3 November 2021
EMA/CAT/574435/2021
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 06-08 October 2021

Chair: Martina Schuessler-Lenz; Vice-Chair: Ilona Reischl

Health and safety information

Some of the information contained in these minutes are considered commercially confidential or sensitive and therefore not disclosed. Regarding 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, these minutes are a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes 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

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants for agenda topics was identified. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Chair welcomed the new member(s) and alternate(s) and thanked the departing members/alternates for their contributions to the Committee.

1.2. Adoption of agenda

CAT agenda for 06-08 October 2021 meeting was adopted with additions in sections 2.6 and 6.2 (ITF meetings in the field of ATMPs).

1.3. Adoption of the minutes

The CAT minutes for 08-11 September 2021 meeting were adopted on 18 October 2021 via written procedure.

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. Lisocabtagene maraleucel / lisocabtagene maraleucel - Orphan - EMEA/H/C/004731

Bristol-Myers Squibb Pharma EEIG; treatment of large B-cell lymphoma, diffuse large B-cell

lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B)

Scope: list of outstanding questions

Action: for adoption

List of Questions (LoQ) adopted on 06.11.2020. List of Outstanding Issues (LoOI) adopted on 16.04.2021

The CAT agreed that an oral explanation was not needed at this time.

The Rapporteurs presented the outcome of the assessment of the list of outstanding issues. On the quality questions, feedback was received from the discussion in BWP.

The second list of outstanding issues was adopted. The evaluation timetable was agreed.

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

2.5.1. Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830

Accelerated assessment

BioMarin International Limited; treatment of severe haemophilia A

Scope: Day 80 assessment report

Action: for information

The information was noted.

2.6. Update on ongoing initial applications

2.6.1. Autologous glioma tumor cells, inactivated / autologous glioma tumor cell lysates, inactivated / allogeneic glioma tumor cells, inactivated / allogeneic glioma tumor cell lysates, inactivated - Orphan - EMEA/H/C/003693

Epitopoietic Research Corporation-Belgium (E.R.C.); treatment of glioma

Scope: MAA's request (dated 06.10.2021) for a clock-stop extension

Action: for information

List of Questions adopted on 22.01.2021.

2.7. New applications

No items

2.8. Withdrawal of initial marketing authorisation application

No items

2.9. Re-examination of initial application procedures under Article 9(2) of Regulation No. 726/2004

No items

2.10. GMP and GCP inspections requests

No items

2.11. Type II variations and variations of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0046

Amgen Europe B.V.

Rapporteur: Heli Suila,

Scope: Clinical. Opinion

Submission of the final report from study 20110265 listed as an obligation in the Annex II of the Product Information. This is a Phase 1b/3, multicenter, trial of talimogene laherparepvec in combination with pembrolizumab for treatment of unresectable stage IIIB to IVM1c melanoma. The Annex II is updated accordingly.

Action: for adoption

The Rapporteur presented the assessment of the type II variation. CAT noted that the study 20110265 showed no difference between pembrolizumab + placebo versus pembrolizumab + Imlygic. The Imlygic product information is unchanged. The opinion is adopted.

2.11.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0040

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.11.3. Libmeldy - atidarsagene autotemcel - Orphan - EMEA/H/C/005321/II/0004

Orchard Therapeutics (Netherlands) BV

Rapporteur: Carla Herberts

Scope: Quality. Request for supplementary information

Action: for adoption

The request for supplementary information was adopted.

2.11.4. Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - Orphan - EMEA/H/C/005102/II/0012

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Request for supplementary information

Action: for adoption

The request for supplementary information was adopted.

2.11.5. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0015

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Clinical. Opinion

Updates to Sections 4.4, 4.8 and 5.1 of the SmPC to reflect the final study results Study AVXS-101-CL-302: a Post-authorisation efficacy study intended to confirm the efficacy and safety and tolerability of a single dose of Zolgensma in patients younger than 6 months of age with SMA Type 1 with One or Two SMN2 Copies.
The package leaflet has been updated accordingly and annex II has been updated to reflect completion of this Specific Obligation.

Action: for adoption

Request for Supplementary Information adopted on 16.07.2021.

The opinion was adopted.

2.11.6. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0017/G

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Quality. Opinion

Action: for adoption

The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - Orphan - EMEA/H/C/002450/R/0039

Holostem Terapie Avanzate s.r.l.

Rapporteur: Egbert Flory, PRAC Rapporteur: Rhea Fitzgerald

Scope: 1-year Renewal of Marketing Authorisation. Opinion

Action: for adoption

The renewal opinion was adopted.

2.13.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/P46/012

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. FINAL STUDY REPORT, Study no. CTL019B2001X, EudraCT no. 2016-001991-31: Phase IIIb study for relapsed/refractory pediatric/young adult acute lymphoblastic leukemia patients to be treated with CTL019.

Action: for adoption

Request for Supplementary Information adopted on 18.06.2021.

The Rapporteur presented the outcome of the assessment. The MAH will submit a variation to change the product information on the experience of treatment in children below 3 years of age. The report was adopted.

2.13.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/REC/013

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: quality

Action: for adoption

The report was adopted.

2.13.4. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/REC/014

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: quality
Action: for adoption

The report was adopted.

2.13.5. Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - Orphan - EMEA/H/C/005102/ANX/002.1

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Scope: Follow-up from ANX-002:
Additional information requested following assessment of the protocol for study KTE-EU-472-6036 entitled: "Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)".

Action: for adoption

CAT noted the question from PRAC.

2.13.6. Impact of tocilizumab potential shortages on CAR-T cell-based ATMPs use in EU – regulatory options and recommendations

Rapporteur: Rune Kjeken, Jan Mueller-Berghaus

Scope: Scientific and regulatory considerations regarding the treatment of cytokine release syndrome following CAR-T cell administration.

Action: for discussion

CAT discussed how to ensure that CAR-T products can be used in case of shortage of tocilizumab. Alternative treatment for cytokine release syndrome were presented. Different regulatory options were discussed. CAT concluded that alternative treatments should not be recommended (this is at the discretion of the treating physician), but that the treating centre have to ensure that that suitable alternative treatments are available; this will have to be verified by the MAHs. An amendment to the Annex IID of the opinions of the approved CAR-T and changes to the product information (SmPC sections 4.2 and 4.4) need to be made. The MAHs will have to submit a type II variation. The recommendation from CAT to CHMP and PRAC was adopted.

3. Certification of ATMPs

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

Timetable:

-Start of the procedure:	11.10.2021
-EMA Coordinator's draft report:	22.10.2021
-CAT Coordinator's comments:	27.10.2021
-Revised scientific recommendation:	29.10.2021
-CAT's discussion of scientific recommendation:	05.11.2021

4.1. New requests – Appointment of CAT Coordinator

4.1.1. CD 19 CAR T-cells transduced with lentiviral vector

Intended for the treatment of adults and children with B-cell non-Hodgkin's lymphoma and acute lymphoblastic leukemia. CD 19 CAR-T cell therapy will be used as first salvage in patients with primary refractory disease or in first relapse, after one line of systemic therapy, and with the presence of least one pre-defined high-risk feature

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Allogeneic adipose-derived mesenchymal stromal cells, ex-vivo expanded

Intended for the treatment of osteoarthritis, knee

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Recombinant adeno-associated virus, serotype 2, containing human ND4 codon-optimised gene (rAAV2-ND4) - EMA/PRIME/21/039

Treatment of Leber's Hereditary Optic Neuropathy (LHON) associated with ND4 G11778A mutation

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. Allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured

Intended for the treatment of paediatric and adult patients undergoing partially human leucocyte antigen (HLA) compatible allogeneic haematopoietic stem cell transplantation to accelerate adaptive immunological reconstitution

Scope: appointment of CAT Coordinator and adoption of timetable

The CAT coordinator was appointed.

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous red blood cells chemically coupled with 12 antigenic peptides

Intended for the treatment of multiple sclerosis

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 22 October 2021.

4.3. Day 60 revised scientific recommendation (following list of questions)

No items

4.4. Finalisation of procedure

4.4.1. Point-of-care skin cell isolation kit

Intended for skin regeneration after burns, skin trauma, invasive surgery

Scope: The European Commission raised no comments. ATMP Scientific Recommendation

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.2. Optimised DNA encoding the sequence of interest COL7A1

Intended for the treatment of dystrophic epidermolysis bullosa (DEB)

Scope: The European Commission raised no comments. ATMP Scientific Recommendation

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.3. Adipose derived Mesenchymal Stem/Stromal Cells

Intended for the treatment of amyotropthic lateral sclerosis

Scope: The European Commission raised no comments. ATMP Scientific Recommendation

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.4. Recombinant adeno-associated virus serotype HSC 15 (rAAVHSC15) expressing human iduronate-2-sulfatase (hIDS)

Intended for the treatment of mucopolysaccharidosis type II (known as Hunter syndrome)

Scope: The European Commission raised no comments. ATMP Scientific Recommendation

Action: for information

The information was noted. The classification report will be sent to the applicant.

4.4.5. Extracellular matrix and non-viable osteogenic cells derived from human adipose-derived stem cells, associated with hydroxyapatite/beta-tricalcium phosphate (HA/βTCP) particles

Intended to stimulate bone regeneration in pathological hypoxic and/or necrotic bone conditions

Scope: Comments raised by the European Commission. Revised ATMP Scientific Recommendation

Action: for discussion

The revised classification report was adopted. The classification report will be sent to the applicant.

4.4.6. Isolated CD31+ cells

Intended for the treatment of erectile dysfunction

Scope: Comments raised by the European Commission. Revised ATMP Scientific Recommendation

Action: for discussion

The revised classification report was adopted. The classification report will be sent to the applicant.

4.5. Follow-up and guidance

No items

5. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.1. New requests - appointment of CAT Rapporteurs

5.1.1. Ongoing scientific advice procedures - Appointment of CAT Peer Reviewers

Timetable:

- Start of procedure at SAWP:	27-30.09.2021
- Appointment of CAT Peer Reviewers:	06-08.10.2021
- SAWP first reports:	18.10.2021
- CAT Peer Reviewer comments:	22.10.2021
- Discussion at SAWP:	25-28.10.2021
- Discussion at CAT and feedback to SAWP:	05.11.2021

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	25-28.10.2021
- Appointment of CAT Peer Reviewers:	03-05.11.2021
- SAWP first reports:	22.11.2021
- CAT Peer Reviewer comments:	26.11.2021
- Discussion at SAWP:	29.11-02.12.2021
- Discussion at CAT and feedback to SAWP:	10.12.2021

5.2. Procedures discussed at SAWP – 1st report and D40 JRs, LoOIs

5.3. Finalisation of D70 procedures – feedback from the discussion meeting

5.4. Final Advice Letters for procedures finalised the previous month

6. Pre-Authorisation Activities

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

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:	
Procedure start:	27-30.09.2021
SAWP recommendation:	28.10.2021
CAT recommendation:	05.11.2021
CHMP adoption of report and final recommendation:	11.11.2021

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

No items

6.3.4. Ongoing support

No items

6.4. Feedback from COMP

6.4.1. Importance of the therapeutic indication for orphan medicinal products

Scope: Feedback from the judgment of the General Court of 23 September 2020 in Medac Gesellschaft für klinische Spezialpräparate v Commission, T-549/19 (Trecondi)

Action: for information

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Action: for information

The Chair welcomed Ebru Karakoc Madsen, as new alternate for Denmark and Maija Tarkkanen as new alternate for Finland.

The Chair thanked Anne Engdahl Pastoft for her contribution as alternate for Denmark.

7.1.2. Vote by proxy

No items

7.1.3. Joint CAT-CHMP Strategic Review & Learning (virtual) meeting (SRLM) under the Slovenian presidency, 21 October 2021, Ljubljana (Slovenia)

CAT: Metoda Lipnik-Štangelj, Martina Schuessler-Lenz

Scope: final agenda and meeting programme

Action: for information

The CAT-CHMP agenda and the CAT-only agenda were presented. CAT members were encouraged to attend the virtual SRLM meeting: a registration link was sent to all members on 1 October 2021.

7.1.4. Call from the European Commission for expression of interest for CAT members representing patients and healthcare professional organisations

Scope: EC published a new call for CAT for expression of interest for CAT members representing patients and healthcare professional organisations.

Action: for information

Note**:** see: Calls for expression of interest | Public Health (europa.eu)

The information was noted.

7.2. Coordination with EMA Scientific Committees

No items

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

No items

7.4. Cooperation with the EU regulatory network

7.4.1. Revision of the EU legislation on blood, tissues and cells (BTC)

CAT: Martina Schüssler-Lenz

Scope: Invitation of the EMA executive director

Action: for discussion

The CAT chair welcomed the EMA executive director, Emer Cooke, who attended this part of the CAT meeting. The aim of this interaction was to brief her on the interactions with the colleagues from the European Commission's BTC unit on the revision of the BTC legislation.

The CAT chair and the CAT members presented their concerns. After almost one year of frequent interactions, there is still no clarity on the how the BTC legislation will be revised. Especially unclarity remains on the scope of the BTC legislation revision and the impact on the ATMP field. Furthermore, the CAT contributions during workshops and interviews and the discussions between CAT and BTC colleagues have been presented in public documents as if CAT agrees with proposals for the revision of the BTC legislation, which is not the case due the many unclarities.

Following additional points were made by the CAT members:

- ATMP are complex products: deregulation of advanced therapies produced in hospitals (regulated under the BTC legislation) versus in a pharmaceutical facility (products to remain under the ATMP regulation) is not an appropriate way forward. CAT has 11 years of experience assessing ATMP and has seen that small change in the manufacturing process can have a serious (negative) effect on the safety or efficacy of the product. It is not because you can make an ATMP in a hospital (using automated machines) that this will result in an efficacious product.
- Also, long term patient follow-up, both for safety and efficacy, is essential for ATMPs: CAT has seen serious safety signals, many years after the administration. This will not be reported in absence of strong post-authorisation and pharmacovigilance follow-up.
- The emphasis put by the BTC unit on patient access and affordability should not result in products with a lower quality, safety and efficacy profile to be made available to patients. Patients are not aware of the difference in treatments under the BTC versus products approved under the ATMP Regulation: they have the right to receive products with a proven efficacy. Less or non-efficacious product will not help them. Accessibility needs to be addressed at another level.
- Deregulation of the ATMP field could be detrimental for novel ATMPs to be developed and approved in the EU. This is not in the benefit of the patients.
- With regards to the classification of borderline products, CAT has a strong record of over 500 ATMP classification: the classification procedure is robust, fast and well accepted by the developers and regulatory authorities.
- CAT has classified over 100 cell-based products (mainly mesenchymal stem cells) as ATMPs for a huge range of therapeutic areas including neurodegenerative diseases and intrathecal or intracerebral administration: based on the information provided by the applicant the mechanism of action in these indication is not always clear, and CAT has serious doubts that it will be possible to demonstrate efficacy and safety in clinical trial settings. In a less regulated field all these products could be administered to patients with efficacy claims that have not been substantiated, thus posing high risks to patients and fostering use of unproven cell-based therapies.
- In conclusion, CAT is of the strong opinion that the current ATMP legal framework is fully suitable for the oversight of all aspects of ATMP development, authorisation and post-authorisation follow-up. It is the best suitable system to ensure public health. The EU regulatory system for ATMP is also acknowledged worldwide as providing high standards for public health protection under the current pharmaceutical frame, and has been used as an example for other regulatory authorities. A system in parallel with the pharmaceutical framework for cell-based ATMPs is unnecessary.

The EMA Executive director thanked the CAT chair and members for the real-life feedback and agreed that a change in the BTC legislation should not result in ATMPs without proven quality, safety and efficacy to be given to patients. She will address this with the Commission services.

7.4.2. Revision of pharmaceutical legislations

CAT: Martina Schuessler-Lenz

Scope: CAT involvement in the development of concept papers

Action: for information

EMA presented the implementation plan of the EU Pharmaceutical strategy. HMA and EMA, in consultation with Committees/CMDh, have been asked to prepare concept papers on 13 topics, to guide DG SANTE in identifying new approaches or practical solutions to be reflected in revision of the Directive and Regulation. An overview was given of the 13 identified topics.

A discussion took place which topics would be considered as 'priority topics' for CAT and CAT members were identified. For the priority topics, (a) CAT member(s) will be closely involved in the drafting of the concept paper. For other topics, the identified CAT member(s) will support the drafting group as reviewers of the drafts.

The identified CAT members will be contacted by the EMA topic coordinators to contribute to the development of the concept papers.

7.5. Cooperation with international regulators

7.5.1. ATMP cluster teleconference with US-FDA, Health Canada and PMDA (Japan)

CAT: Martina Schuessler-Lenz

Scope: Agenda of the teleconference that will take place on 14 October 2021

Action: for information

CAT was informed of the topics on the agenda of the upcoming ATMP cluster TC.

7.5.2. International Pharmaceutical Regulators Programme (IPRP) – Gene therapy and cell therapy working group

CAT: Pille Säälik

Scope: Feedback from the international teleconference that took place on 5 October 2021

Action: for information

Pille Säälik provided a detailed feedback from the topics discussed at the IPRP gene therapy and cell therapy drafting groups.

7.6. CAT work plan

7.6.1. Real World Data (RWD) in regulatory decision making of ATMPs

CAT: Martina Schuessler-Lenz

Scope: Feedback from the third meeting

Action: for information

Topic postponed until the November CAT meeting.

7.6.2. CAT workplan 2021

CAT: Martina Schuessler-Lenz

Scope: Status update and confirmation of drafting group members for the work plan topic: Guideline on requirements for ATMPs in clinical trials.

Action: for discussion

EMA provided a status update on the activities identified in the CAT workplan 2021.

7.7. Planning and reporting

No items

7.8. Others

7.8.1. CAT stakeholder meeting on 26 October 2021

CAT: Martina Schuessler-Lenz

Scope: Stakeholders' proposals for agenda topic; finalisation of the agenda

Action: for discussion

CAT reviewed the proposals received from the stakeholders. The topics for which a good discussion can be expected were added to the agenda. The topics not included in the agenda are either too premature (no discussion possible yet), outside of the remit of CAT or topics that are planned to be discussed in another EMA-Industry stakeholder meeting. CAT also identified topics for specific input from the industry stakeholders. CAT speakers for the different agenda items were identified.

The agenda of the stakeholders meeting will be sent to the industry stakeholders.

7.8.2. Lifecycle Regulatory Submissions Raw Data (LRSR)

Action: for information

EMA presented the LRSR project, which is focusing on utilising raw data to generate evidence for better and more efficient regulatory decision making. This project is part of the Data Analytics Programme, also known as the Agency's vehicle for evolving to data-driven medicines regulation.

8. Any other business

No items

Date of next CAT meeting:

03-05/11/2021

9. Explanatory notes

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

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

EU NTC: European Union Network Training Centre

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Application

MAH: Marketing Authorisation Holder

MNAT: Multinational assessment team

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

QRD: Quality review of documents

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

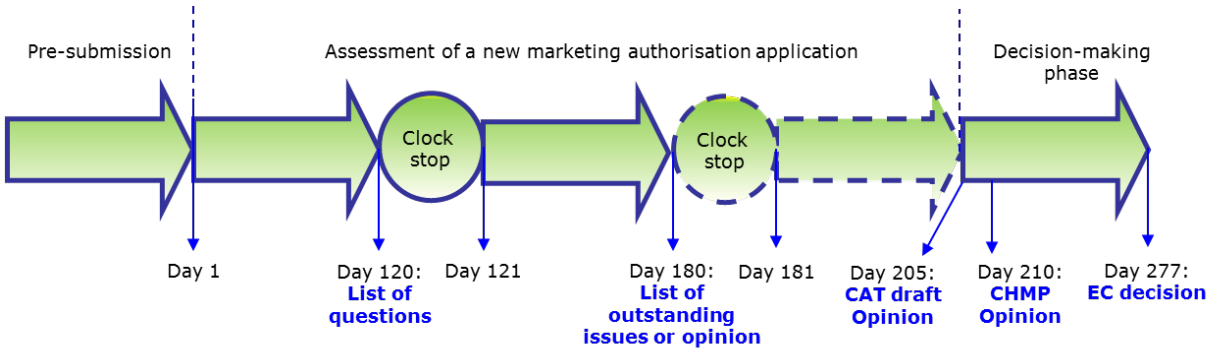
Evaluation of ATMPs (section 2)

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.

Priority Medicines (PRIME)

This section includes the new requests for eligibility to PRIME for ATMPs under development, the discussions in CAT of these eligibility requests and the final recommendations for eligibility of ATMPs adopted by CHMP.

CAT will appoint one of its members as the CAT sponsor for each new ATMP eligibility request who will lead the CAT discussion based on the recommendation from the SAWP.

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/