18 July 2018
EMA/CAT/501027/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 18-20 July 2018

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

18 July 2018, 14:00 – 18:30, room 03-E

19 July 2018, 09:00 – 18:30, room 03-E

20 July 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 18-20 July 2018. See July 2018 CAT minutes (to be published post-September 2018 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 18-20 July 2018 meeting

1.3. Adoption of the minutes

CAT minutes for 20-22 June 2018 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. 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: Opinion

Action: for adoption

List of Outstanding Issues adopted on 25.05.2018. List of Questions adopted on 08.12.2017.

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

No items

2.7. New applications

2.7.1. Autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-A-T87Q-globin gene - Orphan - ATMP - H0003691

bluebird bio GmbH; Treatment of adolescents and adults with transfusion-dependent β-thalassemia (TDT) who do not have a β0 mutation at both alleles of the β-globin (HBB) gene (i.e., patients with a non-β0/β0 genotype).Scope: Briefing note and Rapporteurs' recommendation on the request for accelerated assessment.

Action: for adoption

2.7.2. Adeno-associated viral vector serotype 9 containing the human survival of motor neuron (SMN) gene - Orphan – PRIME - H0004750

AveXis EU Limited; Intended for the treatment of paediatric patients diagnosed with spinal muscular atrophy type 1

Scope: Briefing note and Rapporteurs' recommendation on the request for accelerated assessment.

Action: for adoption

2.8. Withdrawal of initial marketing authorisation application

2.8.1. Axalimogene filolisbac - EMEA/H/C/004473

Treatment of cervical cancer

Scope: Letter for the applicant dated 10 July 2018 informing EMA about the withdrawal of the marketing authorisation application.

Action: for information

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. 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/II/0009/G

MolMed S.p.A

Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinators: Paula Boudewina van Hennik

Scope: Opinion. Quality

Action: for adoption

Request for Supplementary Information adopted on 20.04.2018.

2.12. Other Post-Authorisation Activities

No items

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

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

No items

4.2. Day 30 ATMP scientific recommendation

4.2.1. Adeno-associated viral vector serotype 2 containing a gene encoding the channelrhodopsin-2 protein – H0005122

Intended for the treatment of retinitis pigmentosa

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Autologous blood-derived endothelial and haematopoietic stem/progenitor cells – H0005110

Intended for the treatment of no-option patients with peripheral arterial disease (PAD) and critical limb ischemia (CLI)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Non-viable allogeneic induced pluripotent stem cells – H0005108

Intended for the treatment of epithelial cancers and leukaemia

Scope: classification request withdrawn by the applicant

Action: for information

4.2.4. Combination of four 5' capped single stranded messenger ribonucleic acids encoding one shared tumour-associated antigen - H0005109

Intended for the treatment of malignant melanoma

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. 5´capped single stranded messenger RNA encoding tumour specific neoantigens - H0005111

Intended for the treatment of locally advanced or metastatic tumors

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. Homogenate of antlerogenic stem cells - H0005051/0001

Intended as support for the spinal cord injury in humans

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

Action: for adoption

4.4.2. Homogenate of antlerogenic stem cells - H0005050/0001

Intended for the treatment of recurrent corneal erosion syndrome (RCES)

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

Action: for information

4.4.3. 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: the European Commission raised comments. Revised ATMP scientific recommendation

Action: for information

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

Action: for information

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

Action: for information

4.4.6. Messenger ribonucleic acid, 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: the European Commission raised no comments . Final ATMP scientific recommendation

Action: for information

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

Action: for information

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

Timetable:

-Final Briefing Package:	29.08.2018
-Start of the procedure at SAWP:	3-6.08.2018
-CAT report due by:	07.08.2018
-CAT recommendation:	14.09.2018

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

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME)

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

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting – joint CAT/Clinical trial facilitation group (CTFG), Bucharest, Romania, 13-14 June 2019

CAT resources: Simona Badoi

Scope: confirmation of meeting dates

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 July 2018 meeting

Action: for information

7.2.2. Committee for Orphan Medicinal Products (COMP)

Scope: presentation on the interplay between orphan status and wording of therapeutic indications

Action: for information

7.2.3. Scientific Coordination Board (SciCoBo) – meeting of 16 July 2018

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting that took place on 16 July 2018

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 medicinal products containing genetically modified cells

CAT Rapporteur: Marcos Timón

Scope: revised draft agreed by guideline consistency group (GCG). Guideline for public consultation

Action: for adoption for public consultation

7.3.2. Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container

Scope: presentation of the updated guideline following comments from BWP/CAT

Action: for information

Note: The draft guideline on sterilisation underwent a public consultation from April-October 2016. The guideline has been discussed extensively at QWP, GMDP Inspectors Working Group (IWP) and BWP.

7.3.3. Training in GMP for ATMPs

Scope: training of GMP inspectors and ATMP assessors from national competent authorities will be organised on 27-28 September 2018

Action: for adoption

Note: The training is aimed at those who are active and competent in the inspection of ATMP facilities. Assessors who join the GMP inspectors during an inspection of the ATMP manufacturing site (or who could take up this role in the future) would also benefit from attendance.

7.4. Cooperation within the EU regulatory network

7.4.1. ATMP training curriculum

Scope: ATMP curriculum and composition of the Curriculum Committee members

Action: for adoption and for nomination

Note: CAT will formally adopt the European Union network training centre (EU NTC) Training Curriculum for ATMP. CAT members will be asked to put forward candidatures to become a member of the Curriculum Committee, which will be composed of at least 3 members (one for Quality, Non-clinical and Clinical aspects each). This group will overview the training curriculum and the list of trainings for the next years.

7.5. Cooperation with international regulators

No items

7.6. CAT work plan

7.6.1. CAT 2019 work plan

CAT: Martina Schüßler-Lenz

Scope:
-Topics for the 2019 work plan.
-Feedback from the brainstorming meeting to take place on 18 July 2018

Action: for discussion

7.6.2. Environmental assessment of gene therapy medicinal products

European Commission

Scope: outcome of the meeting between the European Commission and the GMO authorities that took place on 25 June 2018 regarding the assessment of human cells genetically modified.

Action: for information

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming marketing authorisation applications for advanced therapy medicinal products

Scope: MAAs with eligibility for Q2-2018

Action: for information

7.8. Others

7.8.1. EMA implementation of the new medical device and *in* vitro diagnostic regulation

Action: for information

7.8.2. Relocation of EMA to The Netherlands

Scope: update on current state-of-play on EMA relocation

Action: for information

8. Any other business

No items

Date of next CAT meeting:

12-14 September 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

DG: Drafting Group

EC: European Commission

ERA: Environmental Risk Assessment

EU NTC: European Union network training centre

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

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

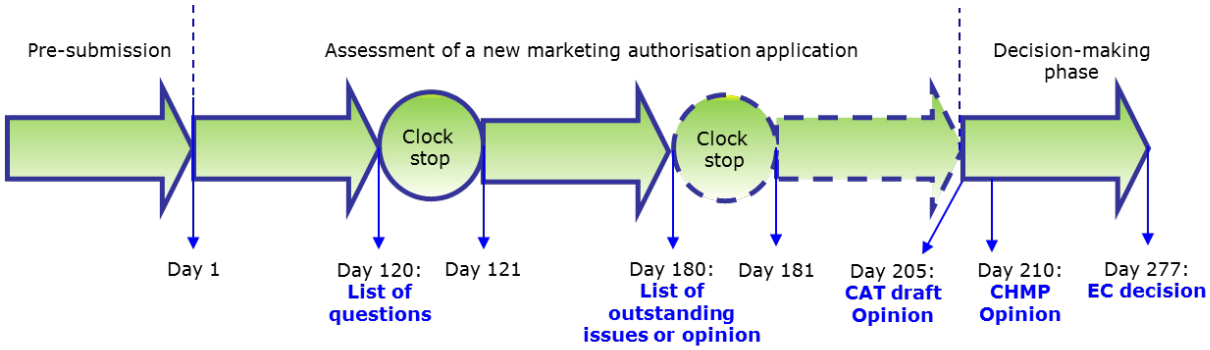
Evaluation of ATMPs (section 2)

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/