20 June 2018
EMA/CAT/426129/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 20-22 June 2018

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

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

21 June 2018, 09:00 – 18:30, room 03-E

22 June 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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2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Tisagenlecleucel - Orphan - EMEA/H/C/004090

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

Scope: Opinion

Action: for adoption

Note: List of Outstanding Issues adopted on 25.05.2018. List of Questions adopted on 16.03.2018.

2.1.2. Axicabtagene ciloleucel - Orphan - EMEA/H/C/004480

Kite Pharma EU B.V.; Intended for the treatment of B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

Scope: Opinion

Action: for adoption

Note: List of Outstanding Issues adopted on 20.04.2018. List of Questions adopted on 08.12.2017.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

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No items

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No items

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No items

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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

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No items

2.11. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

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

CO.DON AG

Rapporteur: Lisbeth Barkholt, CHMP Coordinators: Kristina Dunder

Scope: Safety and efficacy: Opinion

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

Note: requests for Supplementary Information adopted on 25.05.2018, 20.04.2018.

2.12. Other Post-Authorisation Activities

2.12.1. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854/REC/011

GlaxoSmithKline Trading Services Limited

Rapporteur: Christiane Niederlaender, CHMP Coordinator: Robert James Hemmings

Scope: post-authorisation measure from initial opinion/MA

Action: for adoption

2.12.2. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854/REC/012

GlaxoSmithKline Trading Services Limited

Rapporteur: Christiane Niederlaender, CHMP Coordinator: Robert James Hemmings

Scope: post-authorisation measure from initial opinion/MA

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

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

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Intended for the treatment of retinitis pigmentosa

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

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

Intended for the treatment of epithelial cancers and leukaemia

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

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Intended for the treatment of locally advanced or metastatic tumors

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. 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: scientific recommendation

Action: for adoption

4.2.2. *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: scientific recommendation

Action: for adoption

4.2.3. *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: scientific recommendation

Action: for adoption

4.2.4. 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: scientific recommendation

Action: for adoption

4.2.5. 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: scientific recommendation

Action: for adoption

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

4.3.1. Homogenate of antlerogenic stem cells - H0005050/0001

Intended for the treatment recurrent corneal erosion syndrome (RCES)

Scope: Responses from the applicant. Revised ATMP scientific recommendation

Action: for adoption

4.3.2. Biocervin Neuroprotective Matrix - homogenate of antlerogenic stem cells - H0005051/0001

Intended as support for the spinal cord injury in humans.

Scope: Responses from the applicant. Revised ATMP scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Unpurified cell culture of human olfactory ensheathing cells (OECs) and human olfactory nerve fibroblasts (ONFs) - H0005049/0001

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

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

Action: for adoption

4.4.2. Donor-derived CD34+ hematopoietic stem cells with defined dose of donor derived CD3+ T-cells - H0005068/0001

Prevention of kidney graft loss in recipients of human leukocyte antigen-matched living donor kidney transplants

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

Action: for information

4.4.3. CD34+ cells transduced with a lentiviral vector encoding the Fanconi anaemia complementation group A (FANCA) gene - Orphan - H0005064/0001

Treatment of Fanconi anaemia type A patients

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

Action: for adoption

See also 5.2.3

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

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

No item

6.3.3. Month 2 – Recommendation of eligibility

6.3.4. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Slovakia: Lukas Slovak - nominated as the new member from 26 May 2018

Action: for information

7.1.2. Call for expression of interest from civil societies for the position of member of the committee for advanced therapies (CAT)

Scope: European Commission's launch of a selection procedure to appoint the members and alternates representing patients' associations and clinicians in the Committee for Advanced Therapies. Deadline for submission of applications: 18 July 2018

Action: for information

European Commission's website link:
https://ec.europa.eu/health/documents/public_call/call_index_en#fragment0

Note:
-The mandate will run for three years from 1 July 2019
-the EC will appoint the new members after consultation with the European Parliament

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

CAT resources: Martina Schüßler-Lenz

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

Action: for adoption

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 May 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

None

7.4. Cooperation within the EU regulatory network

7.4.1. ATMP training curriculum: assessor trainings on 'Review of quality, non-clinical and clinical aspects of advanced therapy medicinal product clinical trial application and marketing application authorisation' jointly with the Clinical Trial Facilitation Group (CTFG)

Scope: call for 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.

7.4.2. Medical devices and in vitro diagnostic medical devices

CAT: Ilona Reischl

Scope:
- EU Network Awareness session on the new medical devices and in vitro diagnostic medical devices Regulations (2017/745 and 2017/746): Friday 22 June 2018, 12.30 – 14.00 Room 2-F
- Implementation of Art 117 of the medical device Regulation: New requirement that medicinal products with an integral medical device component will require a notified body opinion or conformity assessment before the marketing authorisation can be granted: feedback from the discussions at the BWP interested parties meeting of 20 June 2018
- Feedback from the Pharmacogenics Working Party workshop on predictive biomarker-based assay development in the context of drug development and lifecycle (workshop took place on 18 June 2018).

Action: for information

7.5. Cooperation with international regulators

None

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 discussion

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming advance therapy medicinal products applications

Scope: planning estimates of forthcoming initial ATMPs applications, type II variations and line extensions intended to be submitted within the next 34 months (period covered: March 2018-December 2020).

Action: for information

7.8. Others

None

8. Any other business

No items

Date of next CAT meeting:

18-20 July 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

FDA: Food and Drug Administration

FL: Final Letter

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

MNAT: Multinational Assessment Team

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

RMP: Risk Management Plan

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

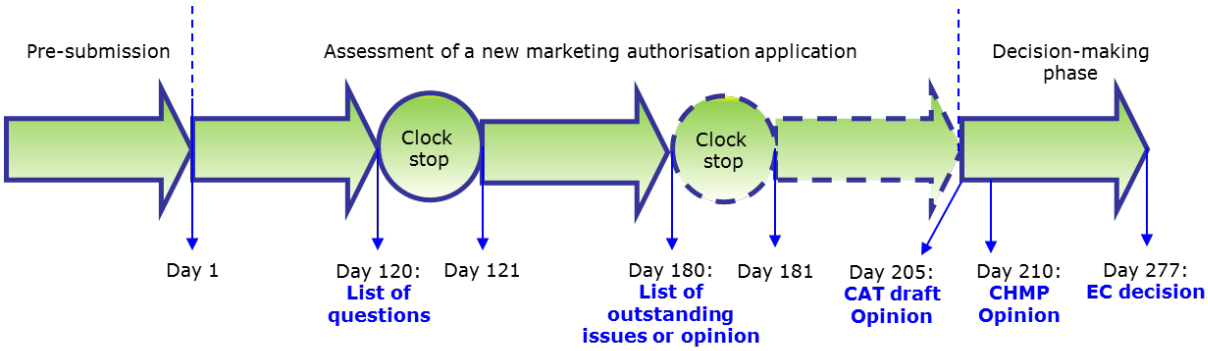
Evaluation of ATMPs (section 2)

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/