12 May 2022
EMA/COMP/214405/2022
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 11-13 April 2022

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).

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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. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held 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, 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. No new or additional interests or restrictions were declared. 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. 22 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

COMP agenda for 11-13 April 2022 was adopted with no amendments.

1.3. Adoption of the minutes

COMP minutes for 15-17 March 2022 were adopted with amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. adeno-associated virus serotype R100 containing the human *RPGRorf15* gene isoform - EMA/OD/0000077548

Pharma Gateway AB; Treatment of inherited retinal dystrophies due to defects in the *RPGR* gene

COMP Rapporteur: Tim Leest

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 sponsor was requested to explain the clinical relevance of the detected differences between treated and untreated eye from the preliminary clinical efficacy data derived from two patients with advanced retinal disease (i.e. data from Ellipsoid Zone Area (EZA) and microperimetry evaluations).

The sponsor was asked to discuss the alignment of subretinal injection site with the therapeutic, the anatomical and functional endpoint changes.

The sponsor was also requested to provide any available updates from patient's efficacy data.

In the written response, the sponsor pointed out that their first in human phase 1/2 study is not powered to demonstrate efficacy but is rather expected to detect trends in activity. The sponsor proposed EZA (obtained by masked expert reading center graders) as the main efficacy endpoint and microperimetry mean retinal sensitivity as intended to be used as secondary supportive evidence. Moreover, the sponsor revised its approach to evaluating EZA data, leveraging data from all time points from a greater number of evaluable subjects in linear regression trend analysis of log transformed data to reduce the effects of individual measurement variability and differences in baseline EZA, and to improve the ability to detect signals of activity of the proposed product.

The sponsor clarified that since the proposed product is not delivered by subretinal injection but by intravitreal injection, there is no subretinal injection site to align with anatomical and functional endpoint measurements.

The COMP discussion included the following points:

Regarding the use of ellipsoid zone (EZ) measure as an early indicator of progression, this was considered acceptable in principle but subject to caveats ie. EZ is an anatomical measure and does not align precisely with retinal sensitivity changes. The use of a slope analysis and log transformation is acceptable in an early setting. However, use of these measures as primary or key secondary endpoints in pivotal clinical trials intended to support licensing of the medicinal product in the EU is not yet regarded as established yet and would need to be discussed through a protocol assistance with the regulators; retinal function and functional vision are considered key primary endpoint in inherited retinal diseases.

Regarding the sponsor's data, the re-analysis and additional references were welcomed. Of 6 evaluation EZA patients, 5 showed a numerical reduction in log EZA slope. The absolute changes from baseline to most recent visit were within the approximately1 mm^2 EZA measurement variability. Two patients may be considered to have some more numerical separation of EZA slope compared to the fellow control eye. The COMP also acknowledged that the study population of this first in human Phase 1/2 4D-125 trial is a population with advanced disease.

Overall, the COMP considered that this data could be indicative of clinical activity of the therapy with uncertainties and assumptions which will need to be further evaluated in the clinical development. Protocol assistance was strongly recommended on the planned clinical development, including the primary and key secondary endpoints for the pivotal licensing studies.

The COMP considered the written response adequately addressed the question raised and cancelled the oral explanation.

The Committee agreed that the condition, inherited retinal dystrophies due to defects in the *RPGR* 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 serotype R100 containing the human *RPGRorf15* gene isoform was considered justified based on preliminary clinical data which suggest a positive trend in preserving photoreceptors.

The condition is chronically debilitating due to the development of nyctalopia and tunnel vision and progression to blindness.

The condition was estimated to be affecting approximately 0.5 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 adeno-associated virus serotype R100 containing the human *RPGRorf15* gene isoform, for treatment of inherited retinal dystrophies due to defects in the *RPGR* gene, was adopted by consensus.

2.1.2. - EMA/OD/0000076540

Treatment of essential thrombocythemia (ET)

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

- Significant benefit

The arguments on significant benefit were based on an alternative mechanism of action to products currently authorised for use in the condition and the potential improved efficacy in the condition.

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

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

In the written response and during an oral explanation before the Committee on 13 April 2022, the sponsor reiterated that all currently used ET therapies only have a cytoreductive effect, with an increased leukaemogenic risk (hydroxyurea, busulfan), unfavourable toxicity profile and therefore were not recommended for ET patients. Although these are valid arguments, treatment with interferon alpha, or with the proposed substance is not possible for all ET patients. While COMP accepted that the proposed long-acting product has less safety concerns than older short-acting ones, there are known side-effects and tolerability issues with it. In addition, when the COMP requested further clarification regarding the previous or concomitant use of anagralide from the clinical data submitted, the sponsor indicated that they did not have any data of this nature.

It was thus noted that the sponsor did not actually provide any direct or in-direct arguments regarding significant benefit against authorised products (namely anagrelide and busulfan), showing better efficacy or major contribution to patient care.

The COMP acknowledged that there is a place for long-acting or short-acting products in the treatment of patients with ET. The sponsor, however, did not provide convincing argumentation. As a result, it was felt that without supporting data, the COMP could not recommend granting the orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 13 April 2022, prior to final opinion.

2.1.3. - EMA/OD/0000075402

Treatment of cystic fibrosis (CF)

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 sponsor's in vitro data with the proposed product and the referenced (indirect) data from various in vitro assays, non-clinical in vivo studies and clinical studies with heparin/heparin derivatives were not considered sufficient to support medical plausibility. The sponsor was asked whether any efficacy/activity data with the proposed product could be presented which demonstrate positive functional effects on clinically relevant aspects of the disease.

- Significant benefit

The arguments on significant benefit appeared to be based on "major contribution to patient care" (MCPC). The sponsor was therefore asked to present data which support comparable activity/efficacy of the proposed product vs relevant authorized products in the standard of care treatment of cystic fibrosis. The sponsor was requested to describe more precisely the expected MCPC.

The response to the COMP's list of questions on medical plausibility and significant benefit were presented in writing and during an oral explanation and include, amongst others, the following arguments/data:

- Medical plausibility

The sponsor clarified that pre-clinical studies were on-going which investigate the effect the proposed product on mucociliary clearance in an in vivo disease model. However, the data were not yet available.

The sponsor presented efficacy data of the proposed product in a non-clinical in vivo model of lipopolysaccharide-induced lung inflammation. Both the proposed product and the oral corticosteroid dexamethasone significantly inhibited neutrophil elastase (NE) activity in bronchial lavage fluid. While such data may be considered supportive, it was not sufficient to support medical plausibility for the following reasons: 1) NE is a biomarker with uncertain translation to clinical efficacy at present, 2) the relevance of the non-clinical model for CF is not clear.

The sponsor emphasised that their data would support a combination use of the proposed product with Pulmozyme. While it is agreed that an enhancer of Pulmozyme activity/efficacy would be of clinical relevance, the COMP expects at least in vivo non-clinical data in a relevant disease model and not only in vitro assay data (DNA degradation assay).

Anti-bacterial effects of the proposed product: the sponsor emphasised that the product used in the study by Lorè et al. 2018 is similar the proposed product. Therefore, applicability of these data by Lorè et al. to the proposed product were expected by the sponsor. While this data may be considered as supportive, it was not considered sufficient as primary data to base proof of concept (POC) for demonstrating anti-bacterial effects of the proposed product

Furthermore, the sponsor described high level results from pre-clinical studies of the effect of the proposed product in non-clinical in vivo models of acute and chronic infection. The proposed product protected from the clinical signs of pneumonia, an effect that was also seen with tobramycin as active comparator. While this data may be potentially valid towards contributing to the POC of the proposed product in CF, insufficient relevant information was presented by the sponsor.

In conclusion, the additional information provided by the sponsor did not change the view of the COMP in that the data is considered insufficient to support medical plausibility for the purpose of this procedure.

- Significant benefit

The sponsor did not provide relevant/convincing data to further support their claim on "major contribution to patient care" (MCPC) of the proposed product vs relevant authorised products in the standard of care treatment of cystic fibrosis. While the sponsor described in more detail the patient burden in CF patients, the sponsor failed to support their claim on MCPC with data that shows that at least similar effects could be obtained with their product as compared to current standard of care (antibacterial, anti-inflammatory, mucolytic).

In addition to the claim on MCPC (single vs multiple product administration to achieve the same effects), the sponsor claimed that the proposed product may be a safer anti-inflammatory agent as currently authorized medicinal products. However, the presented data were considered insufficient to support such claim.

Lastly, the sponsor claimed possible improved efficacy of the proposed product in the combination use of the authorised mucolytic agent Pulmozyme. However, the presented in vitro data was not considered sufficient to support this claim.

In conclusion, the additional information provided by the sponsor did not change the view of COMP in that the data are considered insufficient to support the claim(s) on significant benefit of the proposed product vs relevant authorized medicinal products for the purpose of this procedure.

In communicating the outcome of the discussion to the sponsor, the application for orphan designation was withdrawn on 11 April 2022, prior to the adoption of the final opinion.

2.1.4. - EMA/OD/0000077023

Treatment of Angelman syndrome (AS)

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, the sponsor was asked to further elaborate on the validity of the

Angelman syndrome model used, and the assumption that the seizure types in Angelman syndrome patients are indeed replicated in the non-clinical model especially in relation to the responsiveness to anti-seizure medications.

- Significant benefit

The sponsor was asked to justify the significant benefit assumption in the context of the approved anti-seizure treatments currently used in the therapeutic management of Angelman syndrome patients.

In the written response, and during an oral explanation before the Committee on 11 April 2022, the sponsor defended their position. COMP agreed with the sponsor the existing limitations of the current approaches for managing patients with the condition. However, there is presently no justification as to why the proposed product should provide significant benefit to AS patients compared to the authorized on-label anti-seizure medications. The assumption of significant benefit should be substantiated by data showing that the proposed product might provide benefit in AS patients (as add-on treatment or in patients with refractory seizures) compared to authorized anti-seizure medications. In addition, the proposed product has not proven effective by the sponsor in other domains associated with the condition (e.g., cognitive, motor, behavioural). The COMP concluded that the presented evidence is not sufficient to support an orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 11 April 2022, prior to final opinion.

2.1.5. - EMA/OD/0000077207

Treatment of epidermolysis bullosa

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 1 April 2022, prior to responding to the list of issues.

2.1.6. cannabidiol - EMA/OD/0000077756

Tetra Bio-Pharma Europe Limited; Treatment of epidermolysis bullosa (EB)

COMP Rapporteur: Armando Magrelli

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 sponsor was asked to discuss the validity of the clinical case reports. The sponsor was especially asked to comment on the (expected) comparability of the topical cannabidiol product(s) used in the case reports and the sponsors own product (route of administration, relative cannabidiol content, vehicle) and the interpretability of the uncontrolled data, and whether these could be attributed to a vehicle effect. The sponsor was requested to utilize the totality of non-clinical and clinical data to support the claim for the various effects described in the symptomatic treatment of EB with (topical) cannabidiol.

In the written response, the sponsor clarified that their formulation development is ongoing and while the exact vehicle to be used in the final formulation has not been specified, the

sponsor clarified that their product is intended for cutaneous administration by an airless pump in metered doses, each pump delivering 2.5 mg of cannabidiol to the skin. As certain vehicles can have therapeutic properties as well in EB patients, the specification of the intended vehicle would have been desirable. However, as regards the interpretability of the data by Chelliah et al. 2018, the sponsor emphasised that a vehicle effect is unlikely in view of the fact that:

- the failure to demonstrate clinical improvement in symptoms of EB following treatment with vehicle alone prompted initiation of treatment with cannabidiol;
- specific topical vehicles used to carry cannabidiol were different for each patient treated and included alcohol (tincture), emu oil and a cream and in all cases were applied with different administration techniques, i.e., "misting", topical cream, topical oil.

Therefore, the sponsor proposed that this combined variability in vehicle excipients and formulation, with the exception of the active ingredient, cannabidiol, supports that the reduction in symptoms and positive clinical effects observed across the reported patients was due to cannabidiol. The sponsor further clarified that they will generate controlled data which will account for vehicle only effects.

With regard to the COMP's request to utilize the totality of data, including especially also non-clinical data, to support medical plausibility, the sponsor presented a number of articles which suggest that cannabidiol may indeed have anti-inflammatory, analgesic, wound healing, anti-pruritic, and anti-microbial actions. These data may however be regarded as hypothesis generating and/or supportive, rather than serve as primary evidence to support medical plausibility for the purpose of this procedure.

In conclusion, while the sponsor's clarifications were not considered to address all uncertainties over a possible benefit of the proposed medicinal product in the treatment of EB, a positive conclusion could be drawn considering 1) the overall growing clinical evidence for possible efficacy of CBD in the symptomatic treatment of EB as also described in the publications by Schräder et al. 2019 and Schräder et al. 2021 and as discussed above, and 2) the absence of an established/viable non-clinical disease model in EB. The COMP recommended the sponsor to seek EMA protocol assistance on their future planned clinical development.

The COMP considered the written response adequately addressed the questions raised and cancelled the oral explanation.

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

The intention to treat the condition with the medicinal product containing cannabidiol was considered justified based on preliminary clinical data from case reports, suggesting improvements in disease symptoms such as pain, pruritus, blistering and wound healing. The condition is life-threatening and chronically debilitating due to blister formation following minor friction or trauma, resulting in multiple complications that include life-threatening infections, failure to thrive, and predisposition to the development of squamous cell carcinoma.
The condition was estimated to be affecting approximately 0.7 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 cannabidiol, for treatment of epidermolysis bullosa, was adopted by consensus.

2.1.7. autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD123 - EMA/OD/0000076679

INSERM UMR 1098; Treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN)

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 arguments on significant benefit were based on the alternative mechanism of action and the potential improved efficacy in the condition.
The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the non-clinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.
The sponsor was asked to discuss any available clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients.

In the written responses, the sponsor provided the additional data. In vitro, in vivo and ex vivo studies with CD123 CAR-T in different models reinforce the fact that the CD123 CAR-T cell therapy is more efficient than Elzonris regarding BPDCN blasts elimination. The sponsor also highlighted improved survival in study subjects treated with CD123-CAR-T compared to treatment with Elzonris. Moreover, the persistence of CD123 CAR-T cells, confirmed in the GEN2.2 and CAL-1 non-clinical models, indicated prolonged efficacy compared to chemical agents such Elzonris that requires 5 injections a week and a repetition of this cycle each month. These data suggested that CD123 CAR-T would provide benefit to patients in terms of pharmacokinetics and treatment schema.

Following deliberation of the submitted written response the COMP was of the opinion that it could recommend granting the orphan designation and cancelled the oral explanation.

The Committee agreed that the condition, blastic plasmacytoid dendritic cell neoplasm, 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 cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD123 was considered justified based on non-clinical in vivo data showing prolonged survival.
The condition is life-threatening due to the aggressive progression leading to a mean survival of 12-14 months and overall survival rates of 52-75% after one year.
The condition was estimated to be affecting approximately 0.02 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 T cells transduced with lentiviral vector containing

a chimeric antigen receptor directed against CD123 will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate an improvement in survival through an indirect comparison to the currently authorised medicinal product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD123, for treatment of blastic plasmacytoid dendritic cell neoplasm, was adopted by consensus.

2.1.8. melatonin - EMA/OD/0000076545

Worphmed S.r.l.; Prevention of spaceflight-related radiation and microgravity

COMP Rapporteur: Dinko Vitezic

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 considered that the proposed condition ''prevention of spaceflight-related radiation and microgravity'' is not acceptable as valid.

The proposed condition ''prevention of spaceflight-related radiation and microgravity'' 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 ENTR/6283/00).

In written response and during an oral explanation before the Committee on 12 April 2022, the sponsor described the medical conditions due to long-term space flights. However, since no additional data was presented, the COMP maintained its position that there is no evidence to support the medical plausibility of the proposed condition. Based on this, the COMP could not conclude on the prevalence and the significant benefit.

The COMP considered that the spaceflight-related radiation and microgravity is a physical phenomenon and that the sponsor has not identified a valid clinical setting for drug development. Therefore, the proposed condition is not acceptable for the purpose of orphan designation.

The sponsor has referred to bibliographic studies. However, the data was considered insufficient to support medical plausibility as they could not demonstrate the rationale for the use of the product in the proposed setting. Therefore, the proposed condition 'prevention of spaceflight-related radiation and microgravity' as defined by the sponsor could not be accepted for the purpose of orphan designation.

The sponsor has not established that spaceflight-related radiation and microgravity affects not more than 5 in 10,000 persons in the European Union at the time the application was made, as the proposed condition is not considered to be a valid condition for orphan designation.

The sponsor has not established that the condition is chronically debilitating and life-threatening, as the proposed condition is not considered to be a valid condition for the purpose of orphan designation.

The sponsor has not established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the proposed condition, as this condition is not considered valid for the purpose of orphan designation.

A negative opinion for melatonin, for treatment of prevention of spaceflight-related radiation and microgravity, was adopted by consensus. The sponsor will have 90 days to appeal from the COMP decision.

2.1.9. - EMA/OD/0000077200

Treatment of COVID-19 related ARDS and survival

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 28 March 2022, prior to responding to the list of issues.

2.1.10. fusion protein composed of the first 2 immunoglobulin-like domains of the human roundabout guidance receptor 2 fused to a human IgG1 crystallised fragment - EMA/OD/0000072068

Pfizer Europe MA EEIG; Treatment of focal segmental glomerulosclerosis (FSGS)

COMP Rapporteur: Geraldine O'Dea

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 was asked to recalculate the prevalence estimate without the inclusion of the United Kingdom. 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".

The sponsor was asked to justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor was requested to describe and justify the methodology used for the prevalence calculation.

- Significant benefit

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from their clinical study to justify the assumption of significant benefit over authorised medicinal products with particular attention to the prior use of ciclosporin for the proposed orphan condition.

In the written responses, and during an oral explanation on 11 April 2022, the sponsor presented their answers. COMP accepted the revised prevalence estimate submitted in the written response of 3.38 in 10,000 which was rounded off to 3.4 in 10,000 for the designation.
To support the claim for significant benefit, the sponsor referred to the potential benefit from the proposed product as a result of its mode of action i.e. by acting directly on podocytes as compared to immunotherapeutic options of e.g. glucorticoids and calcineurin inhibitors such as ciclosporin which have a number of safety issues. The sponsor has confirmed that all nine participants included in the first interim analysis of the ongoing

phase 2a study received at least one immunosuppressant for the treatment of focal segmental glomerulosclerosis. Of those nine, three participants continued taking an immunosuppressant at a stable dose throughout the study, one of which was ciclosporin. Each of these three participants with concomitant immunosuppressants were observed to have a reduction in urinary creatinine/protein ratio of at least 33% after 12 weeks of treatment with the proposed product, COMP accepted that this preliminary data indicates that the proposed product has the potential to offer significant benefit on top of authorised medicinal products for patients with FSGS.

The Committee agreed that the condition, focal segmental glomerulosclerosis, is a distinct medical entity and meets the criteria for orphan designation.
The intention to treat the condition with the medicinal product containing fusion protein composed of the first 2 immunoglobulin-like domains of the human roundabout guidance receptor 2 fused to a human IgG1 crystallised fragment was considered justified based on preliminary clinical data in patients with the condition showing a reduction in urinary creatinine/protein ratio.
The condition is life-threatening and chronically debilitating due to the development of end-stage kidney disease.
The condition was estimated to be affecting approximately 3.4 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 exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing fusion protein composed of the first 2 immunoglobulin-like domains of the human roundabout guidance receptor 2 fused to a human IgG1 crystallised fragment will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate an additional reduction in urinary creatinine/protein ratio when their product was used concomitantly with immunosuppressive agents including ciclosporin. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for fusion protein composed of the first 2 immunoglobulin-like domains of the human roundabout guidance receptor 2 fused to a human IgG1 crystallised fragment, for treatment of focal segmental glomerulosclerosis, was adopted by consensus.

2.1.11. - EMA/OD/0000073629

Treatment of glioma

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

- Significant benefit

The arguments on significant benefit were based on the potential improved efficacy in the condition.

The sponsor was requested to further elaborate on the assumption of significant benefit over authorised medicinal products for the proposed orphan condition, e.g. standard of care.

The applicant was asked to elaborate on the non-clinical results given the fact that different modes of administration were used and whether the results from the control groups can be compared.

In the written responses, and during an oral explanation on 11 April 2022, the sponsor defended their position. However, no relevant/convincing data was provided to further support the claim on "clinically relevant advantage" of the proposed product vs relevant authorised products in the standard of care treatment of glioma. With regard to the comparability of the two different routes of administration settings, the sponsor explained satisfactorily that this type of comparison is unavoidable since temozolomide is being compared via its standard way of delivery – systemic administration – to the proposed product that is designed for local delivery. While this limitation was acknowledged by COMP, the resulting indirect comparison was not considered robust enough in order for COMP to conclude on a clinically relevant advantage. Finally, the safety claim by virtue of its structure and its mechanism of action was not accepted by COMP due to the early stage of development, which could support it. COMP concluded that the presented evidence was not sufficient to support an orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 11 April 2022, prior to final opinion.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000076247

Treatment of soft tissue sarcoma

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 May meeting.

2.2.2. - EMA/OD/0000077171

Treatment of chronic myeloid leukemia

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 May meeting.

2.2.3. elezanumab - EMA/OD/0000077407

AbbVie Deutschland GmbH & Co. KG; Treatment of spinal cord injury

COMP Rapporteurs: Jana Mazelova, Armando Magrelli

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

The intention to treat the condition with the medicinal product containing elezanumab was considered justified based on non-clinical in vivo data in valid models of the condition showing improvement of motor function and axonal sprouting at the cellular level in regions around the glial scar.
The condition is chronically debilitating and life-threatening due to sensory and motor loss of function in the limbs and reduced life expectancy.
The condition was estimated to be affecting approximately 4.3 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 elezanumab will be of significant benefit to those affected by the condition. The sponsor has provided in vivo non-clinical data that demonstrate that there was improvement of motor function when the product was given in the sub-acute injury setting where currently there are no authorised medicinal products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for elezanumab, for treatment of spinal cord injury, was adopted by consensus.

2.2.4. - EMA/OD/0000077417

Treatment of tubular aggregate myopathies (including York platelet syndrome and Stormorken syndrome)

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 May meeting.

2.2.5. *streptococcus pyogenes*, group A, type 3, strain Su, inactivated - EMA/OD/0000077676

Pharma Gateway AB; Treatment of lymphatic malformations

COMP Rapporteur: Bozenna Dembowska-Baginska

Following review of the application by the Committee, it was agreed to broaden the indication to treatment of lymphatic malformations.

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

The intention to treat the condition with the medicinal product containing *streptococcus pyogenes*, group A, type 3, strain Su, inactivated was considered justified based on clinical data which showed reduction on lymphatic malformation volume.

The condition is chronically debilitating due to pain, discomfort, swelling, thrombosis and psychologically distressing and life threatening due to impairment of vital functions if left untreated.
The condition was estimated to be affecting approximately 3.7 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 *streptococcus pyogenes*, group A, type 3, strain Su, inactivated, for treatment of lymphatic malformations, was adopted by consensus.

2.2.6. elamipretide - EMA/OD/0000077720

Scendea (NL) B.V.; Treatment of myopathic mitochondrial DNA depletion syndrome

COMP Rapporteur: Dinah Duarte

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

The intention to treat the condition with the medicinal product containing elamipretide was considered justified based on preliminary clinical data showing an improvement in lower limb muscle function.

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 approximately 0.1 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 elamipretide, for treatment of myopathic mitochondrial DNA depletion syndrome, was adopted by consensus.

2.2.7. ibudilast - EMA/OD/0000078233

Healx Technology Limited; Treatment of fragile X syndrome

COMP Rapporteur: Robert Nistico

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 ibudilast was considered justified based on non-clinical in vivo data showing a dose-dependent reversal of the behavioural alterations in a valid model of the condition compared to the wild type control group.

The condition is chronically debilitating due to developmental delay as well as a range of behavioural and cognitive deficits.

The condition was estimated to be affecting approximately 3 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 ibudilast, for treatment of fragile X syndrome, was adopted by consensus.

2.2.8. adeno-associated virus serotype 8 expressing the human gamma-sarcoglycan gene - EMA/OD/0000078678

Atamyo Therapeutics; Treatment of limb-girdle muscular dystrophy (LGMD)

COMP Rapporteur: Dinah Duarte

The Committee agreed that the condition, limb-girdle muscular dystrophy, 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 serotype 8 expressing the human gamma-sarcoglycan gene was considered justified

based on non-clinical in vivo data showing an improvement in global muscle strength, and serum and muscle tissue biomarkers.

The condition is chronically debilitating due to muscle wasting, consequent reduced mobility and debilitating fatigue and potentially life threatening due to respiratory complications.

The condition was estimated to be affecting approximately 1 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 serotype 8 expressing the human gamma-sarcoglycan gene, for treatment of limb-girdle muscular dystrophy, was adopted by consensus.

2.2.9. autologous peripheral blood-derived CD4 T-cells CRISPR-edited at the CD40LG locus - EMA/OD/0000079230

Fondazione Telethon; Treatment of hyper IgM syndromes

COMP Rapporteur: Ingeborg Barisic

Following review of the application by the Committee, it was agreed to rename the indication to treatment of hyper IgM syndromes.

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

The intention to treat the condition with the medicinal product containing autologous peripheral blood-derived CD4 T-cells CRISPR-edited at the CD40LG locus was considered justified based on in vivo non-clinical data in a valid model of the condition which showed partially rescued antigen specific IgG response.

The condition is chronically debilitating and life threatening due to chronic and recurrent infections that could lead to organ damage, autoimmune manifestations including cytopenias, inflammatory bowel disease and reduced life expectancy.

The condition was estimated to be affecting less than 0.005 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 autologous peripheral blood-derived CD4 T-cells CRISPR-edited at the CD40LG locus, for treatment of hyper IgM syndromes, was adopted by consensus.

2.2.10. icerguastat acetate - EMA/OD/0000079683

Inflectis Bioscience S.A.S; 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 icerguastat acetate was considered justified based on non-clinical in vivo data in a model of the condition showing a significant reduction in progressive weight loss as well as the motor function.
The condition is life-threatening and chronically debilitating due to progressive degeneration of motor neurons, ultimately leading to paralysis and respiratory failure. The survival of the patients is usually limited.
The condition was estimated to be affecting approximately 1.2 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 icerguastat acetate will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that showed beneficial effects on motor function loss and delay of disease progression which is not noted with the current authorised medicine. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for icerguastat acetate, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

2.2.11. - EMA/OD/0000080466

Prevention of risk of graft failure following allogenic hematopoietic stem cell transplantation

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 May meeting.

[Post-meeting note: The sponsor withdrew the application for orphan designation on 27 April 2022.]

2.2.12. - EMA/OD/0000080468

Treatment of chromosome 15q11.2-13.1 duplication syndrome (dup15q)

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 May meeting.

2.2.13. - EMA/OD/0000080709

Prevention of retinopathy of prematurity

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 May meeting.

2.2.14. chimeric peptide of human glucagon-like peptide-1, glucagon and gastric inhibitory polypeptide analogues linked to a human immunoglobulin Fc fragment - EMA/OD/0000080809

JVM Europe B.V.; Treatment of idiopathic pulmonary fibrosis

COMP Rapporteur: Eva Malikova

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

The intention to treat the condition with the medicinal product containing chimeric peptide of human glucagon-like peptide-1, glucagon and gastric inhibitory polypeptide analogues linked to a human immunoglobulin Fc fragment was considered justified based on non-clinical in vivo data in a model of the condition showing an improvement in the arterial blood oxygen saturation as well as survival.

The condition is chronically debilitating due to progressive dyspnoea and loss of respiratory function, with limited exercise capability and decreased quality of life. Pulmonary hypertension usually develops. Median survival is less than five years, and death ultimately occurs due to respiratory failure.

The condition was estimated to be affecting approximately 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 chimeric peptide of human glucagon-like peptide-1, glucagon and gastric inhibitory polypeptide analogues linked to a human immunoglobulin Fc fragment will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate improved survival when compared to authorised medicines for the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for chimeric peptide of human glucagon-like peptide-1, glucagon and gastric inhibitory polypeptide analogues linked to a human immunoglobulin Fc fragment, for treatment of idiopathic pulmonary fibrosis, was adopted by consensus.

2.2.15. pasireotide - EMA/OD/0000081138

Recordati Rare Diseases; Treatment of noninsulinoma pancreatogenous hypoglycemia syndrome (NIHPS)

COMP Rapporteur: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing pasireotide was considered justified based on preliminary clinical data showing a reduction or elimination of hypoglycemic episodes.

The condition is life-threatening and chronically debilitating due to the repetitive nature of the associated hypoglycaemia which can be severe leading to neuroglycopenia resulting in dangerous and life-threatening outcomes, such as seizures, loss of consciousness and brain damage.

The condition was estimated to be affecting approximately 3.7 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 pasireotide, for treatment of noninsulinoma pancreatogenous hypoglycemia syndrome, was adopted by consensus.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

None

2.6. Nominations

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

COMP rapporteurs were appointed for 36 applications.

2.7. Evaluation on-going

36 applications for orphan designation will not be discussed as evaluation is ongoing.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of mucopolysaccharidosis type I

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 multiple myeloma

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

3.2. Finalised letters

3.2.1. -

Treatment of acute myeloid leukaemia

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment of multiple myeloma

The new request was noted.

3.3.2. -

Treatment of primary biliary cholangitis

The new request was noted.

3.3.3. -

Treatment of myelodysplastic syndromes

The new request was noted.

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. Carvykti - ciltacabtagene autoleucel - EMEA/H/C/005095/0000, EU/3/20/2252, EMA/OD/0000060914

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

COMP Rapporteurs: Karri Penttila; Maria Elisabeth Kalland

A list of issues was adopted on 17 March 2022.An oral explanation was held on 12 April 2022.

An opinion recommending not to remove Carvykti, ciltacabtagene autoleucel (EU/3/20/2252) 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.

4.1.2. Kymriah – tisangenlecleucel - EMEA/H/C/004090/II/0044, EU/3/21/2464, EMA/OD/0000054173

Novartis Europharm Limited; Treatment of follicular lymphoma

COMP Rapporteurs: Maria Elisabeth Kalland; Frauke Naumann-Winter

A list of issues was adopted on 17 March 2022.

An oral explanation to be held on 13 April 2022, was cancelled.

An opinion recommending not to remove Kymriah, tisangenlecleucel (EU/3/21/2464) 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. Filsuvez - betulae cortex dry extract (DER 5-10: 1), extraction solvent n-heptane 95% (w/w) - EMEA/H/C/005035/0000, EU/3/10/845, EMA/OD/0000070235

Amryt Pharmaceuticals Designated Activity Company; Treatment of epidermolysis bullosa

COMP Rapporteurs: Elisabeth Johanne Rook; Darius MatuseviciusAn opinion recommending not to remove Filsuvez, betulae cortex dry extract (DER 5-10: 1), extraction solvent n-heptane 95% (w/w), EU/3/10/845 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 April meeting.]

4.2.2. Lunsumio - mosunetuzumab - EMEA/H/C/005680/0000, EU/3/21/2517, EMA/OD/0000082933

Accelerated assessment

Roche Registration GmbH; Treatment of follicular lymphoma

COMP Rapporteurs: Karri Penttila; Maria Elisabeth KallandAn opinion recommending not to remove Lunsumio, mosunetuzumab, EU/3/21/2517 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 April meeting.]

4.2.3. – olipudase alfa - EMEA/H/C/004850, EU/3/01/056, EMA/OD/0000072975

Accelerated assessment

Genzyme Europe BV; Treatment of Niemann-Pick disease

The status of the procedure at CHMP was noted.

4.2.4. – fosdenopterin - EMEA/H/C/005378/0000, EU/3/10/777, EMA/OD/0000074822

Accelerated assessment

Comharsa Life Sciences Ltd; Treatment of molybdenum cofactor deficiency type A

The status of the procedure at CHMP was noted.

4.2.5. Imcivree - setmelanotide - EMEA/H/C/005089/II/0002/G, EU/3/19/2192, EMA/OD/0000074865

Rhythm Pharmaceuticals Netherlands B.V.; Treatment of Bardet Biedl syndrome (BBS)

The status of the procedure at CHMP was noted.

4.3. Appeal

4.3.1. Nexviadyme - avalglucosidase alfa - EMEA/H/C/005501/0000, EU/3/14/1251,

Genzyme Europe B.V.; Treatment of Pompe's disease

COMP appeal rapporteurs: Elisabeth Rook, Ingeborg Barisic

In the grounds for appeal, and during an oral explanation before the Committee on 12 April 2022, the sponsor aimed to address the main issues which led to the negative opinion.

The COMP upheld the negative view and an opinion recommending removing Nexviadyme (EU/3/14/1251) 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 April meeting.]

4.4. On-going procedures

COMP co-ordinators were appointed for 5 applications.

4.5. Orphan Maintenance Reports

Documents were tabled for information.

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

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

None

5.3. Appeal

None

5.4. On-going procedures

The COMP noted the review of orphan designation for OMP for MA extension - On-going procedures

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

The COMP was pleased to welcome Mr Vasileios Papadopoulos as new member for Greece.

7.1.2. Vote by proxy

None

7.1.3. Strategic Review & Learning meetings

Feedback from the joint COMP/PDCO meeting under the French Presidency of the Council of the EU, to held virtually on 31 March 2022 was postponed to the next COMP meeting.

7.1.4. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 8 April 2022.

7.1.5. Principal 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.

7.2.2. COMP-CAT Working Group

The meeting was postponed.

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)

Elisabeth Rook was nominated as COMP representative for HCPWP and Tim Leest was re-nominated as COMP representative for PCWP for a three-year mandate (June 2022 to May 2025).

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. Therapeutic Goods Administration (TGA), Australia

None

7.5.4. Health Canada

None

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

None

7.7. COMP work plan

None

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2022

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2022 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. Complex Clinical Trials Question and Answers document

The members were invited to send their comments until the 28th April 2022

8.2. EMA survey on Orphan Maintenance Assessment Report (OMAR)

The COMP noted the OMAR project and proposed updates. Furthermore, the updated summary report template was presented. There were proposals made to improve the process of running the COMP and presentations during the plenaries. The COMP welcomed the improvement proposals. The next steps will be to update the template and test it out when maintenance procedures are discussed.

8.3. Marketing Authorisation Applications 3-year forecast report

COMP noted the information.

8.4. Standard operating procedure (SOP) for orphan medicinal product designation and maintenance

Postponed.

8.5. Inherited Retinal Dystrophies and Orphan Designations - review of approach on conditions

COMP noted the presentation and proposals for the workshop. There were questions to COMP presented by the organisers regarding the workshop. There would be 5-10 experts and patients, and committee members invited to the workshop. The workshop is scheduled to take place on the 17th June 2022 as virtual meeting.

COMP was asked to endorse the expert consultation and deadline 18th April 2022 was noted. Any comments from COMP members on the draft questions, draft agenda and discussion paper were welcome.

9. List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 11-13 April 2022 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	Member (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 Penttilä	Member	Finland	No interests declared	
Cecile Dop	Member	France	No restrictions applicable to this meeting	
Frauke Naumann-Winter	Member	Germany	No interests declared	
Vasileios Papadopoulos	Member	Greece	No interests declared	
Zsofia Gyulai	Member	Hungary	No interests declared	
Geraldine O'Dea	Member	Ireland	No interests declared	
Enrico Costa	Member	Italy	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Irena Rogovska	Member	Latvia	No restrictions applicable to this meeting	
Aušra Matulevičienė	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No restrictions applicable to this meeting	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland	No restrictions applicable to this meeting	
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	
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Giuseppe Capovilla	Member	Expert recommended by EMA	No interests declared	
Maria Cavaller Bellaubi	Expert via WebEx*	Patients' Organisation Representative	No restrictions applicable to this meeting	
Jeanette McCallion	Expert via WebEx*	Ireland	No interests declared	
Jacqueline van Kuijk	Expert via WebEx*	Netherlands	No interests declared	
Jan Span	Expert via WebEx*	Netherlands	No interests declared	
	Patient expert - via WebEx*	European Union - EMA	No interests declared	
Meeting run with support from relevant EMA staff.				

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

10. Explanatory notes

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

Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

market exclusivity) aiming at stimulating the development and availability of treatments for patients suffering from rare diseases.

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

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

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

Sponsor

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

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

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

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