11 April 2022
EMA/CAT/186491/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 16-18 March 2022

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

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 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 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 based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics. Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions 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.

1.2. Adoption of agenda

The CAT agenda for 16-18 March 2022 meeting was adopted with one addition to section 2.6 (Update on ongoing initial applications)

1.3. Adoption of the minutes

CAT minutes for 16-17 February 2022 meeting

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Ciltacabtagene autoleucel - PRIME - Orphan - EMEA/H/C/005095

Janssen-Cilag International NV; treatment of multiple myeloma

Scope: Opinion

Action: for adoption

List of Outstanding Issues adopted on 10.12.2021. List of Questions adopted on 10.09.2021.

The Rapporteurs presented the outcome of the assessment of the List of Outstanding issues. The major objections and the other concerns were resolved.

CAT subsequently discussed the product information. Following wording of the indication was agreed: CARVYKTI is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

CAT agreed that the benefit risk profile of Carvykit in the indication mentioned above is positive and adopted by consensus a positive draft opinion recommending the granting of a conditional marketing authoristion to Carvykti. Norway was in agreement with the position draft opinion from CAT. The CAT draft opinion will be forwarded to CHMP for adoption.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

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

BioMarin International Limited; treatment of severe haemophilia A

Scope: Day 150 list of outstanding issues

Action: for adoption

List of Questions adopted on 05.11.2021.

The Rapporteurs presented the assessment of the responses to the list of questions.

CAT adopted the list of outstanding issues.

2.4. Day 120 list of questions

2.4.1. Tabelecleucel - PRIME - Orphan - EMEA/H/C/004577

Atara Biotherapeutics Ireland Limited; treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV^+ PTLD)

Scope: Day 120 list of questions

Action: for adoption

The Rapporteurs presented the outcome of the assessment of the marketing authorisation application.

CAT adopted the list of questions. The evaluation timetable was reverted to a normal timetable.

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

2.6.1. Eladacagene exuparvovec – Orphan – EMEA/H/C/005352

PTC Therapeutics International Limited; treatment of aromatic L-amino acid decarboxylase (AADC) deficiency

Scope: Organisation of the meeting

Action: for information

2.7. New applications

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/0048

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Clinical. Opinion.

Update of section 4.4 of the SmPC in order to add a new warning about the potential risk of hepatic hemorrhage with the transcutaneous intrahepatic route of administration of talimogene laherparepvec. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

Action: for adoption

The opinion was adopted.

2.11.2. Kymriah - tisagenlecleucel - PRIME - Orphan - EMEA/H/C/004090/II/0044

Novartis Europharm Limited

Rapporteur: Rune Kjeken, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Quality and clinical. Opinion.

Extension of indication to include treatment of adult patients with follicular lymphoma

(FL) after two or more lines of therapy who are refractory or relapsed during or within 6 months after completion of anti-CD20 antibody maintenance or relapsed after autologous haematopoietic stem cell transplantation (HSCT) for Kymriah. As a consequence, Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, the minor editorial corrections are made throughout the SmPC and package leaflet to align with the current QRD template version 10.2.

Action: for adoption

Request for Supplementary Information adopted on 10.12.2021.

The Rapporteur presented the outcome of the assessment. CAT discussed the wording of the indication and agreed on the following wording: treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

CAT adopted the draft opinion.

CAT agreed with the assessment concluding that Kymriah is non orphan similar to Gazyvaro (obinutuzumab, an orphan medicinal product that is indicated for a similar therapeutic indication on basis of a non-similar mechanism of action and principle molecular structure. CAT also agreed with the assessment of the significant clinical benefit in comparison with existing therapies in accordance with art. 14(11) of Regulation 726/2004: Kymriah in the new therapeutic indication brings a significant clinical benefit in comparison with existing therapies and therefore an additional one year marketing protection period can be granted.

2.11.3. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854/II/0033

Orchard Therapeutics (Netherlands) BV

PRAC Rapporteur: Menno van der Elst

Scope: Clinical. Request for Supplementary Information.

Submission of the final report from study STRIM-001 "Evaluation of referring healthcare providers' and parents'/carers' understanding of specific risks associated with Strimvelis treatment" listed as a category 3 study in the RMP. The RMP version 6.1 has also been submitted.

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 - PRIME - Orphan - EMEA/H/C/005102/II/0008/G

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: Quality and clinical. Request for Supplementary Information.

Group of variations including an extension of indication to include treatment of adult patients with relapsed or refractory (r/r) B-cell acute lymphoblastic leukemia (B-ALL) for Tecartus and a type IB variation to change the drug product dose specification for the new indication. As a consequence, sections 2.2, 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template.

Action: for adoption

Request for Supplementary Information adopted on 10.09.2021.

The Rapporteur presented the assessment of the responses to the list of questions. A second request for supplementary information was adopted.

2.11.5. 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 - PRIME - Orphan - EMEA/H/C/005102/II/0016

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality. Opinion.

Action: for adoption

Request for Supplementary Information adopted on 21.01.2022.

The opinion was adopted.

2.11.6. Yescarta - axicabtagene ciloleucel - PRIME - Orphan - EMEA/H/C/004480/II/0042

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, PRAC Rapporteur: Anette Kirstine Stark

Scope: Clinical. Extension of a clock stop.

Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC, Annex II (Section D) and Package Leaflet are proposed to be updated. As a consequence, the RMP (version 5.1) has been updated to align with the indication extension. In addition, the applicant has taken the opportunity to make minor editorial corrections throughout the SmPC and package leaflet to align with the current Quality Review of Documents (QRD) template.

Action: for adoption

Request for Supplementary Information adopted on 18.02.2022, 05.11.2021.

CAT agreed with the extension of the clock stop.

2.11.7. Zolgensma - onasemnogene abeparvovec - PRIME - Orphan - EMEA/H/C/004750/II/0020/G

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Quality. Opinion.

Action: for adoption

Request for Supplementary Information adopted on 10.12.2021.

The opinion was adopted.

2.11.8. Zolgensma - onasemnogene abeparvovec - PRIME - Orphan - EMEA/H/C/004750/II/0024

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Quality and clinical.

Submission of an evaluation of the finished product specifications, in accordance with the obligation in the Annex IID of the Product Information (ANX 004), to be undertaken when primary and key secondary endpoint data from additional patients with 2 copies of SMN2 are available (i.e. completion of CL-302 and CL-304 cohort 1). The Annex II is updated accordingly.

Action: for adoption

The Annex II condition can be considered fulfilled. The opinion was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/MEA/007

Takeda Pharma A/S

Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

Scope: Relates to MEA 002:
Interim Study Result / Study ADMIRE CDII (Cx601-0303)
Title: To evaluate the long-term safety and efficacy of darvadstrocel including adverse events of special interest.

Action: for adoption

The Rapporteur provided short feedback on this post-authorisation measure. The report was agreed.

2.13.2. Glybera – Alipogene tiparvovec – EMA/H/C/0002145/SOB/001.11

uniQure biopharma B.V.; treatment lipoprotein lipase deficiency (LPLD)

Rapporteur: Egbert Flory; CHMP Coordinator: Jan Mueller-Berghaus

Scope: Clinical. Annual safety update report. Long term surveillance programme/ disease registry to collect information on the epidemiology of the disease and the demographics, safety, and the effectiveness outcomes of patients treated with Glybera. The patients enrolled in clinical studies (CT-AMT-010 -10, CT-AMT 011-01, CT-AMT 011-02) should be followed up in the LPLD registry.

Action: for adoption

The report was agreed.

2.13.3. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/MEA/005

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen, CHMP Coordinator: Johanna Lähteenvuo

Scope: Protocol Amendment (v.4) for Study 20130193 (category 3)
A post-marketing, prospective cohort study of patients treated with talimogene laherparepvec in clinical practice to characterize the risk of herpetic illness among patients, close contacts, and healthcare providers; and long term safety in treated patients.

Annual interim reports to be included in the PSUR and DSUR.

Action: for adoption

The report was agreed.

2.13.4. Zolgensma - onasemnogene abeparvovec - PRIME - Orphan - EMEA/H/C/004750/R/0021

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts, Co-Rapporteur: Egbert Flory, PRAC Rapporteur: Ulla Wändel Liminga

Scope: 1-year Renewal of Marketing Authorisation

Action: for adoption

Request for Supplementary Information adopted on 18.02.2022.

The Rapporteur presented outcome of the assessment of the 1-year renewal application.

The renewal was adopted. As all the Annex II conditions are fulfilled, CAT agreed with the reversal of the marketing authorisation from conditional to full.

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

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous transduced CD8+ T cells expressing the Melanoma associated antigen 1-(MAGE-A1)-specific T cell receptor TCR 8001

Intended for the treatment of patients with MAGE-A1 expressing solid tumours

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Suspension of VST cells. Dispersion for infusion

Intended for the treatment of adults and children with therapy-resistant viral infection after allogeneic hematopoietic stem cell transplantation

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Adipose-derived stem cells

Intended for the treatment of type 2 diabetes mellitus, Treatment of cardiac and pulmonary complications after Covid-19

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.2. Day 30 ATMP scientific recommendation

4.2.1. Gingival fibroblast

Intended for the treatment of gonarthrosis

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 1 April 2022.

4.2.2. Recombinant serotype 2 adeno-associated virus (AAV2) carrying a single-stranded expression cassette for human interleukin 12 (IL-12)

Intended for the treatment of advanced solid tumours

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 1 April 2022.

4.2.3. Leukocyte and platelet rich plasma, autologous

Intended for the treatment of critical limb ischemia

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the ATMP classification report. CAT considered that additional information should be provided by the applicant before concluding on the classification

The procedural clock will be stopped awaiting responses from the applicant.

4.2.4. Messenger RNA (mRNA) containing a bicistronic coding sequence that upon translation produces two independent proteins, ZF-DNMT and ZF-KRAB

Intended for the treatment of adult patients with intermediate (stage B) or advanced (stage C) MYC-associated hepatocellular carcinoma (HCC)

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 1 April 2022.

4.2.5. Stimulated anti-viral T-lymphocytes with specific anti-viral activity

Intended for the treatment of resistant viral infections in patients after allo-HSCT

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 1 April 2022.

4.2.6. Plasmid expressing variant of human interleukin-10

Intended for the treatment of osteoarthritis, neuropathic pain, amyotrophic lateral 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 1 April 2022.

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

No items

4.4. Finalisation of procedure

No items

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:	07-10.03.2022
- Appointment of CAT Peer Reviewers:	16-18.03.2022
- SAWP first reports:	28.03.2022
- CAT Peer Reviewer comments:	01.04.2022
- Discussion at SAWP:	04-07.04.2022
- Discussion at CAT and feedback to SAWP:	13.04.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	04-07.04.2022
- Appointment of CAT Peer Reviewers:	11-13.04.2022
- SAWP first reports:	25.04.2022
- CAT Peer Reviewer comments:	29.04.2022
- Discussion at SAWP:	02-05.2022
- Discussion at CAT and feedback to SAWP:	13.05.2022

5.2. Procedures discussed at SAWP – 1st reports, D40 JRs, LoIs

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

No items

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:	02.03.2022
Procedure start:	07-10.03.2022
SAWP recommendation:	07.04.2022

CAT recommendation: 13.04.2022
CHMP adoption of report and final recommendation: 22/04/2022

No items

6.3.2. Month 1 – Discussion of eligibility

No items

6.3.3. Month 2 – Recommendation of eligibility

No items

6.3.4. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

No items

7.1.2. CAT Strategic Review & Learning meeting (SRLM) under the French presidency, 3 March 2022 (virtual)

CAT: Violaine Closson-Carella, Martina Schuessler-Lenz

Scope: feedback from the discussion at the SRLM on 3 March 2022

Action: for discussion

Violaine Closson-Carella and Martina Schuessler-Lenz provided a short feedback from the discussions in the SRLM. Next steps were agreed regarding the regulatory consideration on the toxicities reported with adeno-associated viral vector based ATMPs. This will be further discussed in the April or May CAT meeting.

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Swedish presidency, Q2-Q3/2022

CAT: Lisbeth Barkholt, Martina Schuessler-Lenz

Scope: information about the upcoming SRLM in the Q2/Q3 of 2022

Action: for discussion

CAT members were asked to propose topics for discussion at the SRLM meeting that is tentatively scheduled for 4 – 5 May 2023 in Upsala.

7.2. Coordination with EMA Scientific Committees

No items

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

7.3.1. Clarification on ATMP scientific advice and BWP interaction

Scope: to clarify the interactions with BWP on scientific advices and timing/role of CAT peer review

A presentation was given on how best to incorporate comments from the CAT peer reviewer into the BWP discussion on quality scientific advices for ATMPs. Proposals were made to improve the flow of information and interactions. EMA will further streamline the procedure and report back to CAT in the April or May meeting.

7.4. Cooperation with the EU regulatory network

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: feedback from the teleconference that took place on 24 February 2022

Action: for information

Short feedback was provided from the discussions in the ATMP cluster teleconference.

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

CAT: Pille Säälik, Ivana Haunerova

Scope: Feedback from the international teleconference that took place on 10 March 2022

Action: for information

Short feedback was provided from the discussions in the IPRP cluster teleconference.

7.6. CAT work plan

No items

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q1/2022 update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

7.8. Others

7.8.1. Introducing DARWIN EU Coordination Centre and next steps for RWE

Action: for discussion

CAT noted the presentation on the Data Analysis and Real World Interrogation Network (DARWIN EU®) and RWE pilots. An introduction was given about the DARWIN EU® and the Coordination Centre, explaining what DARWIN EU® will do, the process for conducting studies, and the implementation roadmap. Looking ahead at 2022, DARWIN EU will onboard its first data partners and conduct its first studies for a number of use cases across the medicinal products' lifecycle. Various pilots are ongoing with EMA committees and the SAWP. The pilot with CAT is due to start at the beginning of Q2. Further pilots are expected with HTA and Payers, NCAs and EHDS, later in the year. The current status of RWE studies conducted using in-house databases was shown, together with various studies initiated for each committee and various procedures (signals, referrals, ATMP, PIP, PSUSA etc.). The study on Spinal Muscular Atrophy was presented as a case study. A brief reminder was given on the process for delivering RWE, with a note to continue sending research questions and RWE requests to EMA Secretariat. More information can be found on **Data Analysis and Real World Interrogation Network (DARWIN EU) | European Medicines Agency (europa.eu)**, and for regular updates on DARWIN EU®, committee members are encouraged to subscribe to the big data highlights newsletter by sending an email to: bigdata@ema.europa.eu

A short discussion took place, in which committee members asked questions about the presentation and especially about the current status of the Spinal Muscular Atrophy study. A further update can be expected on the pilot and DARWIN EU® in June/July 2022.

8. Any other business

No items

Date of next CAT meeting:

11-13/04/2022

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

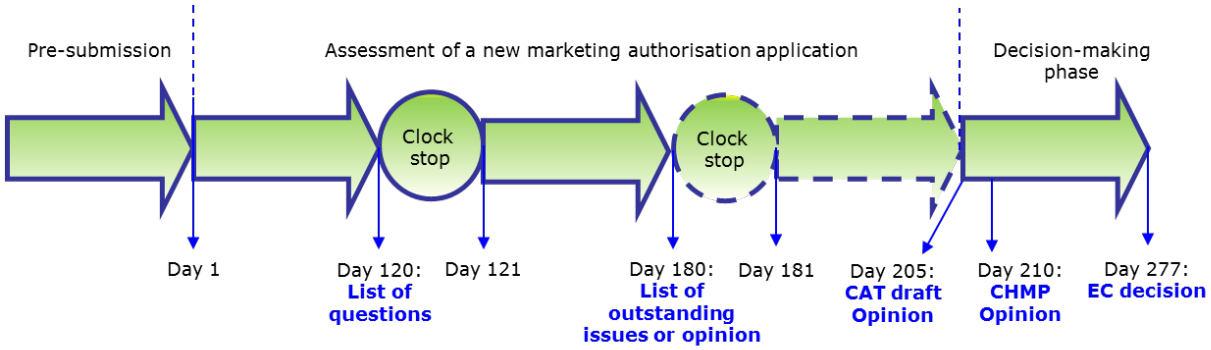
Evaluation of ATMPs (section 2)

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/

10. List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 16-18 March 2022 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martina Schüssler-Lenz	Chair	Germany	No interests declared	
Ilona Reischl	Member (Vice-Chair)	Austria	No interests declared	
Silke Dorner	Alternate	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Belaïd Sekkali	Alternate	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Evelina Shumkova	Alternate	Bulgaria	No interests declared	
Azra Selimovic	Member	Croatia	No interests declared	
Petra Sokol	Alternate	Croatia	No interests declared	
Rafaella Pontou	Member	Cyprus	No interests declared	
Isavella Kyriakidou	Alternate	Cyprus	No interests declared	
Tomas Boran	Member	Czechia	No interests declared	
Petr Soukup	Alternate	Czechia	No interests declared	
vacant	Member	Denmark		
Ebru Karakoc Madsen	Alternate	Denmark	No restrictions applicable to this meeting	
Toivo Maimets	Member	Estonia	No interests declared	
Pille Saalik	Alternate	Estonia	No interests declared	
Heli Suila	Member	Finland	No interests declared	
Maija Tarkkanen	Alternate	Finland	No interests declared	
Violaine Closson	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Egbert Flory	Alternate (to CHMP representative)	Germany	No interests declared	
Maria Gazouli	Member	Greece	No interests declared	
Angeliki Rompoti	Alternate	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Katalin Lengyel	Member	Hungary	No interests declared	
Balázs Sarkadi	Alternate	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Niamh Curran	Alternate	Ireland	No restrictions applicable to this meeting	
Concetta Quintarelli	Member	Italy	No interests declared	
Barbara Bonamassa	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No interests declared	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	
Vlasta Zavadova	Member	Liechtenstein	No interests declared	
Guy Berchem	Alternate	Luxembourg	No restrictions applicable to this meeting	
Nancy De Bremaeker	Member	Luxembourg	No interests declared	
John J. Borg	Member (CHMP member)	Malta	No interests declared	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Babs Fabriek	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Maja Sommerfelt Grønvold	Alternate	Norway	No interests declared	
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Marcin Kolakowski	Alternate	Poland	No interests declared	
Bruno Sepodes	Member (CHMP member)	Portugal	No interests declared	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Silviu Istrate	Member	Romania	No interests declared	
Alexandrina Preda	Alternate	Romania	No interests declared	
Lukas Slovak	Member	Slovakia	No interests declared	
Katarina Vavrová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Suzana Vidic	Alternate	Slovenia	No participation in final deliberations and voting on:	2.11.2., 2.11.7., 2.11.8. & 2.13.4.
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Lisbeth Barkholt	Member	Sweden	No interests declared	
Maria Luttgen	Alternate	Sweden	No participation in final deliberations and voting on:	5.2.4.
Bernd Gänsbacher	Member	Clinicians' Representative	No interests declared	
Alessandro Aiuti	Member	Clinicians' Representative	No participation in discussions, final deliberations and voting on:	2.11.3.
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member	Patients' Representative	No restrictions applicable to this meeting	
Roland Pochet	Alternate	Patients' Representative	No interests declared	
Catherine Milne	Observer/Alternate	EDQM	No interests declared	
Andrea Laslop	Expert - via Webex	AGES AT	No interests declared	
Brigitte Mueller	Expert - via Webex	AGES AT	No interests declared	
Rene Anour	Expert - via Webex	AGES AT	No interests declared	
Florian Klinglmueller	Expert - via Webex	AGES AT	No interests declared	
Philipp Janesch	Expert - via Webex	AGES AT	No interests declared	
Christine Vaculik	Expert - via Webex	AGES AT	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martin Walter	Expert - via Webex	AGES AT	No interests declared	
Harald Bernsteiner	Expert - via Webex	AGES AT	No interests declared	
Tjerk Feenstra	Expert - via Webex	AGES AT	No interests declared	
Johannes Ovelgonne	Expert - via Webex	Netherlands	No interests declared	
Gabriela Ullio-Gamboa	Expert - via Webex	ANSM FR	No interests declared	
Norontsoa Rasolondramanitra	Expert - via Webex	ANSM FR	No interests declared	
Stéphanie Jambon	Expert - via Webex	ANSM FR	No interests declared	
Caroline Matko	Expert - via Webex	ANSM FR	No interests declared	
Nathalie Morgensztejn	Expert - via Webex	ANSM FR	No interests declared	
Sylvie Benchetrit	Expert - via Webex	ANSM FR	No interests declared	
Bruno Delafont	Expert - via Webex	ANSM FR	No restrictions applicable to this meeting	
Paolo Petracci	Expert - via Webex	ANSM FR	No interests declared	
Thomas Hinz	Expert - via Webex	PEI DE	No interests declared	
Dominique Gaston-Tischberger	Expert - via Webex	PEI DE	No interests declared	
Zuzana Jedlickova	Expert - via Webex	PEI DE	No interests declared	
Sven Flindt	Expert - via Webex	PEI DE	No interests declared	
Lukas Aguirre-Dávila	Expert - via Webex	PEI DE	No interests declared	
Michal Zwiewka	Expert - via Webex	PEI DE	No interests declared	
Matthias Renner	Expert - via Webex	PEI DE	No restrictions applicable to this meeting	
Silke Schüle	Expert - via Webex	PEI DE	No interests declared	
Johanna Lähteenvuo	Expert - via Webex	FIMEA FI	No interests declared	
Attila Sebe	Expert - via Webex	PEI DE	No interests declared	
Beate Mosl	Expert - via Webex	PEI DE	No restrictions applicable to this meeting	
Blanca García-Ochoa	Expert - via Webex	AEMPS ES	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Carolina Prieto	Expert - via Webex	AEMPS ES	No interests declared	
Lucia López-Anglada	Expert - via Webex	AEMPS ES	No interests declared	
Maria Kalland	Expert - via Webex	NOMA NO	No interests declared	
Anna Mari Lone	Expert - via Webex	NOMA NO	No restrictions applicable to this meeting	
Ingrid Wang	Expert - via Webex	NOMA NO	No interests declared	
Susanne Mueller	Expert - via Webex	PEI DE	No interests declared	
Ursula Drechsel-Bäuerle	Expert - via Webex	PEI DE	No interests declared	
Meeting run with support from relevant EMA staff				