20 April 2023
EMA/COMP/151364/2023
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 21-23 March 2023

Chair: Violeta Stoyanova-Beninska – Vice-Chair: Armando Magrelli

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 this set of 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 COMP meeting reports once the procedures are finalised.

Of note, this set of minutes is a working document primarily designed for COMP 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 and experts

The Chair opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) pandemic, 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 and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions 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 and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda for 21-23 March 2023 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 14-16 February 2023 were adopted with amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. - EMA/OD/0000112208

Treatment of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 3 March 2023, prior to responding to the list of issues.

2.1.2. - EMA/OD/0000093062

Treatment of spinal cord injury

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of spinal cord injury, the sponsor was requested to further elaborate on the preliminary clinical Phase II study and the inconclusive nature of the findings regarding the primary endpoint, the use on top of pregabalin and the meaningfulness of the responder data. The sponsor was requested to also discuss the reduction of pain relief over time as well as effects on other symptoms of the condition.

The sponsor was asked to further elaborate on the results of the non-clinical in vivo data and their relevance to the target symptom.

- Significant benefit

The arguments on significant benefit were based on an alternative mechanism of action and the potential improved efficacy in the condition.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the Phase II clinical study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

The sponsor was asked to detail the results of any clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients.

In the written response, and during an oral explanation before the Committee on 21 March 2023, the sponsor did not provide any new data. The basis of the argumentation was that the trial design reflected on current medical practice where the dose of pregabalin administered is between 150-300mg per day, as the sponsor claimed that higher doses cause side effects. The COMP noted that the maximal dose administered is 600mg per day and that patients could have been underdosed. The criteria for inclusion regarding prior medication and the control of these patients' neuropathic pain were not clarified either making an understanding of the management of the patients very difficult. The COMP asked the sponsor if they expected the add-on effect on top of maximally tolerated doses of pregabalin would offer additional benefits. The sponsor reiterated several times that the patients were difficult to treat and that they had attempted to standardise the dose given. The COMP concluded that the add-on effect to underlying pregabalin treatment was difficult to establish and that the finding that the dose 2.1 g/day of the sponsors' product could be a chance finding when considering the responder rate data submitted, in particular as there was no dose ranging effect. The rebound effect was also noted to a lesser extent in the dose which was claimed to be effective.

The COMP considered that there was insufficient data to support the basis of significant benefit and therefore could not recommend granting the orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 23 March 2023, prior to final opinion.

2.1.3. - EMA/OD/0000118779

Treatment of amyotrophic lateral sclerosis

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 3 March 2023, prior to responding to the list of issues.

2.1.4. - EMA/OD/0000115658

Treatment of pancreatic cancer

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 6 March 2023, prior to responding to the list of issues.

2.1.5. - EMA/OD/0000117508

Treatment of berylliosis (chronic beryllium disease)

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Significant benefit

The arguments on significant benefit were based on an alternative mechanism of action and the potential improved efficacy in the condition.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from their clinical study to justify the assumption of significant benefit over authorised medicinal products such as methylprednisolone which is specifically authorised in member states for the proposed orphan condition.

In the written response, and during an oral explanation before the Committee on 22 March 2023, the sponsor did not have any new data to present. The sponsor provided additional written information regarding the patient characteristics of the 6 patients who were enrolled. They highlighted those who were corticosteroid intolerant of which there were 3 and corticosteroid treated which were another three. They did not, however, separate out the impact on the FEV1 (forced expiratory volume in the 1st second) and FVC (forced vital capacity) based on the previous background treatment making it difficult to see the real impact in the corticosteroid intolerant patients nor did they further elaborate on the potential corticosteroid effect although only one patient appeared to benefit from this.

The COMP could not establish the clinically relevant advantage and thus the significant benefit and thus concluded that they could not recommend granting the orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 23 March 2023, prior to final opinion.

2.1.6. - EMA/OD/0000104687

Treatment of mucopolysaccharidosis type II, MPS II (Hunter syndrome)

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to clarify the following issues:

- Medical plausibility

The sponsor provided data in an in vivo model of the condition, reporting restoration of IDS activity in several tissues as well as reduction of accumulation of IDS substrates. The sponsor was requested to justify the clinical relevance of the obtained results and to provide any available evidence in functional outcomes, such as behavioural or other neurological assessments or survival.

In the written response, and during an oral explanation before the Committee on 22 March 2023, the sponsor further elaborated on the issues raised. The sponsor commented on the feasibility of using behavioural endpoints in the non-clinical model studied. In particular, it was noted that behavioural differences are barely detectable at early timepoints and that the differences between MPS II and wildtype subjects in behavioural tests are very small, not reaching statistical significance in most of the cases. Moreover, given the existence of a motor phenotype, these tests are not suitable for studying behaviour. The committee noted the limitations and discussed the validity of the model used to draw conclusion of the condition in humans. It was considered that in the absence of improvements shown in functional endpoints, medical plausibility would not be considered justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 22 March 2023, prior to final opinion.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000098523

Treatment of adrenal insufficiency

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the April 2023 meeting.

[Post-meeting note: The sponsor withdrew the application for orphan designation on 29 March 2023].

2.2.2. - EMA/OD/0000114003

Treatment of sarcoidosis

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the April 2023 meeting.

[Post-meeting note: The sponsor withdrew the application for orphan designation on 5 April 2023].

2.2.3. autologous adipose-derived mesenchymal stem cells - EMA/OD/0000118464

nicole BEARD; Treatment of oesophageal atresia

COMP Rapporteur: Armando Magrelli

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of oesophageal atresia.

The Committee agreed that the condition, oesophageal atresia, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing autologous adipose-derived mesenchymal stem cells was considered justified based on in vivo non-clinical data showing successful implantation of the newly formed oesophagus.

The condition is life-threatening and chronically debilitating in particular due to malnutrition, failure to thrive and aspiration, commonly necessitating surgical intervention.

The condition was estimated to be affecting approximately 4.6 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for autologous adipose-derived mesenchymal stem cells, for treatment of oesophageal atresia, was adopted by consensus.

2.2.4. - EMA/OD/0000118693

Treatment of myotonic disorders

The COMP adopted a list of issues that will be sent to the sponsor. The Committee will discuss the submitted answers to the list of issues at the April 2023 meeting.

2.2.5. - EMA/OD/0000119243

Treatment of paediatric osteosarcoma (melatonin monotherapy and/or in combination with cisplatin and/or doxorubicin).

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the April 2023 meeting.

[Post-meeting note: The sponsor withdrew the application for orphan designation on 4 April 2023].

2.2.6. *Escherichia coli*, strain Nissle 1917, expressing high affinity phenylalanine transporter, modified phenylalanine ammonia lyase (S92G, H133M, I167K, L432I, V470A) and L-amino acid deaminase - EMA/OD/0000120359

Orphix Consulting GmbH; Treatment of hyperphenylalaninaemia

COMP Rapporteur: Ingeborg Barisic

The Committee agreed that the condition, hyperphenylalaninaemia, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing *Escherichia coli*, strain Nissle 1917, expressing high affinity phenylalanine transporter, modified phenylalanine ammonia lyase (S92G, H133M, I167K, L432I, V470A) and L-amino acid deaminase was considered justified based on preliminary clinical data which showed a dose-related reduction in plasma deuterium-labelled phenylalanine.

The condition is chronically debilitating due to high blood phenylalanine levels which cause cognitive impairment.

The condition was estimated to be affecting approximately 1.9 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing *Escherichia coli*, strain Nissle 1917, expressing high affinity phenylalanine transporter, modified phenylalanine ammonia lyase (S92G, H133M, I167K, L432I, V470A) and L-amino acid deaminase will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a reduction of elevated blood phenylalanine levels in patients in which target levels cannot be achieved with the currently authorised products or in patients not eligible to receive currently authorised treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for *Escherichia coli*, strain Nissle 1917, expressing high affinity phenylalanine transporter, modified phenylalanine ammonia lyase (S92G, H133M, I167K, L432I, V470A) and L-amino acid deaminase, for treatment of hyperphenylalaninaemia, was adopted by consensus.

2.2.7. - EMA/OD/0000120667

Treatment of Charcot-Marie-Tooth disease

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the April 2023 meeting.

2.2.8. lurbinectedin - EMA/OD/0000122029

Pharma Mar S.A.; Treatment of soft tissue sarcoma

COMP Rapporteur: Jana Mazelova

The Committee agreed that the condition, soft tissue sarcoma, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing lurbinectedin was considered justified based on non-clinical data showed delay in tumour growth and increased survival in animals treated with either lurbinectedin as a single agent or in combination with irinotecan and on preliminary clinical data which showed disease control in patients with different types of soft tissues sarcoma who were treated with either lurbinectedin monotherapy or in combination with doxorubicin, irinotecan or gemcitabine.

The condition is chronically debilitating due the possible need for amputation of limbs and life-threatening with a high recurrence and metastasis rate with reduced life expectancy.

The condition was estimated to be affecting approximately 4.7 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing lurbinectedin will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed disease control in a heavily pretreated population. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for lurbinectedin, for treatment of soft tissue sarcoma, was adopted by consensus.

2.2.9. 2-{4-[4-(4-{5-[(1S)-1-amino-1-(4-fluorophenyl) ethyl]pyrimidin-2-yl}piperazin-1-yl)pyrrolo[2,1-f] [1,2,4]triazin-6-yl]-1h-pyrazol-1-yl}ethan-1-ol - EMA/OD/0000122100

Blueprint Medicines (Netherlands) B.V.; Treatment of mastocytosis

COMP Rapporteur: Karri Penttila

The Committee agreed that the condition, mastocytosis, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing 2-{4-[4-(4-{5-[(1S)-1-amino-1-(4-fluorophenyl) ethyl]pyrimidin-2-yl}piperazin-1-yl)pyrrolo[2,1-f] [1,2,4]triazin-6-yl]-1H-pyrazol-1-yl}ethan-1-ol was considered justified based on non-clinical data showing inhibition of tumour growth and improvement in survival and preliminary clinical data showing improvement in patients' symptoms.

The condition is chronically debilitating due to symptoms such as flushing, tachycardia, pruritus, abdominal cramping, peptic ulcers and diarrhoea, and life-threatening due to bone marrow failure, hepatomegaly, splenomegaly, and poor survival with 5-year rates of around 60% in patients with systemic mastocytosis.

The condition was estimated to be affecting less than 3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing 2-{4-[4-(4-{5-[(1S)-1-amino-1-(4-fluorophenyl) ethyl]pyrimidin-2-yl}piperazin-1-yl)pyrrolo[2,1-f] [1,2,4]triazin-6-yl]-1H-pyrazol-1-yl}ethan-1-ol will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that the proposed product is effective in a patient population with indolent mastocytosis that is not covered with currently approved therapies. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 2-{4-[4-(4-{5-[(1S)-1-amino-1-(4-fluorophenyl) ethyl]pyrimidin-2-yl}piperazin-1-yl)pyrrolo[2,1-f] [1,2,4]triazin-6-yl]-1H-pyrazol-1-yl}ethan-1-ol, for treatment of mastocytosis, was adopted by consensus.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

None

2.6. Nominations

2.6.1. New applications for orphan medicinal product designation - Appointment of COMP rapporteurs

COMP rapporteurs were appointed for 11 applications.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 18 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of adult patients with advanced gastrointestinal tumours (GIST) who harbor a KIT exon 11 primary mutation and co-occurring KIT exons 17 and/or 18 mutations (KIT exons 11+17/18 mutations) and who have received prior treatment with imatinib

The Committee was briefed on the significant benefit issues. The COMP adopted the proposed answers on the significant benefit issues.

3.1.2. -

Treatment of pulmonary arterial hypertension

The Committee was briefed on the significant benefit issues. The COMP adopted the proposed answers on the significant benefit issues.

3.1.3. -

Treatment of idiopathic pulmonary fibrosis

The Committee was briefed on the significant benefit issues. The COMP adopted the proposed answers on the significant benefit issues.

3.1.4. -

Treatment of multiple myeloma

The discussion was postponed.

4. Review of orphan designation for orphan medicinal products at time of initial marketing authorisation

4.1. Orphan designated products for which CHMP opinions have been adopted

4.1.1. Elfabrio – pegunigalsidase alfa - EMEA/H/C/005618, EU/3/17/1953, EMA/OD/0000109504

Chiesi Farmaceutici S.p.A.; Treatment of Fabry disease

COMP Rapporteur: Olimpia Neagu; COMP Co-Rapporteur: Armando Magrelli

A list of issues was adopted on 16 February 2023.

An oral explanation was held on 21 March 2023.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the orphan designation from the register of orphan medicinal products, on 23 March 2023, prior to final opinion.

The orphan designation withdrawal assessment report will be publicly available on the EMA website.

4.1.2. Tibsovo – ivosidenib - EMEA/H/C/005936, EU/3/16/1802, EMA/OD/0000115491

Les Laboratoires Servier; Treatment of acute myeloid leukaemia

COMP Rapporteur: Frauke Naumann-Winter; COMP Co-Rapporteur: Maria Elisabeth Kalland

A list of issues was adopted on 18 February 2023.

An oral explanation was held 21 March 2023.

An opinion recommending not to remove Tibsovo, ivosidenib, EU/3/16/1802 from the EC Register of Orphan Medicinal Products was adopted by consensus.

The orphan maintenance assessment report will be publicly available on the EMA website.

4.1.3. Tidhesco – ivosidenib - EMEA/H/C/006174, EU/3/16/1802, EMA/OD/0000117514

Les Laboratoires Servier; Treatment of acute myeloid leukaemia

COMP Rapporteur: Frauke Naumann-Winter; COMP Co-Rapporteur: Maria Elisabeth Kalland

A list of issues was adopted on 18 February 2023.

An oral explanation was held 21 March 2023.

An opinion recommending not to remove Tidhesco, ivosidenib, EU/3/16/1802 from the EC Register of Orphan Medicinal Products was adopted by consensus.

The orphan maintenance assessment report will be publicly available on the EMA website.

*[*Post-*meeting note: The applicant formally withdrew the marketing authorisation application for Tidhesco at the CHMP March meeting.]*

4.2. Orphan designated products for discussion prior to adoption of CHMP opinion

None

4.3. Appeal

None

4.4. On-going procedures

None

4.5. Orphan Maintenance Reports

Documents were tabled for information.

5. Review of orphan designation for authorised orphan medicinal products at time marketing authorisation extension

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

None

5.3. Appeal

None

5.4. On-going procedures

None

6. Application of Article 8(2) of the Orphan Regulation

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the COMP

7.1.1. COMP membership

None

7.1.2. Vote by proxy

Bozenna Dembowska-Baginska gave a proxy to Brigitte Schwarzer-Daum to vote on behalf of Bozenna Dembowska-Baginska during part of the meeting.

Julian Isla gave a proxy to Gloria Palomo Carrasco to vote on behalf of Julian Isla during part of the meeting.

Vallo Tillmann gave a proxy to Karri Penttila to vote on behalf Vallo Tillmann during part of the meeting.

7.1.3. Strategic Review & Learning meetings

None

7.1.4. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 17 March 2023.

7.1.5. COMP Decisions Database

The COMP acknowledged the importance of adding further topics to the database.

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendation on eligibility to PRIME – report

Documents were tabled for information.

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

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

Documents were tabled for information.

The COMP noted the feedback from Elisabeth Rook and Tim Leest related to PCWP/HCPWP activities.

7.3.2. Upcoming ITF meetings

The COMP noted the upcoming ITF meetings. Furthermore, the COMP noted the overview of ITF activities in 2022: Trends and topics in focus.

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. Therapeutic Goods Administration (TGA), Australia

None

7.5.4. Health Canada

None

7.6. Contacts of the COMP with external parties and interaction with the Interested Parties to the Committee

None

7.7. COMP work plan

None

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2023

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2023 were circulated.

7.8.2. Overview of orphan marketing authorisations/applications

An updated overview of orphan applications for Marketing Authorisation was circulated.

8. Any other business

8.1. 4th EAHP Synergy Certification Course on Rare diseases and orphan medicines as an integral part of European healthcare setting – speaker invitation

The COMP agreed that the Armando Magrelli will attend the event as speaker.

8.2. EMA Business Pipeline activity and Horizon scanning

Documents were tabled for information.

8.3. Interim presentation: review of indirect comparisons for demonstration of significant benefit

The COMP noted the presentation.

9. List of participants

including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 21-23 March 2023 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Violeta Stoyanova-Beninska	Chair	Netherlands	No interests declared	
Armando Magrelli	Vice-Chair	Expert recommended by EMA	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	No restrictions applicable to this meeting	
Lyubina Racheva Todorova	Member	Bulgaria	No interests declared	
Dinko Vitezic	Member	Croatia	No interests declared	
Elli Loizidou	Member	Cyprus	No interests declared	
Jana Mazelova	Member	Czechia	No interests declared	
Elisabeth Penninga	Member	Denmark	No interests declared	
Vallo Tillmann	Member	Estonia	No interests declared	
Karri Penttilä	Member	Finland	No interests declared	
Cecile Dop	Member	France	No interests declared	
Frauke Naumann-Winter	Member	Germany	No interests declared	
Zsofia Gyulai	Member	Hungary	No interests declared	
Enrico Costa	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ruta Mameniskiene	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No interests declared	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland	No restrictions applicable to this meeting	
Joao Rocha	Member	Portugal	No restrictions applicable to this meeting	
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	Slovak Republic	No interests declared	
Gloria Maria Palomo Carrasco	Member	Spain	No interests declared	
Darius Matusevicius	Member	Sweden	No restrictions applicable to this meeting	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Julian Isla	Member	Patients' Organisation Representative	No interests declared	
Ines Alves	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Giuseppe Capovilla	Member	Expert recommended by EMA	No interests declared	
Maria Cavaller Bellaubi	Expert - in person*	Patients' Organisation Representative	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Meeting run with support from relevant EMA staff				

* Experts were evaluated against the agenda topics or activities they participated in.

10. Explanatory notes

The notes below give a brief explanation of the main sections and headings in the COMP agenda and should be read in conjunction with the agenda or the minutes.

Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

Orphan Designation *(section 2 Applications for orphan medicinal product designation)*

The orphan designation is the appellation given to certain medicinal products under development that are intended to diagnose, prevent or treat rare conditions when they meet a pre-defined set of criteria foreseen in the legislation. Medicinal products which get the orphan status benefit from several incentives (fee reductions for regulatory procedures (including protocol assistance), national incentives for research and development, 10-year market exclusivity) aiming at stimulating the development and availability of treatments for patients suffering from rare diseases.

Orphan Designations are granted by Decisions of the European Commission based on opinions from the COMP. Orphan designated medicinal products are entered in the Community Register of Orphan Medicinal Products.

Protocol Assistance *(section 3 Requests for protocol assistance with significant benefit question)*

The protocol assistance is the help provided by the Agency to the sponsor of an orphan medicinal product, on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of the medicinal product in view of the submission of an application for marketing authorisation.

Sponsor

Any legal or physical person, established in the Community, seeking to obtain or having obtained the designation of a medicinal product as an orphan medicinal product.

Maintenance of Orphan Designation *(section 4 Review of orphan designation for orphan medicinal products for marketing authorisation).*

At the time of marketing authorisation, the COMP will check if all criteria for orphan designation are still met. The designated orphan medicinal product should be removed from the Community Register of Orphan Medicinal Products if it is established that the criteria laid down in the legislation are no longer met.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/