30 October 2017
EMA/CAT/726328/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 30-31 October 2017

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

30 October 2017, 09:00 – 19:00, room 03-E

31 October 2017, 09:00 – 16:30, 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 30-31 October 2017. See October 2017 CAT minutes (to be published post-November 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 30-31 October 2017 meeting

1.3. Adoption of the minutes

CAT minutes for 4-6 October 2017 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue - Orphan - EMEA/H/C/004258

Tigenix, S.A.U.; treatment of complex perianal fistula(s)

Scope: Oral explanation

Action: Oral explanation

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. Tisagenlecleucel-T - Orphan – H0004090

Novartis Europharm Ltd.; Indicated for:
-the treatment of paediatric and young adult patients 3 to 25 years of age with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL).
- the treatment of adult patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL) who are ineligible for autologous stem cell transplant

Scope: Rapporteurs' recommendation on the request 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

No items

2.12. Other Post-Authorisation Activities

2.12.1. Glybera - alipogene tiparvovec - Orphan - EMEA/H/C/002145/SOB/001.7

uniQure biopharma B.V.; Indicated for the long term correction of lipoprotein lipase deficiency, to control or abolish symptoms and prevent complications in adult patients clinically diagnosed with lipoprotein lipase deficiency (LPLD)

Rapporteur: Christiane Niederlaender; Co-Rapporteur: Egbert Flory; CHMP Coordinators: Greg Markey, Jan Mueller-Berghaus

Scope: proposals for amendments to the registry protocol

Action: for information

Note: a CAT written procedure was finalised on 19 October 2017 to endorse the Rapporteur's assessment report. The MAH is aiming to keep the registry alive after the expiry of the MA (25 October 2017).

2.12.2. Glybera - alipogene tiparvovec - Orphan - EMEA/H/C/002145/SOB/010

uniQure biopharma B.V.; Indicated for the long term correction of lipoprotein lipase deficiency, to control or abolish symptoms and prevent complications in adult patients clinically diagnosed with lipoprotein lipase deficiency (LPLD)

Rapporteur: Christiane Niederlaender; Co-Rapporteur: Egbert Flory; CHMP Coordinators: Greg Markey, Jan Mueller-Berghaus

Scope: monitoring of immune response: validation of assays

Action: for adoption

Note: in view of the expiry of the MA, CAT to consider adoption of the outcome of this post-authorisation measure at the November 2017 CAT meeting (instead of the December 2017 meeting).

3. Certification of ATMPs

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

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous CD34^{+} cells derived from bone marrow - H0004941

Intended for the improvement of neurologic function in patients with non-lacunar acute ischemic stroke infarctions

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. CD1c (BDCA1)+ myeloid dendritic cells (myDC) - H0004927

Intended for the treatment of patients with advanced, pretreated solid tumours with injectable metastases

Scope: scientific recommendation

Action: for adoption

4.2.2. Genetically modified epithelial cells (factor IX), encapsulated – H0004928

Intended for the treatment of haemophilia B

Scope: scientific recommendation

Action: for adoption

4.2.3. Stromal vascular fraction (SVF) – H0004926

Intended to diminish cancer-related lymphedemia in breast cancer patients

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. Allogenic cardiopoietic cells derived from adipose tissue derived stem cells (ADSC) purified from healthy donor's lipoaspirate – H0004911

Intended to help post - myocardial infarction patients in restoring cardiac function to repair the underlying myocardium damage

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

Action: for information

4.4.2. Recombinant adeno-associated virus serotype 2/1 vector encoding human β-hexosaminidase alpha & beta subunits (rAAV2/1 Hex alpha & beta) – H0004906

Intended for the treatment of Tay-Sachs disease & Sandhoff disease monosialic ganglioside 2 (GM2) gangliosidosis

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

Action: for information

4.4.3. Adeno-associated virus (AAV) vector serotype 8 expressing human low-density lipoprotein receptor (hLDLR) - H0004905

Intended for the treatment of hypercholesterolaemia caused by homozygous mutations in the low density lipoprotein receptor (LDLR) gene

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

Action: for information

4.4.4. Skin tissue – H0004907

Intended for the treatment of patients with acute complex skin loss

Scope: comments received by the European Commission. Clarification included in section 2 of the ATMP scientific recommendation. Final ATMP scientific recommendation

Action: for information

4.4.5. Autologous CD34+ cells, freshly isolated – H0004922

Cells to be used to contribute to the regeneration of soft and hard tissues of temporomandibular joints through their immunological action

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

Action: for information

4.4.6. Autologous dental pulp stem cells (DPSC), freshly isolated – H0004923

Intended for the regeneration of soft and hard tissues of temporomandibular joints

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

Action: for information

4.4.7. Cultured dental pulp stem cells (DPSC) – H0004924

Intended for the regeneration of soft and hard tissues of temporomandibular joints

Scope: no comments received by the European Commission. Final ATMP 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

Timetable:
-Final Briefing Package: 22.11.17
-Start of the procedure at SAWP: 27-30.11.17
-CAT report due by: 01.12.17
-CAT recommendation: 08.12.17

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

Timetable for assessment:
Procedure start: 26.10.17.
SAWP recommendation: 30.11.17.
CAT recommendation: 08.12.17.
CHMP adoption of report and final recommendation: 14.12.17.

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

6.3.4 Month 3 – Nomination of Rapporteurs

6.3.5 Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Scope: membership changes

Finland: Heli Suila – member nomination started on 07 October 2017
Lithuania: Vitalis Briedis – alternate membership started on 19 October 2017
Lithuania: Jolanta Gulbinovič – alternate membership ended on 18 October 2017

Action: for information

7.1.2. Strategic Review & Learning meeting – Tallinn, Estonia, 15-17 November 2017

CAT Strategic Review & Learning meeting (SRLM) will take place in Tallinn, Estonia on 15-17 November 2017 under the auspices of the Estonian Presidency of the Council of the European Union

Scope: final programme

Action: for information

7.1.3. User manual on CxMP/EMA external representation

Action: For information

7.1.4. Rapporteurship bidding process for evaluations of centralised procedures

Scope: a new 2-stage bidding process for Rapporteurships

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 October 2017 meeting

Action: for information

7.2.2. Scientific Co-ordination Board (SciCoBo) – meeting of 21 September 2017

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting that took place in September 2017

Action: for information

7.2.3. Cell based ATMP nomenclature

Scope: guidance on the terminology for cell-based medicinal products (currently applied by the COMP)

Action: for information

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

7.3.1. Review and update of EMA guidelines to implement best practice with regard to 3Rs (replacement, reduction and refinement of animal testing) in regulatory testing of medicinal products

Scope:
-review of EMA Guidelines considering 3Rs - report on actions taken
-overview of comments received - JEG 3Rs - best practise

Action: for comments by 10 November 2017

Note: CAT adopted in September 2016 the comments to the ATMP related entries in the tables included in the reflection paper and agreed on the proposed amendments.

The report and overview of comments documents will be submitted to the CHMP and CVMP in December 2017/January 2018 for adoption and publication. CAT will endorse the documents at its December 2017 CAT meeting.

7.3.2. Scientific Advice Working Party (SAWP)

Martina Schüßler-Lenz

Scope: Re-examination of the SAWP composition - call for interest to become one of the CAT representatives in the SAWP.

Action: expression of interest to be sent to CAT secretariat by 27 October 2017

Note: the role and responsibilities: they will act as liaisons between CAT and the SAWP and act as SAWP coordinators for (a limited number) of scientific advices. The joint CAT-SAWP member will have to need access to experts in their agency / organisation to respond to questions related of the quality, non-clinical and clinical development. The CHMP at its December 2017 meeting will adopt the new composition of the SAWP.

7.4. Cooperation within the EU regulatory network

7.4.1. EU Network Pharmacovigilance Oversight Group (EU-POG) (former ERMS FG)

Scope: nomination of a CAT representative to the EU-POG

Action: for nomination

Nominations received: Corina Spreitzer (AT)

Note:
-Overview: the EU-POG (formerly known as the European Risk Management Strategy Facilitation Group) was established as a permanent Working Group in 2005.The group aim is to develop a European Strategy for risk management, built on the National Competent Authorities (NCA's) resources and expertise, and incorporating the EMA's role in the coordination and the supervision of products authorised through the EU.
-Mandate: '*To prioritise issues for HMA and EMA Management Board consideration, on criteria based on public health and risk to operation of the EU network pharmacovigilance system'.*
-Meeting cycle: bi-monthly by teleconference or face to face meetings when needed.

http://www.hma.eu/ermsfg.html

7.5. Cooperation with international regulators

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

The teleconference will take place right after the end of the second day of the plenary meeting

CAT: Martina Schüßler-Lenz

Scope: draft agenda

Action: for adoption

7.6. CAT work plan

7.6.1. CAT 2018 work plan

CAT: Martina Schüßler-Lenz

Scope: CAT 2018 work plan

Action: for adoption

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

CAT: Martina Schüßler-Lenz

Scope: feedback on the proposed actions

Action: for information

Note: this will be a cross-committee activity, involving members/experts from CAT, SAWP, PRAC, CHMP and PDCO.

7.6.3. Expert meeting on genome editing, EMA, London, UK, 18 October 2017

CAT: Martina Schüßler-Lenz, Bernd Gansbacher, Paolo Gasparini

Scope: oral feedback on the expert meeting

Action: for information

7.7. Planning and reporting

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

CAT: Martina Schüßler-Lenz

Scope: The 'European Commission and European Medicines Agency Action Plan on ATMPs' has been published on 20 October 2017

Action: for information

7.8. Others

8. Any other business

No items

Date of next CAT meeting:

06-08 December 2017

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

SB: Significant benefit

SR: Summary Report

SWP: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

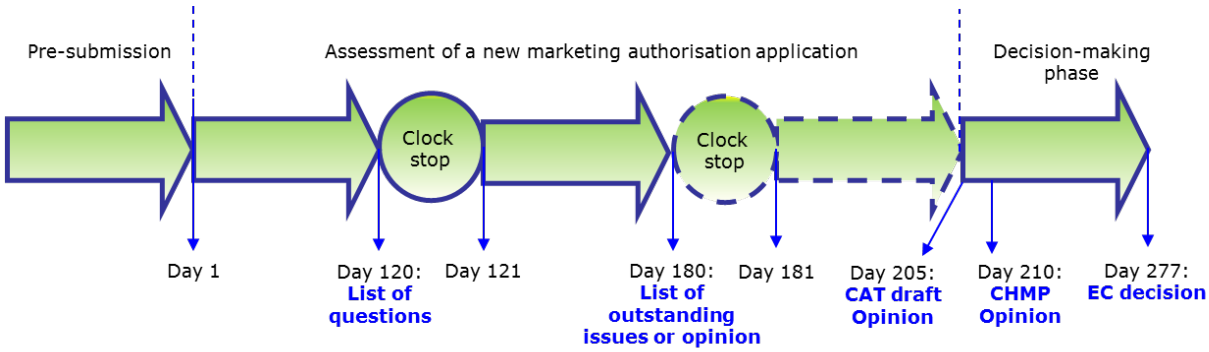
Evaluation of ATMPs (section 2)

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/