



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16 July 2015
EMA/CAT/481509/2015
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 16-17 July 2015

Chair: Paula Salmikangas - Vice-chair: Martina Schübler-Lenz

16 July 2015, 09:00 – 13:00, virtual

17 July 2015, 09:00 – 13:00, virtual

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 16-17 July 2015. See July 2015 CAT minutes (to be published post September 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 16-17 July 2015

1.3. Adoption of the minutes

CAT minutes for 18-19 June 2015

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

None

2.2. Oral explanations

None

2.3. D180 List of outstanding issues (LoOIs)

None

2.4. D120 Lists of questions (LoQs)

None

2.5. Day 80 assessment reports

None

2.6. Re-examination procedure (new applications) under Article 9(2) of Regulation No. 726/2004

2.6.1. Heparesc - allogeneic human heterologous liver cells; Orphan; EMA/H/C/003750

Cytonet GmbH & Co. KG.; treatment of urea cycle disorders

Action:

-for appointment of Re-examination (Co-)Rapporteurs

-request for nominations for expert meeting (date to be confirmed – around 5 October 2015) with expertise in paediatrician and/or paediatric intensive care specialist with expertise in urea cycle disorders; paediatrician hepatologist with expertise in liver genetic diseases; surgeon with expertise in paediatric liver surgery; preclinical lab specialist with expertise in urea cycle disorders

Document(s) tabled:

Notification from the applicant dated 9th July 2015 requesting a re-examination and a SAG consultation

2.7. Withdrawal of initial full application

None

2.8. Ongoing initial full application

2.8.1. talimogene laherparepvec (EMA/H/C/0002771)

treatment of adults with melanoma that is regionally or distantly metastatic.

Scope: feedback from CHMP discussion

Action: for information

Document tabled:

SAG-O LoQs (for information)

Note:

The CAT issued a classification as a gene therapy medicinal product in July 2012

The SAWP gave SA in 2008 and 2013

2.9. New applications

2.9.1. expanded adipose-derived stem cells of allogeneic origin – eASCs; *Orphan*; (EMA/H/C/0004258)

TiGenix S.A.U.; Intended for the treatment of complex perianal fistulas in adult patients

Action: for information

Note:

The CHMP granted at its June 2015 plenary eligibility as a centralised product under Art. 3(1) Indent 1a ATMP Regulation (EC) 126/2004

2.10. GMP and GCP inspections requests

None

2.11. Type II variations

2.11.1. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/34

UniQure Biopharma B.V.; Scope: submission of final study report CT-AMT—011-02

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Action: for adoption

Document(s) tabled:
Revised AR
Opinion

2.11.2. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/37-G

UniQure Biopharma B.V.; Scope: PI update section 4.8 and 5.1 (five years FU of final CSR study 011.01) and FU of 011.3

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Action: for adoption

Document(s) tabled:
Revised AR
Opinion

2.11.3. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/38

UniQure Biopharma B.V.; Scope: PI update section 5.1 (final CSR study 011.05) (FU of 011.03)

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Action: for adoption

Document(s) tabled:
RSI

2.12. Other post-authorisation activities

None

3. Certification of ATMPs

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

3.1. New applications

None

3.2. Day 60 evaluation reports

None

3.3. Opinions

None

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – appointment of CAT Co-ordinators

4.2. Day 30 Co-ordinators' first reports

4.2.1. Adeno-associated virus vector serotype rh10 encoding human factor IX

intended for the treatment of patients with moderate/severe to severe factor IX deficiency, i.e. moderate/severe to severe haemophilia B

Action: for adoption

Document tabled:
Coordinator's Classification report

4.2.2. Concentrate of autologous bone marrow-derived mononuclear cells (BM-MNC)

intended to improve limb perfusion/restore blood flow to previously ischemic tissue, and improve the mobility and quality of life (QoL) of patients with peripheral artery disease (PAD) and critical limb ischemia (CLI)

Action: for adoption

Document tabled:
Coordinator's Classification report

4.3. Finalisation of procedures

4.3.1. Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor

intended for the treatment of various types of cancer

Action: for information:
ATMP Classification report

Note:
The European Commission raised no comments.

4.3.2. Human monocytes-derived suppressive cells (HuMoSC), expanded ex vivo

intended for the treatment of acute Graft-versus-Host Disease refractory to first-line treatment

For action: for information:
Revised ATMP Classification report
Letter from the EC dated 29.06.15.

Note:
The European Commission requested a clarification and raised an editorial comment; these do not require re-adoption of the classification report

4.4. Follow-ups and guidance

None

5. Scientific Advice

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

5.1. New scientific advices – appointment of CAT Rapporteur

5.2. CAT Rapporteurs' reports

5.3. Lists of issues

5.4. Finalisation of Scientific Advice procedures

6. Pre-Authorisation Activities

Disclosure of 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 (PIP)

None

6.2. ITF briefing meetings in the field of ATMPs

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting

CAT-CHMP joint Strategic Review & Learning meeting (formerly known Informal meeting) took place in Ljubljana (Slovenia) on 27th-28th May 2015 under the auspices of the Latvian Presidency of the Council of the European Union

Scope: feedback from the meeting

Action: for discussion

See also 7.3.7., 7.4.2. and 7.4.4.

7.1.2. CAT membership

UK: Christiane Niederlaender – new member nominated on 1st July 2015

UK: Elaine French – termination of mandate for member on 30th June 2015

Action: for information

7.2. Coordination with EMA Scientific Committees

7.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of Outcomes (SoO) for the June 2015 meeting

Action: for information

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

7.3.1. Good Laboratory Practice (GLP) requirements of non-clinical studies for Advanced Therapy Medicinal Products

Action: for discussion

Note:

The EMA GLP IWP gave a presentation to CAT in June 2015 on GLP requirements for ATMPs.

7.3.2. Scientific Co-ordination Board (SciCoBo) - meeting 26th June 2015

Action: for information

7.3.3. Post-authorisation efficacy studies (PAES) - Scientific guidance

Action: for discussion and comments

Note:

The aim of this draft is to provide scientific guidance for MAHs and NCAs on the general need for such studies, on general methodological considerations, on specific situations and on study conduct. Following its adoption by the PRAC the draft guidance will be released for public consultation (foreseen after the summer 2015)

7.3.4. EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP)

Scope: workshop on risk minimisation measures to take place on 16th September 2015

Scope: joint meeting to take place on 17th September 2015

Action: for information

7.3.5. Pharmacovigilance: information systems and services

Update on projects which are currently being implemented to deliver the IT systems required by, or needed to support the business activities of, the new pharmacovigilance legislation.

Action: for information

7.3.6. Enhanced early dialogue to foster development and facilitate accelerated assessment

Scope: nomination of CAT members to review the document and prepare comments

Action: for discussion

Tabled document:
Concept document

7.3.7. Questions and Answers on minimally manipulated ATMPs

Feedback from the discussion that took place at the CAT-CHMP joint Strategic Review & Learning meeting, Ljubljana (Slovenia), May 2015

Action: for appointment of drafting group members

See also 7.1.1.

7.4. Co-operation within the EU regulatory network

7.4.1. GMP requirements for ATMPs

Scope: feedback on the meeting held on 7th July with the GMP inspectors

Action: for information

Tabled document:
Draft guideline

7.4.2. Drafting group for the guideline on requirements for Investigational ATMPs

Scope: discuss the survey targeting the clinical trial authorisation (CTA) assessors. Volunteers to draft the survey and to draft the guideline. Two DGs needed, one for gene therapy and another for cell-based therapies, each consisting experts for quality, nonclinical and clinical

Nominations received: (for gene therapy)

Action: feedback from the discussion in the Strategic Review & Learning meeting – Ljubljana and appointment of DG members

CAT members interested to join the drafting of this guideline should inform the CAT Secretariat.

See also 7.1.1.

7.4.3. European Food Safety Authority (EFSA) - Draft guidance on uncertainty in scientific assessment

Scope: nomination of CAT members to review the document and prepare comments

Guidance on Uncertainty in EFSA Scientific Assessment

<http://www.efsa.europa.eu/en/consultations/call/150618.pdf>

<http://www.efsa.europa.eu/en/consultations/call/150618.htm>

Action: for information

Note:

EFSA's Scientific Committee has developed this guidance document to offer a tool-box of methodologies – both quantitative and qualitative – for analysing scientific uncertainties in all its scientific assessments. EFSA invites input on this draft from other scientific advisory bodies as well as academic or applied experts in uncertainty analysis, particularly on the proposed methods contained in the tool box.

7.4.4. Analysis of European Clinical Trials Database (EudraCT)

Scope: Analysis of EudraCT for trials with ATMPs

Action: for discussion

See also 7.1.1.

7.5. Co-operation with international regulators

7.5.1. International Pharmaceutical Regulators Forum (IPRF), New Orleans (USA), 13-16 May 2015

Scope: Feedback on IPRF Cell Therapy and Gene Therapy Groups

Scope: Feedback from the IPRF - Gene Therapy Working Group meeting

Action: for information

7.5.2. Therapeutics Goods Administration (TGA) – Department of Health, Australia Government. Consultation: regulation of autologous stem cell therapies

Scope: The TGA is considering whether the regulation applied to some autologous cells is appropriate.

<https://www.tga.gov.au/consultation/consultation-regulation-autologous-stem-cell-therapies#documents>

Action: for information

Document table:

Regulation of autologous stem cell therapies – discussion paper for consultation (version 1.0, Jan. 2015)

7.6. Contacts of the CAT with external parties and interaction with the Interested Parties to the Committee

None

7.7. CAT Work Plan

7.7.1. CAT Work Plan 2015

Scope: review of progress

Action: for discussion

7.7.2. CAT Work Plan 2016

Scope: identification of topics for next year

Action: for discussion

- 7.7.3. CAT-ISCT Joint Workshop: *'Challenges and Opportunities for the Successful Development and Approval of Advanced Therapy Medicinal Products'*, Seville (Spain), Friday 25th September 2015, 14:15 – 18:45
-

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/06/news_detail_002357.jsp&mid=WC0b01ac058004d5c1

Action: for information

7.8. Planning and reporting

None

7.9. Others

None

8. Any other business

Date of next CAT meeting:
Thursday 17th – Friday 18th September 2015

9. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

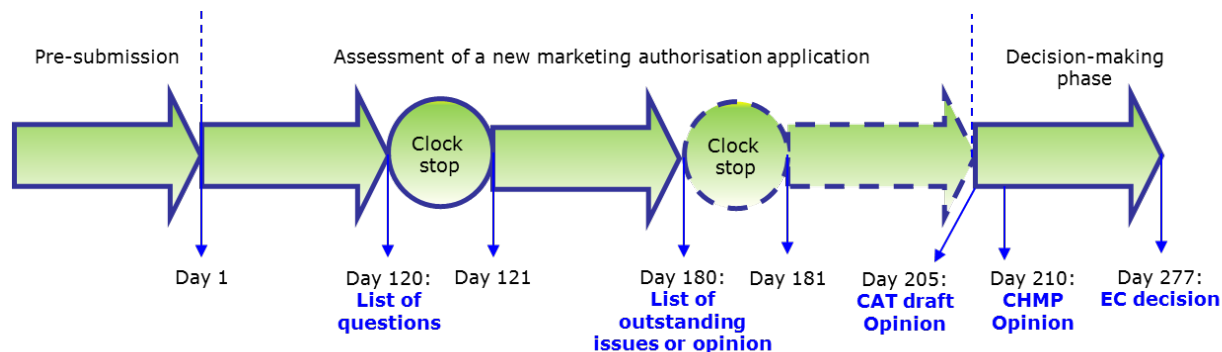
Evaluation of ATMPs (section 2)

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](#).

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/