23 May 2018
EMA/CAT/352923/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 23-25 May 2018

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

23 May 2018, 14:00 – 18:30, room 03-E

24 May 2018, 09:00 – 18:30, room 03-E

25 May 2018, 09:00 – 13:00, 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 on 23-25 May 2018. See May 2018 CAT minutes (to be published post-June 2018 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 24-25 May 2018 meeting

1.3. Adoption of the minutes

CAT minutes for 18-20 April 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

2.3.1. ATIR101 - 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: Day 180 list of outstanding issues

Action: for adoption

List of questions adopted on 08.09.2017.

2.3.2. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451

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

Scope: Day 180 list of outstanding issues

Action: for adoption

List of questions adopted on 08.12.2017.

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

Accelerated assessment

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

Scope: Day 180 list of outstanding issues

Action: for adoption

List of questions adopted on 16.03.2018.

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

No items

2.7. New applications

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

2.11.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0020

Amgen Europe B.V.

Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen

Scope: Safety: Opinion

Update of section 4.8 of the SmPC in order to add the new adverse drug reaction 'hypersensitivity' with a frequency allocation of 'unknown'. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a minor editorial change in section 3 of the SmPC in order to clarify that the current description of the liquid applies to both strengths, and minor changes in section 4.4 of the SmPC and the Package Leaflet regarding sorbitol and sodium subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017).

Action: for adoption

2.11.2. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0002/G

CO.DON AG

Rapporteur: Lisbeth Barkholt; CHMP Coordinator: Kristina Dunder

Scope: Safety and efficacy: RSI

Update of sections 4.2, 4.7, 4.8 and 5.1, of the SmPC in order to revise the wording and to update the safety and efficacy information based on the interim results from studies 16 HS 13 (24-month follow-up data) and 16 HS 14 (48-month follow-up data); the package leaflet is updated accordingly

Action: for adoption

Request for supplementary information adopted on 20.04.2018.

2.12. Other Post-Authorisation Activities

2.12.1. 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 I virus thymidine kinase (HSV-TK Mut2) - Orphan - EMEA/H/C/002801/R/0010

MolMed SpA

Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinator: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 1 year renewal of marketing authorisation

Action: for adoption

Request for supplementary information adopted on 20.04.2018.

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

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous human T cells genetically expressing a chimeric antigen receptor (CAR) for B-cell maturation antigen (BCMA) – H0005095

Intended for the treatment of relapsed or refractory multiple myeloma

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. *Ex vivo* fused allogenic human myoblast (MB^{N}) with autologous human myoblast (MB^{DMD}) forming MB^{N}/MB^{DMD} dystrophin expressing chimeric cells – H0005097

Intended for the treatment of duchenne muscular dystrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. *Ex vivo* fused allogenic human myoblast (MB^{N1}) with allogenic human myoblast (MB^{N2}) forming MB^{N1}/MB^{N2} dystrophin expressing chimeric cells – H0005098

Intended for the treatment of Duchenne muscular dystrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Messenger RNA, codon optimised human, complexed with lipid-based nanoparticles, encoding for the human ornithine transcarbamylase deficiency - H0005081

Intended for the treatment of ornithine transcarbamylase deficiency

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Recombinant adeno-associated viral vector capsid containing the human iduronate-2-sulfatase (hIDS) gene expression cassette - H0005096

Intended for the treatment of mucopolysaccharidosis Type II (Hunter syndrome)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Homogenate of antlerogenic stem cells - H0005050

Intended for the treatment of recurrent corneal erosion syndrome

Scope: scientific recommendation

Action: for adoption

4.2.2. Homogenate of antlerogenic stem cells - H0005051

Intended for therapeutic support in spinal cord injury Scope: scientific recommendation

Action: for adoption

4.2.3. Mixture of cultured human olfactory ensheathing cells and olfactory nerve fibroblasts - H0005049

Intended for the treatment of complete spinal cord injury in human patients

Scope: scientific recommendation

Action: for adoption

4.2.4. CD34+ cells transduced with a lentiviral vector containing the Fanconi anemia complementation group A (FANCA) gene – H0005064

Intended for the treatment of Fanconi anemia type A patientsScope: scientific recommendation

Action: for adoption

4.2.5. Allogeneic CD34+ haematopoietic stem cells and allogeneic CD3+ T-cells – H0005068

Intended for prevention of kidney transplant rejectionScope: 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. Allogeneic foetal neural stem cells (ALS) - H0005022

Intended for the treatment of amyotrophic lateral sclerosis (ALS)

Scope: the European Commission raised no comments. Final ATMP scientific recommendation

Action: for information

4.4.2. Allogeneic foetal neural stem cells (SCI) - H0005023

Intended for the treatment of spinal cord injury (SCI)

Scope: the European Commission raised no comments. Final ATMP scientific recommendation

Action: for information

4.4.3. Fat graft - H0005024

Intended for lipofilling of anal fistula

Scope: the European Commission raised no comments. Final ATMP scientific recommendation

Action: for information

4.4.4. Pegylated exosomes carrying recombinant cystic fibrosis transmembrane conductance regulator (CFTR) mRNA and microRNA-17 – H0005021

OmniSpirant Limited; Intended for the treatment of cystic fibrosis

Scope: scientific recommendation

Action: for information

4.5. Follow-up and guidance

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

No items

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

No items

6.3.4. Month 3 – Nomination of Rapporteurs

No items

6.3.5. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Croatia: Nenad Medić -nominated as the new member from 16 May 2018
Croatia: Ivica Malnar -membership ended on 15 May 2018
Slovakia: Jan Kyselovic - membership ended on 30 April 2018

Action: for information

7.1.2. Strategic Review & Learning meeting - Joint CHMP/PDCO/CAT, Oslo, Norway, 07-09 May 2018

Postponed to June 2018

CAT resources: Martina Schüßler-Lenz

Scope: feedback from the meeting that took place on 07-09 May 2018

Action: for adoption

Note: Strategic Review & Learning meeting partnered with CAT/CHMP/PDCO.

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 April 2018 meeting

Action: for information

7.2.2. Scientific Coordination Board (SciCoBo) – meeting of 03 May 2018

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting on 3 May 2018

Action: for information

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

7.3.1. Guideline on quality of water for pharmaceutical use

CAT: Margarida Menezes-Ferreira; QWP Rapporteur/Coordinator: Eugenia Cogliandro

Scope: CAT's input to the guideline

Action: for discussion

Note: the revision of the guideline aims at harmonisation with US and Japanese pharmacopeias. The guideline is currently being revised by QWP (with input from BWP and GMDP IWG). It is planned to be adopted by QWP/CHMP/CVMP and released for public consultation in June 2018. The background to the revision is outlined in this Concept paper (EMA/CHMP/CVMP/QWP/BWP/428135/2016).

7.4. Cooperation within the EU regulatory network

7.4.1. Guidelines on good clinical practice for advanced therapy medicinal products

CAT drafting group: Simona Badoi, Maura O'Donovan, Kieran Breen

Scope: draft GCP for ATMP guidelines is open for consultation.

Action: for discussion

7.4.2. ATMP training curriculum: assessor trainings on *'Review of Quality, Non-Clinical and Clinical aspects of ATMP CTA and MAA'* jointly with the Clinical Trial Facilitation Group (CTFG)

Scope: call of expression of interest from CAT and CTFG members to present relevant case studies to cover review of quality, non-clinical and clinical aspects of ATMP clinical trial applications.

Action: for discussion

Note: an e-mail calling for volunteers to present their case studies was sent to CAT members on 10 May 2018.

7.4.3. Orphan similarity for ATMPs

CAT drafting group: Margarida Menezes-Ferreira, Christiane Niederlaender, Violaine Closson Carella, Simona Badoi, Guido Pantè.

Scope: Questions and Answers (Q&A) document

Action: for information

Note: amendments were introduced in response to question 3 and agreed by written procedure on 11 May 2018.

The Q&A will be published by the European Commission and will accompany the revised legislation on orphan similarity .

7.4.4. Pharmacogenomics Working Party (PGWP)

Scope: EMA multi-stakeholder workshop on predictive biomarker-based assay development in the context of drug development and lifecycle (EMA/136048/2018) - scheduled on 18 June 2018

Action: for information

7.5. Cooperation with international regulators

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

The teleconference will take place

CAT: Martina Schüßler-Lenz

Scope: draft agenda

Action: for discussion

7.6. CAT work plan

7.6.1. CAT 2019 work plan

CAT: Martina Schüßler-Lenz

Scope: initial discussions of topics for the 2019 work plan

Action: for discussions

7.6.2. Environmental assessment of gene therapy medicinal products

Scope: presentation on outcome of discussions with GMO authorities regarding the assessment of human cells genetically modified.

Action: for discussion

7.7. Planning and reporting

7.7.1. European Commission and European Medicines Agency Action Plan on ATMPs

CAT: Martina Schüßler-Lenz

Scope: status update of the European Commission and European Medicines Agency Action Plan on ATMPs

Action: for information

7.8. Others

None

8. Any other business

No items

Date of next CAT meeting:
20-22/06/2018

9. Explanatory notes

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

Abbreviations / Acronyms

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

QWP: Quality Working Party

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

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 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

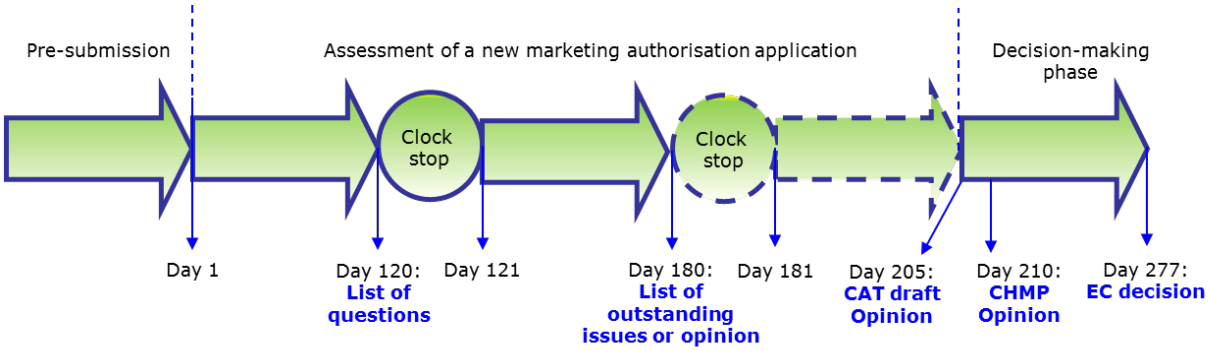
Evaluation of ATMPs (section 2)

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/