EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 June 2014
EMA/CAT/368856/2014
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda of the 19 – 20 June 2014 meeting

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

19th June 2014, 11:00hrs – 18:30hrs, Room 3A
20th June 2014, 09:00hrs – 13:00hrs, Room 3A

Declaration on conflict of interest

In accordance with the Agency's revised policy and procedure on the handling of conflicts of interests, participants in this meeting are asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests). Discussions, deliberations and voting will take place in full respect of the restricted involvement of Scientific Committee members and, where relevant, experts attending the plenary meeting, as announced by the Scientific Committee Secretariat at the start of meeting.

Health & 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 regards to therapeutic indications listed against products, it must be noted that these may not reflect the full wording proposed by the applicant and may also vary during the course of the review. The procedures discussed at CAT are on-going and therefore certain aspects are considered confidential. Additional details on some of the procedures (for example the ATMP classification procedure) will be published in the CAT monthly report. For orphan medicinal products the product name and the applicant are published to be consistent with already publicly available information. Of note, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes. Further information with relevant explanatory notes can be found at the end of this document.

Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present within the framework of Regulation (EC) No 1049/2001 on access to documents because 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. PLENARY RELATED DOCUMENTS

1.1. AGENDA (EMA/CAT/318496/2014) and **TIMESCHEDULE** (EMA/CAT/337347/2014) for the CAT plenary to be held on 19th and 20th June 2014: **for adoption**

1.2. TABLE OF DECISIONS CAT plenary held on 15th and 16th May 2014 (EMA/CAT/301148/2014): **for information**

1.3. MINUTES of the CAT plenary held on 15th and 16th May 2014 (EMA/CAT/333504/2014): **for adoption**

1.4. 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 of 19th – 20th June 2014: **for information**

See June minutes (to be published post July 2014 CAT meeting)

2. EVALUATION OF ATMPS

2.1. OPINION

No items on the agenda

2.2. ORAL EXPLANATION

No items on the agenda

2.3. LoOI

No items on the agenda

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 APPLICATIONS)+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. (allogeneic human heterologous liver cells) (EMA/H/C/003750). Therapeutic indication: Treatment of urea cycle disorders.

For discussion:

- Request from the applicant of 26th May 2014, requesting a three-month extension of the clock stop to respond to the D120 LoQs

For adoption:

- Revised timetable to response to LoQs

2.9. NEW APPLICATIONS

2.9.1. (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:
- Nominations received for Rapporteurship:
- Nominations received for Co-rapporteurship:
- Nominations received for Peer reviewers:

2.10. GMP and GCP INSPECTIONS REQUESTS

No items on the agenda

2.11. POST-AUTHORISATION

2.11.1. Type II Variations

2.11.1.1. **Glybera** MAH: UniQure Biopharma B.V. (EMEA/H/C/002145/II/30)
Orphan
II/30
Scope: update of the protocol of the CM efficacy and safety study requested in Annex II
For discussion:
- Oral explanation by the MAH

CAT Rapporteur: E. French (UK)
CHMP Co-ordinator: G. Markey (UK)

See also 2.11.2.1.

2.11.1.2. **Glybera** (EMEA/H/C/002145/II/33 MAH: UniQure Biopharma B.V.
Orphan
II/33
Scope: Quality.
For discussion/adoption:
- Draft opinion /RSI

CAT Rapporteur: E. French (UK)
CHMP Co-ordinator: G. Markey (UK)

2.11.1.3. **Glybera** (EMEA/H/C/002145/II/05 MAH: UniQure Biopharma B.V.
Orphan
II/05
Scope*:* Quality.
For adoption – no discussion required:
- Draft opinion

CAT Rapporteur: E. French (UK)
CHMP Co-ordinator: G. Markey (UK)

2.11.2. Other PA Activities

2.11.2.1. Glybera (EMEA/H/C/002145) MAH: UniQure Biopharma B.V. *Orphan*	CAT Rapporteur: E. French (UK) CHMP Co-ordinator: G. Markey (UK) See also 2.11.1.1.
2.11.2.2. ChondroCelect (characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins) (EMA/H/C/00878/R/09). MAH: TiGenix N.V. **Scope:** Five-year renewal **For adoption:** ▪ Draft opinion ▪ CAT draft AR	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinator: J. Müller-Berghaus (DE) The CAT adopted a second request for supplementary information to the applicant at its May 2014 plenary.
2.11.2.3. ChondroCelect (characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins) MAH: TiGenix N.V. (EMA/H/C/00878/MEA 16.2) **Scope:** Randomised control trial protocol TIG/ACT/04/2009 **For information:** ▪ Reflection paper on chondrocyte products **For discussion:** ▪ Overview of comments received to the LoQs from the experts consultation (Healthcare Professional Organisations) **For adoption:** ▪ Draft AR of responses to the RSI	CAT Rapporteur: E. Flory (DE) CAT Co-Rapporteur: T. Palomäki CHMP Co-ordinator: J. Müller-Berghaus (DE) CAT adopted the second RSI in March 2014 CAT adopted a LoQs to HCPOs in April 2014 http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/05/WC500090887.pdf See also 2.11.2.4.

2.11.2.4.	**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:** ▪ Overview of comments received to the LoQs from the experts consultation (Healthcare Professional Organisations) **For adoption:** ▪ Draft AR of responses to the RSI	CAT Rapporteur: E. Flory (DE) CAT Co-Rapporteur: T. Palomäki CHMP Co-ordinator: J. Müller-Berghaus (DE) The second RSI was adopted at the March CAT meeting. The CAT adopted a LoQs to HCPOs in April 2014. See also 2.11.2.3.
2.11.2.5.	**PROVENGE** (autologous peripheral blood mononuclear cells activated with pap-gm-csf (sipuleucel-T)). MAH: Dendreon UK Ltd. (EMA/H/C/002513/MEA 005) **Scope:** Interventional PASS Protocol P13-2, Phase 2 study of coagulation parameters in men with metastatic castrate-resistant prostate cancer who receive Sipuleucel-T] including statistical analysis plan **For adoption:** ▪ Timetable	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinators: J. Müller-Berghaus (DE)
2.11.2.6.	**MACI** [matrix-assisted autologous chondrocyte implantation]. MAH: Genzyme Europe BV. (EMA/H/C/002522)	CAT Rapporteur: E. French (UK) CAT Co-Rapporteur: H. Ovelgönne (NL) CHMP Co-ordinators: G. Markey (UK) and J. Lodewijk Hillege (NL)

3. CERTIFICATION

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. [concentrate of autologous, uncultured, custom prepared bone marrow aspirate]. Proposed indication: field of regenerative medicine: bone damaged by disease (e.g. ostenecrosis), fracture or age-related loss of bone function.

For discussion:

- Comments received from the European Commission on 6 June 2014

For adoption:

- Revised ATMP Classification report

4.2. [an antiinfectious naked DNA vaccine encoding mutationinactivated E7-E6 fusion protein from Human Papillomavirus 16 linked to the human chemokine hMIP-1α via a dimerization module derived from human IgG3.]. Proposed indication: to prevent and treat HPV16 induced pre-malignancies and malignancies.

For discussion:

- Response to the LoQ received on 3rd June 2014

For adoption:

- Revised ATMP Classification report

4.3. [active substance (NTC8685-eRNA41H-Ubi-hTERT) is a double-stranded naked DNA plasmid of 7120 bp encoding an inactive human telomerase reverse transcriptase protein fused to ubiquitin (Ubi-hTERT)]. Proposed indication: immunotherapy (therapeutic DNA vaccination) for the treatment of various malignancies and the prevention of tumour relapse.

For adoption:

- ATMP Classification report

4.4. [an oncolytic virus derived from type 1 herpes simplex virus (HSV-1) by deletion of two genes (ribonucleotid reductase RR/ICP6, and gamma34.5) and re-insertion of one copy of gamma34.5 gene under expression control of b-myb transcription factor inserted upstream]. Proposed indication: treatment of advanced pancreatic cancer and / or unresectable hepatocellular carcinoma

For adoption:

- ATMP Classification report

4.5. [allogeneic peripheral blood mononuclear cells induced to an early apoptotic stage)]. Proposed indication: prevention of graft versus host disease.

For adoption:

- ATMP Classification report

4.6. [allogeneic expanded CD34+HSC issue from cord blood unit allogeneic lymphoid cells CD34- issue from cord blood unit]. Proposed indication: malignant hemopathies.

For information:

- Request received on 27 May 2014

For adoption:

- Appointment of CAT Co-ordinator
- Timetable

4.7. [autologous dendritic cells pulsed with tumour antigen-derived synthetic peptides]. Limited, USA. Proposed indication: treatment of glioblastoma

For information:

- Request received on 27 May 2014

For adoption:

- Appointment of CAT Co-ordinator
- Timetable

4.8. [AAV containing DNA encoding an RNAi targeting rhodopsin in combination with an AAV containing DNA encoding a rhodopsin gene]. Proposed indication: treatment of autosomal dominant rhodopsin-linked retinitis pigmentosa

For information:

- Request received on 5 June 2014

For adoption:

- Appointment of CAT Co-ordinator
- Timetable

4.9. [autologous bone marrow-derived progenitor cells in a suspension form for infusion]. Proposed indication: intended for chronic heart disease

For information:

- Request received on 6 June 2014

For adoption:

- Appointment of CAT Co-ordinator
- Timetable

4.10. [lysate of tumor cells associated to hydroxylapatite particles]. Proposed indication: intended for a therapeutic vaccine

For information:

- Request received on 10 June 2014

4.11. Reflection paper on classification of ATMPs: **for adoption for external consultation**

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)

No items on the agenda

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. Presentation on the Conflict of Interest revised policy: **for information**

8.1.2. Multinational Assessment Teams for initial marketing authorisation applications.

For discussion:

- Registry to list possible/available CAT-related expertise/resources in each MS for MN-teams

8.1.3. Report from the European Commission to the European Parliament and the Council on the application of the ATMP Regulation: **for information**

Following CAT members expressed interest to take part in CAT reflection groups:
- Quality related issues:
- Risk based approach:

8.2. CAT Meeting Organisation

8.2.1. CAT Membership
For information:
- Finland: Tiina Palomäki – new member nominated on 14th May 2014

8.2.2. CAT/CHMP/COMP joint informal meeting to be held in Rome on 28th – 30th October 2014 under the auspices of the Italian Presidency of the Council of the European Union
For information:
- Feedback on topics for the agenda

8.3. Co-ordination with Committees/WPs/SAGs

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

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

8.4. CAT's Workplan

8.4.1. CAT Workplan 2015
For discussion:
- List of proposed topics

Link to the EMA Work Programme 2014: http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2014/03/WC500163394.pdf

9. CAT's DGs / PCWP and HCPWP

9.1. DG on GTMP Guidelines

9.1.1. Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products
For discussion:
- Comments received from Finland

9.2. DG on CTMP and TEP Guidelines

10. OTHER SCIENTIFIC TOPICS

10.1. Regulation Forum Gene Therapy discussion Group (RFGTDG)
For information:
- Agenda of the international telecon which took place in April 2014
- Agenda of the international telecon to take place on 23 June 2014

10.2. EMA/CAT/FDA/Health Canada bimonthly teleconference on ATMP cluster

For adoption:

- Agenda

11.A.O.B.

11.1. Project 2014: move to 30, Churchill Place, Canary Wharf

For information:

- Last presentation
- Visit by the committee to the new building organised for Thursday 17th July at 7pm (after the CAT meeting)

Date of next CAT meeting:
Thursday 17th – Friday 18th July 2014

The notes below give a brief explanation of the main sections and headings in the CAT agenda and should be read in conjunction with the agenda or the minutes.

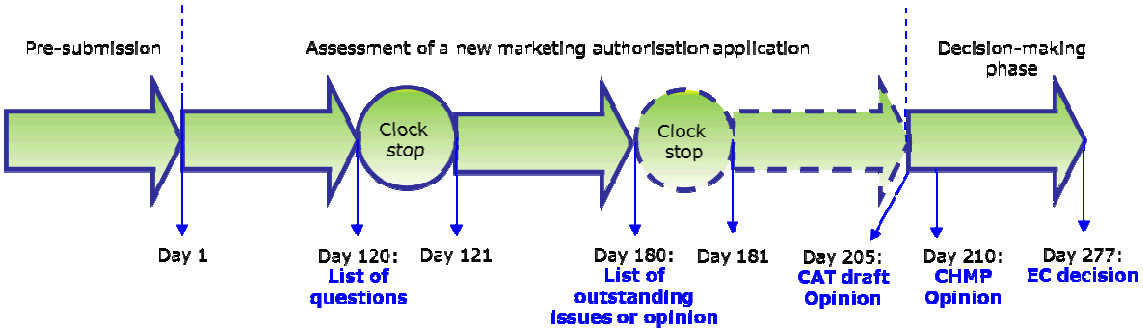
Evaluation of ATMPs (section 2)

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 2.5*)

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 2.6*)

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 2.8*)

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 2.9*)

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 2.10*)

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.