18 June 2015
EMA/CAT/358344/2015
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 18-19 June 2015

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

18 June 2015, 09:00 – 18:00, room 03-F

19 June 2015, 09:00 – 15:00, room 03-F

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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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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 18-19 June 2015. See June 2015 CAT minutes (to be published post July 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 18-19 June 2015

1.3. Adoption of the minutes

CAT minutes for 12-13 May 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)

2.3.1. - talimogene laherparepvec (EMA/H/C/0002771)

treatment of adults with melanoma that is regionally or distantly metastatic

Action: for adoption

Documents tabled:
LoOIs
Draft questions to SAG
PP on GMO ERA consultation
BWP report

Note:
The SAWP gave SA in 2008 and 2013
The CAT issued a classification as a gene therapy medicinal product in July 2012

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

None

2.7. Withdrawal of initial full application

None

2.8. Ongoing initial full application

2.8.1. allogeneic human heterologous liver cells; Orphan; EMA/H/C/003750

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

Scope: Oral feedback from the discussion that took place at CHMP in April 2015

Action: for information

Note:

2.8.2. human autologous spheroids of matrix – associated chondrocytes for transplantation; EMA/H/C/0002736

Treatment is eligible for single as well as multiple adjacent defects. Cartilage defects of the knee, hip, elbow, shoulder and ankle joints were treated successfully. In a few cases, defect sizes between 11 and 23 cm^2 were treated successfully. The product is indicated for adults and adolescents with a closed epiphyseal growth platecancer.

Scope: to discuss the feasibility analysis and reach an agreement on whether a further clock stop can be granted.

Action: for discussion

Document tabled:

2.9. New applications

None

2.10. GMP and GCP inspections requests

None

2.11. Type II variations

None

2.12. Other post-authorisation activities

2.12.1. ChondroCelect – characterised viable autologous cartilage cells expanded in vivo expressing specific marker proteins; EMA/H/C/00878/MEA 16.3 and 18.3

TiGenix N.V.;

Scope 16.3: randomised control trial protocol TIG/ACT/04/2009

Scope 18.3: Non-interventional registry on the use of ChondroCelect to document the clinical effectiveness and safety outcome of treatment with ChondroCelect in real life in a patient population within the authorised indication

Rapporteur: Egbert Flory; Co-rapporteur: Tiina Palomäki; CHMP Coordinators: Jan Müller-Berghaus; PRAC Rapporteur: Brigitte Keller-Stanislawski

Action: for adoption

Document tabled:

Assessment reports of the PAMs

2.12.2. Provenge - autologous peripheral blood mononuclear cells activated with PAP-GM-CSF (Sipuleucel-T); EMA/H/C/002513

Dendreon UK LTD; Treatment of metastatic castrate resistant (hormone refractory) prostate cancer.Rapporteur: Egbert Flory; Co-rapporteur: Nicolas Ferry; CHMP Coordinators: Jan Mueller-Berghaus, Pierre Demolis; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: withdrawal of the MA

EPAR - summary for public

Action: for information

Notes:
Valeant reached a business decision to discontinue the commercial availability of Provenge in Europe and to withdraw the Marketing Authorization (letter dated 21.04.15.).

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

4.1.1. 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:
Request received on 29th May 2015

Notes:
Appointment of CAT Co-ordinator

Timetable:

4.1.2. 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:
Request received on 4th June 2015

Notes:
Appointment of CAT Co-ordinator

Timetable:

4.2. Day 30 Co-ordinators' first reports

4.2.1. 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 adoption

Document tabled:
Co-ordinator's Classification report

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

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

Action: for adoption

Document tabled:
Co-ordinator's Classification report

4.3. Finalisation of procedures

None

4.4. Follow-ups and guidance

4.4.1. Informal classification discussion from the Danish Health and Medicines Authority

Action: for discussion

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)

6.2. ITF briefing meetings in the field of ATMPs

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

7.1.2. Training on Meeting Management Documents application (CAT-MMD)

Scope: how to use the search functionality in MMD

Action: for discussion

7.2. Coordination with EMA Scientific Committees

7.2.1. Committee for Medicinal Products for Veterinary Use (CVMP): Ad Hoc Group on Veterinary Novel Therapies (ADVENT)

Scope: oral feedback on the work of the Advent Group

Action: for information

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

Summary of Outcomes (SoO) for the May 2015 meeting

Action: for information

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

7.3.1. Draft update of CHMP guidelines concerning tools for early access to medicines: release for consultation

Scope: Revised guideline on Accelerated Assessment
Scope: Conditional Marketing Authorisation – guideline on

Action: for information

Note: both guidelines will be adopted by the CHMP at their July 2015 meeting.

7.3.2. Training on the structure of the Benefit-risk in the assessment report

The new template for assessment report was presented at the CAT in February 2015

Action: for information

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

The upcoming clinical trial regulation requires that all non-clinical testing is performed under GLP

Action: for discussion

~~7.3.4.~~ Postponed to July 2015. ~~CAT involvement in scientific advice procedures for ATMPs:~~

~~**Action**: for discussion~~

7.3.5. Human Scientific Committees' Patients and Consumers Working Party (PCWP) and Healthcare Professionals' Organisations (HCPWP)

Scope: meeting taking place on 3-4 June 2015

Action: for information

Documents tabled:
PCWP agenda of 3rd June 2015
PCWP-HCPWP agenda of 4th June 2015
HCPWP agenda of 4th June 2015

7.4. Cooperation within the EU regulatory network

7.4.1. EU Medicines Agencies Network Strategy to 2020: *'Working Together to Improve Health'* – consultation phase

The European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) have released the 'EU Medicines Agencies Network Strategy to 2020', a draft common strategy to 2020 for the European medicines agencies network, for a three-month public consultation. Stakeholders are invited to send their comments before 30 June 2015.

Action: for information

Link to Network Strategy:
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/03/WC500185138.pdf

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/03/news_detail_002301.jsp&mid=WC0b01ac058004d5c1

7.4.2. GMP requirements for investigational ATMPs

Scope: feedback on the meetings held on 28th May, 4th and 17th June

Action: for discussion

7.4.3. Drafting group for a guideline on requirements for Investigational Medicinal Products (IMPs)

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

Action: for discussion

7.4.4. Consultation of the EU Environmental Agencies during the evaluation of medicinal products containing Genetically Modified Organisms (GMO): presentation of the procedure

Action: for information

Document tabled:
Presentation

7.5. Co-operation with international regulators

7.5.1. ATMP cluster teleconference with FDA and Health Canada

The teleconference will take place during the plenary meeting on Thursday 18th June from 14.00hrs – 15.00hrs

Action: for adoption

Document table:
Agenda

7.5.2. 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

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

EMA resources:

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)

Timetable:
-Documents released for consultation: 06.01.15.
-Interested parties responded by closed of business: 03.03.15.
-Feedback will be released following consideration of submission

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 2016 drafting process

Action: for information

7.8. Planning and reporting

None

7.9. Others

7.9.1. EMA Cross-Committee Task Force on Patient Registries

Feedback from the CAT representative on the second meeting of the Task Force that took place in June 2015.

Action: for information

Note:
The Task Force will finalise a strategy paper, identify/develop tools and make a proposal for a pilot phase to develop and test an EU collaborative framework for patient registries that would facilitate the collection and analysis of high quality data to inform regulatory decisions and the benefit-risk profile of medicinal products.

8. Any other business

8.1.1. Biennial on-line survey on the quality of the services and support provided by the Agency

In addition to the EMA's meeting services, the survey will also cover participation in virtual meetings and videoconferences. The survey was sent out on 10th June 2015 to the MB, all scientific committees and several working parties

Action: for information

Document table:
Survey

Date of next CAT meeting:
Thursday 16th – Friday 17th July 2015

9. Explanatory notes

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

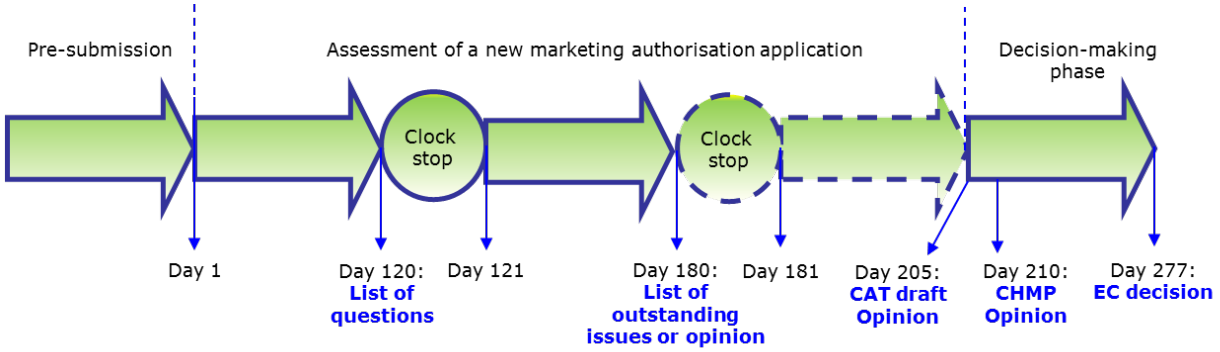
Evaluation of ATMPs (section 2)

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/