10 April 2017
EMA/CAT/242785/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 10-12 April 2017

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

10 April 2017, 14:00 – 18:30, room 02-A

11 April 2017, 09:00 – 18:30, room 02-A

12 April 2017, 09:00 – 12:00, room 02-A

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 10-12 April 2017. See April 2017 CAT minutes (to be published post-May 2017 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 10-12 April 2017 meeting

1.3. Adoption of the minutes

CAT minutes for 15-17 March meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. Human autologous spheroids of matrix– associated chondrocytes for transplantation; EMA/H/C/0002736

Claimed indication: repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (International Cartilage Repair Society [ICRS] grade III or IV) with defect sizes up to 10 cm^2 in adults

Scope: Oral explanation

Action: Oral explanation to be held on 11 April 2017 from 09:30hrs

List of Outstanding Issues adopted on 17.02.2017. List of Questions adopted on 19.04.2013

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

2.8. Withdrawal of initial marking 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 - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0008

Amgen Europe B.V.

Rapporteur: Olli Tenhunen; CHMP Coordinator: Tuomo Lapveteläinen; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Quality

Action: for adoption

Request for Supplementary Information adopted on 17.02.2017.

2.12. Other Post-Authorisation Activities

Annex C - Post-Authorisation Measures (PAMs): Line listing of ATMPs post authorisation measures with procedures starting in April 2017 will be tabled in CAT MMD two weeks after current CAT meeting

Annex D - Post-Authorisation Measures (PAMs): Line listing of ATMPs post authorisation measures with procedures concluded in April 2017 will be tabled in CAT MMD two weeks after current CAT meeting

2.12.1. Zalmoxis – Allogeneic t cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ðlngfr) and the herpes simplex i virus thymidine kinase (hsv-tk mut2); Orphan; EMEA/H/C/002801/R/0003

MolMed SpA; Treatment of adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies

Rapporteur: Hans Ovelgönne; CHMP Coordinator: Paula Boudewina van Hennik

Scope: 1st annual reassessment for renewal of conditional MA. Opinion

Action: for adoption

3. Certification of ATMPs

Disclosure of 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

4. Scientific Recommendation on Classification of ATMPs

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

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous adipose derived mesenchymal stem cells; EMA/H0004813

Intended for the treatment of chronic wound

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Mesenchymal stem cells isolated from umbilical cord; EMA/H0004815

Intended for the treatment of chronic obstructive pulmonary diseas

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Bilayer, engineered, collagen hydrogel-based skin graft composed of autologous keratinocytes and fibroblasts; EMA/H0004817

Intended for the treatment of partial deep dermal and full thickness burn wounds

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Replication incompetent adenoviral serotype 5 vector encoding the human interleukin-12 p70 (hIL-12) transgene under the control of the activator ligand, veledimex; EMA/H0004805

Intended for the treatment of recurrent or progressive glioblastoma

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Adenovirus-associated viral vector serotype 5 containing CRISPR Cas9 and guide RNAs targeting intron 26 of the centrosomal protein 290 gene (AAV5-GRK1-SauCas9-CEP290gRNA 323/64); EMA/H0004818

Intended for the treatment of patients aged 3 years and older with Leber Congenital Amaurosis type 10 (LCA10) caused by a homozygous or compound heterozygous intron 26 mutation, c.2991+1655 A>G, in the CEP290 gene

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Autologous human adipose perivascular stromal cells genetically modified to secrete soluble tumour necrosis factor-related apoptosis-inducing ligand (sTRAIL); EMA/H0004820

Intended for the treatment of TRAIL-sensitive cancers such as Ewing sarcoma and pancreatic ductal adenocarcinoma

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. Resorbable, viscoelastic matrix for use with autologous stromal vascular fraction (SVF); EMA/H0004819

A resorbable matrix to be used for the delivery of autologous SVF adipose derived cells for the treatment of HIV-related facial lipoatrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. Allogeneic unexpanded amniotic fluid derived cells suspended with dried and cryofractured amniotic tissue; EMA/H0004816

Intended for the treatment of chronic wound care

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.9. Human autologous stromal vascular fraction (SVF); EMA/H0004822

Intended for the treatment of articular cartilage and bone defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.10. Human autologous adipose-derived stromal/stem cells (ADSCs); EMA/H0004823

Intended for the treatment of articular cartilage and bone defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Human induced pluripotent stem cell derived natural killer cells expressing high-affinity non-cleavable CD16 Fc; EMA/H0004784

Intended for the treatment of advanced solid tumour malignancies

Scope: scientific recommendation

Action: for adoption

4.2.2. Autologous cultured Wharton jelly derived mesenchymal stem cells; EMA/H0004795

Intended for the treatment of amyotrophic lateral sclerosis or other central or peripheral nervous system repair

Scope: scientific recommendation

Action: for adoption

4.2.3. Allogeneic cultured Wharton jelly derived mesenchymal stem cells; EMA/H0004796

Intended for the treatment of amyotrophic lateral sclerosis or other central or peripheral nervous system repair

Scope: scientific recommendation

Action: for adoption

4.2.4. Autologous cultured adipose regenerative mesenchymal stem cells; EMA/H0004797

Intended for the treatment of autoimmune epilepsy and other central or peripheral nervous system repair

Scope: scientific recommendation

Action: for adoption

4.2.5. Autologous adipose derived mesenchymal stem cells; EMA/H0004798

Intended for the treatment of autoimmune epilepsy and other central or peripheral nervous system repair

Scope: scientific recommendation

Action: for adoption

4.2.6. Autologous cultured adipose derived mesenchymal stem cells - EMA/H0004799

Intended for the treatment of autoimmune epilepsy and other central or peripheral nervous system repair

Scope: scientific recommendation

Action: for adoption

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

4.3.1. Stimulated resistant cells suspension cancer vaccine; H0004763/0001

Colorectal cancer

Scope: revised scientific recommendation

Action: for adoption

4.4. Finalisation of procedure

4.4.1. Allogenic human mesenchymal stem cells - mesenchymal stem cells, umbilical cord derived; EMA/H0004758/0001

Intervertebral disc regeneration

Scope: No comments raised by the European Commission

Action: for information

4.4.2. Recombinant adeno-associated virus serotype 8 (rAAV8) thyroxine-binding globulin (TBG) human uridine diphosphate glucuronosyltransferase 1A1 (hUGT1A1); EMA/H0004757/0001

Treatment of Crigler-Najjar (CN) syndrome.

Scope: No comments raised by the European Commission

Action: for information

4.4.3. Autologous human mesenchymal stem cells - mesenchymal stem cells, bone marrow derived; EMA/H0004766/0001

Faculty of Medical Sciences, University of Warmia and Mazury; Coma (brain injury, stroke)

Scope: No comments raised by the European Commission

Action: for information

4.4.4. Banked allogenic leukocytes - Leukocytes with high cancer killing activity (CKA); EMA/H0004785/0001

Metastatic Pancreatic Ductal Adeno Carcinoma

Scope: No comments raised by the European Commission

Action: for information

4.4.5. Implantable continuous glucose monitoring system; EMA/H0004762/0001

Adjunct glucose monitoring in diabetes patients

Scope: No comments raised by the European Commission

Action: for information

4.4.6. Recombinant adeno-associated virus serotype 8 (rAAV8) thyroxine-binding globulin (TBG) human uridine diphosphate glucuronosyltransferase 1A1 (hUGT1A1); EMA/H0004757

Intended for the treatment of Crigler-Najjar (CN) syndrome

Scope: No comments raised by the European Commission

Action: for information

4.4.7. Oncolytic adenovirus; EMA/H0004767

Intended for the treatment of pancreatic cancer

Scope: scientific recommendation

Action: No comments raised by the European Commission

4.5. Follow-up and guidance

5. Scientific Advice

Disclosure of 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 Coordinators

5.2. CAT reports

5.3. List of Issues

5.4. Finalisation of SA procedures

6. Pre-Authorisation Activities

Disclosure of 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

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

Intended for the treatment of Fanconi anaemia type AScope: CHMP at its March 2017 denied eligibility to PRIME

6.3.4. Month 3 – Nomination of Rapporteurs

6.3.5. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting – Malta, June 2017

CAT Strategic Review & Learning meeting (SRLM) will take place in Gozo, Malta on 1-2 June 2017 under the auspices of the Maltese Presidency of the Council of the European Union

Scope: draft programme

Action: for information

7.1.2. CAT - Best practice guide

Scope: Proposal for a best practice guide

Action: for discussion

7.1.3. Good manufacturing practice (GMP) requirements for ATMPs

Scope: proposed way forward. Drafting group meeting will take place on 26 April 2017 (date is to be confirmed)

Action: for information

7.1.4. CAT meeting dates 2019 - 2021

Scope: meeting dates for 2019 – 2021

Action: for adoption

7.2. Coordination with EMA Scientific Committees

7.2.1. Procedural advice on the evaluation of advanced therapy medicinal products

Scope: revised document for presentation to Committees

Action: for discussion

7.2.2. Committee for Medicinal Products for Human Use (CHMP)

Scope: Summary of Outcomes (SoO) for the 15-17 March 2017 meeting

Action: for information

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

7.3.1. Working Party with Patients' and Consumers' Organisations (PCWP)

Scope: minutes of the PCWP with all eligible organisations that took place on 30 November 2016

Action: for information

7.3.2. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope: agenda of the workshop on personalised medicines: role of patients, consumers and healthcare professionals, 14 March 2017 and agenda of the PCWP/HCPWP joint meeting, 15 March 2017

Action: for information

7.3.3. Guideline on quality, non-clinical and clinical aspects of gene therapy medicinal products

Scope: Drafting group will take place on 10 May 2017 from 10:00-13:30hrs to finalise the revision. Call for interest for additional CAT members can join the Drafting group

Action: for discussion

Drafting group composition:
-Quality: M. Menezes-Ferreira, C. Niederlaender, S. Ruiz and P. Salmikangas
-Non-clinical: K. Breen, B. Sarkadi, M. Renner
-Clinical: P. Gasparini, B. Klug, M. Hystad, O. Tenhunen

7.4. Cooperation within the EU regulatory network

7.4.1. Orphan similarity for ATMPs

CAT drafting group: Simona Badoi, Violaine Closson-Carella, Michele Lipucci, Martina Menezes-Ferreira, Christiane Niederlaender, Ilona Reischl, Paula Salmikangas

Scope: Reflection from the perspective of ATMPs on the concept of 'similar active substance' as referred to in Art 3(3)c of Reg (EC) No 847/2000 of April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concept 'similar medicinal product' and 'clinical superiority'. Review of comments received from the public consultation. Feedback from the breakout meeting that will take place on Monday 10 April 2017.

Action: for information

Timeline:
-Break out meeting organised for Monday 10 April 2017.
-The drafting group participated in two virtual meetings on 09 February and 07 March 2016 and two break-out meetings on 19 February and 23 March 2016
-CAT agreed to a proposal at its March 2016 plenary. CHMP adopted the proposal (from QWP, BWP and CAT) in March 2016.

Consultation document published by the European Commission

http://ec.europa.eu/health/sites/health/files/files/orphanmp/2016_07_pc_orphan/2016_07_consultation_paper.pdf

7.5. Cooperation with international regulators

None

7.6. CAT work plan

7.6.1. CAT 2017 work plan

Scope: Work plan was adopted via written procedure on 22 March 2017

Action: for information

7.6.2. Questions and Answers document on minimally manipulated ATMPs

Scope: draft Questions & Answers

Action: for adoption

7.7. Planning and reporting

None

7.8. Others

8. Any other business

No items

Date of next CAT meeting:

10-12 May 2017

9. Explanatory notes

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

Abbreviations / Acronyms

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

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

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 Applicant

MAH: Marketing Authorisation Holder

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

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: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

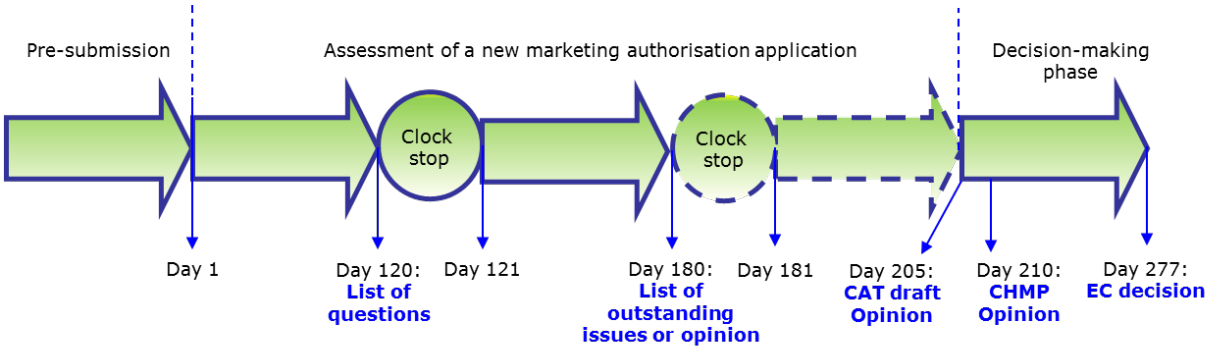
Evaluation of ATMPs (section 2)

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.

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/