EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 May 2017
EMA/COMP/174237/2017
Inspections, Human Medicines Pharmacovigilance and Committees

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 14-15 March 2017

Chair: Bruno Sepodes – Vice-Chair: Lesley Greene

14 March 2017, 08:30-19:30, room 2F

15 March 2017, 08:30-17:30, room 2F

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.

Further information with relevant explanatory notes can be found at the end of this document.

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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members and experts

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 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 as included in the pre-meeting list of participants and restrictions.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion.

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 (i.e. 23 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda for 14-15 March 2017 was adopted with amendments.

1.3. Adoption of the minutes

The minutes for 14-16 February 2017 were adopted with no amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. N-[(1R)-1-phenylethyl]-6-{1H-pyrazolo[3,4-d]pyrimidin-4-yl}quinazolin-2-amine - EMA/OD/293/16

Sentinel Oncology Limited; Treatment of fragile X syndrome

COMP coordinator: Giuseppe Capovilla

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

The COMP is of the opinion that audiogenic seizures are not a sufficiently justified endpoint in the sought indication. The sponsor is invited to elaborate on the relevance of the endpoints studied in the in vivo model, and provide any additional data in relevant preclinical or clinical settings to justify the medical plausibility in the scope of the proposed indication.

In the written response, and during an oral explanation before the Committee on 14 March 2017, the sponsor presented additional data from a pre-clinical in vivo model of the condition which was not in the initial submission. In this model they showed behavioural improvements by treatment with the proposed product.

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

The intention to treat the condition with the medicinal product containing N-[(1R)-1-phenylethyl]-6-{1H-pyrazolo[3,4-d]pyrimidin-4-yl}quinazolin-2-amine was considered justified based on improved behaviour in an in vivo model of the proposed condition.

The condition is chronically debilitating due to developmental delay, severe neuro-behavioural and neurocognitive complications.

The condition was estimated to be affecting approximately 2 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 N-[(1R)-1-phenylethyl]-6-{1H-pyrazolo[3,4-d]pyrimidin-4-yl}quinazolin-2-amine, for treatment of fragile X syndrome, was adopted by consensus.

2.1.2. - EMA/OD/308/16

Treatment of acromegaly

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 are based on improved safety, when the proposed product is used as second line somatostatin analogue. The sponsor provides preclinical data versus authorised pasireotide in support of this argumentation.

It is well known that extrapolation from preclinical studies cannot predict the safety of a product in its clinical setting, thus more relevant data is mandatory to justify safety arguments in most cases. Without clinical experience, the sponsor should justify the relevance of preclinical safety data on diabetes.

Furthermore, the sponsor is invited to provide significant benefit consideration versus GH receptor antagonist pegvisomant, which exhibits a favourable benefit for glycaemic control and is currently authorised for patients with acromegaly intolerant to authorised somatostatin analogues.

In the written response, and during an oral explanation before the Committee on 14 March 2017, the sponsor discussed the adequacy of the preclinical model to demonstrate an improved safety of their product within the context of significant benefit. The COMP stressed that the argument of an improved safety as a ground for significant benefit could not be accepted without clinical evidence on the safety profile of the proposed product. Furthermore, the COMP noted that additional significant benefit argumentation was only theoretical in nature and was not supported by any clinical or preclinical evidence.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 14 March 2017, prior to final opinion.

2.1.3. - EMA/OD/253/16

Treatment of invasive aspergillosis

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 if there exists a scientific rationale for the development of the proposed product for treatment of invasive aspergillosis, the sponsor should further elaborate on:

– the results obtained in vitro in the treatment of invasive aspergillosis,

– the relevance of the preclinical model used for the treatment of invasive aspergillosis, and the interpretation of the results obtained in the experiments,

– the absence of any in vivo data in Aspergillus infection settings.

- Significant benefit

The arguments on significant benefit are based on an alternative mechanism of action and the potential improved efficacy and safety in the condition applied for designation.

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on any available data in Aspergillus infection settings to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan indication.

It is well known that extrapolation from preclinical or early clinical studies cannot predict the safety of a product in its clinical setting, thus more relevant data is mandatory to justify safety arguments in most cases. The sponsor should further elaborate on the potential risks with the product and how this compares with the safety profile of current authorised medicinal products for the same condition.

In the written response, and during an oral explanation before the Committee on 14 March 2017, the sponsor did not submit any new data and no in vivo data in any Aspergillus model were discussed. In the absence of such data the criteria of the medical plausibility may not be considered justified. With regards to the significant benefit, the applicant discussed that the product acts via a different mechanism of action than the authorised products, and that its safety may be considered improved but no new data was provided. In the absence of such data the criteria of significant benefit may not be considered justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 March 2017, prior to final opinion.

2.1.4. - EMA/OD/314/16

Treatment of ovarian cancer

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:

- Number of people affected

The sponsor presented prevalence estimate assuming the median duration of the condition to be 5 years. Instead, an attempt to calculate the point prevalence of the condition would be expected.

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor should re-calculate the prevalence estimate based on relevant epidemiological studies and registers for the proposed orphan condition.

- Significant benefit

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition. The sponsor presented non-clinical data to demonstrate the potential improved efficacy of the product in cisplatin and paclitaxel resistant tumours. No discussion of the efficacy of the product versus remaining authorised products was provided. In particular, bevacizumab, pegylated liposomal doxorubicin and topotecan were not discussed and no data was presented to demonstrate benefits of the proposed product over these agents.

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from non-clinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan indication.

In the written response, and during an oral explanation before the Committee on 14 March 2017, the sponsor provided a revised and acceptable prevalence calculation. The sponsor highlighted where in the current treatment algorithm they believed the product would offer a clinically relevant advantage in the treatment of ovarian cancer. The COMP was of the opinion that the data submitted could not establish if indeed there was a clinically relevant advantage of using the product in the target patient population indicated.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 14 March 2017, prior to final opinion.

2.1.5. (S)-8-{2-Amino-6-[1-(5-chloro-biphenyl-2-yl)-(R)-2,2,2-trifluoro-ethoxy]-pyrimidin-4-yl}-2,8-diaza-spiro[4.5]decane-3-carboxylic acid ethyl ester - EMA/OD/299/16

Biological Consulting Europe Ltd; Treatment of pulmonary arterial hypertension

COMP coordinator: Dan Henrohn/Eva Malikova

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

In order to justify the significant benefit of the proposed product the sponsor is invited to provide a more in depth comparative discussion *vis a vis* the authorised products for the treatment of PAH and the current management algorithm of the condition. Such discussion should be as much as possible supported by any available data.

In the written response, the sponsor further elaborated on the pre-clinical in vivo data, demonstrating the additional efficacy when the product was administered in addition to other products used to treat the condition.

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

The intention to treat the condition with the medicinal product containing (S)-8-{2-amino-6-[1-(5-chloro-biphenyl-2-yl)-(R)-2,2,2-trifluoro-ethoxy]-pyrimidin-4-yl}-2,8-diaza-spiro[4.5]decane-3-carboxylic acid ethyl ester was considered justified based on preclinical data showing reduction of mean pulmonary arterial pressure and of pulmonary vessel wall thickness in valid models of the condition.

The condition is chronically debilitating and life threatening due to progressive dyspnoea and right heart failure, leading to death in an average period of approximately 3 years after diagnosis.

The condition was estimated to be affecting less than 2 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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing (S)-8-{2-amino-6-[1-(5-chloro-biphenyl-2-yl)-(R)-2,2,2-trifluoro-ethoxy]-pyrimidin-4-yl}-2,8-diaza-spiro[4.5]decane-3-carboxylic acid ethyl ester will be of significant benefit to those affected by the condition. The sponsor has provided preclinical data showing that the combination of the proposed product with one endothelin receptor antagonist currently authorised is more efficacious in reducing mean pulmonary arterial pressure and pulmonary vessel wall thickness than either products used alone or than the combination of the endothelin receptor antagonist with a phosphodiesterase type 5 inhibitor, which is also authorised for the treatment of the condition. The Committee considered that this constitutes a clinically relevant advantage for the patients affected by the condition.

A positive opinion for (S)-8-{2-amino-6-[1-(5-chloro-biphenyl-2-yl)-(R)-2,2,2-trifluoro-ethoxy]-pyrimidin-4-yl}-2,8-diaza-spiro[4.5]decane-3-carboxylic acid ethyl ester, for treatment of pulmonary arterial hypertension, was adopted by consensus.

2.1.6. Rituximab - EMA/OD/286/16

Hôpital Foch; Treatment in solid organ transplantation

COMP coordinator: Frauke Naumann-Winter

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

The proposed condition "graft rejection following solid organ transplantation" should be justified as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

The sponsor is invited to specify the scope of the application, detail how the product will be used, and define the proposed indication with reference to both antibody mediated and

cellular rejection. A "treatment" indication should also be discussed in view of administration of the product to donor specific antibody positive or presymptomatic patients.

The sponsor is also invited to discuss the proposed condition in the context of the exceptional circumstances of guideline ENTR/6283/00 Rev 04, referring to “treatment modalities”.

With regards to the clinical studies presented in the application, the sponsor is also invited to comment on the expected effects of IVIG alone in order to show to what extent the effects may be attributed to rituximab.

- Prevalence

In case of an amended indication to “treatment in solid organ transplantation” in line with the special considerations of guideline ENTR/6283/00 Rev 04, the sponsor is invited to supplement the estimate with the annual number of eligible patients.

- Significant benefit

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition.

The sponsor is requested to further discuss the arguments by providing a data-driven comparative discussion versus all other authorised products for the sought indication.

In the written response, and during an oral explanation before the Committee on 15 March 2017, the sponsor presented a table with unpublished data comparing and contrasting three eras of rejection treatment, with regards to survival and freedom from chronic transplant dysfunction. The COMP considered that this historical comparison supports the assumption that use of the product may result in improved graft survival.

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment in solid organ transplantation.

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

The intention to treat the condition with the medicinal product containing rituximab was considered justified based on preliminary clinical observations supporting increased graft survival in treated patients.

The condition is life-threatening and chronically debilitating due to complications such as ischemia - reperfusion injury, delayed graft function, and graft rejection.

The condition was estimated to be affecting approximately 1 in 10,000 persons in the European Union, at the time the application was made; this was based on the number of annual solid organ transplantations in the EU.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing rituximab will be of significant benefit to those affected by the condition. The sponsor has provided observational studies including an historical comparison supporting the assumption that use of the product may result in improved graft survival. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for rituximab, for treatment in solid organ transplantation, was adopted by consensus.

2.1.7. Human normal immunoglobulin - EMA/OD/287/16

Hôpital Foch; Treatment in solid organ transplantation

COMP coordinator: Frauke Naumann-Winter

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

The proposed condition "graft rejection following solid organ transplantation" should be justified as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

The sponsor is invited to specify the scope of the application, detail how the product will be used, and define the proposed indication with reference to both antibody mediated and cellular rejection. A "treatment" indication should also be discussed in view of administration of the product to donor specific antibody positive or presymptomatic patients.

The sponsor is also invited to discuss the proposed condition in the context of the exceptional circumstances of guideline ENTR/6283/00 Rev 04, referring to "treatment modalities".

With regards to the clinical studies presented in the application, the sponsor is also invited to comment on the expected effects of rituximab alone in order to show to what extent the effects may be attributed to IVIG.

- Number of people affected

In case of an amended indication to "treatment in solid organ transplantation" in line with the special considerations of guideline ENTR/6283/00 Rev 04, the sponsor is invited to supplement the estimate with the annual number of eligible patients.

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

- Significant benefit

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition.

The sponsor is requested to further discuss the arguments by providing a data-driven comparative discussion versus all other authorised products for the sought indication.

In the written response, and during an oral explanation before the Committee on 15 March 2017, the sponsor presented a table with unpublished data comparing and contrasting three eras of rejection treatment, with regards to survival and freedom from chronic transplant dysfunction. The COMP considered that this historical comparison supports the assumption that use of the product may result in improved graft survival.

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment in solid organ transplantation.

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

The intention to treat the condition with the medicinal product containing human normal immunoglobulin was considered justified based on preliminary clinical observations supporting increased graft survival in treated patients.

The condition is life-threatening and chronically debilitating due to complications such as ischemia - reperfusion injury, delayed graft function, and graft rejection.

The condition was estimated to be affecting approximately 1 in 10,000 persons in the European Union, at the time the application was made; this was based on the number of annual solid organ transplantations in the EU.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing human normal immunoglobulin will be of significant benefit to those affected by the condition. The sponsor has provided observational studies including an historical comparison supporting the assumption that use of the product may result in improved graft survival. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for human normal immunoglobulin, for treatment in solid organ transplantation, was adopted by consensus.

2.1.8. Autologous adult bone marrow-derived non-expanded CD 133+ hematopoietic stem cells - EMA/OD/313/16

Igenomix, S.L.; Treatment of Asherman's syndrome

COMP coordinator: Armando Magrelli/Violeta Stoyanova

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

Asherman's syndrome should be justified as a distinct medical entity. Specifically, the COMP intends to discuss with the sponsor if the proposed condition is a distinct medical entity in contrast to an iatrogenic complication, which would not be acceptable for orphan designation. To support this discussion, please also outline and discuss all potential causes for Asherman's syndrome. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of AS, the sponsor should further elaborate on:

– the methodology and study protocol of the trial

– the results of the trial and the contextualisation with available literature data

– the use of hormonal treatment in the patients enrolled into the trial and the outcome related to hormonal treatment

- Number of people affected

The current estimate is not based on primary epidemiological literature on the proposed condition. This might also indicate that the proposed condition is an iatrogenic complication rather than a distinct medical entity. If possible, the sponsor should re-calculate the prevalence estimate based on relevant epidemiological studies and registers for the proposed orphan condition.

The current proposed prevalence estimate is close to the threshold of 5 per 10,000 and is based on indirect assumptions. Given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations including a worst case figure that is based on the most conservative estimations. For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

- Significant benefit

The COMP invites the sponsor to further discuss the current methods to treat these patients (e.g surgery and hormonal treatment) and if they can be considered satisfactory methods for treating patients affected by the condition. In this context, the sponsor should outline significant benefit argumentation of their proposed product versus such methods.

In the written response, and during an oral explanation before the Committee on 15 March 2017, the sponsor proposed a definition of Asherman's syndrome, which is exclusively based on clinical symptoms related to intrauterine adhesions including pelvic pain, amenorrhea, recurrent miscarriage, abnormal placentation, infertility, and psychological distress associated with the latter. The COMP agreed with this definition. The sponsor presented preliminary clinical data from the uncontrolled pilot clinical trial in comparison to published literature and also clarified the role of previous and concomitant hormonal replacement therapy. The COMP accepted this clarification for the basis of medical plausibility. The sponsor provided a sensitivity analysis of the data submitted for the prevalence calculation to support the calculation provided. The COMP accepted these additional findings. The sponsor presented further information on preliminary clinical data confirming that these patients have failed previous methods of treatment. Therefore, the COMP acknowledged that the outcomes measured in this preliminary clinical data was sufficient to support the assumption of significant benefit for the purpose of orphan designation.

Following review of the application by the Committee, it was agreed to broaden/rename the active substance to autologous adult bone marrow-derived non-expanded CD133+ haematopoietic stem cells.

The Committee agreed that the condition, Asherman's syndrome, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing autologous adult bone marrow-derived non-expanded CD133+ haematopoietic stem cells was considered justified based on preliminary clinical data demonstrating that the treatment could improve pregnancy rates in patients affected by the condition.

The condition is chronically debilitating due to pelvic pain, amenorrhea, retrograde menstruation, recurrent miscarriage and infertility.

The condition was estimated to be affecting approximately 4.4 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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous adult bone marrow-derived non-expanded CD133+ haematopoietic stem cells will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that the treatment could improve pregnancy rates in patients affected by the condition, who failed previous satisfactory methods. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous adult bone marrow-derived non-expanded CD133+ haematopoietic stem cells, for treatment of Asherman's syndrome, was adopted by consensus.

2.1.9. - EMA/OD/315/16

Treatment of acute myeloid leukaemia

As agree d 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

In order to justify the significant benefit of the proposed product the sponsor is invited to further discuss the claimed benefits in terms of last line efficacy and/or safety *vis a vis* all products currently authorised for the treatment of acute myeloid leukaemia. This or any other claim of significant benefit should be supported by data.

In absence of data the significant benefit cannot be assessed.

In the written response, and during an oral explanation before the Committee on 15 March 2017, the sponsor has not provided additional data to help establish what the clinically relevant advantage and/or major contribution to patient care is. The COMP could not conclude on the hypothetical basis that the sponsor provided to support significant benefit.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 March 2017, prior to final opinion.

2.1.10. - EMA/OD/301/16

Treatment of narcolepsy

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 are based on the new mechanism of action and the potential improved efficacy in the condition.

The sponsor is invited to further elaborate on the potential place of this treatment in Narcolepsy and in particular Type 1 where there is a current proposed algorithm regarding the optimal use of currently approved products.

In the written response, and during an oral explanation before the Committee on 15 March 2017, the sponsor did not provide any further data to support the claim that the product could offer a significant benefit within the current treatment algorithms regarding authorised products for this condition. The COMP could not therefore conclude on this key criterion in establishing the recommendation to grant an orphan medicinal designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 March 2017, prior to final opinion.

2.1.11. - EMA/OD/294/16

Treatment of calciphylaxis

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

In order to justify the medical plausibility of the proposed product the sponsor is invited to further discuss the methodology and results of the preclinical study, and in particular:

– the rationale for administering at the start of the induction of chronic kidney and cardiovascular disease rather than at later stage of the study, and the impact of this early administration on the results;

– the relevance of the preclinical model to the clinical presentation and pathogenesis of calciphylaxis;

– the extrapolation of the results from the preclinical model to the intended clinical use in calciphylaxis.

In the absence of results from clinical studies, the sponsor is invited to present data from the use of the product in the clinical setting, including case reports.

In the written response, and during an oral explanation before the Committee on 15 March 2017, the sponsor did not provide any further data to support the claim that the product could support the medical plausibility for use of this product in this condition. The COMP could not therefore conclude on this key criterion in establishing the recommendation to grant an orphan medicinal designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 March 2017, prior to final opinion.

2.1.12. - EMA/OD/302/16

Treatment of epidermolysis bullosa due to mutations in the *COL7A1* gene

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 23 February 2017, prior to responding to the list of issues.

2.1.13. Estetrol - EMA/OD/309/16

Mithra Pharmaceuticals S.A.; Treatment of neonatal encephalopathy

COMP coordinator: Giuseppe Capovilla/Dinah Duarte

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 if there exists a scientific rationale for the development of the proposed product for treatment of neonatal encephalopathy, the sponsor should further elaborate on the mechanism of action and the presented data on animal well-being and the methodology of the studies.

- Number of people affected

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor should update the prevalence to take into account perinatal asphyxia/ hypoxic ischaemic encephalopathy, which were previously designated by the COMP as having a higher prevalence of less than 1 per 10,000.

- Significant benefit

The COMP invites the sponsor to discuss therapeutic hypothermia and if it can be considered a satisfactory method for treating patients affected by the condition. In this context, the sponsor should outline significant benefit argumentation versus therapeutic hypothermia.

In the written response, the sponsor further elaborated on the mechanism of action and the outcomes of the preclinical studies. The COMP acknowledged the data in support of medical plausibility for orphan designation. The COMP also accepted the revised prevalence calculation. The sponsor outlined that the proposed treatment could be used in patients that are failing or are not eligible for other methods as well as being used in addition to current satisfactory methods. The COMP accepted these arguments as the basis for significant benefit.

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

The intention to treat the condition with the medicinal product containing estetrol was considered justified based on preclinical data from a valid disease model showing improvements regarding pathophysiology, general well-being and motor function.

The condition is life-threatening and chronically debilitating to the long lasting neurological and developmental sequelae. The most severe cases are associated with high mortality.

The condition was estimated to be occurring in less than 1 in 10,000 persons per year in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing estetrol will be of significant benefit to those affected by the condition. The sponsor has provided preclinical data from a valid

disease model showing improvements regarding pathophysiology, general well-being and motor function. The proposed product could improve outcome in patients not eligible for therapeutic hypothermia or in addition to therapeutic hypothermia. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for estetrol, for treatment of neonatal encephalopathy, was adopted by consensus.

2.1.14. Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains- EMA/OD/270/16

Bluebird bio France; Treatment of multiple myeloma

COMP coordinator: Frauke Naumann-Winter

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:

- Number of people affected

The sponsor presented a calculation of the prevalence assuming 5-year duration of the disease. The sponsor did not offer an estimate of point prevalence of multiple myeloma, which is expected for an orphan drug designation.

For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor should re-calculate the prevalence estimate based on relevant epidemiological studies and registers for the proposed orphan condition, and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

- Significant benefit

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition, leading to a curative potential. The sponsor presented clinical data in RRMM patients demonstrating partial and complete responses. Patients enrolled in the study have previously received a median of 6 prior treatment lines, which included most products authorised for the treatment of MM, with the exception of ixazomib, elotuzumab and panobinostat. A discussion of these products would be expected, in particular in the view of the reported late line efficacy of panobinostat in multiple myeloma.

The sponsor is requested to further discuss the intended positioning of the product in the treatment algorithm of RRMM and to elaborate on the results from the clinical study to justify the assumption of significant benefit.

In the written response, the sponsor proposed a revised prevalence calculation. The final value was discussed and very similar to the more recent calculations so the COMP brought it into line with recent values accepted. The arguments for significant benefit included indirect comparison between expected responses to last line authorised treatments in patients with relapsed refractory multiple myeloma compared to the proposed product. Based on the potential of achieving stringent complete responses in relapsed refractory multiple myeloma

patients treated with the proposed product the COMP accepted the proposed assumptions for significant benefit.

Following review of the application by the Committee, it was agreed to broaden/rename the active substance to autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains.

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

The intention to treat the condition with the medicinal product containing autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains was considered justified based on data showing that patients with relapsed refractory multiple myeloma achieve partial or complete responses.

The condition is chronically debilitating and life threatening due to the poor survival of patients with relapsed or refractory disease.

The condition was estimated to be affecting approximately 3.6 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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that patients with relapsed refractory multiple myeloma achieve partial and stringent complete responses. This compared favourably with a long list of authorised products to which these patients were not responding anymore. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains, for treatment of multiple myeloma, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/319/16

Treatment of acute myeloid leukaemia

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 meeting.

2.2.2. - EMA/OD/323/16

Treatment of Herpes simplex encephalitis

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 meeting.

2.2.3. Emeramide - EMA/OD/329/16

NBMI Science Limited; Prevention of mercury toxicity

COMP coordinator: Olimpia Neagu

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

The intention to prevent the condition with the medicinal product containing emeramide was considered justified based on preclinical in vivo data demonstrating that preventive administration of the proposed product was able to improve survival after mercury intoxication.

The condition is chronically debilitating due to symptoms such as unsteadiness of gait and limbs, muscle weakness, irritability, memory loss, depression and sleeping difficulties. It is life-threatening when there is acute exposure to high doses.

The population of patients eligible for prevention of the condition was estimated to be approximately less than 0.1 in 10,000 persons per year in the European Union, at the time the application was made.

The sponsor has also established that there exists no satisfactory method of prevention that has been authorised in the European Union for the population at risk of developing the condition.

A positive opinion for emeramide, for prevention of mercury toxicity, was adopted by consensus.

2.2.4. - EMA/OD/260/16

Treatment of glioma

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 meeting.

2.2.5. Modified messenger ribonucleic acid encoding human ornithine transcarbamylase enzyme encapsulated into lipid nanoparticles - EMA/OD/326/16

PhaseRx Ireland, Ltd; Treatment of ornithine transcarbamylase deficiency

COMP coordinator: Kerstin Westermark

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

The intention to treat the condition with the medicinal product containing modified messenger ribonucleic acid encoding human ornithine transcarbamylase enzyme encapsulated into lipid nanoparticles was considered justified based on pre-clinical in vivo data using a model of the condition which showed normalisation of plasma ammonia and orotic acid levels.

The condition is life-threatening and chronically debilitating due to the metabolic decompensation that can lead to irreversible neurological damage.

The condition was estimated to be affecting approximately 0.1 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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing modified messenger ribonucleic acid encoding human ornithine transcarbamylase enzyme encapsulated into lipid nanoparticles will be of significant benefit to those affected by the condition. The sponsor has provided pre-clinical data that demonstrate a reduction in plasma ammonia and orotic aciduria, which may reduce the need for ammonia scavangers. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for modified messenger ribonucleic acid encoding human ornithine transcarbamylase enzyme encapsulated into lipid nanoparticles, for treatment of ornithine transcarbamylase deficiency, was adopted by consensus.

2.2.6. Thymidine and deoxycytidine - EMA/OD/317/16

Vall d'Hebron Institute of Research; Treatment of mitochondrial DNA depletion syndrome, myopathic form

COMP coordinator: Frauke Naumann-Winter

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of mitochondrial DNA depletion syndrome, myopathic form.

The Committee agreed that the condition, mitochondrial DNA depletion syndrome, myopathic form, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing thymidine and deoxycytidine was considered justified based on non-clinical data in disease models demonstrating improved survival.

The condition is life-threatening due to muscle wasting leading to respiratory failure and chronically debilitating due to generalised hypotonia, proximal muscle weakness, loss of motor skills, poor feeding, fatigue and respiratory difficulties.

The condition was estimated to be affecting less than 0.01 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 thymidine and deoxycytidine, for treatment of mitochondrial DNA depletion syndrome, myopathic form, was adopted by consensus.

2.2.7. - EMA/OD/316/16

Treatment of Niemann-Pick disease, type C

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 meeting.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

2.5.1. 20% I.V. fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection - EMA/OD/062/16

Alan Boyd Consultants Ltd; Treatment of poisoning by local anesthetics

COMP coordinator: Karri Penttilä / Roberto Nistico

In the grounds for appeal, and during an oral explanation before the Committee on 14 March 2017, the sponsor applied for “treatment of poisoning by local anaesthetics” but limited the discussion of the condition to the inclusion of local anaesthetics systemic toxicity (LAST) in this indication, without differentiating it from other types of anaesthetic toxicities such as local toxicity. Therefore, LAST was the subject of the discussion and the COMP’s questions to the sponsor aimed at clarifying whether LAST is a distinct medical entity or a subset of a broader condition. LAST is a complication of an appropriate use of local anaesthetics (LA) or accidental inappropriate use and it is recognised in the literature. The pathophysiology of LAST is understood within the context of the known mode of action for local anaesthetics. There was an extensive discussion between the sponsor and the COMP on this and if there was any specificity for LAST which could differentiate it from other forms of local anaesthetic toxicity. It was concluded there were none. COMP acknowledged that clinical characteristics of LAST are different to those of toxicity caused by general anaesthesia. It was noted that LAST may be viewed as a severity grade of anaesthetics toxicity, rather than a distinct condition. As “treatment of poisoning by local anaesthetics” is not rare, the uncertainty around the prevalence criterion was raised during the oral explanation. The sponsor did not address the prevalence criterion for broader inclusion criteria and only the prevalence of LAST was proposed. Therefore, the COMP could not conclusively establish the prevalence for a broader medical entity and maintained its position as adopted during the initial assessment.

The intention to treat poisoning by local anaesthetics with the medicinal product containing 20% intravenous fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection was argued on the basis of preclinical and preliminary clinical data supporting increased survival in treated subjects affected by local anaesthetic toxicity; however, the sponsor did not sufficiently justify the definition of the proposed condition and has not established that the proposed product is intended to treat a distinct medical entity in terms of pathophysiology.

The sponsor has not established that poisoning by local anaesthetics (hereinafter referred to as ‘the condition’) affects not more than 5 in 10,000 persons in the European Union at the time the application was made.

Poisoning by local anaesthetics is life-threatening due to neurological and cardiac toxicity which may lead to respiratory and cardiac arrest.

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

A final negative opinion for 20% intravenous fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection, for treatment of poisoning by local anaesthetics, was adopted by consensus.

[*Post-meeting note: The COMP adopted the opinion by written procedure following its March meeting.*]

2.6. Nominations

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

COMP coordinators were appointed for 12 applications submitted.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 21 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of Gaucher disease

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 narcolepsy

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 Langerhans cell histiocytosis

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 Wolfram syndrome

The discussion was postponed.

3.1.5. -

Treatment of Wolfram syndrome

The discussion was postponed.

3.1.6. -

Treatment of paroxysmal nocturnal haemoglobinuria

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

3.1.7. -

Treatment of beta-thalassemia intermedia and major

The Committee was briefed on the significant benefit issues in preparation of the April meeting.

3.2. Finalised letters

3.2.1. -

Treatment of amyotrophic lateral sclerosis

The finalised letter was circulated for information.

3.3. New requests

None

4. Review of orphan designation for orphan medicinal products for marketing authorisation

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

None

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

4.2.1. - pentosan polysulfate sodium – EMA/OD/179/14, EU/3/14/1411, EMEA/H/C/004246

Bene-Arzneimittel GmbH; Treatment of interstitial cystitis

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 meeting.

4.2.2. Dinutuximab beta Apeiron - dinutuximab beta - EMA/OD/112/12, EU/3/12/1062, EMEA/H/C/003918

APEIRON Biologics AG; Treatment of high-risk neuroblastoma

COMP coordinator: Violeta Stoyanova / Brigitte Bloechl-Daum

The COMP concluded that:

The proposed therapeutic indication, treatment of high-risk neuroblastoma falls entirely within the scope of the orphan indication of the designated orphan medicinal product, treatment of neuroblastoma.

The prevalence of neuroblastoma (hereinafter referred to as “the condition”) was estimated to remain below 5 in 10,000 and was concluded to be 1.1 in 10,000 persons in the European Union, at the time of the review of the designation criteria.

The condition is life-threatening and median survival is 1 year, the condition is chronically debilitating due to growth reduction, thyroid function disorders, learning difficulties, and greater risk of secondary cancers in survivors of high-risk disease.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, Dinutuximab beta Apeiron is of significant benefit to those affected by the orphan condition. This is based on clinical data demonstrating that treatment with Dinutuximab beta Apeiron improved survival in neuroblastoma patients after induction chemotherapy and in patients with a history of relapsed or refractory neuroblastoma. The Committee considered that this constitutes a clinically relevant advantage.

An opinion not recommending the removal of Dinutuximab beta Apeiron, chimeric monoclonal antibody against GD2 (EU/3/12/1062) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The draft public summary of the COMP opinion will be endorsed for publication on the EMA website.

[*Post-meeting note: The COMP formally adopted the final opinion by written procedure following its April meeting.*]

4.2.3. - cerliponase alfa - EMA/OD/177/12, EU/3/13/1118, EMEA/H/C/004065

BioMarin International Limited; Treatment of neuronal ceroid lipofuscinosis type 2

The COMP discussed the responses from the sponsor and the status of the procedure at CHMP was noted.

4.2.4. - nonacog beta pegol – EMEA/OD/005/09, EU/3/09/640, EMEA/H/C/004178

Novo Nordisk A/S; Treatment of haemophilia B

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 meeting.

4.2.5. - nusinersen – EMEA/H/C/004312, EMA/OD/141/11, EU/3/12/976

Biogen Idec Ltd; Treatment of 5q spinal muscular atrophy

The status of the procedure at CHMP was noted.

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 3 applications.

4.5. Public Summary of Opinions

The draft public summaries of the COMP opinions adopted last month were endorsed for publication on the EMA website.

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

5.2.1. Nplate - recombinant megakaryopoiesis-stimulating protein – EMEA/OD/008/05, EU/3/05/283, EMA/H/C/000942/II/0060/G

Amgen Europe BV - The Netherlands; Treatment of idiopathic thrombocytopenic purpura

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.

5.3. Appeal

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. Protocol Assistance Working Group

The working group on Protocol Assistance met on 14 March 2017 at 13:00

7.1.2. COMP Strategy Review & Learning meetings, 19-20 March 2017, Valletta, Malta

The updated draft agenda was presented.

7.1.3. COMP meeting dates for 2019, 2020 and 2021

COMP meeting dates for 2019, 2020 and 2021 were adopted by the committee.

Document(s) tabled:
COMP meetings dates for 2019-2021

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. PDCO/COMP Working Group

The PDCO/COMP working group took place on 15 March 2017 by teleconference.

7.2.2. Recommendations on eligibility to PRIME – report from CHMP

Documents were circulated in MMD.

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

None

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)

The draft agenda of the monthly teleconference with FDA held on 21 February 2017 was circulated in MMD for information.

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. The 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

7.7.1. COMP Work Plan 2017

Documents were circulated in MMD.

Document(s) tabled:
COMP Work Plan 2017

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2017

An updated list of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2017 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. EMA Business Pipeline activity and Horizon scanning

Documents were circulated in MMD.

Document tabled:
Upcoming Q1/2017 Update of the Business Pipeline report for the human scientific committees

List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 14-15 March 2017 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bruno Sepodes	Chair	Expert recommended by EMA	No interests declared	
Brigitte Blöchl-Daum	Member	Austria	No interests declared	
Lyubina Racheva Todorova	Member	Bulgaria	No interests declared	
Dinko Vitezic	Member	Croatia	No restrictions applicable to this meeting	
Ioannis Kkolos	Member	Cyprus	No restrictions applicable to this meeting	
Katerina Kopeckova	Member	Czech Republic	No restrictions applicable to this meeting	
Jens Ersbøll	Member	Denmark	No interests declared	
Vallo Tillmann	Member	Estonia	No interests declared	
Karri Penttilä	Member	Finland	No interests declared	
Annie Lorence	Member	France	No interests declared	
Frauke Naumann-Winter	Member	Germany	No interests declared	
Nikolaos Sypsas	Member	Greece	No restrictions applicable to this meeting	
Melinda Sobor	Member	Hungary	No interests declared	
Sigurdur B. Thorsteinsson	Member	Iceland	No interests declared	
Geraldine O'Dea	Member	Ireland	No interests declared	
Armando Magrelli	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Aušra Matulevičienė	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No interests declared	
Violeta Stoyanova-Beninska	Member	Netherlands	No interests declared	
Ingrid Wang	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland	No restrictions applicable to this meeting	
Dinah Duarte	Member	Portugal	No interests declared	
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	Slovak Republic	No interests declared	
Martin Mozina	Member	Slovenia	No interests declared	
Fernando Mendez Hermida	Member	Spain	No interests declared	
Dan Henrohn	Member	Sweden	No restrictions applicable to this meeting	
Daniel O'Connor	Member	United Kingdom	No interests declared	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Lesley Greene	Member (Vice-Chair)	Patients' Organisation Representative	No interests declared	
Mario Ricciardi	Member	Patients' Organisation Representative	No interests declared	
Kerstin Westermark	Member	Expert recommended by EMA	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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Virginie Hivert	Expert - in person*	Patients' Organisation Representative	No restrictions applicable to this meeting	
Julian Isla	Expert - in person*	Patients' Organisation Representative	No interests declared	
Rizwan Hamid	Expert - via telephone*	University College London	No restrictions applicable to this meeting	
Liesbeth Van Vlijmen	Expert - in person*	Netherlands - CBG/MEB	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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

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/