16 April 2015
EMA/CAT/258888/2015
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 16-17 April 2015

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

16 April 2015, 09:00 – 18:00, room 02-F

17 April 2015, 09:00 – 15:00, room 02-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).

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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 April 2015. See April 2015 CAT minutes (to be published post May 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 16-17 April 2015

1.3. Adoption of the minutes

CAT minutes for 19-20 March 2015

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

None

2.2. Oral Explanations

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

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

Action: for discussion

Document tabled:

Joint AR of the responses to the LoOIs
BWP report

Note:
Oral Explanation to take place at 09:30hrs on 16th April 2015

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

None

2.8. Ongoing Initial Full Application

2.8.1. - Characterized viable haploidentical Herpes Simplex Virus Thymidine Kinase (HSV-Tk) and Human Low Affinity Nerve Growth Factor Receptor (ΔLNGFR) transfected donor lymphocytes; *Orphan*; EMA/H/C/002801

MolMed SpA; treatment of adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies

Action: for discussion

Documents tabled:
Rapporteurs' feasibility analysis

Request of extension of the clock stop .
Notes:

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.

Action: for adoption

Documents tabled:
Applicant's submission of 13th March requesting an accelerated assessment procedure

Rapporteurs' draft briefing note for the accelerated assessment

Notes:

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: E. French; CHMP Coordinators: G. Markey

Action: for adoption

Document tabled:
RSI

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: E. French; CHMP Coordinators: G. Markey

Action: for adoption

Document tabled:
RSI

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: E. French; CHMP Coordinators: G. Markey

Action: for adoption

Document tabled:
RSI
Presentation on regulatory options

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: E. Flory; Co-rapporteur: T. Palomäki; CHMP Coordinators: J. Müller-Berghaus

Action: for discussion

Action: for adoption
Timetable:

Document tabled:

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

None

4.2. Day 30 Co-ordinators' First Reports

4.2.1. - 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:
Co-ordinator's Classification report

4.2.2. - Autologous chondrocyte transplantation system

intended for the treatment of articular cartilage defect of the knee

Action: for adoption

Document tabled:
Co-ordinator's Classification report

4.2.3. - 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 adoption

Document tabled:
Co-ordinator's Classification report

4.3. Finalisation of Procedure

4.3.1. - autologous mononuclear cells derived from human cord blood

intended for the treatment of paediatric brain damage, hypoxic-ischaemic encephalopathy, and cerebral palsy

Action: for adoption

Documents tabled:
Revised Co-ordinator's Classification report
Comments by the European Commission dated 30th March 2015

4.3.2. - allogeneic *ex-vivo* expanded placental adherent stromal cells

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

Action: for adoption

Documents tabled:
Revised Co-ordinator's Classification report
Comments by the European Commission dated 30th March 2015

Note:

4.3.3. - allogeneic somatic cells therapy medicinal product derived from the isolation and *ex vivo* expansion of human Umbilical Tissue-Derived Cells

intended improvement of visual acuity in patients with vision loss from geographic atrophy secondary to age-related macular degeneration

Action: for adoption

Documents tabled:
Revised Co-ordinator's Classification report
Comments by the European Commission dated 30th March 2015

4.3.4. - autologous dendritic cells loaded with autologous irradiated tumour stem cells suspended in a cryopreservation medium

intended for the treatment of melanoma.

Action: for adoption

Documents tabled:

Revised Co-ordinator's Classification report
Comments by the European Commission dated 30th March 2015

4.3.5. -suspension of allogeneic human adult stern cells, isolated from skeletal muscle

intended for the treatment of Duchenne Muscular

Action: for information

Document tabled:
ATMP Classification report

Note:
The European Commission raised no comments

4.4. Follow-up and Guidance

4.4.1. Reflection Paper on Classification of ATMPs

DG on substantial manipulation:
DG on non-homologous use:

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. CAT Rapporteurs' Reports

5.3. List of Issues

5.4. Finalisation of SA procedures

5.4.1.

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:
Draft agenda

7.1.2. CAT membership

Italy: Paolo Gasparini's re-nomination as member started on 27th March 2015.

Action: for information

7.2. Coordination with EMA Scientific Committees

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

Table of Decisions for the March 2015 meeting

Action: for information

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

7.3.1. GMP requirements for investigational ATMPs

CAT drafting group members: **Action:** for discussion

Notes:
Feedback on the outcome of the DG meeting's discussion on chapters 4, 5 and 6 which took place on 16th April 2015

7.3.2. Scientific Co-ordination Board (SciCoBo) meeting of 29th January 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

None

7.5. Cooperation 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 16th April from 14.00 – 15.00hrs

Action: for adoption

Document table:
Agenda

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

None

7.9. Others

7.9.1. Cross-Committee Task Force on Patient Registries

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

CAT resources: K. Breen

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

None

Date of next CAT meeting:
Tuesday 12th – Wednesday 13th May 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.

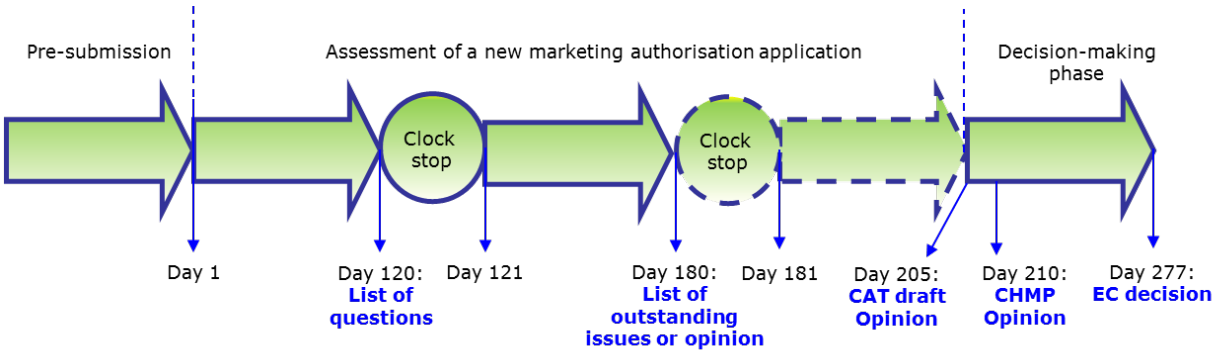
Evaluation of ATMPs (section 2)

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/