EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 December 2014
EMA/CAT/652186/2014
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 11–12 December 2014

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

11 December 2014, 09:00hrs – 18:30hrs, room 3-E
12 December 2014, 09:00hrs – 15:00hrs, room 3-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 monthly reports once the procedures are finalised and start of referrals will also be available.

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 11 - 12 December 2014.

See December 2014 minutes (to be published post January 2015 CAT meeting)

1.2. Adoption of agenda of the meeting of 11-12 December 2014

1.3. Adoption of the minutes of the previous CAT meeting on 13-14 November 2014

1.4. Table of Decisions of the previous CAT meeting on 13-14 November

2. Evaluation of ATMPs

2.1. Opinion

2.1.1. (formerly known as GPLSCD01) (*ex vivo* expanded autologous human corneal epithelial cells containing stem cells). (EMA/H/C/H0002450).

For information:

- PRAC RMP AR

For discussion:

- D180 Joint AR to the responses to the LoOIs
- BWP Report

For adoption:

- Draft CAT AR
- Draft Opinion
- Draft PI
- Draft SPC

2.2. Oral Explanation

No items on the agenda

2.3. List of Outstanding Issues

2.3.1. (allogeneic human heterologous liver cells) (EMA/H/C/003750).

For discussion:

- Joint response AR
- Joint inspection assessment (JIA)
- BWP report
- Request from the MAA dated 5th December 2014 requesting a one-month clock-stop to respond to the D180 LoOIs.

For adoption:

- LoOIs
- Revised Response Timetable

2.4. List of Questions

No items on the agenda

2.5. Day 80 Assessment Report

No items on the agenda

2.6. Re-Examination Procedure (New Application)+Under Article 9(2) of Regulation No. 726/2004

No items on the agenda

2.7. Withdrawal of Application

No items on the agenda

2.8. Ongoing Evaluation Procedures

2.8.1. (talimogene laherparepvec) (EMA/H/C/H0002771).

For information:

- Oral report by the Rapporteurs on possible major issues in the forthcoming LoQs

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

2.9. New Applications

2.9.1. (haploidentical donor lymphocytes depleted of alloreactive T cells, Donor T-lymphocytes depleted ex vivo of host alloreactive T-cells). EMA/H/C/0002397. Therapeutic indication: for the treatment of prevention (reduction) of transplant-related mortality (caused by graft-versus-host disease and/or infections) following haploidentical allogeneic hematopoietic stem cell transplantation (HSCT). Orphan

For information:

- Nominations received for Rapporteurship:
- Nominations received for Co-Rapporteurship:
- Nominations received for Peer reviewers:

2.9.2. (autologous CD34+ cells transduced with retroviral vector containing the adenosine deaminase gen), (EMA/H/C/H0003854). Therapeutic indication: treatment of severe combined immunodeficiency due to adenosine deaminase deficiency. 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. *Orphan*

For information:

- Letter from the applicant dated 21st October 2014 notifying of a delay in the anticipated submission date

2.10. GMP and GCP Inspections Requests

No items on the agenda

2.11. Post-Authorisation

No items on the agenda

2.11.1. Type II Variations

No items on the agenda

2.11.2. Other PA Activities

2.11.2.1.	**ChondroCelect** (characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins) MAH: TiGenix N.V. (EMA/H/C/00878/MEA 18.2) **Scope:** 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 **For discussion:** ▪ Oral update on the outcome	CAT Rapporteur: E. Flory CAT Co-Rapporteur: T. Palomäki CHMP Co-ordinator: J. Müller-Berghaus

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.

4. Scientific Recommendation on Classification of ATMPs

4.1.	[platelet generated from in-vitro derived megakaryocytes]. Proposed indication: intended for the treatment of thrombocytopenia in patients at risk of bleeding or with haemorrhagic events **For information**: ▪ ATMP Classification report	*The European Commission raised no comments*
4.2.	[allogeneic cord blood cells, *ex vivo* modulated with 16,16 dimethyl prostaglandin E2 (dmPGE2/ FT1050)]. Proposed indication: intended for the treatment of patients undergoing allogeneic hematopoietic reconstitution after high dose conditioning therapy for haematologic malignancies and certain rare genetic disorders. *Orphan* **For information:** ▪ ATMP Classification report	*The European Commission raised no comments*

4.3. [autologous differentiated adipose cells isolated from adipose tissue]. Proposed indication: intended for the treatment of primary perianal fistula **For information:** ▪ ATMP Classification report	*The European Commission raised no comments*
~~**4.4.** [living human mesenchymal stem cells derived from Wharton's jelly tissue of umbilical cord].~~ ~~**Proposed indications:**~~ ~~1. Acute and chronic Graft-versus-Host-Disease (aGvHD and cGvHD);~~ ~~2. Cartilage lessions;~~ ~~3. Cerebral palsy;~~ ~~4. Amyotrophic lateral sclerosis (ALS)~~ ~~**For information:**~~ ~~▪ ATMP Classification reports~~	
4.5. [solid flexible implant with chondrocytes fixed in biodegradable human origin fibrin based excipient]. Proposed indication: intended for the treatment of focal non-arthrotic cartilage defects of Outerbridge Grade III or IV of the femoral condyle including the trochlea **For adoption**: ▪ ATMP Classification report	
4.6. [adipose-derived mesenchymal stem cells]. Proposed indication: intended for the treatment of autoimmune diseases. **For information:** ▪ Request for ATMP Classification received on 24.11.14. **For adoption**: ▪ Appointment of CAT Co-ordinator ▪ Timetable	
4.7. [Tumour-infiltrating lymphocytes derived from metastatic melanoma]. Proposed indication: intended for the treatment of metastatic melanoma **For information:** ▪ Request for ATMP Classification received on 24.11.14. **For adoption**: ▪ Appointment of CAT Co-ordinator ▪ Timetable	
4.8. [human extracellular matrix on a absorbable polymer matrix]. Proposed indication: intended for the surgical/ interventional treatment of congenital heart malformations **For information:** ▪ Request for ATMP Classification received on 20.11.14. **For adoption**: ▪ Appointment of CAT Co-ordinator ▪ Timetable	

4.9.	Reflection Paper on Classification of ATMPs **For information:** ▪ Update on the comments received **For agreement:** ▪ Appointment of drafting group members **For discussion:** ▪ Briefing from the DG members on the lines to take during the discussion with the CAT's Its	Following CAT members will take part in the review of the comments received: - Drafting group on substantial manipulation: - Drafting group on non-homologous use

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.

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)

7. ITF Briefing Meetings in the field 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.

8. Organisational Matters

8.1. Regulatory and Procedural Guidance

8.1.1.	Application of ATMP Regulation **For discussion:** ▪ Oral feedback from the joint telecon of the CAT reflection groups on quality-related issues and risk based approach ▪ 'Aspects to consider on questions to SAWP of ATMPs'	CAT reflection groups: - Quality related issues: - Risk based approach: **Timetable** for document *'Aspects to consider on questions to SAWP on ATMPs'*: -Comments by CAT: Friday 5th December 2014 -Discussion at CAT: 11-12 December 2014
8.1.2.	Draft Guidance on meetings with applicants on responses to questions received from EMA Scientific Committees during the evaluation within the centralised procedure **For adoption:** ▪ Draft guidance document	Committees drafting group members: **Timetable:** Comments by committees: 05.12.14 to

8.2. CAT Meeting Organisation

8.2.1. CAT/CHMP/COMP joint informal meeting took place in Rome on 28th – 30th October 2014 under the auspices of the Italian Presidency of the Council of the European Union

For information:

- Oral debriefing / minutes

8.2.2. Revised Declaration of Interest form. Submission before end of January 2015: **for information**

Note: reference is made to the EMA's Chief Policy Adviser's presentation in June 2014 on the revised policy on Conflict of Interest.

8.3. Co-ordination with Committees/WPs/SAGs

8.3.1. CHMP November 2014 ToD: **for information**

8.3.2. COMP December 2014 agenda: **for information**

8.4. CAT's Workplan

8.4.1. European Meeting of the ISCT to be held on 24-26 September 2015, Seville (Spain): '*What should and can we do to make cellular therapies that bring value to patients available to these patients as soon as possible?'*

For agreement:

- Potential participation of CAT members

8.5. Interested Parties to CAT

8.5.1. CAT meeting with Interested Parties

For information:

- List of participants
- List of questions

For adoption:

- Agenda

This meeting will take place on Thursday 11th December from 15.00 – 18.00, room 3-E

9. CAT's DGs / PCWP and HCPWP

9.1. DG on GTMP Guidelines

No items on the agenda

9.2. DG on CTMP and TEP Guidelines

No items on the agenda

9.3. PCWP and HCPWP

9.3.1. PCWP

For information:

- Agenda - EMA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) meeting with all eligible organisations – 26 Nov. 2014
- Agenda - Training session for patients and consumers involved in EMA activities – 25 November

9.3.2. PCWP / HCPWP

For information:

- Minutes of the EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP) joint meeting in September 2014.
- Report on the workshop (which took place in September 2014) on: *'Benefit-risk communication to medicines users - How can regulators best meet the information needs of patients and healthcare professionals?'*

10. Other Scientific Topics

10.1. Council of Europe – Guide to the Quality and Safety of Tissues and Cells for Human Application, second edition

For information:

- CAT comments on Chapters 1, 20, 21 and 22 related to ATMPs to be sent to EDQM

Note: the Council of Europe is preparing a revision of the Tissues & Cells Guide. Chapters 1, 20, 21 and 22 are making reference to ATMP and are significantly extending the scope of chapter 20 ATMP, 1st edition TC guide.

CAT comments were sent to EDQM on 18th November 2014

CAT drafting members

10.2. Draft INN naming scheme for cell therapy products

For discussion :

- INN scheme
- Comments by CAT and BWP

Note: the draft has been developed by the WHO INN secretariat in collaboration with the INN expert group.

10.3. '*Development pathways for advanced therapy medicinal products*': workshop organised by Emerging Biopharmaceutical Enterprises (EBE) in collaboration with EMA and Italian Embassy's Scientific Office in London – 15 December 2014

For information:

- Programme

Registration and agenda

10.4.	Joint meeting between CAT and Competent Authorities for tissues and cells to take place in Brussels in the 1Q of 2015, to discuss topics of common interest. **For information:** ▪ Debriefing on the two meetings	Two meetings on 4 December: -morning meeting with the CA for tissues and cells; -afternoon meeting will be a preparation for a larger meeting between CAT and CA for tissues and cells in the beginning of 2015.
10.5.	The British Standard Institute (BSI) is running a Public Review for their Guide: *'PAS 157, Selection of materials of biological origin used in the design and development of cell-based medicinal products for clinical application'*: **for comments**	Click in the link to comment on the draft: http://drafts.bsigroup.com/Home/Details/53891 Deadline for comments: 10th December 2014.
10.6.	European Directorate for the Quality of Medicines & HealthCare (EDQM). Meeting of the Advisory Group of the Official Control Authority Batch Release (OCABR) Network for Human Biologicals which took place in October 2014, Strasbourg. **For information:** ▪ Letter to the CAT from the OCABR dated 19th November 2014 on the outcome of their discussion on *'Batch release requirements for human blood and plasma derived excipients used in ATMPs'* ▪ Annex IIf	

11. Any Other Business

Date of next CAT meeting:
Thursday 15th – Friday 16th January 2015

Explanatory notes

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

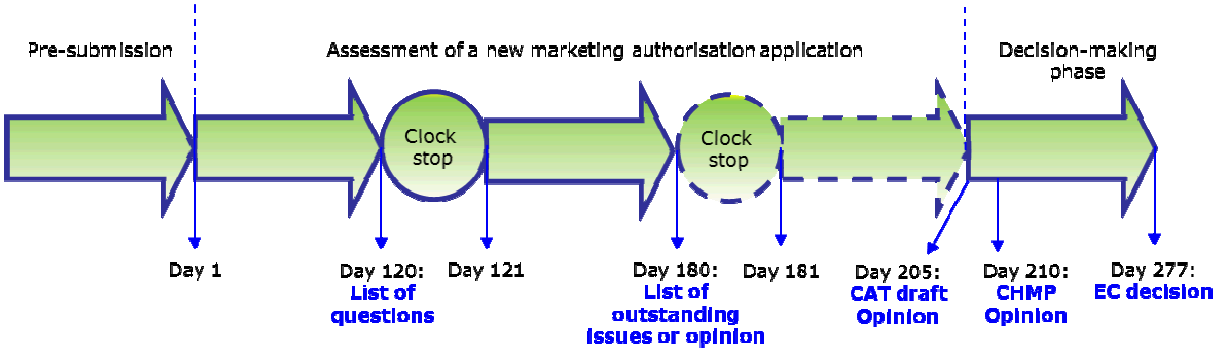
Evaluation of ATMPs (section 2)

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 2.9*)

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.

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 2.11.*)

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.

ATMP Certification (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)

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 (Section 7)

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 matters (section 8)

This section includes topics related to Regulatory and Procedural Guidance, CAT meeting organisation (including CAT membership) and Co-ordination with other Committees, Working Parties, Scientific Advisory Groups and other groups.

CAT's DGs / PCWP and HCPWP (section 9)

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, the EMA/CAT-Notified Body Collaboration Group, the Patient and Consumer Working Party (PCWP) and the Healthcare Professionals Working Party (HCPWP).

Other Scientific Topics (section 10)

This section 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.

More detailed information on the adobe terms can be found on the EMA website: www.ema.europa.eu/