08 September 2017
EMA/CAT/599328/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 06-08 September 2017

Chair: Martina Schüßler-Lenz; Vice-Chair: Ilona Reischl

06 September 2017, 10:00 – 18:30, room 02-A

07 September 2017, 09:00 – 18:30, room 02-A

08 September 2017, 09:00 – 12:00, room 02-A

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 06-08 September 2017. See September 2017 CAT minutes (to be published post-October 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for the 06-08 September 2017 meeting

1.3. Adoption of the minutes

CAT minutes for the 12-14 July 2017 meeting

1.4. August 2017 Written Procedure

CAT minutes of the August 2017 Written Procedure

1.5. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

2.4.1. Haploidentical donor lymphocytes depleted of alloreactive T cells, donor T-lymphocytes depleted ex vivo of host alloreactive T-cells- Orphan - EMEA/H/C/002397

Kiadis Pharma Netherlands B.V.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: D120 List of questions

Action: for adoption

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

2.6.1. Axicabtagene ciloleucel – Orphan - EMA/H/0004480

Kite Pharma UK Ltd; treatment of B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

Scope: timetable for assessment

Action: for information

2.6.2. Voretigene neparvovec - Orphan - EMEA/H/C/0004451

Spark Therapeutics Ireland Ltd.; treatment of patients with vision loss due to leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

Scope: timetable for assessment

Action: for information

2.7. New applications

No items

2.8. Withdrawal of initial marking 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

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

2.11.1. Zalmoxis – allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (δlngfr) and the herpes simplex in virus thymidine kinase (hsv-tk mut2) – Orphan - EMEA/H/C/002801/II/0005/G

MolMed SpA; adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies

Rapporteur: Hans Ovelgönne; CHMP Coordinator: Paula Boudewina van Hennik

Scope: Quality

Action: timetable for adoption

2.12. Other Post-Authorisation Activities

2.12.1. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854/REC/010

GlaxoSmithKline Trading Services Limited

Rapporteur: Christiane Niederlaender, CHMP Coordinator: Robert James Hemmings

Scope: Quality:

Action: for information

3. Certification of ATMPs

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

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogenic cardiopoietic cells derived from adipose tissue derived stem cells (ADSC) purified from healthy donor's lipoaspirate – H0004911

Intended to help post - yocardial infarction patients in restoring cardiac function by targeting for repair the underlying myocardium damage

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Recombinant adeno-associated virus serotype 2/1 vector encoding human β-hexosaminidase alpha & beta subunits (rAAV2/1 Hex alpha & beta) – H0004906

Intended for the treatment of Tay-Sachs disease & Sandhoff disease monosialic ganglioside 2 (GM2) gangliosidosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Adeno-associated virus (AAV) vector serotype 8 expressing human low-density lipoprotein receptor (hLDLR) - H0004905

Intended for the treatment of hypercholesterolaemia caused by homozygous mutations in the low density lipoprotein receptor (LDLR) gene

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Skin tissue – H0004907

Intended for the treatment of patients with acute complex skin loss

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Autologous CD34+ cells, freshly isolated – H000

Cells will be used to contribute the regeneration of soft and hard tissues of temporomandibular joints through their immunological action

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Autologous dental pulp stem cells (DPSC), freshly isolated – H000

Intended for the regeneration of soft and hard tissues of temporomandibular joints

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. Cultured dental pulp stem cells (DPSC) – H000

Intended for the regeneration of soft and hard tissues of temporomandibular joints

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Allogeneic human glial-restricted precursors - H0004887/0001

Intended for the treatment of amyotrophic lateral sclerosis

Scope: scientific recommendation

Action: for adoption

4.2.2. Allogeneic human glial-restricted precursors - H0004898/0001

Intended for the treatment of spinal cord injuries

Scope: scientific recommendation

Action: for adoption ribonucleic acid (RNA) molecules small interfering

4.2.3. Nuclease-resistant, synthetic double-stranded, small interfering ribonucleic acid (siRNA) designed to temporarily inhibit the expression of the collagen-specific chaperone, heat shock protein 47 (HSP47) - H0004900/0001

Intended for the treatment of hepatic fibrosis

Scope: scientific recommendation

Action: for adoption

4.2.4. Messenger RNA encoding immunostimulatory proteins constitutively active Toll-like receptor 4 (caTLR4), cluster of differentiation 40 ligand (CD40L) and cluster of differentiation 70 (CD70) and tumour associated antigens (TAA) tyrosinase, gp100, MAGE A3, MAGE C2 and PRAME - H0004899/0001

Intended for the treatment of melanoma

Scope: scientific recommendation

Action: for adoption

4.2.5. Cultured viable chondrocytes in a 3-dimensional hydrogel - H0004901/0001

Intended for the treatment of articular cartilage defect of the knee

Scope: scientific recommendation

Action: for adoption

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

No items

4.4. Finalisation of procedure

No items

4.5. Follow-up and guidance

No items

5. Scientific Advice

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 Rapporteurs

5.2. CAT reports

5.3. List of Issues

5.4. Finalisation of SA procedures

6. Pre-Authorisation Activities

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

6.1. Pediatric investigation plans

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

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting – Tallinn, Estonia, 15-17 November 2017

CAT Strategic Review & Learning meeting (SRLM) will take place in Tallinn, Estonia on 15-17 November 2017 under the auspices of the Estonian Presidency of the Council of the European Union

CAT: Toivo Maimets, Martina Schüßler-Lenz

Scope: topics for the first draft of the programme

Action: for discussion

7.1.2. Multinational Assessment Team (MNAT) concept: the next phase – broadening the concept to the post-authorisation phase

Scope: broadening the concept to the post-authorisation phase

Action: For information

Note: the broadening of the MNAT concept to post-authorisation was adopted by EMA Management Board in December 2016.

7.2. Coordination with EMA Scientific Committees

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

Scope: Summary of Outcomes (SoO) for 14-17 August 2017 Written Procedure

Action: for information

7.2.2. Pharmacovigilance Risk Assessment Committee (PRAC)

Scope: comments on post consultation on *'Guideline on good pharmacovigilance practices (GVP), Module XV – Safety communication (Rev 1)'* should be sent by 18 September 2017

Action: for information

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

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

Scope:
-Report on the workshop on personalised medicines
-Draft agenda AMR workshop - 19 September 2017
-Draft agenda PCWP-HCPWP – 20 September 2017

Action: for information

7.4. Cooperation within the EU regulatory network

No items

7.5. Cooperation with international regulators

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

CAT: Martina Schüßler-Lenz

Scope: draft agenda

Action: for adoption

7.6. CAT work plan

7.6.1. Expert meeting on adeno-associated viral vectors, 06 September 2017, EMA, London

CAT: Martina Schüßler-Lenz

Scope: feedback on the expert meeting that will take place on the first day of the CAT, 6 September 2017

Action: for information

7.6.2. Expert meeting on genome editing, 18 October 2017, EMA, London

CAT: Paolo Gasparini

Scope: updated agenda

Action: for information

This meeting is open to all CAT members. Alternatively, members can join virtually (via Adobe Connect application).

7.6.3. CAT 2017 work plan

Scope: status of the CAT work plan

Action: for information

Note: Work plan was adopted via written procedure on 22 March 2017

7.6.4. CAT 2018 work plan

Scope: proposals for the CAT work plan 2018

Action: for discussion

7.7. Planning and reporting

7.7.1. Update on ongoing ATMP-related activities

CAT: Martina Schüßler-Lenz

Scope: at the publication on 2 February 2017 of the document 'Issues identified by stakeholders: follow-up from EMA's ATMP workshop', the development of a broader EU plan, prepared jointly by EMA, CAT, the European Commission and the National Competent Authorities was announced. CAT members are asked for their contributions and input.

Two documents are tabled: the 'List of proposed actions to improve the regulatory framework for ATMPs' from the Commission and an EMA working document (based on the above mentioned document published in February 2017) 'Update on ongoing ATMP-related activities'.

Action: for discussion

7.8. Others

7.8.1. Interaction with EBMT

Proposal for a meeting with EBMT in the margins of the December 2017 CAT meeting, with the involvement of PRAC members, to discuss amongst others, a common protocol for registries for CAR-T cells

CAT: Martina Schüßler-Lenz

Action: for discussion

8. Any other business

No items

Date of next CAT meeting:
04-06 October 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

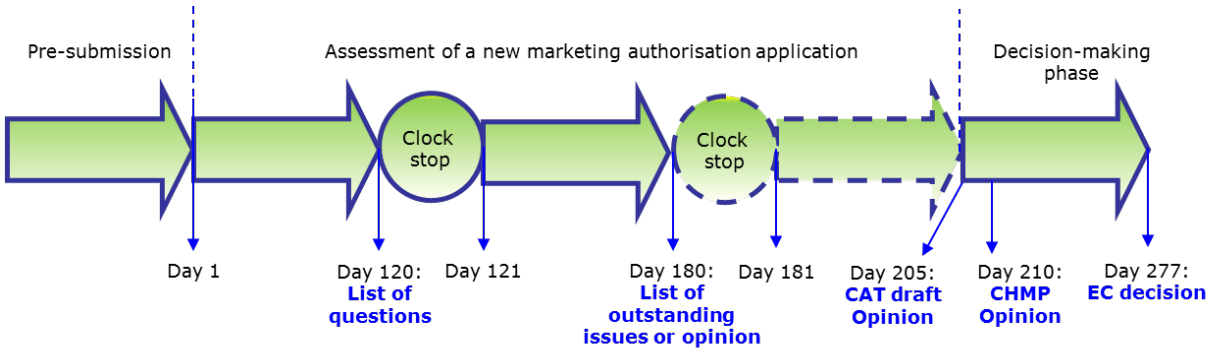
Evaluation of ATMPs (section 2)

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.

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/