commercial purposes.

Action: for discussion

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 September 2016 meeting

Action: for information

Documents:
-Summary of Outcomes

7.2.2. Review of experience with the Early Background Summary

Action: for information

Note: at the plenaries end of 2015, the committees agreed to perform a review of experience with the Early Background Summaries. A survey amongst CAT/CHMP/PRAC assessors was conducted following the pilot starting at the end of 2014.

7.3. Co-ordination with EMA Working Parties / Working Groups / Drafting Groups

7.3.1. PCWP and HCPWP membership

Scope: call of interest for nomination of CAT representatives

Action: for nomination

7.3.2. Extrapolation Working Group

Scope: report on public workshop on extrapolation of efficacy and safety in medicine development across age groups

Action: For information

Note: the report will be published end of October 2016.

7.4. Co-operation within the EU regulatory network

7.4.1. Environmental assessment for gene therapy products

Scope: feedback by the European Commission representative

Action: for information

Note: topic discussed at the Strategic Review and Learning meeting in Utrecht (1-2 June 2016. See June 2016 CAT meeting minutes, item 7.1.1.

7.4.2. European Medicines Agencies Group on the Co-operation on Legal and Legislative Issues (EMACOLEX). Meeting in Uppsala (Sweden), 8 -9 September 2016

Scope: feedback by the European Commission representative

Action: for information

7.5. Co-operation with international regulators

7.5.1. ATMP cluster teleconference with FDA, Health Canada and PMDA (Japan)

The teleconference will take place during the plenary meeting on Thursday 6 October from 14.00hrs – 15.00hrs

CAT resource: Paula Salmikangas

Action: for adoption

Document table:
Agenda

7.6. CAT Work Plan

7.6.1. 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: feedback on the break-out meeting held on 5 and 6 October 2016

Action: for information

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, Marit Hystad, Mikuláš Hrubiško

Scope: feedback on the break-out meeting held on 5 and 6 October 2016

Action: for information

Note:
The Questions-and-Answers will describe 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.

7.6.3. CAT Workshop on cell-based cancer immunotherapies, EMA, London, 15-16 November 2016

CAT resources: Rune Kjeken, Björn Carlsson

Action: for information

7.7. Planning and reporting

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

Postponed to November 2016

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

7.7.2. Planning estimates of Q3/2016 ATMP MAAs

Action: for information

7.8. Others

No items

8. Any other business

No items

Date of next CAT meeting:
Thursday 03 to Friday 04 November 2016

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

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

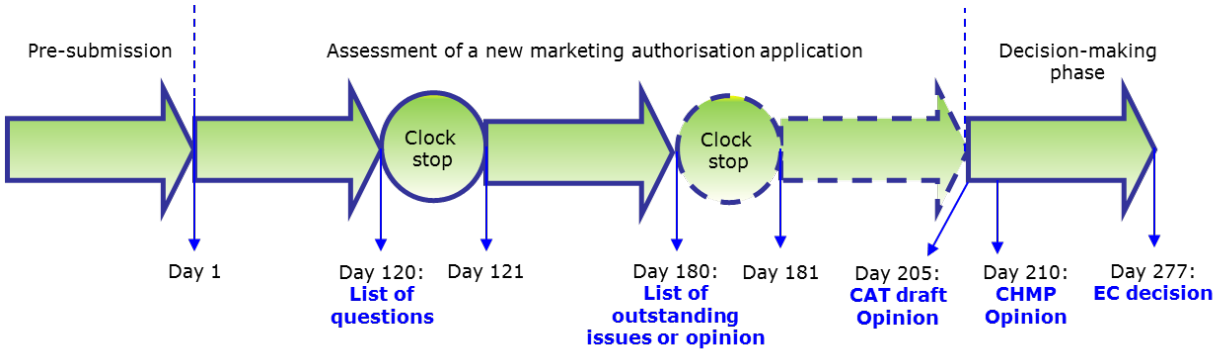
Evaluation of ATMPs (section 2)

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/