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SCIENCE MEDICINES HEALTH

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Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 17-19 January 2024

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

Disclaimers

Some of the information contained in these minutes 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, 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 ongoing 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. 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 current meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

Participants 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.

The Chair welcomed the new members and alternates and thanked the departing members/alternates for their contributions to the Committee.

The Chair announced the start of the Belgian presidency of the Council of the European Union (EU).

1.2. Adoption of agenda

The CAT agenda for 17-19 January 2024 meeting was adopted.

1.3. Adoption of the minutes

The CAT minutes of 06-09 December 2023 meeting were adopted.

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

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

No items

2.6. Update on ongoing initial applications

No items

2.7. New applications

2.7.1. Autologous cartilage-derived articular chondrocytes, in-vitro expanded - EMEA/H/C/004594

TETEC Tissue Engineering Technologies AG; Repair of symptomatic, localised, full-thickness cartilage defects of the knee joint grade III or IV

Scope: Timetable for assessment

Action: for adoption

The timetable for assessment was adopted.

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. Companion diagnostics

2.10.1. Initial consultation

No items

2.10.2. Follow-up consultation

No items

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

2.11.1. Abecma - Idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0031

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjekken, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Clinical, opinion

Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least two prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD-38 antibody and have demonstrated disease progression on the last therapy for Abecma (idecabtagene vicleucel, ide-cel), based on results from study BB2121-MM-003 (MM-003, KarMMa-3). This is a Phase 3, multicentre, randomised, open-label study to compare the efficacy and safety of ide-cel versus standard regimens in subjects with RRMM. As a consequence, sections 2.1, 2.2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.3, 6.4 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 3.0 of the RMP has also been submitted. Furthermore, the product information (PI) is brought in line with the Guideline on core SmPC, Labelling and Package Leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells.

Action: for adoption

Request for supplementary information adopted on 16.06.2023 and 31.10.2023.

The rapporteur presented the assessment of the responses by the MAH. Based on final assessment, CAT agreed that the benefit risk of Abecma is positive for the extension of indication. CAT discussed the wording of a warning in the SmPC (section 4.4) on the treatment of patients with rapidly progressing disease. CAT agreed with the recommendation for the MAH to submit the final overall survival (OS) data. CAT subsequently discussed what further data could be considered interesting to be collected by the MAH to confirm an optimised bridging therapy.

A positive opinion was adopted by CAT. CAT also concluded that the specific obligation is considered fulfilled, therefore the conditional marketing authorisation (MA) can be converted to a full MA.

2.11.2. Alofisel - Darvadstrocel - Orphan - EMEA/H/C/004258/II/0047/G

Takeda Pharma A/S

Rapporteur: Maria Luttgen

Scope: Quality, opinion

Action: for adoption

The opinion was adopted.

2.11.3. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0023

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality

Action: for adoption

Request for supplementary information adopted on 06.10.2023.

The opinion was adopted.

2.11.4. Upstaza - Eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0013

PTC Therapeutics International Limited

Rapporteur: Joseph De Courcey

Scope: Quality, request for supplementary information

Action: for adoption

Request for supplementary information adopted on 08.09.2023.

A second request for supplementary information was adopted.

2.11.5. Upstaza - Eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0014/G

PTC Therapeutics International Limited

Rapporteur: Joseph De Courcey

Scope: Clinical

Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update information on safety and efficacy, based on final results from studies NTUH-AADC-010 and NTUH-AADC-011. NTUH-AADC-010 is an open-label, single arm, externally controlled trial to evaluate safety, efficacy, pharmacodynamics and immunogenicity of AGIL-AADC in children from 18 months to less than 18 years of age with severe AADC deficiency, while NTUH-AADC-011 is an open-label, single arm, externally controlled trial to evaluate efficacy and safety of AGIL-AADC in children from 18 months to less than 6 years of age with severe AADC deficiency. In addition, sections 4.5, 4.9 and 6.6 of the SmPC are updated in order to provide better clarification and guidance for the medical practice. The Package Leaflet is updated accordingly. The MAH also took the opportunity to update the due date of the final report of study AADC-1602 in the Annex II, considering the 10-year follow up of the last patient in study AADC-011, and to introduce minor editorial changes to the product information.

Action: for adoption

Request for supplementary information adopted on 06.10.2023.

The opinion was adopted.

2.11.6. Tecartus; Yescarta - Axicabtagene ciloleucel; Brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2607

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.

2.11.7. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0021

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jo Robays

Scope: Extension of indication, request for supplementary information

Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 1 prior therapy, including an immunomodulatory imide drug (IMiDs) and a proteasome inhibitors (PI), have demonstrated disease progression on or after the last therapy and are refractory to lenalidomide for CARVYKTI, based on interim results from study MMY3002 listed as a specific obligation (SOB/006) in the Annex II. This is an ongoing, phase 3, randomised, open-label, multicentre study to determine whether treatment with cilta-cel provides an efficacy benefit compared to standard therapy in participants with relapsed and lenalidomide-refractory multiple myeloma. As a consequence, sections 4.1, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update Annex II of the product information. As part of the application the MAH is requesting a 1-year extension of the market protection.

Action: for discussion (feedback on the ongoing procedure)

Request for supplementary information adopted on 08.09.2023.

CAT requested a reminder of the available data for Carvykti-II-21 in light of a parallel procedure of similar nature.

The Carvykti extension of indication will be discussed at the February 2024 CAT meeting following the assessment of the responses to the request for supplementary information .

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Abecma - Idecabtagene vicleucel - Orphan - EMEA/H/C/004662/MEA/007

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeklen

Scope: Pharmacovigilance, opinion

From Initial MAA: Long-term follow-up study (GC-LTFU-001) to assess the risk of delayed adverse events (AEs) following exposure to GM T cells, to monitor for long-term persistence of GM T cells, including analysis of vector integration sites, as appropriate and to monitor for generation of replication competent retroviruses.

Action: for adoption

No new safety signals were identified in the first interim report of the study GC-LTFU-001.

The conclusion of the report was agreed.

2.13.2. [Abecma - Idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/016.1](#)

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeklen

Scope: Quality

Action: for adoption

The conclusion of the report was agreed.

2.13.3. [Breyanzi - Lisocabtagene maraleucel / Lisocabtagene maraleucel - EMEA/H/C/004731/MEA/007](#)

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Pharmacovigilance

From Initial MAA:

LTFU study (GC LTFU 001): Long-term follow-up of safety and efficacy for all paediatric and adult subjects exposed to a GM T cell therapy in Bristol-Myers Squibb sponsored, or Bristol Myers Squibb alliance partner sponsored, clinical trials in accordance with Health Authorities' guidance for long-term (up to 15 years) follow-up of subjects treated with gene therapy products (interim report 5 year)

Action: for adoption

The conclusion of the report and the request for supplementary information were agreed.

2.13.4. [Breyanzi - Lisocabtagene maraleucel / Lisocabtagene maraleucel - EMEA/H/C/004731/REC/017](#)

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, request for supplementary information

Action: for adoption

The conclusion of the report and the request for supplementary information were agreed.

2.13.5. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/ANX/003.1

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Pharmacovigilance

PASS STUDY First Interim Report (Study 68284528MMY4004: An observational post-authorization safety study to evaluate the safety of multiple myeloma patients treated with ciltacabtagene autoleucel)

Action: for adoption

The conclusion of the report was agreed.

2.13.6. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/R/0025

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Marcos Timón, PRAC Rapporteur: Jo Robays

Scope: 1-year renewal of marketing authorisation

Action: for adoption

The 1-year renewal of marketing authorisation was adopted.

2.13.7. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/REC/013.1

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Clinical

MAH Response to REC 013 [Study MMY2003 Cohort A] Request for supplementary information as adopted in June 2023: safety and efficacy analysis of the subjects who received cilta-cel manufactured with Bern-LV in Study MMY2003 Cohort A.

Action: for adoption

The conclusion of the report was agreed. This recommendation is closed as the scientific issue is part of the variation II/21 for the extension of indication.

2.13.8. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/009.7

Novartis Europharm Limited

Rapporteur: Rune Kjekken

Scope: Pharmacovigilance

MAH's response to ANX 009.6 [Study CCTLO19H2301:PAES]: Request for supplementary

information as adopted in October 2023.

Action: for adoption

The MAH provided an interim report of study CCTL019H2301 (overall survival data). The conclusion of the report was agreed.

2.13.9. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/LEG/021.1

Novartis Europharm Limited

Rapporteur: Rune Kjekken

Scope: Pharmacovigilance

MAH's response to LEG 021 [potential secondary malignancy cases including the case number NVS2022DE245136]. Request for supplementary information was adopted in September 2023.

Action: for adoption

The conclusion of the report was agreed.

2.13.10. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/P46/022

Novartis Europharm Limited

Rapporteur: Rune Kjekken

Scope: Clinical

Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Final study report NO. CCTL019C2202: a phase II, single arm, multicentre open label trial to determine the safety and efficacy of tisagenlecleucel in paediatric patients with relapsed or refractory mature B-cell non-Hodgkin lymphoma (NHL) (BIANCA)

Action: for adoption

The conclusion of the report was agreed. The product information is unchanged.

2.13.11. Luxturna - Voretigene neparvovec - Orphan - EMEA/H/C/004451/REC/012

Novartis Europharm Limited

Rapporteur: Sol Ruiz

Scope: Quality

Action: for adoption

The conclusion of the report was agreed.

2.13.12. ROCTAVIAN - Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/SOB/006

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Clinical, pharmacovigilance

Study 270-303 1-Year CSR: a phase 3b, single arm, open-label study to evaluate the efficacy and safety of BMN 270, an adeno-associated virus vector-mediated gene transfer of human factor VIII, with prophylactic corticosteroids in haemophilia A patients.

Action: for adoption

The conclusion of the report was agreed.

2.13.13. Abecma - idecabtagene vicleucel; Breyanzi - lisocabtagene maraleucel; Carvykti - ciltacabtagene autoleucel; Kymriah - tisagenlecleucel; Tecartus - brexucabtagene autoleucel; Yescarta - axicabtagene ciloleucel

Bristol-Myers Squibb Pharma EEIG (Abecma, Breyanzi), Janssen-Cilag International NV (Carvykti), Novartis Europharm Limited (Kymriah), Kite Pharma EU B.V. (Tecartus, Yescarta)

CAT Rapporteurs: Rune Kjekken (Kymriah, Abecma), Jan Mueller-Berghaus (Carvykti, Tecartus, Yescarta), Concetta Quintarelli (Breyanzi)

PRAC Rapporteur (for the signal): Ulla Wändel Liminga

Scope: Feedback from PRAC discussion on signal of secondary malignancies of T-cell origin (EPITT 20040)

Action: for information

CAT was informed about the PRAC discussion on the signal of secondary malignancies of T-cell origin. The signal is under review and is scheduled for further PRAC discussion in April 2024. CAT will be informed of the outcome of the PRAC discussion.

2.14. GMP and GCP inspections requests

No items

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:	19.01.2024
-EMA Coordinator's draft report:	02.02.2024
-CAT Coordinator's comments:	07.02.2024
-Revised scientific recommendation:	09.02.2024
-CAT's discussion of scientific recommendation:	16.02.2024

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Modified measles vaccine virus

For the treatment of solid cancer tumours

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. Allogeneic expanded natural killer cells

For the treatment of acute myeloid leukaemia

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report.

4.2.2. Autologous tissue generated in the human body (in vivo) through the foreign body reaction

For tissue augmentation

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 02.02.2024.

4.2.3. Dendritic cells activated by lysate of circulating tumour cells

For the treatment of solid tumours in metastatic stage

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific

recommendation to the European Commission for comments by 02.02.2024.

4.2.4. Autologous T Lymphocytes engineered with nanoparticles with curcumin encapsulated

For the treatment of melanoma

Scope: ATMP scientific recommendation

Action: for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 02.02.2024.

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

4.3.1. Spermatogonial stem cells, propagated *in vitro*

Male infertility due to gonadotoxic treatment

Scope: ATMP scientific recommendation

Action: for adoption

The CAT coordinator presented the updated classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 02.02.2024.

CAT was informed of scientific developments specifically in the field of infertility treatments: reference was made to national scientific advice requests . The developer should be recommended to come for ATMP classification early on to confirm the regulatory framework for its product.

4.4. Finalisation of procedure

4.4.1. Allogeneic peripheral blood-derived HSPC, Treg cells and Tcon cells

Prevention of moderate to severe chronic graft-vs.-host disease and/or death in patients with acute leukaemias and in patients with myelodysplastic syndrome (MDS) undergoing HLA-matched allogeneic haematopoietic stem cell transplant (alloHCT)

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does not fulfil the definition of an advanced therapy medicinal product as provided in Article 2(1) of Regulation (EC) No. 1394/2007.

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:	08-11.01-2024
- Appointment of CAT Peer Reviewers:	17-19.01.2024
- SAWP first reports:	29.01.2024
- CAT Peer Reviewer comments (NC/C):	02.02.2024
- CAT Peer Reviewer comments (Q):	07.02.2024
- Discussion at SAWP:	05-08-02.2024
- Discussion at CAT and feedback to SAWP:	14-16.02.2024

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	05-08.02.2024
- Appointment of CAT Peer Reviewers:	14-16.02.2024
- SAWP first reports:	26.02.2024
- CAT Peer Reviewer comments (NC/C):	01.03.2024
- CAT Peer Reviewer comments (Q):	06.02.2024
- Discussion at SAWP:	04-07.03.2024
- Discussion at CAT and feedback to SAWP:	13-15.03.2024

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

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: 08-11.01.2024

SAWP recommendation: 08.02.2024

CAT recommendation: 16.02.2024

CHMP adoption of report and final recommendation: 22.02.2024

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

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

Action: for information

The CAT Chair welcomed Anna Katalin Barane Gilicse and Viola Bardczy as the new member and alternate for Hungary and thanked Balázs Sarkadi for his contribution as the alternate for Hungary.

The CAT Chair welcomed Joseph De Courcey and Richard Carroll as the new member and alternate for Ireland and thanked Maura O'Donovan and Niamh Curran for their contribution as member and alternate for Ireland.

The CAT Chair welcomed Vilma Petrikaite as the new member for Lithuania.

The CAT Chair welcomed Alessia Pochesci and Nancy De Bremaeker as the new member and alternate for Luxembourg and thanked Guy Berchem for his contribution as alternate for Luxembourg.

7.1.2. Vote by proxy

Action: for information

None

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Belgian presidency – 15-17 May 2024

CAT: Claire Beuneu

Scope: Draft agenda of the upcoming SRLM

Action: for discussion

A first discussion took place on the agenda of the CAT-only meeting and the joint CAT-PDCO meeting during the upcoming SRLM.

7.2. Coordination with EMA Scientific Committees

7.2.1. BWP/CAT training on AAV based gene therapy

Scope: Discussion on upcoming training on AAV based gene therapy

Coordinator: Sean Barry, Ilona Reischl

Action: for information

CAT was informed on the planned training on quality requirements for AAV based gene therapy products.

7.2.2. Update on revamp project: available new templates, ongoing template revision and industry pilot

Scope: Provide update to the CAT members of the ongoing project and the achievements reached to this point

Action: for information

CAT was informed on the second phase of the Revamp project on revision of Initial Marketing Authorisation templates for assessment. A pilot project with industry has started whereby selected applicants on a voluntary basis will include factual data in the D80 clinical/non-clinical assessment reports. ATMPs have not been selected so far for this pilot but will be included for consideration from now on if criteria used for the pilot industry involvement are being satisfied. As an incentive, the involved companies will have more dedicated interactions with the rapporteurs and assessors, which would allow for simple issues (such clarification or mistakes in the dossier, or the provision of missing documents) to be resolved without the need for committee involvement: this should give the opportunity to reduce the number of questions and the time for assessment.

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

No items

7.4. Cooperation with the EU regulatory network

No items

7.5. Cooperation with international regulators

No items

7.6. CAT work plan

7.6.1. CAT work plan for 2024

CAT: Ilona Reischl

Scope: Draft CAT work plan for 2024

Action: for discussion

The CAT work plan for 2024 was adopted and will now be published on the EMA website. The activity related to the SMA registry study (see agenda point 7.6.2) was removed from the 2024 work plan.

7.6.2. Update on real-world evidence (RWE) studies to support EMA scientific committees

Scope: Outcome of the SMA registry study

Action: for information

CAT received detailed feedback on the outcome of the Spinal muscular atrophy (SMA) registry study. CAT was informed that the final report is being finalised and a manuscript is under preparation. No additional activities involving CAT are planned on this SMA registry study.

7.6.3. Reflection paper on the use of real-world data to generate real-world evidence in non-interventional studies

CAT: Ilona Reischl, Rozalina Kuloksozova

Scope: Comment from CAT on the draft Reflection Paper on real-world evidence

Action: for discussion

Rozalina Kuloksozova and Ilona Reischl informed CAT of their observations on the above mentioned reflection paper. The main concern is that less experienced applicants might misunderstand or misuse the reflection paper to replace clinical trial data by real-world evidence data obtained from non-interventional studies. It is proposed that the reflection paper includes cautionary statements in this respect.

EMA thanked the CAT members for the careful review and comments provided. The comments will be addressed in due course by the drafting group. Concerning the main point described above, EMA mentioned that, while the reflection paper already includes statements to make clear that real-world evidence is to complement and not to replace

evidence from clinical trials, the drafting group will consider emphasising that message to mitigate the risk of misinterpretation or misuse of the reflection paper by sponsors.

7.6.4. Guideline on quality, non-clinical and clinical requirements for investigational ATMPs in clinical trials

CAT: Ilona Reischl

Scope: Draft guideline, updated following the external consultation

Action: for discussion

CAT was informed that the comments from the external consultation have now been reviewed and incorporated in the guideline where relevant. CAT members are invited to review the updated guideline and provide comments by 9 February 2024. The guideline will be adopted at the February 2024 CAT meeting. In view of the many changes to the guideline text (especially to the quality part), a short second public consultation is scheduled.

7.7. Planning and reporting

No items

7.8. Others

No items

8. Any other business

8.1. Demo of the Scientific Explorer tool

Scope: AI/Knowledge Mining driven tool that EMA is developing to allow easy and accurate searching, finding, interrogating and accessing of scientific information to inform scientific decisions. The scope of the tool's first version are scientific advice letters.

Action: for information

A demonstration of the search engine that is under development for data mining in scientific advice letters was given. The tool will become available later this year.

Date of next CAT meeting:

14-16 February 2024

9. List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 16-19 January 2024 meeting.

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Ilona Reischl	Chair	Austria	No interests declared	
Silke Dorner	Member	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Olga Kholmanskikh	Alternate	Belgium	No interests declared	
Rozalina Kulaksazova	Member	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	
Petr Soukup	Member	Czechia	No interests declared	
Ebru Karakoc Madsen	Member	Denmark	No restrictions applicable to this meeting	
Bibi Fatima Syed Shah	Alternate	Denmark	No interests declared	
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 Carella	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 restrictions applicable to this meeting	
Anna Katalin Barane Gilicze	Member	Hungary	No restrictions applicable to this meeting	

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Viola Bardoczy	Alternate	Hungary	No restrictions applicable to this meeting	
Joseph De Courcey	Member	Ireland	No interests declared	
Concetta Quintarelli	Member	Italy	No interests declared	
Una Riekstina	Member	Latvia	No interests declared	
Villma Perikaite	Member (CHMP member)	Lithuania	No restrictions applicable to this meeting	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	
Nancy De Bremaeker	Alternate	Luxembourg	No interests declared	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Emmely de Vries	Member	Netherlands	No interests declared	
Berendina Maria (Tineke) van den Hoorn	Alternate	Netherlands	No interests declared	
Rune Kjeklen	Member	Norway	No participation in discussion, final deliberations and voting on:	Bizalimogene ralaplasamid, mavilimogene ralaplasamid
Dariusz Sladowski	Member	Poland	No restrictions applicable to this meeting	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Silviu Istrate	Member	Romania	No interests declared	
Katarina Kollarova	Member	Slovakia	No interests declared	
Margareta Fogelová	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:	2.13.8, 2.13.9; 2.13.10 Kymriah 2.13.11 Luxturna
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Maria Luttgen	Member	Sweden	No restrictions applicable to this meeting	
Charlotte Anderberg	Alternate	Sweden	No interests declared	
Paolo Gasparini	Member	Clinicians' Representative	No interests declared	
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant Melefors	Member	Patients' Representative	No interests declared	
Mencia de Lemus Belmonte	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member (Vice- Chair)	Patients' Representative	No interests declared	
Federica Chiara	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Torjorn Callreus	Expert	Malta	No interests declared	
Lothar Bergmann	Expert	Germany		
Lena Eroukhanoff	Expert	Norway	No restrictions applicable to this meeting	
Fabrice Eroukhanoff	Expert	Norway	No interests declared	
Nina Pettersen Hessvik	Expert	Norway	No interests declared	
Ingrid Wang	Expert	Norway	No interests declared	
Ulla Wändel Liminga	Expert	Sweden	No interests declared	
Beate Mosl	Expert	Germany	No interests declared	
Attila Sebe	Expert	Germany	No interests declared	
Karri Penttilä	Expert	Finland	No interests declared	
Johanna Lähteenhuo	Expert	Finland	No interests declared	
Odoardo Maria Olimpieri	Expert	Italy	No interests declared	
Antonella Isgro	Expert	Italy	No interests declared	

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Federico de Angelis	Expert	Italy	No interests declared	
Meeting run with support from relevant EMA staff				

10. Explanatory notes

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

For a list of acronyms and abbreviations, see:

[List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in relation to EMA's regulatory activities](#)

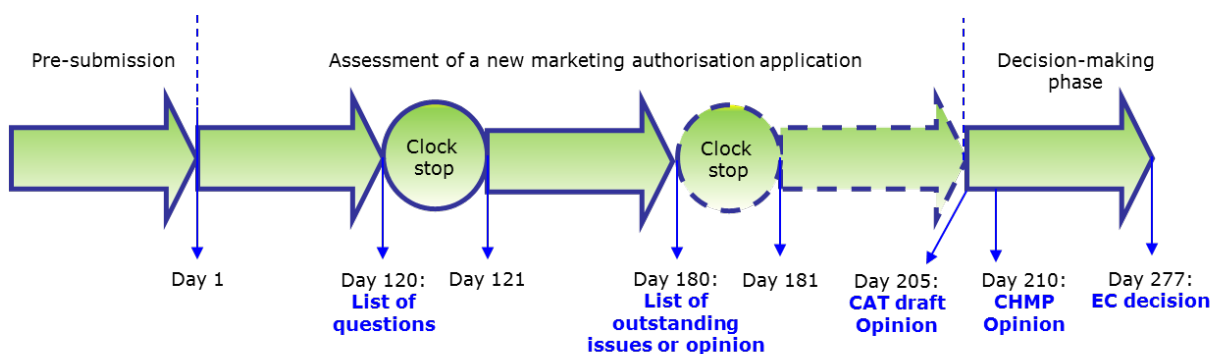
Evaluation of ATMPs (section 2)

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 Post-authorisation activities (section 2.11-2.13) and any ATMP related inspection requests (section 2.14).

New applications (sections 2.1. to 2.9.)

Section 2.1 is for ATMPs nearing the end of the evaluation and for which the CAT is expected to adopt a draft **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CAT opinion is transmitted to the CHMP for final adoption. The CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU. More information on the evaluation of ATMPs can be found [here](#).

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CAT. The clock stop happens after day 120 and may also happen after day 180, when the CAT has adopted respectively a **Day 120 list of questions** (section 2.4) 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 2.3)). Section 2.6 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.

New applications (section 2.7.)

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.

Withdrawal of applications (section 2.8.)

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.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.9.)

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.

Companion diagnostics (section 2.10)

This section lists applications for initial and follow-on consultation of companion diagnostics.

Post-authorisation activities (section 2.11-2.13.)

Section 2.11 lists type II variations, including extension of indication applications and re-examination procedures for type II variations for which the applicant has requested re-examination of the opinion previously issued by the CHMP. Section 2.12 list extension application according to Annex I of Reg. 1234/2008 and section 2.13 includes all other post-authorisation activities concerning authorised ATMPs that are not covered elsewhere in the agenda such as post-authorisation measures, 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.

GMP and GCP Inspections Issues (section 2.14.)

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).

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/