19 April 2023
EMA/CAT/143498/2023
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 22-23 March 2023

Chair: Ilona Reischl; Vice-Chair: Carla Herberts

Health and safety information

In accordance with the Agency's health and safety policy, delegates were 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 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 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. The meeting was held in-person with some members connected 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 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 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 member and alternate for Austria.

1.2. Adoption of agenda

The CAT agenda for 22-23 March 2023 meeting was adopted.

1.3. Adoption of the minutes

The CAT minutes for 15-16 February 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. In vitro diagnostic medical device - EMEA/H/D/006255

Indicated as an aid in the selection of adult haemophilia A patients for whom valoctocogene roxaparvovec treatment is being considered

Scope: Timetable for assessment

Action: for adoption

The assessment timetable 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. 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. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0022/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, Opinion

Action: for adoption

Request for supplementary information adopted on 17.02.2023.

The opinion was adopted.

2.11.2. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0026

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, Opinion

Action: for adoption

The opinion was adopted.

2.11.3. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0027

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, Opinion

Action: for adoption

The opinion was adopted.

2.11.4. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0005

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, PRAC Rapporteur: Gabriele Maurer

Scope: Clinical, Opinion

Extension of indication to include treatment of adult patients with second-line (2L) transplant intended (TI) large B-cell lymphoma (LBCL) for Breyanzi, based on interim analyses from pivotal study JCAR017-BCM-003; this is a global randomised multicentre phase III trial to compare the efficacy and safety of JCAR017 to standard of care in adult subjects with high-risk, transplant-eligible relapsed or refractory aggressive B-cell non-Hodgkin lymphomas (TRANSFORM); as a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted.

Action: for adoption

Request for supplementary information adopted on 09.09.2022 and 17.02.2023.

The Rapporteur presented the outcome of the assessment of the responses to the request for supplementary information. . The indication wording (section 4.1 of SmPC) was agreed; the SmPC will indicate that limited data are available on the efficacy of Breyanzi in CD19-negative patients and the MAH agreed to study this patient population. Information on the treatment of cytokine release syndrome will be included in SmPC section 4.8 and cross-

referred in section 4.4.

The opinion was adopted.

2.11.5. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0014

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, PRAC Rapporteur: Gabriele Maurer

Scope: Clinical, Request for supplementary information

Update of section 5.1 of the SmPC in order to update efficacy information based on final results from studies 017001 and JCAR-017-BCM-001 listed as obligations in the Annex II. These studies aimed to further characterise the long-term efficacy and safety of Breyanzi in patients treated with relapsed or refractory diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), and follicular lymphoma grade 3B (FL3B) after two or more lines of systemic therapy. Study 017001 is a phase I, open-label, single-arm, multicohort, multicentre seamless design trial, while study JCAR-017-BCM-001 is a phase II, open-label, single-arm, multicohort, multicentre trial. The Annex II is updated accordingly. The RMP version 3.0 has also been submitted.

Action: for adoption

The Rapporteur presented the outcome of the assessment. Some other concerns were identified . The request for supplementary information was updated following the discussion and subsequently adopted.

2.11.6. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0005

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, Opinion

Action: for adoption

Request for supplementary information adopted on 09.12.2022.

The opinion was adopted.

2.11.7. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0057

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, Request for supplementary information

Action: for adoption

Request for supplementary information adopted on 20.01.2023.

The second request for supplementary information was adopted.

2.11.8. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0036/G

Novartis Europharm 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. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/014.1

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, Fulfilled

Action: for adoption

The outcome was adopted.

2.13.2. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/011.1

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, Opinion

Action: for adoption

The outcome was adopted.

2.13.3. Glybera (EXP) - alipogene tiparvovec - EMEA/H/C/002145/SOB/001.12

uniQure biopharma B.V.

Rapporteur: Egbert Flory

Scope: Pharmacovigilance

Annual safety update report: 25.10.2021 – 24.10.2022. 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.

Action: for adoption

The outcome was adopted. CAT agreed that no further annual safety update reports for Glybera should be provided.

2.13.4. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/MEA/005.1

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Pharmacovigilance, Opinion

Submission of Protocol Amendment (amendment 5 and superseding amendment 5) of Study 20130193 (cat 3): A post-marketing, prospective cohort study of patients treated with talimogene laherparepvec in clinical practice to characterise the risk of herpetic illness among patients, close contacts, and healthcare providers; and long-term safety in treated patients.

Action: for adoption

The outcome was adopted.

2.13.5. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/003.10

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Pharmacovigilance

Sixth semi-annual report (EBMT data only). Study CCTL019B2401: Non-interventional post-authorisation safety study (PASS) in order to further characterise the safety – including long-term safety – of Kymriah, the applicant should conduct and submit a study based on data from a disease registry in acute lymphoblastic leukaemia (ALL) and diffuse large B-Cell lymphoma (DLBCL) patients.

Action: for adoption

EMA presented the outcome of the sixth semi**-**annual assessment for Kymriah. The analysis is based on aggregated data : the benefit risk profile is unchanged. The outcome was adopted.

2.13.6. Tecartus - brexucabtagene autoleucel - Orphan - EMEA/H/C/005102/ANX/011

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Clinical & Pharmacovigilance

Protocol of Study No. KTE-EU-474-6644: Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory acute lymphoblastic leukaemia (ALL) [From II-008-G]

Action: for adoption

The Rapporteur presented the outcome of the review of the protocol of the post

authorisation safety study. The protocol at this point in time is not agreed and some questions will be send to the applicant . The outcome was adopted.

2.13.7. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/MEA/007

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Clinical

Feasibility assessment to determine the suitability of adding the registry of the International Working Group On Neurotransmitter Related Disorders (iNTD) as a secondary data source to the PTC-AADC-MA-406 registry [From initial MAA RMP]

Action: for adoption

The Rapporteur presented the outcome of the assessment of the feasibility analysis. The Rapporteur was not in agreement with the company's feasibility conclusion . Further to the discussion, the Rapporteur will amend the conclusion of the report.

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:	24.03.2023
- EMA Coordinator's draft report:	05.04.2023
- CAT Coordinator's comments:	12.04.2023
- Revised scientific recommendation:	14.04.2023
- CAT's discussion of scientific recommendation:	21.04.2023

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Ixoberogene soroparvovec (genetically engineered, replication-incompetent adeno-associated virus vector comprising the AAV.7m8 capsid proteins, carrying a version of complementary deoxyribonucleic acid for aflibercept, under the control of a ubiquitous promoter)

Treatment of neovascular (wet) age-related macular degeneration

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.2. Ex vivo fused allogeneic human myoblasts (MB-N) with autologous human myoblast (MB-ALS)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.3. Ex vivo fused allogeneic human myoblasts (MB-N) with autologous human bone marrow derived mesenchymal stem cells (MSC-ALS)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.4. Ex vivo fused allogeneic human mesenchymal stem cell (MSC-N) with autologous human myoblast (MB-ALS)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.5. Ex vivo fused allogeneic human myoblasts (MBN1) with allogeneic human myoblasts (MBN2)

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.6. Helper-dependent adenovirus vector coding for interleukin-1 receptor antagonist

Treatment of osteoarthritis of the knee

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.7. Autologous CD34+ cells from mobilised peripheral blood

Treatment of amyotrophic lateral sclerosis (ALS)

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT coordinator was appointed.

4.1.8. Biotinylated cultured reticulocytes, cultured from haematopoietic stem cells

Treatment of red cell suppletion (e.g. trauma/anaemia)

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. Lyophilised supernatant of a pathogen inactivated and gamma sterilised platelet lysate

Treatment of topical treatment of skin ulcers

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 05.04.2023

4.2.2. Autologous intestinal organoid derived from adult stem cells from intestinal epithelial tissue

Treatment of intractable ulcer

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 05.04.2023.

4.2.3. Autologous chondrocytes cultured in hyaluronan-derived scaffold

Repair of cartilage defects

Scope: ATMP scientific recommendation

Action: for discussion

CAT discussed the 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.

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

No items

4.4. Finalisation of procedure

4.4.1. Umbilical Cord Wharton Jelly-derived mesenchymal stem cells (MSCs) cells

Treatment of spinal cord injury; drug resistant epilepsy; hypoxia ischemia encephalopathy

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of an advanced therapy medicinal product as provided in Article 2(1) of Regulation (EC) No 1394/2007. CAT considered that the applicant has not provided sufficient information on the claimed mode of action of the product in the indication sought and therefore CAT concluded that the product is an ATMP but did not decide yet if it is a tissue engineered product or a somatic cell therapy medicinal product.

4.4.2. Bladder acellular matrix (BAM) based scaffold seeded with allogenic or autologous adipose-derived stromal cells

Treatment of urinary bladder wall augmentation in patients with small capacity high pressure urinary bladder

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of tissue engineered product as provided in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.3. Fibrin gel containing autologous leucocyte- and platelet-rich plasma, autologous thrombin, and ascorbic acid

Treatment of wounds

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.

4.4.4. Ex-vivo expanded allogeneic human corneal endothelial cells

Treatment of diseases of the corneal endothelium

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definitions of tissue engineered product and a combined ATMP as provided in Article 2(1) of Regulation (EC) No 1394/2007.

4.4.5. Recombinant Adeno-Associated Viral Vector expressing a codon optimised human RPGR gene (rAAV2tYF-GRK1-RPGR)

Treatment of X-linked retinitis pigmentosa (XLRP) caused by mutations in the RPGR gene

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

The classification report was adopted. The product does fulfil the definition of gene 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:	13-16.03.2023
- Appointment of CAT Peer Reviewers:	22-24.03.2023
- SAWP first reports:	03.04.2023
- CAT Peer Reviewer comments (NC/C):	05.04.2023
- CAT Peer Reviewer comments (Q):	12.04.2023
- Discussion at SAWP:	11-14.04.2023
- Discussion at CAT and feedback to SAWP:	19-21.04.2023

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	06-09.02.2023
- Appointment of CAT Peer Reviewers:	15-17.02.2023
- SAWP first reports:	06.03.2023
- CAT Peer Reviewer comments (NC/C):	10.03.2023
- CAT Peer Reviewer comments (Q):	15.03.2023
- Discussion at SAWP:	22-24.03.2023
- Discussion at CAT and feedback to SAWP:	19-21.04.2023

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

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	13-16.03.2023

SAWP recommendation:	14.04.2023
CAT recommendation:	21.04.2023
CHMP adoption of report and final recommendation:	26.04.2023

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

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 Silke Dorner as the new member for Austria and Corina Spreitzer as the new alternate for Austria.

7.1.2. Vote by proxy

Action: for information

None

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Sweden presidency, 4 and 5 May 2023, Upsala (Sweden)

CAT: Lisbeth Barkholt, Maria Lüttgen

Scope: Topics for discussion at the upcoming SRLM

Action: for discussion

Lisbeth Barkholt presented the revised agenda for the joint meeting with COMP.

7.2. Coordination with EMA Scientific Committees

7.2.1. Companion Diagnostics (CDx)

CAT: Ilona Reischl

Scope: Update from the Companion Diagnostics (CDx) Expert group meeting (10.03.2023); in vitro diagnostics (IVD) wording in the SmPC

Action: for information

Feedback was provided from the last CDx Expert group meeting. The following topics were presented: the Scientific Advice questions and answers document on CDx for which a clean version will be circulated to CAT for information; the IVD wording in the SmPC; the experience so far with the CDx consultation process mentioning the issue with legacy IVD where a follow on CDx was discussed in the consultation procedure according to the IVDR already, while the reference IVD according to the IVD Directive has not yet undergone the CDx consultation and therefore only limited information is available.

7.2.2. CHMP AR template – Revamp Project

Presentation on the new CHMP AR template

Action: For discussion

EMA presented the project aiming to take out repetitions and redundancies from the assessment report template. The response document template was presented: the applicant will be able to include the response to the questions, and the rapporteurs would add their assessment in the same document. The response document will be implemented next month (a communication will go out to companies: they will be asked to use, on a voluntary basis, the response template).

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

7.5.1. 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 07.03.2023

Action: for information

Pille Säälik provided detailed feedback from the discussions in the last International Pharmaceutical Regulators Programme (IPRP) meeting.

It was noted that the IPRP reflection paper on raw materials has been published on the IPRP website.

7.5.2. WHO approach towards the development of a global regulatory framework for cell and gene therapy products

CAT: Ilona Reischl

Scope: Final WHO paper

Action: for information

Topic postponed to the April CAT meeting.

7.5.3. Strategic approach to international harmonization of cell and gene therapy products

Scope: Bio Reflection paper on ICH harmonisation of cell and gene therapy products

Action: for discussion

CAT members provided feedback in the BIO reflection paper to set up a discussion group to determine the further ICH guideline development on cell and gene therapy products. Overall, this initiative could be supported. CAT indicated that there is value of harmonisation of guidance for mature products (such as AAVs and CAR-Ts). It was noted that some of the examples of potential guideline development are outside of the remit of EMA (e.g. on clinical trial requirements). Key will be to have sufficient resources available to contribute to the activities of the proposed discussion group and afterwards for the drafting of multidisciplinary guidelines in the field of gene and cell therapies.

7.6. CAT work plan

No items

7.7. Planning and reporting

7.7.1. Update of the Business Pipeline report - Q1-2023

Action: for information

The information was noted.

7.8. Others

7.8.1. CAT stakeholder meeting 2023

CAT: Dariusz Sladowski, Ilona Reischl, Kerstin Sollerbrandt

Scope: Topics proposed by the CAT stakeholders and plan of actions to prepare the agenda of the stakeholders meeting to take place on 16.05.2023

Action: for discussion

EMA presented the proposals received from the stakeholders. Some of the topics proposed are outside of the remit of CAT, so CAT can listen to the concerns raised but will not be able

to offer solutions.

It was agreed that the following CAT members together with CAT secretariat will look at proposals and bring back a draft agenda to the April CAT: Ilona Reischl, Carla Herberts, Dariusz Sladowski and Violaine Closson Carella.

7.8.2. EMAN-EIT Expert workshop on Genome editing

CAT: Ilona Reischl, Kieran Breen, Sol Ruiz, Alessandro Aiuti, Alessandra Renieri

Scope: Oral feedback from the workshop held on 21.03.2023

Action: for information

EMA gave a high-level feedback from the discussions in the genome editing workshop.

7.8.3. Consensus of scientific principles and experimental approaches for the assessment of potential carcinogenicity of gene therapies

CAT: Carla Herberts

Scope: Feedback from a workshop held on 7-8.03.2023 on the development of a Consensus on the Scientific principles and experimental approaches for the assessment of potential carcinogenicity of gene therapies

Action: for information

The CAT Vice-Chair provided feedback from the workshop. The updated consensus document will be circulated to CAT when it becomes available.

7.8.4. ISCT Global Regulators Summit on the use of unproven cell and gene products – 30 May 2023 Paris, France

CAT: Ilona Reischl

Action: for information

The CAT Chair presented an outline of the messages she plans to bring at the ISCT Global Regulator Summit.

8. Any other business

No items

Date of next CAT meeting:

19-21 April 2023

9. List of participants

Including any restrictions with respect to involvement of members / alternates / experts

following evaluation of declared interests for the 22-23 March 2023 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ilona Reischl	Chair	Austria	No interests declared	
Silke Dorner	Member	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Azra Selimovic	Member	Croatia	No interests declared	
Rafaella Pontou	Member	Cyprus	No interests declared	
Petr Soukup	Member	Czechia	No interests declared	
Ebru Karakoc Madsen	Member	Denmark	No interests declared	
Bibi Fatima Syed Shah	Alternate	Denmark	No interests declared	
Pille Saalik	Alternate	Estonia	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	
Balázs Sarkadi	Alternate	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Concetta Quintarelli	Member	Italy	No interests declared	
Barbara Bonamassa	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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 (Vice-Chair)	Netherlands	No interests declared	
Babs Fabriek	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Katarina Vavrová	Member	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Lisbeth Barkholt	Member	Sweden	No interests declared	
Paolo Gasparini	Member	Clinicians' Representative	No interests declared	
Alessandro Aiuti	Member	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant	Member	Patients' Representative	No interests declared	
Mencia de Lemus Belmonte	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member	Patients' Representative	No interests declared	
Odoardo Olimpieri	Expert - in person*	Italy	No interests declared	
Jörg Engelbergs	Expert - in person*	Germany	No interests declared	
Olga Kholmanskikh	Expert - via telephone*	Belgium	No interests declared	
Ivana Haunerova	Expert - via telephone*	Czech Republic	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Anna Vikerfors	Expert - via telephone*	Sweden	No interests declared	
Torbjorn Callreus	Expert - via telephone*	Malta	No interests declared	
A representative from the European Commission attended the meeting 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.

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

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

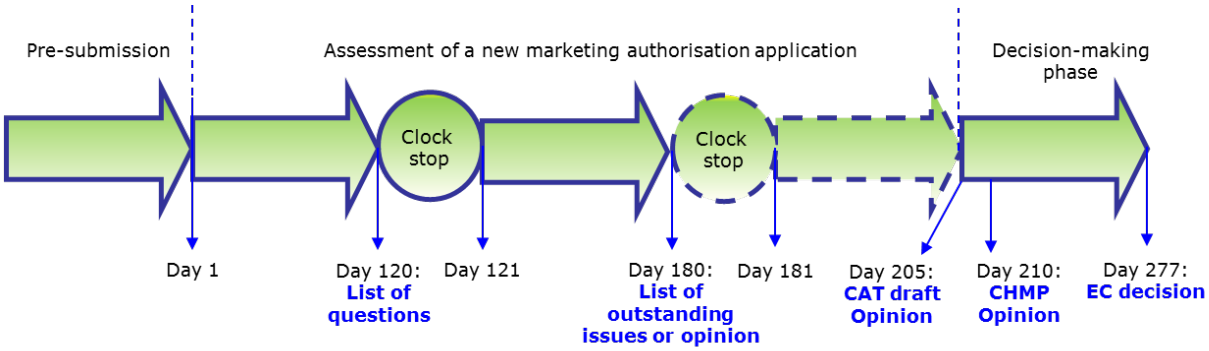
Evaluation of ATMPs (section 2)

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 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/