15 June 2023
EMA/COMP/248545/2023
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 15-17 May 2023

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

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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
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1. Introduction

1.1. Welcome and declarations of interest of members and experts

The Chairperson opened the meeting by welcoming all participants. The meeting was held in-person with some members connected remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members 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. 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 15-17 May 2023 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 18-20 April 2023 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. exenatide - EMA/OD/0000112308

Boyd Consultants Limited; Treatment of moderate and severe closed traumatic brain injury (TBI)

COMP Rapporteur: Michel Hoffmann

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

Moderate and severe closed traumatic brain injury 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 relevant guidelines (especially section A of the guideline).

- Significant benefit

The arguments on significant benefit were based on an alternative mechanism of action which could offer an additional therapeutic approach to treating the condition.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from their non-clinical in vivo studies to justify the assumption of significant benefit within the context of the use of barbiturates in the proposed orphan condition.

In the written response, the sponsor offered further argumentation to support the condition. In this response it was highlighted that, the condition targeted, is very different in both morbidity and mortality to the milder forms of traumatic brain injury which generally only involve concussion.

The COMP accepted the sponsor's argumentation and agreed that the condition continued to be accepted for orphan designation.

The sponsor also provided a written response for the question on significant benefit. It was noted that the principal therapeutic approaches to reduce raised intracranial pressure (ICP) in TBI include osmotic therapy, barbiturates, decompressive craniotomy, and hypothermia. In their question the COMP requested that the sponsor should further elaborate on the place of their product in the treatment armamentarium and the use of barbiturates.

The results of 5 clinical studies analysing the impact of barbiturate therapy on survival in severe TBI, who developed intracranial hypertension, was submitted. Outcome in barbiturate treated patients was in general not superior to the control groups and barbiturate treated patients where a coma was induced through barbiturates did not show improvement in survival.

The COMP noted that barbiturate treatment is recommended as a second- or third-line therapy for high and refractory intracranial hypertension and is believed to improve longer term outcome. It was however noted that no significant effect on survival has been demonstrated and that high-dose barbiturates therapy can only be used in haemodynamically stable patients.

The sponsor also considered that a direct comparison of exenatide and barbiturates was not feasible.

Significant benefit could be accepted based on the alternative mechanism of action of exenatide with the potential to be used in all TBI patients with raised ICP due to its rapid and prolonged lowering effect on elevated ICP.

Although the sponsor did not provide new pre-clinical or clinical data to show significant benefit of exenatide over barbiturates they did successfully argue that the alternative mode of action of their product allowed early treatment after the brain injury. This was considered a significant benefit over the second- and third-line use of barbiturates.

The COMP accepted the written response and agreed to recommend granting the orphan designation. The oral explanation was cancelled.

The Committee agreed that the condition, moderate and severe closed traumatic brain injury, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing exenatide was considered justified based on non-clinical in vivo data in a model of the condition which shows a reduction in intracranial pressure and significant improvement of sensorimotor functional recovery.

The condition is chronically debilitating and life threatening due to the high fatality rate and likelihood of permanent functional neurological impairment in surviving patients.

The condition was estimated to be affecting approximately 3.9 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 exenatide will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that support the assumption of an improvement in sensorimotor functional recovery supporting the use of the product in first line offering prolonged administration compared with authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for exenatide, for treatment of moderate and severe closed traumatic brain injury, was adopted by consensus.

2.1.2. - EMA/OD/0000127495

Treatment of idiopathic pulmonary fibrosis

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 27 April 2023, prior to responding to the list of issues.

2.1.3. - EMA/OD/0000117653

Treatment of pouchitis

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 pouchitis, the sponsor was asked to further elaborate on the preliminary clinical observations discussing the particulars of the studied population, concomitant treatments, history, assessments and results.

- Significant benefit

The sponsor was requested to detail the results of any clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients. A comparative discussion was expected versus the authorised treatment(s) in the treatment of pouchitis to justify a clinically relevant advantage or major contribution to patient care.

It is well known that extrapolation from non-clinical or early clinical studies cannot fully predict the safety of a product in its clinical setting, thus other relevant data is required to justify safety arguments in most cases. The sponsor was asked to 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.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 15 May 2023, the sponsor updated the information on patients treated with the product. Patients included in the study had moderately severe symptoms, but severe enough to seek medical care.

The data was considered insufficient, but the patients seemed to respond to the treatment and this could be enough to support the medical plausibility.

During the oral explanation, the results on the Pouchitis Disease Severity Index (PDAI score -symptoms, physician assessment, histology) of the patients were discussed.

The sponsor hypothesised that their product would likely be used before treatment with vedolizumab, as local treatment could be preferred before introducing a systemic treatment. However, they envisaged a comparator trial versus vedolizumab as the pivotal study.

The COMP was of the opinion that the data were not sufficient and that the results in the PDAI score was too heterogeneous to be able to draw conclusions on a significant benefit, in particular over vedolizumab.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 May 2023, prior to final opinion.

2.1.4. - EMA/OD/0000117747

Treatment of pouchitis

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 pouchitis, the sponsor should further elaborate on the preliminary clinical observations discussing the particulars of the studied population, concomitant treatments, history, assessments and results.

- Significant benefit

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. A comparative discussion was expected versus the authorised treatment(s) in the treatment of pouchitis to justify a clinically relevant advantage or major contribution to patient care.

It is well known that extrapolation from non-clinical or early clinical studies cannot fully predict the safety of a product in its clinical setting, thus other relevant data is required to justify safety arguments in most cases. The sponsor was asked to 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.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 15 May 2023, the sponsor updated the information on patients treated with the product. Patients included in the study had moderately severe symptoms, but severe enough to seek medical care.

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The sponsor hypothesised that their product would likely be used before treatment with vedolizumab, as local treatment could be preferred before introducing a systemic treatment. However, they envisaged a comparator trial versus vedolizumab as the pivotal study.

The COMP was of the opinion that the data were not sufficient and that the results in the PDAI score was too heterogeneous to be able to draw conclusions on a significant benefit, in particular over vedolizumab.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 May 2023, prior to final opinion.

2.1.5. - EMA/OD/0000117752

Treatment of pouchitis

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 pouchitis, the sponsor was asked to further elaborate on the preliminary clinical observations discussing the particulars of the studied population, concomitant treatments, history, assessments and results.

- Significant benefit

The sponsor was requested to detail the results of any clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients. A comparative discussion was expected versus the authorised treatment(s) in the treatment of pouchitis to justify a clinically relevant advantage or major contribution to patient care.

It is well known that extrapolation from non-clinical or early clinical studies cannot fully predict the safety of a product in its clinical setting, thus other relevant data is required to justify safety arguments in most cases. The sponsor was asked to 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.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 15 May 2023, the sponsor updated the information on patients treated with the product . Patients included in the study had moderately severe symptoms, but severe enough to seek medical care.

The data was considered insufficient, but the patients seem to respond to the treatment and this could be enough to support the medical plausibility

During the oral explanation, the results on the Pouchitis Disease Severity Index (PDAI score -symptoms, physician assessment, histology) of the patients were discussed.

The sponsor hypothesised that their product would likely be used before treatment with vedolizumab, as local treatment could be preferred before introducing a systemic treatment. However, they envisaged a comparator trial versus vedolizumab as the pivotal study.

The COMP was of the opinion that the data were not sufficient and that the results in the PDAI score was too heterogeneous to be able to draw conclusions on a significant benefit, in particular over vedolizumab.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 May 2023, prior to final opinion.

2.1.6. - EMA/OD/0000116156

Treatment of prosthetic joint infection

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 27 April 2023, prior to responding to the list of issues.

2.1.7. - EMA/OD/0000128546

Treatment of pemphigus

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

A claim based solely on a novel mechanism of action is generally not accepted as sufficient in supporting significant benefit. The sponsor was therefore requested to further substantiate their claims for significant benefit with relevant data, to allow a conclusion on the product's potential clinically relevant advantage vis-à-vis the authorised therapies.

In the written response, and during an oral explanation before the Committee on 16 May 2023, the sponsor provided new clinical data from pemphigus vulgaris (PV) patients, whose responses to the proposed product were monitored for 12 weeks and compared to baseline values. The data suggested that the proposed product may modulate the immune response by increasing Treg and decreasing Th17 and CD27+ memory B cells. In some patients, the decrease in memory B cells and Th17 cells was associated with decreased anti-Dsg3 antibodies. While COMP acknowledged that the chosen parameters may be considered

relevant biomarkers of tolerance induction, their link with a clinical benefit in PV patients was not clear and seems not to be established yet.

The sponsor clarified that an efficacy comparison of the proposed product with the authorised medicinal products for PV treatment is not yet possible due to the early stage of development. However, the current unmet medical need in pemphigus was highlighted as well as the potential promise of such a novel mechanism of action which may modify the patho-mechanism of the condition and minimises the risk of generalised immunosuppression. While COMP acknowledged these arguments, it was pointed out again that a novel mechanism of action is not sufficient to establish significant benefit and the safety data was too preliminary to allow a conclusion on improved safety vis-à-vis the authorised therapies for PV.

While COMP acknowledged the new and targeted mechanism of action of the proposed product, the Committee concluded that the presented data was insufficient to establish a significant benefit of the proposed product versus the authorised therapies, in the proposed condition. The patients included in the sponsor's clinical study did either have no or only low disease activity, which did not allow for the assessment of trends in symptomatic changes following treatment with the proposed product. In addition, the link between the observed specific changes in the pharmacodynamic markers and possible positive changes in clinical symptoms were not deemed to be sufficiently established.

Moreover, the COMP noted that the chosen non-clinical model did not display any disease phenotypes and therefore the effect of the proposed products on clinically relevant symptoms could also not be assessed in this specific non-clinical model.

Furthermore, the overall safety data package of the proposed product was considered too limited to allow a conclusion on a claim of improved safety of the proposed product versus the authorised therapies, in the proposed condition.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 16 May 2023, prior to final opinion.

2.1.8. autologous CD34+ haematopoietic stem and progenitor cells transduced with a lentiviral vector encoding the interferon alpha-2 gene - EMA/OD/0000122073

Genenta Science S.p.A.; Treatment of glioma

COMP Rapporteur: Brigitte Schwarzer-Daum

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 of the proposed product versus the authorised treatments were based on 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 clinical data presented providing more details on the treatments used in the ongoing study including standard of care.

In the written response, and during an oral explanation before the Committee on 16 May 2023, the sponsor presented update clinical data the with a cut-off of 30th April 2023. Based on this data, the median overall survival (OS) following first surgery was 15 months

(11.3 months after the infusion with the proposed product). The sponsor also compared the OS results with historical OS data. Previous evidence showed that patients, treated with radiation and temozolomide, with O(6)-Methylguanine DNA methyltransferase (MGMT)-methylated tumours had a median OS of 21.7 (17.4-30.4) months compared 12.7 (11.6-14.4) months for those patients with non-MGMT-methylated tumours [Hegi et al, 2005].The COMP concluded that the preliminary clinical data demonstrate increased survival with the proposed product compared to the standard of care in patients with newly diagnosed glioblastoma multiforme who have an unmethylated MGMT promoter.

Four COMP members were of the opinion that the OS data from the applicant's study are in the same range as recent data on standard of care. Therefore, they were of the opinion, that the provided data was not sufficient to support the assumption of significant benefit to receive orphan status.

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

The intention to treat the condition with the medicinal product containing autologous CD34+ haematopoietic stem and progenitor cells transduced with a lentiviral vector encoding the interferon alpha-2 gene was considered justified based on preliminary clinical data which showed increased survival in patients with glioma.

The condition is chronically debilitating due to symptoms caused by the tumour compressing the surrounding brain tissue including headache, anorexia, nausea, vomiting, seizures, neurological deficits, personality changes and cognitive decline. The condition is also life-threatening, with a limited median overall survival.

The condition was estimated to be affecting approximately 2.6 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 exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous CD34+ haematopoietic stem and progenitor cells transduced with a lentiviral vector encoding the interferon alpha-2 gene will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate increased survival with the proposed product compared to the standard of care in patients with glioma. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for glioma, for treatment of autologous CD34+ haematopoietic stem and progenitor cells transduced with a lentiviral vector encoding the interferon alpha-2 gene, was adopted by majority (23 out of 27). The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

The divergent positions (Brigitte Schwarzer-Daum, Michel Hoffmann, Ingeborg Barisic, Elisabeth Penninga) were appended to this opinion.

2.1.9. [(2S,3S,4E,6S,7R,10R)-7,10-Dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-pyridin-2-ylhepta-2,4-dien-2-yl]-1-oxacyclododec-4-en-6-yl]4-methylpiperazine-1-carboxylate - EMA/OD/0000126745

Voisin Consulting Life Sciences; Treatment of myelodysplastic syndrome (MDS)

COMP Rapporteur: Karri Penttila

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 sponsor was requested to further substantiate the claim of significant benefit of the proposed product versus luspatercept with relevant data. In this regard, the sponsor should also clarify the ring sideroblast (RS) status in the 8 MDS patients who achieved at least one transfusion independent interval following treatment with oral RVT-2001.

In the written response, the sponsor provided the requested data regarding ring sideroblast (RS) status in the 8 MDS patients who achieved at least one transfusion independent interval following treatment with the proposed product. The data showed that also some patients with RS negative status achieved at least one transfusion independent interval. As patients with RS negative status are currently not covered by the therapeutic indication of luspatercept, the COMP considered that this constitutes a clinically relevant advantage of the proposed product at time of initial orphan designation. The planned oral explanation was cancelled.

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

The intention to treat the condition with the medicinal product containing [(2S,3S,4E,6S,7R,10R)-7,10-dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-pyridin-2-ylhepta-2,4-dien-2-yl]-1-oxacyclododec-4-en-6-yl]4-methylpiperazine-1-carboxylate was considered justified based on preliminary clinical data which demonstrated haematologic improvement resulting in the reduction of the need for red-blood-cell transfusions.

The condition is life-threatening and chronically debilitating in particular due to anaemia, thrombocytopenia, and neutropenia, as well as transformation into acute myeloid leukaemia.

The condition was estimated to be affecting approximately 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 exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing [(2S,3S,4E,6S,7R,10R)-7,10-dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-pyridin-2-ylhepta-2,4-dien-2-yl]-1-oxacyclododec-4-en-6-yl]4-methylpiperazine-1-carboxylate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that suggests haematologic improvement resulting in a reduced need for red-blood-cell transfusions, in patients with myelodysplastic syndromes with and without ring sideroblasts, who have failed or were not eligible to prior treatment with erythropoietin stimulating agents and who were pretreated with azacitidine and/or lenalidomide. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for [(2S,3S,4E,6S,7R,10R)-7,10-Dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-pyridin-2-ylhepta-2,4-dien-2-yl]-1-oxacyclododec-4-en-6-yl]4-methylpiperazine-1-carboxylate, for treatment of myelodysplastic syndrome, was adopted by consensus.

2.1.10. efzofitimod - EMA/OD/0000126335

FGK Representative Service GmbH; Treatment of systemic sclerosis

COMP Rapporteur: Elisabeth Johanne Rook

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 systemic sclerosis the sponsor should further elaborate on the non-clinical in vivo data used to support the treatment of systemic sclerosis, and the interpretation of the results obtained in the experiments. In order to address this issue, the sponsor is requested to submit the final study reports of the main non-clinical studies, and any publications in the public domain which have been recently released regarding this data.

- Number of people affected

The sponsor provided a prevalence estimate which is limited to one publication. The sponsor was requested to further provide a more detailed estimate using all relevant sources.

For the estimation and presentation of the prevalence estimate the sponsor is advised to refer to the "Points to Consider on the Estimation and Reporting of a Prevalence of a Condition for Orphan Designation".

In the written response, the sponsor explained answers to the list of questions raised. Regarding the medical plausibility the final study reports of the non-clinical studies in relevant disease models, which were summarised and referenced in the application, are now submitted conform COMP's request. These have not appeared in publications.

Additional information was now also available on skin outcomes, indicating an antifibrotic effect on a par with nintedanib.

The COMP accepted the response for medical plausibility.

Concerning the prevalence estimate the sponsor provided a written response and discussed the variance of their estimate with the COMP rapporteur who suggested that more recent data suggested that the prevalence was higher at 3.5 in 10,000. This higher number was accepted by the sponsor and the oral explanation was cancelled as the COMP believed that all the issues had been adequately addressed.

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

The intention to treat the condition with the medicinal product containing efzofitimod was considered justified based on non-clinical in vivo data in two different models of the condition showing a reduction in fibrosis both in the skin and the lungs.

The condition is chronically debilitating and life-threatening due to the deposition of collagen in the skin leading to skin ulcers and in internal organs such as kidneys, heart, lungs and gastrointestinal tract, which may lead to severe complications such as pulmonary arterial hypertension, interstitial lung disease, progressive dysphagia, scleroderma renal crisis and cardiac failure.

The condition was estimated to be affecting approximately 3.5 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 efzofitimod will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate a greater reduction in the decline of lung function and dermal fibrosis which cannot be achieved with authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for efzofitimod, for treatment of systemic sclerosis, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. nicotinamide mononucleotide - EMA/OD/0000104786

Lgd; Treatment of sickle cell disease

COMP Rapporteur: Enrico Costa

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

The intention to treat the condition with the medicinal product containing nicotinamide mononucleotide was considered justified based on non-clinical in vivo data showing an improvement in erythropoiesis, an increase in foetal haemoglobin and a reduction in sickling of red blood cells.

The condition is chronically debilitating in particular due to vaso-occlusive crises, haemolytic anaemia, stroke, chronic kidney disease, pulmonary hypertension, susceptibility to infections and skin ulcers and life-threatening with reduced life expectancy.

The condition was estimated to be affecting approximately 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 exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing nicotinamide mononucleotide will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate an increase in foetal haemoglobin when the product is used in combination with hydroxyurea which targets more aspects of the condition as compared to other authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for nicotinamide mononucleotide, for treatment of sickle cell disease, was adopted by consensus.

2.2.2. - EMA/OD/0000116655

Treatment of patients with light chain (AL) amyloidosis

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 June meeting.

2.2.3. - EMA/OD/0000119470

Treatment of osteosarcoma

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 June meeting.

2.2.4. evorpacept - EMA/OD/0000124587

Alx Oncology Limited; Treatment of gastric cancer

COMP Rapporteur: Frauke Naumann-Winter

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

The intention to treat the condition with the medicinal product containing evorpacept in combination with anti-tumour agents and was considered justified based on in vivo non-clinical data which showed anti-tumour activity and preliminary clinical data which showed responses in patients with HER2-overexpressing gastric tumours that have progressed upon prior systemic therapy.

The condition is chronically debilitating due to dysphagia, weight loss and gastric bleeding and life threatening with poor overall survival.

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 exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing evorpacept will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that evorpacept in combination with anti-tumour agents showed responses in patients with HER2-overexpressing gastric tumours that have progressed upon prior systemic therapy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for evorpacept, for treatment of gastric cancer, was adopted by consensus.

2.2.5. - EMA/OD/0000124780

Treatment of pre-eclampsia

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 June meeting.

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 30 May 2023.]

2.2.6. - EMA/OD/0000124931

Treatment of primary biliary cholangitis

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 June meeting.

2.2.7. adeno-associated virus vector serotype 8 encoding the ABCA4 protein, C-region - EMA/OD/0000125116

Splicebio S.L.; Treatment of inherited retinal dystrophy due to dysfunction in the *ABCA4* gene

COMP Rapporteur: Zsofia Gyulai

The Committee agreed that the condition, inherited retinal dystrophy due to dysfunction in the *ABCA4* gene, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing adeno-associated virus vector serotype 8 encoding the ABCA4 protein, C-region, adeno-associated virus vector serotype 8 encoding the ABCA4 protein, N-region was considered justified based on the effects of the product in a non-clinical model of the condition resulting in reduction in accumulation of N-retinyl-N-retinylidene ethanolamine (A2E) in photoreceptor cells.

The condition is chronically debilitating, in particular due to loss of visual acuity and central vision loss, which may progress to complete blindness.

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 in the European Union for patients affected by the condition.

A positive opinion for adeno-associated virus vector serotype 8 encoding the ABCA4 protein, C-region, for treatment of inherited retinal dystrophy due to dysfunction in the *ABCA4* gene, was adopted by consensus.

2.2.8. - EMA/OD/0000125383

Treatment of cryopyrin associated periodic syndromes

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 June meeting.

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 26 May 2023.]

2.2.9. fasudil hydrochloride - EMA/OD/0000127302

MDC RegAffairs GmbH; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Darius Matusevicius

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

The intention to treat the condition with the medicinal product containing fasudil hydrochloride was considered justified based on non-clinical in vivo data in a model of the condition showing improved survival and motor function.

The condition is chronically debilitating and life-threatening due to progressive degeneration of motor neurons, ultimately leading to paralysis and respiratory failure with shortened life expectancy.

The condition was estimated to be affecting approximately 1.3 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 fasudil hydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate that fasudil can attenuate motor function decline in a valid model of the condition. In addition, preliminary clinical data showed a positive trend in possibly attenuating the decline in motor function, in combination with the only approved medicinal product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for fasudil hydrochloride, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

2.2.10. - EMA/OD/0000130058

Treatment of congenital diaphragmatic hernia

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 June meeting.

2.2.11. autologous dendritic cells pulsed with allogeneic tumour cell lysate - EMA/OD/0000130111

Amphera B.V.; Treatment of pancreatic cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

The intention to treat the condition with the medicinal product containing autologous dendritic cells pulsed with allogeneic tumour cell lysate was considered justified based on in vivo non-clinical data which showed antitumour activity and on preliminary clinical data which showed increased survival in patients with pancreatic ductal adenocarcinoma.

The condition is chronically debilitating due to pain in the upper abdomen, loss of appetite, nausea, vomiting, weight loss, jaundice, fatigue, weakness and depression and life-threatening with a markedly reduced life expectancy.

The condition was estimated to be affecting approximately 2.3 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 autologous dendritic cells pulsed with allogeneic tumour cell

lysate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed increased survival in patients with pancreatic ductal adenocarcinoma who were pre-treated with the currently authorised treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous dendritic cells pulsed with allogeneic tumour cell lysate, for treatment of pancreatic cancer, was adopted by consensus.

2.2.12. - EMA/OD/0000130960

Treatment of acute lymphoblastic 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 June meeting.

2.2.13. 5-(3,4-Dichloro-phenyl)-N-((1R,2R)-2-hydroxy-cyclohexyl)-6-(2,2,2-trifluoro-ethoxy)-nicotinamide - EMA/OD/0000131549

Veristat Spain S.L.; Treatment of Alport syndrome

COMP Rapporteur: Elisabeth Penninga

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

The intention to treat the condition with the medicinal product containing 5-(3,4-dichloro-phenyl)-N-((1R,2R)-2-hydroxy-cyclohexyl)-6-(2,2,2-trifluoro-ethoxy)-nicotinamide was considered justified based on non-clinical data in a relevant model of the condition showing improved kidney function and prolonged survival.

The condition is chronically debilitating due to kidney insufficiency, sensorineural hearing loss and ocular manifestations and life-threatening in particular due to end stage renal disease leading to kidney failure.

The condition was estimated to be affecting less than 1.5 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 in the European Union for patients affected by the condition.

A positive opinion for 5-(3,4-dichloro-phenyl)-N-((1R,2R)-2-hydroxy-cyclohexyl)-6-(2,2,2-trifluoro-ethoxy)-nicotinamide, for treatment of Alport syndrome, was adopted by consensus.

2.2.14. - EMA/OD/0000131821

Treatment of nontuberculous mycobacterial pulmonary disease (NTM-PD)

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 June meeting.

2.2.15. (3S,3'S,3a'S,10a'S)-6-chloro-3'-(3-chloro-2-fluorophenyl)-1'-(cyclopropylmethyl)-6'-methyl-2-oxo-1,2,3',3a',10',10a'-hexahydro-1'H-spiro[indole-3,2'-pyrrolo[2',3':4,5]pyrrolo[1,2-b]indazole]-7'-carboxylic acid - EMA/OD/0000131872

Boehringer Ingelheim International GmbH; Treatment of soft tissue sarcoma

COMP Rapporteur: Brigitte Schwarzer-Daum

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 (3S,3'S,3a'S,10a'S)-6-chloro-3'-(3-chloro-2-fluorophenyl)-1'-(cyclopropylmethyl)-6'-methyl-2-oxo-1,2,3',3a',10',10a'-hexahydro-1'H-spiro[indole-3,2'-pyrrolo[2',3':4,5]pyrrolo[1,2-b]indazole]-7'-carboxylic acid was considered justified based on non-clinical data which showed delay in tumour growth and preliminary clinical data which showed responses in patients with different types of soft tissue sarcoma.

The condition is chronically debilitating due to 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 (3S,3'S,3a'S,10a'S)-6-chloro-3'-(3-chloro-2-fluorophenyl)-1'-(cyclopropylmethyl)-6'-methyl-2-oxo-1,2,3',3a',10',10a'-hexahydro-1'H-spiro[indole-3,2'-pyrrolo[2',3':4,5]pyrrolo[1,2-b]indazole]-7'-carboxylic acid will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed responses in a heavily pretreated population. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for (3S,3'S,3a'S,10a'S)-6-chloro-3'-(3-chloro-2-fluorophenyl)-1'-(cyclopropylmethyl)-6'-methyl-2-oxo-1,2,3',3a',10',10a'-hexahydro-1'H-spiro[indole-3,2'-pyrrolo[2',3':4,5]pyrrolo[1,2-b]indazole]-7'-carboxylic acid, for treatment of soft tissue sarcoma, 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

None

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 25 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of Fabry disease

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

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. Lytgobi - futibatinib - EMEA/H/C/005627/0000, EU/3/19/2146, EMA/OD/0000122904

Taiho Pharma Netherlands B.V.; Treatment of biliary tract cancer

As agreed during the previous meeting, a list of issues was sent to the sponsor for response.

The sponsor formally withdrew the orphan designation from the EC register of orphan medicinal products, on 05 May 2023.

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

4.1.2. Columvi – glofitamab - EMEA/H/C/005751, EU/3/21/2497, EMA/OD/0000091986

Roche Registration GmbH; Treatment of diffuse large B-cell lymphoma

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

A list of issues was adopted on 20 April 2023.

An oral explanation was held on 16 May 2023.

An opinion recommending not to remove Columvi, glofitamab, EU/3/21/2497 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. Jaypirca - pirtobrutinib - EMEA/H/C/005863, EU/3/21/2450, EMA/OD/0000124200

Eli Lilly Nederland B.V.; Treatment of mantle cell lymphoma

COMP Rapporteur: Maria Elisabeth Kalland; COMP Co-Rapporteur: Cécile Dop

A list of issues was adopted on 20 April 2023.

An oral explanation was held on 16 May 2023.

An opinion recommending the removal of Jaypirca, pirtobrutinib, EU/3/21/2450 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.

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

4.2.1. Ztalmy - ganaxolone - EMEA/H/C/005825, EU/3/19/2224, EMA/OD/0000071368

Marinus Pharmaceuticals Emerald Limited; Treatment of CDKL5 deficiency disorder

COMP Rapporteur: Elisabeth Johanne Rook; COMP Co-Rapporteur: Giuseppe Capovilla

An opinion recommending not to remove Ztalmy, ganaxolone, EU/3/19/2224 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 COMP adopted the opinion by written procedure following its May meeting.]

4.2.2. – sodium phenylbutyrate / ursodoxicoltaurine - EMEA/H/C/005901, EU/3/20/2284, EMA/OD/0000096503

Amylyx Pharmaceuticals EMEA; Treatment of amyotrophic lateral sclerosis

The status of the procedure at CHMP was noted.

4.2.3. Sohonos - palovarotene - EMEA/H/C/004867, EU/3/14/1368, EMA/OD/0000101938

Ipsen Pharma; Treatment of fibrodysplasia ossificans progressiva

CHMP negative opinion was noted.

4.2.4. - talquetamab - EMEA/H/C/005864, EU/3/21/2486, EMA/OD/0000126657

Accelerated assessment

Janssen-Cilag International N.V.; Treatment of multiple myeloma

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 July meeting.

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 1 application.

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

5.2.1. Aspaveli - pegcetacoplan- EMEA/H/C/005553/II/0011, EU/3/17/1873, EMA/OD/0000140083

Swedish Orphan Biovitrum AB (publ); Treatment of paroxysmal nocturnal haemoglobinuria

CHMP Rapporteur: Alexandre Moreau; CHMP Co-Rapporteur: Selma Arapovic-Dzakula

The COMP agreed that a formal review of the maintenance of the orphan designation for the applied indication is needed.

5.3. Appeal

None

5.4. On-going procedures

COMP co-ordinators were appointed for 1 application.

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

New membership:

The Chair welcomed Evangelia Yannaki, as the new member for EL.

End of membership:

The Chair thanked Giuseppe Capovilla for their contribution as a member for IT.

7.1.2. Vote by proxy

Robert Nistico gave a proxy to Armando Magrelli to vote on behalf of Robert Nistico during the entire duration of meeting.

7.1.3. Strategic Review & Learning meetings

Feedback was noted from the COMP SRLM under the Swedish Presidency of the Council of the EU held F-2-F on 3-4 May 2023 in Uppsala, Sweden.

7.1.4. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met face-to-face on 15 May 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.

7.3.2. Upcoming ITF meetings

The COMP noted the upcoming ITF meetings.

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)

COMP noted update from Rare Disease Cluster on Accelerating Access to Critical Therapies for amyotrophic lateral sclerosis (ALS) Act.

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. Discussion on OMARs

Postponed.

8.2. Business Pipeline Report - 3 year Forecast report

COMP noted the presentation on the business analysis and forecasting. The data in the report represent an outlook of the initial MAAs planned for the next three years (March 2023 - December 2025).

8.3. ACT EU PA04 - Multi-stakeholder Workshop on ICH E6 R3 - Public Consultation

COMP noted the presentation of the ICH E6 GCP public communication, intended to be published on 26th May. The multi-stakeholder workshop will take place on 13 and 14 July. The agenda and its topics were presented.

8.4. Report on experience with RWE studies to support EMA scientific committees

COMP noted the presentation that focused on the 1.5 year long experience with regulatory-led real world evidence (RWE) studies from September 2021 until February 2023. Overview of RWE Pilots was presented with various committees and SAWP. It was noted that there are 3 main pathways for generating RWE.

Overall, a total of 61 research topics were considered during the reporting period resulting in 30 studies that were initiated, of which 27 studies were completed. Out of 18 replies on the usefulness of the studies, 12 responders indicated that the results were considered for the assessment (supportive). The COMP noted that further granularity would be of interest on how the study results were used for decision making. The majority of the research topics emerged in the context of scientific assessments by the PRAC and PDCO followed by COMP and SAWP. Most studies fell within the use case category of safety studies. No study in the area of effectiveness or representativeness/validity of applicant studies was requested.

Overview of studies in the context of regulatory procedures was presented.

Regarding studies specifically conducted to support COMP, the total number of research topics was six. Five studies were feasible and completed. COMP-specific learning include (amongst other) that rare disease research may be best performed using (networks of) disease registries, hospital databases or primary/secondary care linked databases. In future studies, the target population will need to be carefully defined. Information data source characteristics and healthcare system organisation will help to better understand strengths and limitations of the studies. During the discussion it was noted that one of the main challenges for rare disease research is the fragmentation of data.

As next steps, the report will be circulated for a 2 weeks commenting period. Findings of the report will be published by end of June. A multi-stakeholder workshop on RWE for regulatory decisions is taking place on 26-27 June 2023. Furthermore, as a last item in the presentation, update on DARWIN EU was provided. As a next step, the COMP welcomed

discussions with EMA on how to best implement the recommendations of the report and if to proceed with a new DARWIN EU study.

8.5. Format of OEs during COMP meetings

COMP was informed on the new arrangement and format of the oral explanations during the plenary meetings. Companies will have an enhanced experienced being able to see both the live video feeds and the presentation slides. This would allow the experience for companies to be as close as possible to the face-to-face setting.

9. List of participants

including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 15-17 May 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	
Tim Leest	Member	Belgium	No interests declared	
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 Penttila	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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Enrico Costa	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No restrictions applicable to this meeting	
Ruta Mameniskiene	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	
Bożenna Dembowska-Baginska	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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Maria Cavaller Bellaubi	Expert - in person*	Patients' Organisation Representative	No restrictions applicable to this meeting	
Meeting run with support from relevant EMA staff				

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/