10 October 2018
EMA/CAT/709578/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 10-12 October 2018

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

10 October 2018, 14:30 – 17:30, room 03-E

11 October 2018, 09:00 – 17:00, room 03-E

12 October 2018, 09:00 – 12:00, room 03-E

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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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 October 2018. See October 2018 CAT minutes (to be published post-November 2018 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 10-12 October 2018 meeting

1.3. Adoption of the minutes

CAT minutes for 12-14 September 2018 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

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

2.6.1. Viable 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: request by the applicant for a clock stop extension .

Action: for adoption

Oral Explanation took place on 12.09.2018. List of Outstanding Issues adopted on 14.09.18 and 25.05.2018. List of Questions adopted on 08.09.2017.

2.7. New applications

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

No items

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/ANX/001

Amgen Europe B.V.; treatment of 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: clinical: submission of the preliminary results

of Study 20120325 (a phase 2, multicenter, open-label, single-arm trial to evaluate the correlation between objective response rate and baseline intratumoral CD8+T-lymphocyte density in subjects with unresected stage IIIB to IVM1c melanoma treated with talimogene laherparepvec). Assessment Report

Action: for adoption

2.12.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090

Novartis Europharm Limited; treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL)

Rapporteur: Rune Kjeken, Co-Rapporteur: Christiane Niederlaender, CHMP Coordinators: Bjorg Bolstad and Greg Markey

Scope: quality

Action: for information

2.12.3. Holoclar - *Ex vivo* expanded autologous human corneal epithelial cells containing stem cells - Orphan - EMEA/H/C/002450/R/0021

Chiesi Farmaceutici S.p.A.

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

Scope: 4th annual reassessment for renewal of marketing authorisation. Opinion/RSI

Action: for adoption

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. Allogeneic Wharton's jelly mesenchymal stem cells (MSCs) on dermal scaffold - H0005198

Intended for the treatment of epidermolysis bullosaScope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Genetically modified bone marrow derived allogeneic mesenchymal stem cells (MSCs) expressing human alpha-1 antitrypsin (AAT) - H0005206

Intended for the treatment of steroid refractory acute graft-versus-host-disease (GvHD), grades II-IV

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Suspension of human olfactory ensheathing cells (OECs) and olfactory nerve fibroblasts (ONFs) – H0005197

Indicated for the treatment of complete and incomplete spinal cord injuries in human patients, aiming to support neuroregeneration

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Whole lipoaspirate containing viable autologous adipose-derived regenerative cells - H0005212

Intended for the treatment of progressive hemifacial atrophy (Parry-Romberg syndrome)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Viable autologous adipose-derived regenerative cells (Celution Technology) combined with whole lipoaspirate - H0005213

Intended for the treatment of progressive hemifacial atrophy (Parry-Romberg syndrome)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Viable autologous adipose-derived regenerative cells (Lipogems Technology) combined with whole lipoaspirate - H0005214

Intended for the treatment of progressive hemifacial atrophy (Parry-Romberg syndrome)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. Whole lipoaspirate containing viable autologous adipose-derived regenerative cells - H0005215

Intended for the treatment of burn scars

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. Viable autologous adipose-derived regenerative cells (Celution Technology) - H0005216

Intended for the treatment of burn scars

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.9. Viable autologous adipose-derived regenerative cells (Lipogems Techonology) - H0005217

Intended for the treatment of burn scars

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.10. Human donor haematopoietic stem cells treated *ex vivo* - H0005195

Intended for the treatment of severe combined immunodeficiency

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.11. Recombinant adeno-associated virus serotype 1 (AAV1) containing a transgene that encodes a microRNA (miRNA) targeting huntingtin - H0005196

Intended for the treatment of Huntington's disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Allogeneic Epstein-Barr virus (EBV)-specific cytotoxic T cells – H0005168

Intended for the treatment of refractory / relapsed EBV-associated post-transplant lymphoproliferative disease (PTDL)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Autologous bone marrow derived mesenchymal stem cells – H0005176

Intended for the treatment of ischemic stroke

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Autologous bone marrow derived mesenchymal stem cells – H0005177

Intended for the regeneration of cartilage, ligamentum bone and muscle defects

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Codon-optimised human cystic fibrosis transmembrane conductance regulator messenger ribonucleic acid complexed with lipid-based nanoparticles – H0005111

Intended for the treatment of cystic fibrosis

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Adeno-associated virus (AAV) vector containing a human neuronal ceroid lipofuscinosis (CLN2) (hCLN2) expression cassette encoding for the soluble lysosomal enzyme tripeptidyl-peptidase 1 (TPP1) – H0005160

Intended for the treatment of late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease

Scope: ATMP scientific recommendation

Action: for adoption

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

No items

4.4. Finalisation of procedure

4.4.1. Genetically modified adeno-associated virus 9 (AAV9) expressing short hairpin RNA (shRNA) targeting mutant polyadenylate RNA binding protein nuclear 1 (PABPN1) as well as a codon-optimised shRNA-insensitive wildtype poly(A) binding protein nuclear 1 (PABPN1) - H0005142

Intended for the treatment of oculopharyngeal muscular dystrophy

Scope: the European Commission raised editorial comments. Revised final ATMP scientific recommendation

Action: for information

4.4.2. Organ donor derived haematopoietic stem cells and defined dose of donor-derived immune cells - H0005143

Intended for the treatment of solid organ transplantation

Scope: the European Commission raised minor comments. Revised final ATMP scientific recommendation

Action: for information

4.4.3. Stromal vascular fraction - H0005151

Intended for the regeneration of epithelial fibrosis as a result of vulvar lichen sclerosis

Scope: the European Commission raised editorial comments. Revised final ATMP scientific recommendation

Action: for information

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. 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 0 - Start of the procedure

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Denmark: Anne Pastoft becomes the member and Nanna Aaby Kruse becomes the alternate from 06 October 2018

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) from the September 2018 meeting

Action: for information

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

7.3.1. Guideline on requirements for investigational ATMPs

Drafting group: Ilona Reischl (Rapporteur), Tiina Palomäki (Rapporteur), Martina Schüßler-Lenz, Simona Badoi, Tomáš Boráň, Violaine Closson-Carella, Paolo Gasparini, Carla Herberts, Metoda Lipnik-Stangelj, Margarida Menezes Ferreira, Christiane Niederlaender, Maura O'Donovan, Olli Tenhunen, Barbara Bonamassa, Giuseppa Pistritto, Marcel Hoefnagel

Scope: update on progress

Action: for information

7.3.2. Organising Committee on EMA/FDA workshop on quality support to PRIME/Breakthrough, 26 November 2018

Scope: update on the organisation of the workshop. Draft agenda and case study selection

Action: for discussion

7.3.3. Scientific Advice Working Party (SAWP)

Scope: call for nomination of CAT members to join the SAWP

Action: for agreement

7.4. Cooperation within the EU regulatory network

None

7.5. Cooperation with international regulators

None

7.6. CAT work plan

7.6.1. Genome editing technologies on drug development editing

CAT: Martina Schüßler-Lenz

Scope: publication on the EMA's website of the report on the genome editing expert meeting organised by CAT and the CHMP's Pharmacogenomics Working Party (PGWP) that took place in October 2017.

Action: for information

Note: the report can be found here

7.6.2. Genome editing technologies on drug development editing – regulatory considerations

Scope: feedback from the drafting group discussion of 01.10.2018.

Action: for discussion

7.7. Planning and reporting

None

7.8. Others

7.8.1. Concepts of significant benefit (follow-up to CHMP/COMP/PDCO Work Plan 2017)

Action: For information

8. Any other business

Date of next CAT meeting:
07-09 November 2018

9. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

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

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HMA: Heads of Medicines 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 Application

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

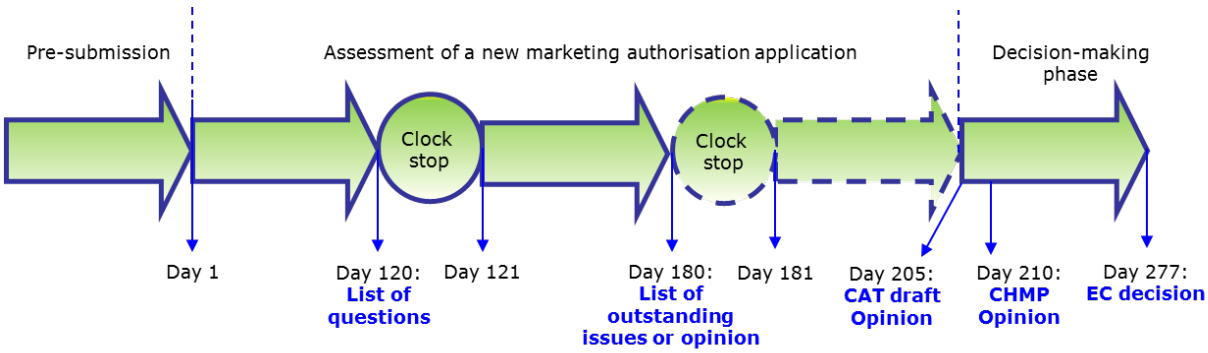
Evaluation of ATMPs (section 2)

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/