10 May 2017
EMA/CAT/303936/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 10-12 May 2017

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

10 May 2017, 14:00 – 18:30, room 02-A

11 May 2017, 09:00 – 18:30, room 02-A

12 May 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).

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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 10-12 May 2017. See May 2017 CAT minutes (to be published post June 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 10-12 May 2017 meeting

1.3. Adoption of the minutes

CAT minutes for 10-12 April 2017 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736

Claimed indication: repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (International Cartilage Repair Society [ICRS] grade III or IV) with defect sizes up to 10 cm^2 in adults

Scope: Opinion

Action: for adoption

List of Outstanding Issues adopted on 17.02.2017. and 12.04.2017. List of Questions adopted on 19.04.2013.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue; Orphan; EMA/H/C/0004258TiGenix S.A.U.; Treatment of complex perianal fistula(s)

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 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

No items

2.12. Other Post-Authorisation Activities

2.12.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/MEA/006

Amgen Europe B.V.; Indicated for the treatment of adults with unresectable melanoma that is regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a) with no bone, brain, lung or other visceral disease

Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen

Scope: extension of the submission time (from February 2021 to October 2021) of study 20120324 (category 3): a phase 2, multicenter, single-arm trial to evaluate the biodistribution and shedding of talimogene laherparepvec in subjects with unresected, stage IIIB to IVM1c melanoma.

Action: for adoption

Note: Extension agreed by Rapporteur in Variation IB/0007

See also 2.12.2. and 5.1.4.

2.12.2. Imlygic – ta imogene laherparepvec - EMEA/G/C/2771/PSUSA/10459/201610

Amgen Europe B.V.; Indicated for the treatment of adults with unresectable melanoma that is

regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a) with no bone, brain, lung or other visceral disease.

Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen

Scope: PRAC assessment of PSUSA, of the following adverse event: fatal event of arterial haemorrhage/carotid blow out syndrome following administration of Imlygic

Action: for information

See also 2.12.1. and 5.1.4.

2.12.3. Glybera - Alipogene tiparvovec; Orphan; EMA/H/C/002145/R/0062

UniQure; Indicated for the long term correction of lipoprotein lipase deficiency, to control or abolish symptoms and prevent complications in adult patients clinically diagnosed with lipoprotein lipase deficiency (LPLD)

Rapporteur: Christiane Niederlaender; Co-Rapporteur: Egbert Flory; CHMP Coordinators: Greg Markey, Jan Mueller-Berghaus

Scope: Formal notification letter by the MAH informing the EMA of the withdrawal of the 5-year renewal application in view of allowing the marketing authorisation to expire on 25 October 2017 based on economic reasons

Action: for information

2.12.4. Zalmoxis – Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ðlngfr) and the herpes simplex i virus thymidine kinase (hsv-tk mut2); Orphan; EMEA/H/C/002801/R/0003

MolMed SpA; Treatment of 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: 1st annual reassessment for renewal of conditional MA. Opinion

Action: for adoption

Note: CAT adopted an RSI at is 10-12 April 2017 meeting

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

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 Coordinator

4.1.1. Stromal vascular fraction cells for autologous use; EMA/H0004838

Intended for the relief of symptoms of osteoarthritis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Autologous human keratinocytes; EMA/H0004841

Intended for the treatment of burns and chronic, severe wounds

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Autologous human chondrocytes; EMA/H0004840

Intended for the repair of single symptomatic cartilage defect of the knee or ankle

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Allogeneic human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSC); EMA/H0004839

Intended for the treatment of atopic dermatitis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous adipose derived mesenchymal stem cells; EMA/H0004813

Intended for the treatment of chronic wound

Scope: scientific recommendation

Action: for adoption

4.2.2. Allogenic human mesenchymal stem cells - Mesenchymal stem cells isolated from umbilical cord; EMA/H0004815

Intended for the treatment of chronic obstructive pulmonary disease

Scope: scientific recommendation

Action: for adoption

4.2.3. Bilayer, engineered, collagen hydrogel-based skin graft composed of autologous keratinocytes and fibroblasts; EMA/H0004817

Intended for the treatment of partial deep dermal and full thickness burn wounds

Scope: scientific recommendation

Action: for adoption

4.2.4. Replication incompetent adenoviral serotype 5 vector encoding the human interleukin-12 p70 (hIL-12) transgene under the control of the activator ligand, veledimex; EMA/H0004805

Intended for the treatment of recurrent or progressive glioblastoma

Scope: scientific recommendation

Action: for adoption

4.2.5. Adenovirus-associated viral vector serotype 5 containing CRISPR Cas9 and guide ribonucleic acids (RNAs) targeting intron 26 of the centrosomal protein 290 gene (AAV5-GRK1-SauCas9-CEP290gRNA 323/64); EMA/H0004818

Intended for the treatment of patients aged 3 years and older with Leber congenital amaurosis type 10 (LCA10) caused by a homozygous or compound heterozygous intron 26 mutation, c.2991+1655 A>G, in the CEP290 gene

Scope: scientific recommendation

Action: for adoption

4.2.6. Autologous human adipose perivascular stromal cells genetically modified to secrete soluble tumour necrosis factor-related apoptosis-inducing ligand (sTRAIL); EMA/H0004820

Intended for the treatment of TRAIL-sensitive cancers such as Ewing sarcoma and pancreatic ductal adenocarcinoma

Scope: scientific recommendation

Action: for adoption

4.2.7. Resorbable, viscoelastic matrix for use with autologous stromal vascular fraction (SVF); EMA/H0004819

A resorbable matrix to be used for the delivery of autologous SVF adipose derived cells for the treatment of HIV-related facial lipoatrophy

Scope: scientific recommendation

Action: for adoption

4.2.8. Allogeneic unexpanded amniotic fluid derived cells suspended with dried and cryofractured amniotic tissue; EMA/H0004816

Intended for the treatment of chronic wound care

Scope: scientific recommendation

Action: for adoption

4.2.9. Human autologous stromal vascular fraction (SVF); EMA/H0004822

Intended for the treatment of articular cartilage and bone defects

Scope: scientific recommendation

Action: for adoption

4.2.10. Human autologous adipose-derived stromal/stem cells (ADSCs); EMA/H0004823

Intended for the treatment of articular cartilage and bone defects

Scope: scientific recommendation

Action: for adoption

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

4.3.1. Cultured autologous Wharton jelly derived mesenchymal stem cells; EMA/H0004795

Intended for the treatment of amyotrophic lateral sclerosis (ALS)

Scope: revised scientific recommendation

Action: for adoption

4.3.2. Cultured allogeneic Wharton jelly derived mesenchymal stem cells; EMA/H0004796

Intended for the treatment of amyotrophic lateral sclerosis (ALS)

Scope: revised scientific recommendation

Action: for adoption

4.3.3. Cultured autologous adipose derived regenerative mesenchymal stem cells; EMA/H0004797

Intended for the treatment of autoimmune drug resistant epilepsy

Scope: revised scientific recommendation

Action: for adoption

4.3.4. Autologous adipose derived mesenchymal stem cells; EMA/H0004798

Intended for the treatment of autoimmune drug resistant epilepsy

Scope: revised scientific recommendation

Action: for adoption

4.3.5. Cultured autologous adipose derived mesenchymal stem cells - EMA/H0004799

Intended for the treatment of autoimmune drug resistant epilepsy

Scope: revised scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Stimulated resistant cells suspension cancer vaccine; H0004763

Colorectal cancer

Scope: revised scientific recommendation following comments by the European Commission

Action: for adoption

4.4.2. Human induced pluripotent stem cell derived natural killer cells expressing high-affinity non-cleavable CD16 Fc; EMA/H0004784

Intended for the treatment of advanced solid tumour malignancies

Scope: No comments raised by the European Commission

Action: for information

4.5. Follow-up and guidance

No items

5. Scientific Advice

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

5.1. New requests – appointment of CAT Coordinators

5.2. CAT 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

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 1 – Discussion of eligibility

No items

6.3.2. Month 2 – Recommendation of eligibility

6.3.3. Month 3 – Nomination of Rapporteurs

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting – Malta, June 2017

CAT Strategic Review & Learning meeting (SRLM) 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 information

7.1.2. Good manufacturing practice for advanced therapy medicinal products

Scope: feedback from drafting group 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 18-21 April 2017 meeting

Action: for information

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

7.3.1. Guideline on quality, non-clinical and clinical aspects of gene therapy medicinal products

CAT: drafting group members

Scope: feedback on the revision of the guideline by the DG in their meeting of 10 May 2017

Action: for discussion

Drafting group composition:
-Quality: M. Menezes-Ferreira, C. Niederlaender, S. Ruiz and P. Salmikangas
-Non-clinical: K. Breen, B. Sarkadi, M. Renner, Tiina Palomäki
-Clinical: P. Gasparini, B. Klug, M. Hystad, O. Tenhunen, B. Gänsbacher

7.3.2. Guideline on genetically modified cells

CAT: Marcos Timón, Paolo Gasparini, Olli Tenhunen

Scope: review of draft concept paper; call for additional clinical expertise to join the drafting group

Action: for discussion

7.4. Cooperation within the EU regulatory network

7.4.1. Orphan similarity for ATMPs

CAT drafting group: Simona Badoi, Violaine Closson-Carella, Michele Lipucci, Margarida Menezes-Ferreira, Christiane Niederlaender, Ilona Reischl, Paula Salmikangas

Scope: Reflection from the perspective of ATMPs on the concept of 'similar active substance' as referred to in Art 3(3)c of Reg (EC) No 847/2000 of April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concept 'similar medicinal product' and 'clinical superiority'. Review of comments received from the public consultation.

Action: for adoption

Consultation document published by the European Commission

http://ec.europa.eu/health/sites/health/files/files/orphanmp/2016_07_pc_orphan/2016_07_consultation_paper.pdf

7.5. Cooperation with international regulators

7.5.1. International Pharmaceutical Regulators Forum (IPRF) gene therapy working group (GTWG)

Scope: feedback from the meeting of 2-3 May 2017 on the topic of IPRF biodistribution reflection paper studies

Action: for information

7.6. CAT work plan

7.6.1. Expert meeting on adeno-associated viral vectors

Scope: feedback from the organising committee

Action: for information

Note: expert meeting to take place on 06 September 2017

7.7. Planning and reporting

None

7.8. Others

7.8.1. EMA framework of collaboration with academia

Scope: presentation on the scope, objectives and methodology

Action: for information

Note: The EMA's management board adopted the framework on 16 March 2017

7.8.2. EMA's ATMP matrix team

Scope: presentation of the new EMA – ATMP team

Action: for discussion

8. Any other business

No items

Date of next CAT meeting:
14-16 June 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

EDQM: European Directorate for the Quality of Medicines

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

GTMP: Gene therapy medicinal product

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

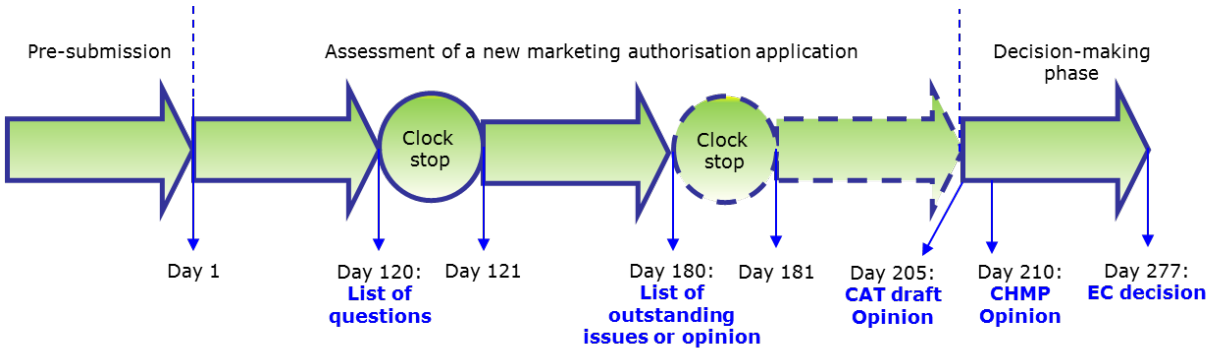
Evaluation of ATMPs (section 2)

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/