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SCIENCE MEDICINES HEALTH

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Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 15-16 February 2018

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

15 February 2018, 09:00 – 14:00

16 February 2018, 09:00 – 14:00

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 ongoing 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 15-16 February 2018. See February 2018 CAT minutes (to be published post-meeting March 2018 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 15-16 February 2018 meeting

1.3. Adoption of the minutes

CAT minutes for 17-19 January 2018 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

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

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

Action: for discussion

2.7. New applications

2.8. Withdrawal of initial marketing 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. Spherox – spheroids of human autologous matrix-associated - EMEA/H/C/002736/II/001

CO.DON AG

Rapporteur: Lisbeth Barkholt; CHMP Coordinator: Kristina Dunder

Scope: quality/non-clinical: update of Annex II to delete the condition “To re-validate the potency assay post marketing and to monitor its correlation with the efficacy outcome” following the submission of the revalidation of potency assay study report.

Action: for adoption of timetable

2.11.2. Spherox – spheroids of human autologous matrix-associated - EMEA/H/C/002736/II/002/G

CO.DON AG

Rapporteur: Lisbeth Barkholt; CHMP Coordinator: Kristina Dunder

Scope: safety and efficacy – 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 of timetable

Note:

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

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic umbilical cord derived mesenchymal stem cells – H0004999

Intended for the treatment of multiple sclerosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Autologous bone marrow derived mesenchymal stem cells - H0004998

Intended for the treatment of multiple sclerosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Allogeneic human neural stem cells - H0004995

Intended for the treatment of traumatic brain injuries (e.g. coma, minimally conscious state, persistent vegetative state) & stroke

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Autologous bone marrow derived mesenchymal stem cells - H0004997

Intended for the treatment of articular cartilage damage and tendon injuries

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. *Ex vivo* fused autologous human bone marrow-derived mesenchymal stem cell with allogenic human myoblast - H0004994

Intended for the treatment of Duchenne muscular dystrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Expanded autologous auricular chondrocytes - H0004979

Intended for the surgical implantation for the repair of microtia

Scope: scientific recommendation

Action: for adoption

4.2.2. Elastin recombinamer (ELR)-encapsulated allogeneic pancreatic islets - H0004980

Intended for treatment of severe forms of type 1 diabetes

Scope: scientific recommendation

Action: for adoption

4.2.3. Autologous CD31+ Cells - H0004981

Intended as adjunct therapy during primary care of proximal humeral fracture to decrease incidence of non-union and secondary displacement

Scope: 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. Autologous dendritic cells pulsed with allogeneic tumour cell lysate - H0004949

Intended for the treatment of malignant mesothelioma

Scope: minor comments received by the European Commission. Final scientific recommendation

Action: for information

4.4.2. Allogeneic mesenchymal stem cells suspended in cell supernatant - H0004952

Intended for the treatment of osteoarthritis

Scope: minor comments received by the European Commission. Final scientific recommendation

Action: for information

4.5. Follow-up and guidance

No items

5. Scientific Advice

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

5.1. New requests – appointment of CAT Rapporteurs

5.2. CAT reports

5.3. List of Issues

5.4. Finalisation of SA procedures

6. Pre-Authorisation Activities

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

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

No items

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

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

CAT resources: Helga Olsen, Rune Kjekken

Scope: agenda building

Action: for discussion

Note: Strategic Review & Learning meeting will be 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 January 2018 meeting

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: draft guideline

Action: for discussion

Note: the draft guideline will be presented to the BWP and the CAT in February for a one month reflection; adoption by CAT is anticipated for March 2018.

7.3.2. ATMP guideline on safety and efficacy follow-up and risk management

Drafting group: Rob Hemmings, Sol Ruiz, Maura O'Donovan, Tomas Boráň, Julie Williams, Brigitte Keller-Stanislawski, Pierre Demolis

Action: for information

Note: the guideline has been adopted by the CHMP and released for public consultation.

7.3.3. Guideline on quality, non-clinical and clinical aspects of gene therapy medicinal products

CAT Rapporteurs: Quality: Christiane Niederlaender; Non-clinical: Kieran Breen; Clinical: Bettina Klug

Action: for adoption

Note: comments raised by the Guideline Consistency Group were discussed with the drafting group chairs and incorporated where appropriate.

7.3.4. PRIME for ATMPs

CAT: Martina Schübler-Lenz, Rune Kjekken, Jimmy McBlane, Jan Müller-Berghaus, Maura O'Donovan, Hans, Ovelgönne, Ilona Reischl, Olli Tenhunen,

Scope: ATMP input in PRIME-related documents

Action: for discussion

7.3.5. PRIME Oversight Group – Monitoring of fulfilment of PRIME eligibility criteria

CAT: Martina Schübler-Lenz

Scope: feedback on the discussion of the PRIME oversight group that took place on 1 February 2018

Action: for information

7.4. Cooperation within the EU regulatory network

7.4.1. ATMP training curriculum

CAT: Ilona Reishl

Scope: proposal of the curriculum

Action: for discussion

Note: the training on clinical trial approval with focus on ATMP will be included (provisionally) in the draft training curriculum and feedback will be awaited from CTFG on potential co-management of this topic.

7.4.2. Orphan similarity for ATMPs

CAT: Rocío Salvador-Roldán – European Commission

Scope: development of a Q&A document

Action: for appointment of volunteers

7.5. Cooperation with international regulators

7.5.1. International Pharmaceutical Regulators Forum Gene Therapy Working Group (IPRF-GTWG)

CAT experts: Björn Carlsson, Tiina Palomäki

Scope: IPRF Reflection paper on biodistribution (BD) for gene therapy products.

Action: for agreement

Background: this reflection paper describing the expectations for BD for GTMP has been developed by a drafting group from the IPRF-GTWG. Drafting took place virtually and during the in-person IPRF-GTWG meeting that was organised at EMA on 2-3 May 2017 (see [minutes of May 2017 CAT meeting](#), agenda point 7.5.1). Björn Carlsson and Tiina Palomäki were part of this drafting group.

7.6. CAT work plan

7.6.1. Registry requirements for chimeric antigen receptor T (CAR-T) cells

CAT: Martina Schübler-Lenz

Scope: feedback on the workshop that took place on 9th February 2018

Action: for information

7.6.2. Expert meeting on adeno-associated viral vectors

CAT: Martina Schübler-Lenz

Scope: publication strategy for the report of the meeting that took place on 6 September 2017

Action: for discussion

7.6.3. Environmental assessment of gene therapy medicinal products

CAT: Rocío Salvador-Roldán – European Commission

Scope: feedback from discussions with GMO authorities regarding the assessment of human cells genetically modified.

Action: for discussion

7.7. Planning and reporting

None

7.8. Others

7.8.1. AAV gene therapy: finding from high dose administration to non-human primates

CAT: Rune Kjeklen

Scope: Information provided by University of Pennsylvania (Dr Wilson) on findings from two studies in juvenile and adult rhesus macaque monkeys administering high doses of systemic (IV) AAV serotypes hu68 and AAV.PHP.B, respectively

Action: for discussion

8. Any other business

No items

Date of next CAT meeting:

14-16 March 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 Applicant

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

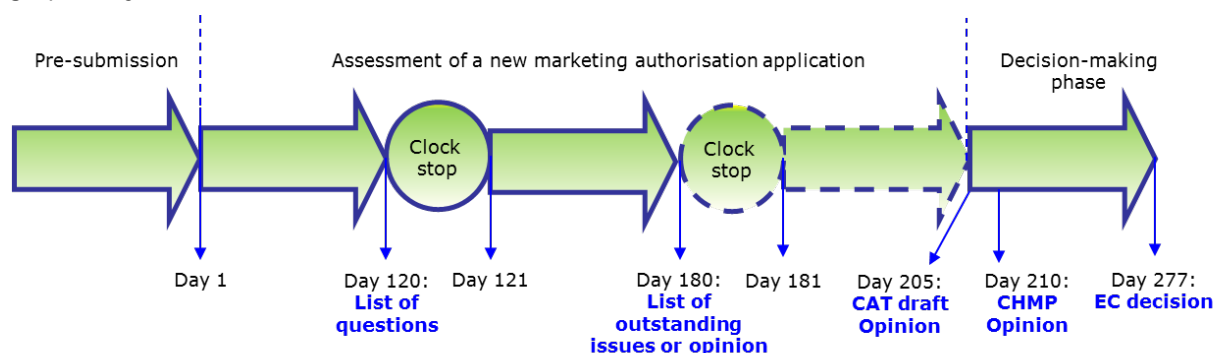
Evaluation of ATMPs (section 2)

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/