EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

08 April 2022
EMA/CAT/184995/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 11-13 April 2022

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

11 April 2022, 14:00 – 18:30, room 01-D

12 April 2022, 09:00 – 18:30, room 01-D

13 April 2022, 09:00 – 13:00, room 01-D

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CAT meeting reports once the procedures are finalised.

Of note, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CAT plenary session to be held 11-13 April 2022. See 11-13 April 2022 CAT minutes (to be published post 11-13 May 2022 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 11-13 April 2022 meeting

1.3. Adoption of the minutes

CAT minutes for 16-18 March 2022 meeting

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. Eladocagene exuparvovec - Orphan - EMEA/H/C/005352

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

Scope: oral explanation

Action: for adoption

List of Outstanding Issues adopted on 05.11.2021, 16.04.2021. List of Questions adopted on 20.05.2020.

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

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

Scope: oral explanation

Action: for information

List of Questions adopted on 22.01.2021. List of outstanding issues adopted on 16.07.2021

Note: the revised timetable was adopted via written procedure.

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

2.6.1. Lenadogene nolparvovec - Orphan - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of vision loss due to Leber hereditary optic neuropathy (LHON)

Scope: MAA's request for additional clock stop extension

Action: for adoption

D120 List of Questions adopted in February 2021

2.7. New applications

2.7.1. Etranacogene dezaparvovec - PRIME - Orphan - EMEA/H/C/004827

Accelerated assessment

CSL Behring GmbH; treatment of adults with Haemophilia B (congenital Factor IX deficiency) and with a pre-existing neutralising anti-AAV5 antibody titre below 1:700 to reduce the frequency of bleeding episodes and the need for Factor IX replacement therapy

Scope: Timetable for assessment

Action: for adoption

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. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0050

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Request for Supplementary Information

Action: for adoption

2.11.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0052

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality. Opinion

Action: for adoption

2.11.3. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451/II/0026/G

Novartis Europharm Limited

Rapporteur: Sol Ruiz

Scope: Quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 21.01.2022.

2.11.4. Yescarta - axicabtagene ciloleucel - 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. Opinion

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.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Abecma - idecabtagene vicleucel - Orphan - EMEA/H/C/004662/R/0014

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Annika Folin

Scope: 1-year Renewal of Marketing Authorisation

Action: for adoption

2.13.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/003.7

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: 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 ALL and DLBCL patients. Fourth semi-annual report (EBMT data only)**Action:** for adoption

2.13.3. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/P46/018

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

Scope: Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.
FINAL STUDY REPORT, Study AVXS-101-CL-306 (CL-306): a Phase 3, Open-Label, Single Arm, Single-dose Gene Replacement Therapy Clinical Trial for Patients with Spinal Muscular Atrophy Type 1 with One or Two SMN2 Copies Delivering AVXS-101.

Action: for adoption

Request for Supplementary Information adopted on 18.02.2022.

2.13.4. CAT recommendation to MAHs of CAR-T cell-based therapies with regards to long-term safety and efficacy follow-up studies using EBMT as a data source

Scope: Following the trilateral with EBMT and MAHs and following consultation with CAT and

PRAC Rapporteurs of affected products, EMA is presenting a draft recommendation for CAT discussion and endorsement, with various options.

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. Ex-vivo expanded autologous Wharton's Jelly derived mesenchymal stem cells (WJ-MSCs)

Intended for the treatment of autism spectrum disorder

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Ultra-purified adipose tissue-derived product devoid of mature adipocytes

Intended for fat grafting, augmenting and managing soft tissue defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Cultured human adipose derived stromal cells

Intended for the treatment of stress urinary incontinence in men after radical prostatectomy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Human autologous tumour and hypoxia educated macrophages

Intended for the treatment of spinal cord injury

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. 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: ATMP scientific recommendation

Action: for adoption

4.2.2. Suspension of VST cells

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

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Adipose-derived stem cells

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

Scope: ATMP scientific recommendation

Action: for adoption

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

4.3.1. Leukocyte and platelet rich plasma, autologous

Intended for the treatment of critical limb ischemia

Scope: ATMP scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Gingival fibroblast

Intended for the treatment of gonarthrosis

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.2. 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: The European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.3. 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: The European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

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

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

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.5. Plasmid expressing variant of human interleukin-10

Intended for the treatment of osteoarthritis, neuropathic pain, amyotrophic lateral sclerosis

Scope: The European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

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: 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

5.1.2. 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:	02-05.05.2022
- Discussion at CAT and feedback to SAWP:	13.05.2022

No items

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:	04-07.04.2022
SAWP recommendation:	05.05.2022
CAT recommendation:	13.05.2022
CHMP adoption of report and final recommendation:	19.05.2022

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

Action: for information

7.1.2. Vote by proxy

No items

7.2. Coordination with EMA Scientific Committees

No items

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

7.3.1. Working party review - nomination of ESEC members

CAT: Martina Schüssler-Lenz

Action: for information

7.3.2. Core SmPC for genetically modified cells

CAT drafting group: Martina Schüssler-Lenz, Ilona Reischl, Violaine Closson Carella, Isabel Vieira, Metoda Lipnik-Stangelj, Carla Herberts, Alessandro Aiuti

Scope: Core SmPC for genetically modified cells

Action: for adoption

7.3.3. EC/EMA/CTCG (ACT-EU) Complex Clinical trials Q&A – Final Draft

CAT: Ilona Reischl, Alessandra Renieri

Action: for adoption

7.3.1. Procedure on ATMP scientific advice and BWP interaction

Scope: procedure for interactions with BWP on scientific advices and timing/role of CAT peer review

7.4. Cooperation with the EU regulatory network

7.4.1. Revision of the EU pharmaceutical legislation (Directive 2001/83/EC and Regulation (EC) No 726/2004

Action: for discussion

7.4.2. Revision of the EU pharmaceutical legislation

Action: for information

7.5. Cooperation with international regulators

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

CAT: Martina Schuessler-Lenz

Scope: Agenda of the teleconference that will take place on 21 April 2022

Action: for information

7.6. CAT work plan

No items

7.7. Planning and reporting

7.7.1. Marketing authorisation applications: 3-year forecast report

Scope: Update of the business pipeline report for the human scientific committees

Action: for information

7.8. Others

7.8.1. Adeno-associated viral (AAV) vector toxicities: regulatory considerations

CAT: Carla Herberts, Egbert Flory

Scope: CAT discussion paper: follow-up of patients treated with AAV-based gene therapies

Action: for discussion

7.8.2. DIA Europe

CAT: Ilona Reischl

Scope: Feedback from the panel session: 'A future vision for cell & gene therapies in Europe' and from the session: 'The future of Drug-Device combination product registries'

Action: for information

8. Any other business

No items

Date of next CAT meeting:

11-13/05/2022

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

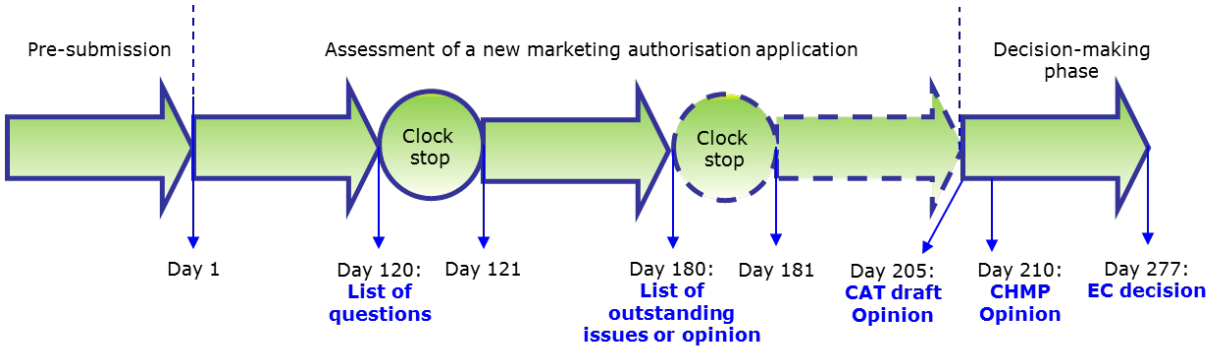
Evaluation of ATMPs (section 2)

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/