12 May 2015
EMA/CAT/282059/2015
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 12-13 May 2015

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

12 May 2015, 11:00 – 18:00, room 02-A

13 May 2015, 09:00 – 17:00, room 02-A

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

Table of contents

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 12-13 May 2015. See May 2015 CAT minutes (to be published post June 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 12-13 May 2015

1.3. Adoption of the minutes

CAT minutes for 16-17 April 2015

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. - Allogeneic human heterologous liver cells; *Orphan*; EMA/H/C/003750

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

Action: for adoption

Documents tabled:
Draft CAT AR
Draft Opinion

Note:
OE took place on 16th April 2015

2.2. Oral Explanations

None

2.3. D180 List of Outstanding Issues (LoOIs)

None

2.4. D120 List of Questions (LoQs)

None

2.5. Day 80 Assessment Report

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

2.8. Ongoing Initial Full Application

2.8.1. 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.

Action: for information

2.9. New Applications

2.9.1. autologous CD34+ cells transduced with retroviral vector containing the adenosine deaminase gen; *Orphan*; EMA/H/C/003854

GlaxoSmithKline Trading Services- UK; indicated for the treatment of children aged 0-18 diagnosed with ADA-SCID and for whom no suitable HLA-identical sibling bone marrow donor is available.

Notes:
CAT granted an accelerated assessment in April 2015

2.9.2. talimogene laherparepvec; EMA/H/C/H0002771

indicated for the treatment of adults with melanoma that is regionally or distantly metastatic

Action: for information

Notes:
-CAT issued a classification as a gene therapy medicinal product in July 2012
-CAT adopted the List of Questions in January 2015

2.10. GMP and GCP Inspections Requests

None

2.11. Type II Variations

2.12. Other Post-Authorisation Activities

2.12.1. 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 Coordinators: Brigitte Keller-Stanislawski, PRAC Co-Rapporteur: Arnaud Batz

Action: for discussion

Document tabled:
Letter from the MAH dated 21.04.15. withdrawing their MA

Notes:
After acquiring Dendreon and world-wide rights to Provenge, Valeant Pharmaceuticals performed a comprehensive review of Dendreon's portfolio, which included a careful examination of the viability of the European operations. Through this review, Valeant reached a business decision to discontinue the commercial availability of Provenge in Europe and to withdraw the Marketing Authorization

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. Opinion

4. Scientific Recommendation on Classification of ATMPs

4.1. New Requests – Appointment of CAT Co-ordinators

4.1.1. 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:
Request received on 28th April 2015

Notes:
Appointment of CAT Co-ordinator
See also 5.2.1. and 5.2.2.

Timetable:

4.1.2. 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:
Request received on 28th April 2015

Notes:
Appointment of CAT Co-ordinator

Timetable:

4.2. Day 30 Co-ordinators' First Reports

4.3. Finalisation of Procedure

4.3.1. Cell-based product made of a plasmacytoid dendritic cell line loaded with peptides from tumour antigens and irradiated

intended for the treatment of metastatic stages of cancer

Action: for adoption

Document tabled:

Revised CAT Classification report
Comments by the European Commission dated 29th April 2015

4.3.2. Autologous chondrocyte transplantation system

intended for the treatment of articular cartilage defect of the knee

Action: for adoption

Document tabled:

Revised CAT Classification report
Comments by the European Commission dated 29th April 2015

4.3.3. autologous human peripheral blood Vδ1+ T lymphocytes activated in vitro by cytokine and monoclonal antibody treatment

intended for the treatment of Chronic Lymphocytic Leukaemia, Acute Lymphoblastic Leukaemia.

Action: for information

Document tabled:
The European Commission raised no comments

4.4. Follow-up and Guidance

4.4.1. allogeneic ex-vivo expanded placental adherent stromal cells

intended for the treatment of Peripheral Arterial Occlusive Disease (PAOD)

Action: for discussion in view of the update of the reflection paper on classification

Documents tabled:
E-mail from the applicant dated 4th May 2015
Response from EMA to the applicant dated 6th May 2015

Note:
CAT classified it as Tissue Engineered Product (TEP) in March 2015
See also 5.2.3.

4.4.2. Informal classification query from the National Transplant Bureau (Lithuania)

National Transplant Bureau (the competent authority on tissue, cell and organ donation and transplantation) asks for interpretation of treatment, which may belong to advanced therapies.

Action: for discussion

Documents tabled:
E-mails from the NTB (Lithuania) dated 7th May 2015

4.4.3. Reflection Paper on Classification of ATMPs

DG on substantial manipulation:

DG on non-homologous use:
EMA resources:

Action: for adoption

Documents tabled:
Reflection Paper
Overview of comments

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 SAs – Appointment of CAT Rapporteur

5.2. List of Issues

5.3. Finalisation of SA 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 Plan (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) to be held in Ljubljana (Slovenia) on 27th-28th May 2015 under the auspices of the Latvian Presidency of the Council of the European Union

CAT resources: Metoda Lipnik-Stangelj, Una Riekstina

Action: for discussion

Documents tabled:
Final agenda

7.1.2. CAT membership

Poland: Dariusz Śladowski re-nomination as member started on 28th April 2015.

Action: for information

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

Send any questions/query/issues in advanced to CATSecretariat@ema.europa.eu

CAT resources:

Action: for discussion

Document(s) tabled:
Questions

7.2. Coordination with EMA Scientific Committees

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

Table of Decisions for the April 2015 meeting

Action: for information

7.2.2. EU Good Pharmacovigilance Practices (GVP)

Public consultation of GVP Module XVI Addendum I on educational materials. This has been developed within the governance structure for the implementation and maintenance in relation to the pharmacovigilance legislation and lead mainly by Portugal and other Member States, as it provides guidance on the submission and approval of educational materials for implementation at national level.

Action: for public consultation until 30 June

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c#section4

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

7.3.1. GCP guideline specific to ATMPs: need for revision

Action: for discussion

CAT members interested to join:

Notes:
Call of expression of interest

7.3.2. Scientific Co-ordination Board (SciCoBo): meeting of 30th March 2015

CAT resources: Paula Salmikangas
Action: for information

Documents tabled:
Minutes
Summary of meeting

Various meeting presentations

7.4. Cooperation within the EU regulatory network

7.4.1. GMP requirements for investigational ATMPs

CAT drafting group members:
Action: for discussion

Notes:
Feedback on the outcome of the DG meetings' discussions which will take place on 5 and 12 May 2015

7.4.2. National Competent Authorities: tissues and cells / medicines

Joint meeting between CAT and NCAs responsible for tissues and cells / medicines took place on 23rd April 2015 at the European Commission

Action: for information

Document tabled:
Agenda

7.4.3. Review of 3Rs (replacement, reduction and refinement) recommendations in the guidelines for cell based and gene therapy products

JEG 3Rs (joint Expert Group on the Application of the 3Rs in Regulatory Testing of Medicinal Products) review of EMA guidelines with regard to application of 3Rs approaches in regulatory testing. Annex table concerning the guidelines for cell based and gene therapy products to review and collect the relevant information on recommendations to reduce *in vivo* animal testing.

Action: for discussion

Note:
Agreement from CAT is sought on the part concerning guidelines for ATMPs. The final annex table will contain information from all non-clinical guidelines; relevant working parties will be consulted.

~~7.4.4. Pharmacovigilance: Information systems and services.~~ Postponed to July

~~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.~~

~~CAT resources:~~

~~**Action:** for information~~

7.5. Cooperation with International Regulators

None

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

None

7.7. CAT work plan

None

7.8. Planning and reporting

7.8.1. Planning estimates of forthcoming Advanced Therapies Medicinal Products (ATMP) MAAs for the period March. 2015 - Dec. 2017

7.9. Others

7.9.1. Talk on: *'Orphan medicines* 12th May 2015, 12:30-13:30hrs, Room 3E

This event will be a panel discussion and open floor debate.
Speakers: Bruno Sepodes, chair of COMP; Paula Salmikangas, chair of CAT; Yann le Cam, CEO of Eurordis; and Ad Schurmann, Head of the Reimbursement Department at the Dutch Health Care Insurance Board

CAT resources:

Action: for information

Note:
Delegates are invited to join the discussion and open floor debate organised by the Communications Department. This discussion is part of the EMA's 20th anniversary monthly event series entitled: *'Debating Science, Medicines, Health'*.

7.9.2. EMA Cross-Committee Task Force on Patient Registries

Feedback from the CAT representative on the first meeting of the Task Force that took place on 30th March 2015.

CAT resources:

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.

7.9.3. Article on regulatory/scientific issues related to stem cell containing medicinal products, to be published in the journal: Cell and Gene Therapy Insights.

Lead author:

Following members indicated their interest to participate in the drafting:

Action: for discussion

Authors to confirm their active participation to the drafting of this article.
Rapporteurs of Holoclar (E. Flory, P. Gasparini) to agree to contribute.

8. Any other business

8.1.1. Parental Drug Association: 2015 Europe Conference, Advanced Therapy Medicinal Products, 2-3 June, Amsterdam (The Netherlands)

CAT resources:

Action: for information

Date of next CAT meeting:
Thursday 18th – Friday 19th June 2015

Explanatory notes

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

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

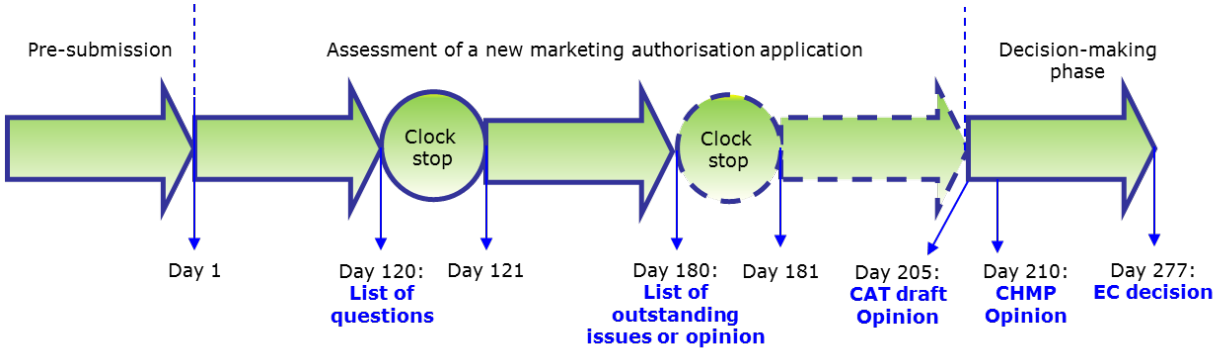
8.2. Evaluation of ATMPs (section 2)

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.

8.3. 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.

8.4. 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.

8.5. 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.

8.6. 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.

8.7. 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.

8.8. 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/