12 September 2018
EMA/CAT/628659/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 12-14 September 2018

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

12 September 2018, 14:15 – 19:30, room 03-E

13 September 2018, 08:30 – 18:15, room 03-E

14 September 2018, 08:30 – 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 12-14 September 2018. See September 2018 CAT minutes (to be published post-October 2018 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 12-14 September 2018 meeting

1.3. Adoption of the minutes

CAT minutes for 18-20 July 2018 meeting

1.4. August 2018 Written Procedure

CAT minutes of the August 2018 Written Procedure

1.5. Technical information

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. 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 20.07.2018, 25.05.2018. List of Questions adopted on 08.12.2017.

2.2. Oral explanations

2.2.1. 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: Oral Explanation held on 12.09.2018

Action: for adoption

List of Outstanding Issues adopted on 25.05.2018. List of Questions adopted on 08.09.2017.

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 CD34+ cells transduced with a lentiviral vector encoding the human βA-T87Q-globin gene (LentiGlobin-BB305) – Orphan – EMA/H/C/0003691

Bluebird bio France; Indicated for the treatment of transfusion-dependent beta-thalassaemia (also referred to as beta-thalassaemia major).

Scope: timetable for accelerated assessment

Action: for adoption

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/0024

Amgen Europe B.V.

Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Opinion. Quality.

Action: for adoption

2.12. Other Post-Authorisation Activities

2.12.1. 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, Peer Reviewer: Dariusz Sladowski, CHMP Coordinators: Bjorg Bolstad and Greg Markey, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: quality

Action: for information

3. Certification of ATMPs

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

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic EBV-specific cytotoxic T cells – H0005168

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Autologous bone marrow derived mesenchymal stem cells – H0005176

Intended for the treatment of ischemic stroke

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Autologous bone marrow derived mesenchymal stem cells – H0005177

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Adeno-associated virus (AAV) vector containing a human CLN2 (hCLN2) expression cassette encoding for the soluble lysosomal enzyme TPP1 – H0005160

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Genetically modified AAV9 expressing shRNA as well as a codon-optimised shRNA-insensitive wildtype PABPN1 - H0005142

Intended for the treatment of oculopharyngeal muscular dystrophy

Scope: ATMP scientific recommendation

Action: for adoption

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

Intended for the treatment of solid organ transplantation

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Stromal vascular fraction - H0005151

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

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. Adeno-associated viral vector serotype 2 containing a gene encoding the channelrhodopsin-2 protein - H0005112

Treatment of retinitis pigmentosa

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

Action: for information

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

Action: for information

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

Action: for information

4.4.4. 5´capped single stranded messenger RNA encoding tumour specific neoantigens - H0005111

Intended for the treatment of locally advanced or metastatic tumors

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

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. Regulatory Science Engagement Plan to 2025

Scope: presentation of EMA's regulatory science engagement plan

Action: for discussion

7.1.2. Abolishment of physical signatures for divergent positions for centrally authorised products (CAPs)

Scope: The divergent position members will be approached to confirm the agreed final wording for the divergent position.

Action: for information

Note: this proposal has already been presented to the PRAC and CHMP

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. Scientific Coordination Board (SciCoBo) – meeting of 10 September 2018

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting that took place on 10 September 2018

Action: for information

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

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

Scope: updated guideline following comments from BWP/CAT

Action: for discussion

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

Scope:
PCWP: draft agenda PCWP meeting 25 Sep 2018
PCWP/HCPWP: draft agenda joint PCWP/HCPWP meeting 25 Sep 2018
HCPWP: draft agenda HCPWP meeting 26 Sep 2018

Action: for information

7.4. Cooperation within the EU regulatory network

7.4.1. ATMP training curriculum

CAT Curriculum Committee: Claire Beuneu (non-clinical); Lisbeth Barkholt (clinical)

Scope: guidance document on the organisation of the ATMP trainings

Action: for information

CAT members who wish to volunteer to cover the quality part of the Curriculum Committee to send expression of interest to CATSecretariat@ema.europa.eu

7.4.2. European Commission - draft guidelines on good clinical practice for advanced therapy medicinal products

Scope: public consultation on draft guidelines on GCP for ATMPs.

Action: for information

Note: the European Commission - DG Health and Food Safety has launched an online targeted public consultation on the draft guidelines on good clinical practice for advanced medicinal products addressed particularly to small and medium-sized enterprises (SMEs), academia, hospitals and patient organisations. Comments are invited to be sent by 31 October 2018 to sante-pharmaceuticals-B5@ec.europa.eu.

https://ec.europa.eu/health/human-use/consultations/2018_gcp_atmp_en

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

7.5.2. International pharmaceutical regulators forum (IPRF) - gene therapy working group (GTWG): publication of the reflection paper on expectations for biodistribution assessment for gene therapy products

Scope: reflection paper can be found in the IPRF website: https://www.i-p-r-f.org/index.php/en/news/gene-therapy-working-group-reflection-paper/ .

Action: for information

Note: this reflection paper was discussed and agreed at the February 2018 CAT meeting.

7.6. CAT work plan

7.6.1. CAT meeting with Interested Parties, September 2018, EMA, London

EMA: Martina Schüßler-Lenz

Scope: meeting with interested parties to take place on 13 September 2018, at 15:15hrs

Action: for discussion

7.6.2. CAT 2019 work plan

CAT: Martina Schüßler-Lenz

Scope: updated CAT work plan 2019 (following July 2018 CAT discussion)

Action: for adoption

7.6.3. Genome editing – scientific considerations

Scope: report from the ad hoc expert meeting of 18 October 2017

Action: for information

Note: the report will be published on the EMA website shortly.
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2018/07/event_detail_001672.jsp&mid=WC0b01ac058004d5c3

7.6.4. Genome editing – regulatory considerations

Scope: Reflection on regulatory aspects of medicinal product based on or produced using genome editing technologies

Action: for discussion of next steps

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q3/2018 update of the business pipeline report for the human scientific committees

Action: for information

7.8. Others

7.8.1. Global consultation on the review and update of the Changsha Communique on Xenotranplantation, 12 – 14 December 2018, Changsha, China

CAT: Martina Schüßler-Lenz

Scope: nomination of Ralf Tönjes (PEI-DE) as EMA representative at the Global consultation meeting

Action: for agreement

8. Any other business

8.1. International Conference of Drug Regulatory Authorities (ICDRA), 04 September 2018, Dublin, Ireland

CAT: Martina Schüßler-Lenz

Scope: Pre-ICDRA, workshop 8: 'Regulation of advanced therapies', 04 September 2018, Ireland. Summary of discussion and draft recommendation

Action: for information

8.2. Telematics - Concept paper on strategy 2020-2025

Action: For discussion

Date of next CAT meeting:
10-12/10/2018

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

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

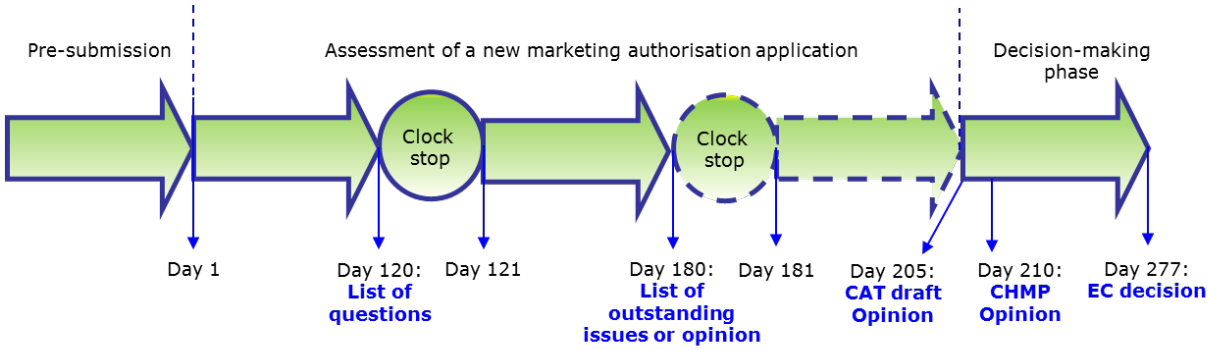
Evaluation of ATMPs (section 2)

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/