18 January 2024
EMA/COMP/582760/2023
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 05-07 December 2023

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

Health & safety

In accordance with the Agency's health and safety policy, delegates were briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the COMP meeting reports once the procedures are finalised.

Of note, this set of minutes is a working document primarily designed for COMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members and experts

The Chair opened the meeting by welcoming all participants. The meeting was held in-person.

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.

The EMA Secretariat announced the names of the Committee members who delegated their vote via proxy and the Committee members who received such proxy.

1.2. Adoption of agenda

The agenda for 05-07 December 2023 was adopted with amendments.

Topic added:

5.2.1. Kaftrio – ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/WS2551/0043, EU/3/18/2116, EMA/OD/0000160021

1.3. Adoption of the minutes

The minutes for 07-09 November 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. - EMA/OD/0000150558

Treatment of eosinophilic esophagitis

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 appeared to have included older data in the prevalence estimate. As the incidence of the condition has significantly increased in the last ten years due to changing diagnostic criteria, the sponsor should use more current data to provide an updated estimate. The prevalence should be for the entire population (paediatric and adults) affected by the condition.

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

For the estimation and presentation of the prevalence estimate the sponsor was 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, and during an oral explanation before the Committee on 6 December 2023, the sponsor provided a written response and presented an oral explanation. The prevalence estimate was primarily based on a recent publication *Hahn JW et al., Global Incidence and Prevalence of Eosinophilic Esophagitis, 1976- 2022: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2023 Jun*. It was also highlighted that there were publications from Spain: Overall prevalence 111.9 cases per 100,000 (Arias A et al., 2019) and Denmark: eosinophilic esophagitis (EoE) prevalence resulted 22.2 per 100,000 individuals in 2011 and 69.7 per 100,000 in 2018 (Allin KH et al., 2022) which indicated that recently the prevalence had gone over the threshold of 5 in 10,000. The sponsor, however, argued that Hahn et al. (2023) was the more representative as it considered the totality of the data available in Europe. They therefore considered that their proposed prevalence estimate of 4.2 in 10,000 represented the true prevalence in Europe.

The COMP noted that since 2018 and the introduction of new guidelines the incidence of EoE has substantially risen as cases that were not included in the condition before were now diagnosed. It was felt that publications prior to 2018 did not accurately reflect the current situation and that Hahn et al. fell into this category as it included publications from 1976 to 2022 and did not adequately reflect the current situation in Europe. The sponsor was invited to further elaborate on the impact of the new guidelines and the higher numbers that further reinforced the trend seen already in the late 2000s. They were not able to satisfactorily address the issue.

The COMP decided that insufficient data had been provided to support the prevalence estimate for EoE and therefore could not recommend granting the orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 6 December 2023, prior to final opinion.

2.1.2. anti-(insulin receptor) human monoclonal antibody - EMA/OD/0000149464

Rezolute (Bio) Ireland Limited; Treatment of insulinoma

COMP Rapporteur: Vallo Tillmann

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

Treatment of hyperinsulinism 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 was drawn to the orphan regulations and relevant guidelines (especially section A of 2022/C 440/02). The COMP considered the proposed condition to be a symptom of an underlying condition, namely insulinoma.

- Number of people affected

The sponsor proposed a prevalence estimate based on establishing the number of patients who have hyperinsulinism associated with insulinoma. As the orphan condition is insulinoma they should provide a revised estimate for insulinoma. They should justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor should describe and justify the methodology used for the prevalence calculation.

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

- Significant benefit

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

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

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

In the written response, the sponsor changed the condition to insulinoma as recommended by the COMP. The prevalence estimate was adjusted to reflect the estimate of the numbers of patients with insulinomas in Europe. This number did not change from the initial prevalence estimate submitted by the sponsor which the COMP accepted as approximately 1 in 10,000.

The sponsor provided data from two more patients with hyperinsulinism associated with insulinoma. As of today, a total of three insulinoma patients with metastatic disease have received the proposed product under an extended access programme (EAP) for treatment of severe hypoglycaemia refractory to available standard of care therapies.

The change of the condition to insulinoma and the supporting prevalence estimate was agreed by the COMP for the purpose of an initial orphan designation. The significant benefit was further supported by data from three patients, refractory to standard of care and who responded adequately to the sponsors' product. The COMP accepted the responses to the LoQ and decided to cancel the oral explanation.

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

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

The intention to treat the condition with the medicinal product containing anti-(insulin receptor) human monoclonal antibody was considered justified based on non-clinical in vivo and preliminary clinical data showing a reduction of hypoglycaemia following treatment.

The condition is life-threatening and chronically debilitating due to severe hypoglycaemia, with possible progression to loss of consciousness, seizures, grand mal seizures and coma.

The condition was estimated to be affecting approximately 1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing anti-(insulin receptor) human monoclonal antibody will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo and preliminary clinical data that demonstrate a reduction of hypoglycaemia in patients who are refractory to medicines used to treat hypoglycaemia associated with insulinoma. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for anti-(insulin receptor) human monoclonal antibody, for treatment of insulinoma, was adopted by consensus.

2.1.3. golcadomide hydrochloride - EMA/OD/0000149222

Bristol-Myers Squibb Pharma EEIG; Treatment of diffuse large B-cell lymphoma

COMP Rapporteur: Bozenna Dembowska-Baginska

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 applied for the treatment of diffuse large B-cell lymphoma based on preliminary clinical data in patients with diffuse large B-cell lymphoma. However, the sponsor should further discuss whether large B-cell lymphoma is a more suitable condition taking into consideration the WHO classification of lymphoid neoplasm (5th edition, Alaggio et al., 2022).

- Number of people affected

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

The sponsor should re-calculate the prevalence considering the change in the applied condition.

- Significant benefit

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

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the clinical studies to justify the assumption of

significant benefit over authorised medicinal products for the proposed orphan condition. For this purpose, direct or indirect comparisons would be needed against all authorised treatments considered satisfactory methods in first line and in the relapse or refractory disease setting.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development and the positioning of this product in the treatment algorithm.

In the written response, and during an oral explanation before the Committee on 5 December 2023, the sponsor defended their position.

Regarding the condition, the sponsor elaborated on the changes introduced as part of the 5th edition of the WHO classification of haematolymphoid neoplasms from 2022 and confirmed that diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) and DLBCL/high-grade B-cell lymphoma (HGBL) are the target patient populations for a future indication, and these are the populations included in ongoing and planned clinical studies. Overall, the Committee discussed the suitability of the proposed condition and the risk of excluding patients at the time of marketing authorisation that would otherwise benefit from the proposed treatment, an element that was discussed in depth. However, at this present time, the Committee considered that DLBCL can continue to be designated as a valid orphan condition. Answering to the queries on the prevalence calculation, the sponsor leveraged sources such as cancer registries (e.g., GLOBOCAN), publications, and other publicly available sources of information and concluded on a prevalence estimate range in line with the initial discussion and with previous orphan designation that was considered satisfactory.

Regarding the significant benefit, the sponsor provided additional information on two Phase 1 ongoing clinical trials in subjects with previously untreated disease and in subjects with relapsed or refractory disease. Overall, the results demonstrated high response rates which would support the significant benefit claims. In addition, a summary of available data including baseline characteristics and best overall response was provided in combination with individual comparisons against authorised treatments for the applied condition. Overall, although preliminary, the clinical data can be supportive of a positive opinion.

The COMP adopted a positive opinion after the oral explanation. The COMP advised the sponsor to request EMA protocol assistance for further development given the changing nature of the treatment paradigm.

The Committee agreed that the condition, diffuse large B-cell lymphoma, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing golcadomide hydrochloride was considered justified based on non-clinical data in a model of the condition showing a dose-dependent antitumour activity, and preliminary clinical data showing responses to treatment with golcadomide hydrochloride in previously untreated and in relapsed/refractory patients.

The condition is chronically debilitating due to constitutional symptoms, local symptoms of lymphadenopathy, end-organ damage from disease involvement, and bone marrow failure that may lead to infections, anaemia, and thrombocytopenia, and life-threatening in patients not responding to treatment.

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

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 golcadomide hydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrated high response rates in previously untreated high-risk diffuse large B-cell lymphoma patients when the product was used in combination with R-CHOP. In addition, the sponsor provided data indicating a potential effect in patients with relapsed/refractory diffuse large B-cell lymphoma. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for golcadomide hydrochloride, for treatment of diffuse large B-cell lymphoma, was adopted by consensus.

2.1.4. apilimod dimesilate - EMA/OD/0000148755

Maxia Strategies-Europe Limited; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Maria Judit Molnar

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

With regards to the exploratory clinical trial, no positive trend toward functional improvement was observed in C9ALS patients. The clinical relevance of the GPNMB or poly (GP) biomarkers in amyotrophic lateral sclerosis (ALS) has not been established to date. The sponsor was therefore invited to provide further arguments and/or data that would substantiate the translation of the observed effect of attenuation of motor function decline in the TDP-43 model into the clinic.

In addition, an update of the long-term extension data (24 weeks) of the clinical study is requested.

The sponsor was invited to elaborate on the clinical development plan.

- Significant benefit

The sponsor was invited to further substantiate the significant benefit of apilimod dimesilate vs the authorised product riluzole with relevant evidence.

In the written response, the sponsor clarified key aspects pertaining to the COMPs list of questions on medical plausibility and significant benefit. The COMP considered that especially the positive functional effects observed in the non-clinical in vivo model could be sufficient to support the medical plausibility and the significant benefit for the purpose of initial orphan designation. Attenuation of motor function decline cannot be expected from the authorised medicinal product riluzole. The COMP acknowledged also the clinical data with modest positive trends possibly suggestive of stabilisation or improvement on selected clinical endpoints (e.g. respiratory and cognitive-behavioural domain). However, the data was considered too preliminary on the clinical/functional endpoints (owing mostly to the small sample size over time and large variability), to be taken into consideration for decision making during this procedure. The COMP accepted the responses to the LoQ and decided to cancel the oral explanation.

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 apilimod dimesilate was considered justified based on non-clinical in vivo data in a model of the condition showing improved 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 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 apilimod dimesilate will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data in a model of the condition that demonstrate that the product can attenuate motor function decline which cannot be expected from the currently authorised medicinal product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for apilimod dimesilate, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

2.1.5. - EMA/OD/0000149631

Treatment of amyotrophic lateral sclerosis

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 invited to justify the medical plausibility of the proposed product in amyotrophic lateral sclerosis (ALS) and better explain the existing data and/or provide additional data which could further support the proof of concept of the proposed product in ALS, as further specified above in the relevant section of the report.

- Number of people affected

The sponsors literature review in support of the proposed prevalence estimate was considered to be very limited. The sponsor was asked to consider a revision of their review for relevant and up-to-date epidemiologic data of ALS in the EU and revise their final estimate as/if needed.

With regards to the Logroscino et al. (2009) publication and the reported annual incidence rate of ALS, the sponsor was asked to also provide an estimate for the ALS disease duration in order to derive a prevalence estimate.

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

- Significant benefit

The sponsor was requested to further support the significant benefit of the proposed product vis a vis the authorised product Rilutek and support their claim with relevant evidence, as further specified above in the relevant section of the report.

In the written response, the sponsor submitted new non-clinical data in a model of the condition and also provided additional epidemiologic references to better support their prevalence calculation.

The non-clinical data considered of most relevance for the purpose of this procedure was the rotarod performance data. Rotarod performance was measured every two weeks. All SOD1 groups declined over time in their latency time on rotarod, independent of their treatment (active or vehicle control). Only at one timepoint, i.e. at 13 weeks of age, the riluzole and one dose group of the proposed product treated groups spent significantly more time on the rotarod before falling compared with the vehicle group. Other endpoints including neurological scores, Compound Motor Action Potential (CMAP) latency/amplitude and survival, either the effects of the SOD1 groups treated with the proposed product were not significant as compared to the groups treated with the vehicle control or the single components of the proposed product and/or not different from effects achieved with riluzole. Furthermore, treatment with the proposed product did not significantly affect disease onset score in any of the treatment groups, compared with vehicle treatment.

The COMP concluded that the newly provided data were not sufficient to support the medical plausibility and the significant benefit over the authorised medicinal product riluzole, for the purpose of initial orphan designation.

In order to further support the prevalence in ALS the sponsor provided the following data/arguments, considering also the additional epidemiology data on ALS published by Longinetti et al. in 2019 as well as by Puopolo et al. in 2021, the COMP concluded that a prevalence estimate of approximately 1 in 10.000 is acceptable, which is also in line with previously agreed values.

Of note, the sponsor decided to not attend the oral hearing with the COMP.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 6 December 2023, prior to final opinion.

2.1.6. methyl-(1-{[6-{[(1S)-1-cyclopropylethyl]amino}-2-(pyrazolo[5,1-b][1,3]thiazol-7-yl)-pyrimidin-4-yl]carbonyl}piperidin-4-yl)carbamate mono(4-methylbenzenesulfonate) - EMA/OD/0000150398

Syneos Health Netherlands B.V.; Treatment of eosinophilic granulomatosis with polyangiitis

COMP Rapporteur: Ingeborg Barisic

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 new 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 justify the assumption of significant benefit over the authorised medicinal product for the proposed orphan condition.

In the written response, the sponsor provided an additional study which was conducted to evaluate reslizumab in the eosinophilic vasculitis model. Since there are no pharmacologically relevant non-clinical models to test this particular product, mepolizumab was not evaluated. Mepolizumab and reslizumab both bind to epitope of IL-5 within the IL-5Rα-binding domain with similar affinity (Amini-Vaughan et al., 2012). The efficacy of reslizumab injection was evaluated using the same model of eosinophilic vasculitis used in the non-clinical study which evaluated the efficacy of the proposed product. Reslizumab significantly suppressed the number of eosinophils in the peripheral blood and BALF to a same degree showed by the administration of the proposed product. Reslizumab, however, did not suppress the vascular lesion grade in the pulmonary arteries, while the proposed product significantly suppressed the vascular lesions. The significant increase in the number of lymphocytes in the BALF by the exposure to OVA aerosol/vehicle was not suppressed by reslizumab. Several upregulated pro-inflammatory, Th1-, and Th2-related cytokines in the peripheral blood and BALF in the model were not suppressed well by reslizumab.

The COMP concluded that the non-clinical study data collectively support the evidence that the proposed product is expected to provide significant benefit over the authorised medicinal product mepolizumab for the treatment of eosinophilic granulomatosis with polyangiitis (EGPA). The COMP accepted the responses to the LoQ and decided to cancel the oral explanation.

The Committee agreed that the condition, eosinophilic granulomatosis with polyangiitis, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing methyl-(1-{[6-{[(1S)-1-cyclopropylethyl]amino}-2-(pyrazolo[5,1-b][1,3]thiazol-7-yl)-pyrimidin-4-yl]carbonyl}piperidin-4-yl)carbamate mono(4-methylbenzenesulfonate) was considered justified based on non-clinical data which showed reduction in the vascular lesion grade and eosinophil numbers in the blood and bronchoalveolar lavage fluid.

The condition is chronically debilitating due to the inflammatory involvement of the lungs, heart, kidneys, gastrointestinal and musculoskeletal system, and life-threatening with reduced life expectancy.

The condition was estimated to be affecting less than 0.5 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 methyl-(1-{[6-{[(1S)-1-cyclopropylethyl]amino}-2-(pyrazolo[5,1-b][1,3]thiazol-7-yl)-pyrimidin-4-yl]carbonyl}piperidin-4-yl)carbamate mono(4-methylbenzenesulfonate) will be of significant benefit to those affected by the condition. The sponsor has provided in vivo non-clinical data that demonstrate that the product is expected to be more efficacious compared to the authorised treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for methyl-(1-{[6-{[(1S)-1-cyclopropylethyl]amino}-2-(pyrazolo[5,1-b][1,3]thiazol-7-yl)-pyrimidin-4-yl]carbonyl}piperidin-4-yl)carbamate mono(4-methylbenzenesulfonate), for treatment of eosinophilic granulomatosis with polyangiitis, was adopted by consensus.

2.1.7. - EMA/OD/0000150249

Treatment of autosomal dominant polycystic kidney disease

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

- Significant benefit

The sponsor was invited to further support their claim(s) for significant benefit vis a vis the authorised product tolvaptan with relevant data with the proposed product in the proposed condition autosomal dominant polycystic kidney disease (ADPKD).

In the written response, and during an oral explanation before the Committee on 7 December 2023, the sponsor's line of argumentation further stressed the putative validity of extrapolating between allopurinol and the proposed product and between gout/hyperuricemia, chronic kidney disease (CKD) and ADPKD. The sponsor stressed that from a pharmacodynamic (PD) perspective, the reliance on the proposed product as the key therapeutic moiety is supported by clinical data showing that hyperuricemia is modified to the same degree using allopurinol or the proposed product. However, the COMP considered that the PD effect on hyperuricemia of these two components cannot be extrapolated to ADPKD. Therefore, the reliance on data with allopurinol as a surrogate for the proposed product in support of the sponsors significant benefit arguments could not be accepted.

The study by Han and co-workers (Han et al., 2014) within a subgroup of 53 ADPKD hyperuricemic patients treated with xanthine oxidase inhibitors (12 of whom were given allopurinol) showed attenuation of annual eGFR decline after hyperuricemia treatment. However, the COMP pointed out that it was difficult to know if the improvement in eGFR was due to treating the hyperuricemia or the ADPKD in these patients. Possible effects on total kidney volume or renal cysts were not evaluated in this study.

The COMP also emphasised the HALT PKD trials which were randomised, double-blind, placebo-controlled, multi-centre trials and which concluded that elevated serum uric acid is not an independent risk factor for disease progression in ADPKD (Brosnahan et al., 2021). Furthermore, the latest KDIGO guideline from October 2023 was referred to by the COMP.

Overall, the COMP was not convinced that the indirect data from the sponsor could support a significant benefit of the proposed product over tolvaptan.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 7 December 2023, prior to final opinion.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000139765

Treatment of glioma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the January 2024 meeting.

2.2.2. (4R)-3-(4-fluoro-2-hydroxyphenyl)-4-methyl-4,5-dihydro-1H-pyrazole-1-carboximidamide hydrochloride - EMA/OD/0000144447

AnaMar AB; Treatment of systemic sclerosis

COMP Rapporteur: Joao Rocha

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 (4R)-3-(4-fluoro-2-hydroxyphenyl)-4-methyl-4,5-dihydro-1H-pyrazole-1-carboximidamide hydrochloride was considered justified based on non-clinical in vivo data showing a reduction in skin fibrosis and dermal thickness as well as in lung fibrosis.

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, renal crisis and cardiac failure.

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.

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 (4R)-3-(4-fluoro-2-hydroxyphenyl)-4-methyl-4,5-dihydro-1H-pyrazole-1-carboximidamide hydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate a reduction in skin fibrosis and dermal thickness which currently is not treated with authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for (4R)-3-(4-fluoro-2-hydroxyphenyl)-4-methyl-4,5-dihydro-1H-pyrazole-1-carboximidamide hydrochloride, for treatment of systemic sclerosis, was adopted by consensus.

2.2.3. - EMA/OD/0000144999

Treatment of glioma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the January 2024 meeting.

2.2.4. thiophene methylimidazole pentahydrogen - EMA/OD/0000145710

Celluminova AB; Diagnosis of glioma

COMP Rapporteur: Dinko Vitezic

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

The intention to diagnose the condition with the medicinal product containing thiophene methylimidazole pentahydrogen was considered justified based on preliminary clinical data

which supports the added benefit of identifying glioma stems cells associated with the borders of a glioma at the time of surgical resection.

The condition is life-threatening with poor 5-year survival of less than 5% for glioblastoma multiforme patients and chronically debilitating due to symptoms caused by compression by the tumour on the surrounding brain tissue including headache, anorexia, nausea, vomiting, seizures, neurological deficits, personality and cognitive impairment.

The condition was estimated to be affecting approximately 1.6 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of diagnosis of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing thiophene methylimidazole pentahydrogen will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate the additional benefit of using the sponsor's diagnostic product in identifying the limits of a glioma at the time of surgical resection in combination with Gliolan. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for thiophene methylimidazole pentahydrogen, for diagnosis of glioma, was adopted by consensus.

2.2.5. tarlatamab - EMA/OD/0000146101

Amgen Europe B.V.; Treatment of small cell lung cancer

COMP Rapporteur: Elisabeth Johanne Rook

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

The intention to treat the condition with the medicinal product containing tarlatamab was considered justified based on non-clinical data in models of the condition showing an inhibition of tumour growth, in combination with clinical data demonstrating a tumour response in patients affected by the condition and whose disease progressed after two prior lines of treatment.

The condition is chronically debilitating and life-threatening due to its rapid progression and the development of widespread metastases, with a poor 5-year overall survival.

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 tarlatamab will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in relapsed or refractory patients with small cell lung cancer who had progressed after two prior lines of treatment including atezolizumab and durvalumab, and who responded to treatment with the proposed product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for tarlatamab, for treatment of small cell lung cancer, was adopted by consensus.

2.2.6. - EMA/OD/0000149117

Treatment of cystic fibrosis

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 January 2024 meeting.

2.2.7. - EMA/OD/0000149156

Treatment of cholangiocarcinoma

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 January 2024 meeting.

2.2.8. adenine - EMA/OD/0000149689

Raremoon Consulting Esp S.L.; Treatment of epidermolysis bullosa

COMP Rapporteur: Elisabeth Johanne Rook

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 adenine was considered justified based on preliminary clinical data in patients with dystrophic epidermolysis bullosa, showing improvements in wound healing and complete wound closure as compared to placebo-vehicle control.

The condition is life-threatening and chronically debilitating due to blister formation following minor friction or trauma, resulting in multiple complications that include painful wounds, secondary infections, failure to thrive, and predisposition to the development of squamous cell carcinoma.

The condition was estimated to be affecting approximately 0.6 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 adenine will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data in epidermolysis bullosa patients which showed a shortening of the time to complete closure of the wounds treated with the proposed product, versus the authorised medicinal product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adenine, for treatment of epidermolysis bullosa, was adopted by consensus.

2.2.9. ziftomenib - EMA/OD/0000150090

MWB Consulting; Treatment of acute myeloid leukaemia

COMP Rapporteur: Karri Penttila

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

The intention to treat the condition with the medicinal product containing ziftomenib was considered justified based on non-clinical data in models of the condition supporting inhibition of tumour growth and increased survival, as well as preliminarily clinical observations reporting durable responses in relapsed/refractory patients.

The condition is life-threatening and chronically debilitating due to the consequences of bone marrow dysfunction, such as intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, and the risk of severe infections. The condition progresses rapidly and is fatal within days to weeks or a few months if left untreated.

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 ziftomenib will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data which showed durable responses in heavily pretreated patients with acute myeloid leukaemia. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for ziftomenib, for treatment of acute myeloid leukaemia, was adopted by consensus.

2.2.10. cutamesine - EMA/OD/0000152508

3R Pharma Consulting GmbH; Treatment of alpha-thalassaemia X-linked intellectual disability syndrome (due to mutations in the *ATRX* gene)

COMP Rapporteur: Enrico Costa

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of alpha-thalassaemia X-linked intellectual disability syndrome (due to mutations in the *ATRX* gene).

The Committee agreed that the condition, alpha-thalassaemia X-linked intellectual disability syndrome (due to mutations in the *ATRX* gene), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing cutamesine was considered justified based on non-clinical data in a model of the condition showing an amelioration of biomarkers of the disease, and an improvement in cognitive deficits as measured by memory-related tests.

The condition is life-threatening and chronically debilitating due to severe intellectual disability and developmental delays, haemoglobin H disease, facial dysmorphism and anomalies, skeletal and genital abnormalities, heart defects, eye anomalies, respiratory complications, renal abnormalities and gastrointestinal dysfunction.

The condition was estimated to be affecting less than 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 cutamesine, for treatment of alpha-thalassaemia X-linked intellectual disability syndrome (due to mutations in the *ATRX* gene), was adopted by consensus.

2.2.11. adeno-associated viral vector serotype 9 containing the human *MECP2* gene, an intron encoding a miRNA generating sequence, and complementary miRNA binding sites - EMA/OD/0000152994

Transcrip Ireland Limited; Treatment of Rett syndrome

COMP Rapporteur: Ingeborg Barisic

Following review of the application by the Committee, it was agreed to broaden/rename the active substance to adeno-associated viral vector serotype 9 containing the human *MECP2* gene, an intron encoding a miRNA generating sequence, and complementary miRNA binding sites.

The Committee agreed that the condition, Rett syndrome, 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 viral vector serotype 9 containing the human *MECP2* gene, an intron encoding a miRNA generating sequence, and complementary miRNA binding sites was considered justified based on non-clinical in vivo data in a valid model of the disease which showed improved survival and ameliorated RTT-like phenotypes, including mobility, gait, and breathing abnormalities, as quantified using an observational scoring system.

The condition is life-threatening and chronically debilitating due to severe neurodevelopmental delay, sleep disturbances, seizures, respiratory complications and development of arrhythmias resulting in decreased life-expectancy.

The condition was estimated to be affecting less than 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 viral vector serotype 9 containing the human *MECP2* gene, an intron encoding a miRNA generating sequence, and complementary miRNA binding sites, for treatment of Rett syndrome, was adopted by consensus.

2.2.12. motixafortide - EMA/OD/0000153654

Granzer Regulatory Consulting & Services GmbH; Treatment of patients undergoing haematopoietic stem cell transplantation

COMP Rapporteur: Evangelia Yannaki

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of patients undergoing haematopoietic stem cell transplantation.

The Committee agreed that the condition, treatment of patients undergoing haematopoietic stem cell transplantation, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing motixafortide was considered justified based on clinical data demonstrating that in a significant proportion of subjects the product was able to mobilise the optimal amount of haematopoietic stem cells in up to two apheresis sessions.

Haematopoietic stem cell transplantation is a preferred method for the treatment of a variety of haematologic conditions, including leukaemias and lymphomas. Left untreated, these conditions are life-threatening and patients suffering from one of these malignancies have little prospects for survival.

The condition was estimated to be affecting approximately 1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing motixafortide will be of significant benefit to those affected by the condition. The sponsor has provided clinical data which demonstrates that motixafortide in combination with G-CSF is more effective in mobilising relevant numbers of haematopoietic stem cells, than the authorised product G-CSF alone. The sponsor has also provided non-clinical in vivo data which suggests that motixafortide is more effective than the authorised method plerixafor in mobilising haematopoietic stem cells. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for motixafortide, for treatment of patients undergoing haematopoietic stem cell transplantation, was adopted by consensus.

2.2.13. human coagulation factor X - EMA/OD/0000153667

BPL Bioproducts Laboratory GmbH; Treatment of acquired factor X deficiency

COMP Rapporteur: Karri Penttila

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

The intention to treat the condition with the medicinal product containing human coagulation factor X was considered justified based on reported literature cases which showed haemostatic response in patients with acquired factor X deficiency.

The condition is chronically debilitating and life-threatening due to risk of bleeding including recurrent haemorrhages that can result in chronic and major haemorrhages that carry a direct vital risk.

The condition was estimated to be affecting approximately 0.6 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for human coagulation factor X, for treatment of acquired factor X deficiency, was adopted by consensus.

2.2.14. gorilla adenovirus vector expressing HPV6 and HPV11 antigens - EMA/OD/0000154030

Granzer Regulatory Consulting & Services GmbH; Treatment of recurrent respiratory papillomatosis

COMP Rapporteur: Elisabeth Johanne Rook

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

The intention to treat the condition with the medicinal product containing gorilla adenovirus vector expressing HPV6 and HPV11 antigens was considered justified based on preliminary clinical data which showed reduction on the number of surgical procedures in patients.

The condition is chronically debilitating and life-threatening due to airway obstruction, the spread of the disease and dysplastic changes leading to development of malignancies.

The condition was estimated to be affecting approximately 0.3 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 gorilla adenovirus vector expressing HPV6 and HPV11 antigens, for treatment of recurrent respiratory papillomatosis, was adopted by consensus.

2.2.15. human heparan N-sulfatase, recombinant - EMA/OD/0000154059

3R Pharma Consulting GmbH; Treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome)

COMP Rapporteur: Cécile Dop

The Committee agreed that the condition, mucopolysaccharidosis type IIIA (Sanfilippo A syndrome), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing human heparan N-sulfatase, recombinant was considered justified based on non-clinical in vivo studies in a valid model of the condition that show dose-dependent reduction of heparan sulfate levels in the brain and cerebrospinal fluid, as well as functional improvement on cognitive and behavioural endpoints.

The condition is life-threatening and chronically debilitating due to complications arising from N-sulfoglucosamine sulfohydrolase deficiency, including severe neurological symptoms, organ failure, and death in the second or third decade of life.

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.

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 human heparan N-sulfatase, recombinant, for treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome), was adopted by consensus.

2.2.16. - EMA/OD/0000154242

Treatment of ATTR 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 January 2024 meeting.

2.2.17. mitapivat sulfate - EMA/OD/0000154838

Agios Netherlands B.V.; Treatment of alpha-thalassaemia intermedia and major

COMP Rapporteur: Enrico Costa

The Committee agreed that the condition, alpha-thalassaemia intermedia and major, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing mitapivat sulfate was considered justified based on preliminary clinical data which showed an increase in haemoglobin levels and a decrease in haemolysis and erythropoietin.

The condition is chronically debilitating due to a number of problems, including delayed growth during childhood, iron overload, gallstones, cholecystitis, skeletal abnormalities, osteoporosis, and reduced fertility. Other serious types such as Bart's hydrops fetalis syndrome is fatal.

The condition was estimated to be affecting approximately 1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing mitapivat sulfate will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo and preliminary clinical data that demonstrate an increase in haemoglobin and reduction in haemolysis and erythropoietin. This is associated with a reduction in iron overload in target end organs and supports an important therapeutic effect which can be translated into a reduced need for chelating agents. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for mitapivat sulfate, for treatment of alpha-thalassaemia intermedia and major, 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 10 applications.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 12 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of gastrointestinal stromal tumours

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 immune thrombocytopenia

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. Omjjara - momelotinib dihydrochloride - EMEA/H/C/005768/0000

GlaxoSmithKline Trading Services Limited;

COMP Rapporteur: Frauke Naumann-Winter; COMP Co-Rapporteur: Karri Penttila

a) Treatment of post-polycythaemia vera myelofibrosis, EU/3/11/886, EMA/OD/0000129901

A list of issues was adopted on 9 November 2023.

An oral explanation was held on 6 December 2023.

An opinion recommending not to remove Omjjara, momelotinib dihydrochloride, EU/3/11/886 from the EC Register of Orphan Medicinal Products was adopted by majority (23 out of 28 votes). The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

The divergent positions (Brigitte Schwarzer-Daum, Tim Leest, Jana Mazelova, Elisabeth Johanne Rook, Ines Alves) were appended to this opinion.

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

b) Treatment of post-essential thrombocythaemia myelofibrosis, EU/3/11/887, EMA/OD/0000130955

A list of issues was adopted on 9 November 2023.

An oral explanation was held on 6 December 2023.

An opinion recommending not to remove Omjjara, momelotinib dihydrochloride, EU/3/11/887 from the EC Register of Orphan Medicinal Products was adopted by majority (23 out of 28 votes). The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

The divergent positions (Brigitte Schwarzer-Daum, Tim Leest, Jana Mazelova, Elisabeth Johanne Rook, Ines Alves) were appended to this opinion.

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

c) Treatment of primary myelofibrosis, EU/3/11/888, EMA/OD/0000130957

A list of issues was adopted on 9 November 2023.

An oral explanation was held on 6 December 2023.

An opinion recommending not to remove Omjjara, momelotinib dihydrochloride, EU/3/11/888 from the EC Register of Orphan Medicinal Products was adopted by majority (23 out of 28 votes). The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

The divergent positions (Brigitte Schwarzer-Daum, Tim Leest, Jana Mazelova, Elisabeth Johanne Rook, Ines Alves) were appended to this opinion.

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. Livmarli - maralixibat - EMEA/H/C/005857/II/0003/G, EU/3/13/1216, EMA/OD/0000136132

Mirum Pharmaceuticals International B.V.; Treatment of progressive familial intrahepatic cholestasis

CHMP Rapporteur: Martina Weise; The status of the procedure at CHMP was noted.

4.2.2. Casgevy – exagamglogene autotemcel - EMEA/H/C/005763

Vertex Pharmaceuticals (Ireland) Limited

COMP Rapporteur: Karri Penttila; COMP Co-Rapporteur: Enrico Costa

a) Treatment of sickle cell disease, EU/3/19/2242, EMA/OD/0000146415

An opinion recommending not to remove Casgevy, exagamglogene autotemcel, EU/3/19/2242 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 December 2023 meeting.]

b) Treatment of beta-thalassaemia intermedia and major, EU/3/19/2210, EMA/OD/0000146264

An opinion recommending not to remove Casgevy, exagamglogene autotemcel, EU/3/19/2210 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 December 2023 meeting.]

4.2.3. - sparsentan - EMEA/H/C/005783, EU/3/20/2345, EMA/OD/0000110380

Vifor France; Treatment of primary IgA nephropathy

The status of the procedure at CHMP was noted.

4.2.4. Skyclarys – omaveloxolone - EMEA/H/C/006084, EU/3/18/2037, EMA/OD/0000156841

Reata Ireland Limited; Treatment of Friedreich's ataxia

COMP Rapporteur: Gloria Palomo Carrasco; COMP Co-Rapporteur: Elisabeth PenningaAn opinion recommending not to remove Skyclarys, omaveloxolone, EU/3/18/2037 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 December 2023 meeting.]

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 6 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

5.2.1. Kaftrio – ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/WS2551/0043, EU/3/18/2116, EMA/OD/0000160021

Vertex Pharmaceuticals; Treatment of cystic fibrosis

CHMP Rapporteur: Peter Mol; CHMP Co-Rapporteur: Finbarr Leacy

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

None

7.1.2. Vote by proxy

Dinko Vitezic gave a proxy to Ingeborg Barisic to vote on behalf of Dinko Vitezic during the entire meeting.

Eva Malikova gave a proxy to Michel Hoffmann to vote on behalf of Eva Malikova during the entire meeting.

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

Julian Isla gave a proxy to Jana Mazelova to vote on behalf of Julian Isla during part of the meeting.

Joao Rocha gave a proxy to Enrico Costa to vote on behalf of Joao Rocha during part of the meeting.

Gloria Maria Palomo Carrasco gave a proxy to Cecile Dop to vote on behalf of Gloria Maria Palomo Carrasco during part of the meeting.

Bozenna Dembowska-Baginska gave a proxy to Vallo Tillmann to vote on behalf of Bozenna Dembowska-Baginska during part of the meeting.

7.1.3. Strategic Review & Learning meetings

None

7.1.4. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 1 December 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)

The COMP was informed about the PCWP-HCPWP and all eligible organisations meeting held on 14-15 November 2023.

7.3.2. Upcoming Innovation Task Force (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)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. Therapeutic Goods Administration (TGA), Australia

None

7.5.4. Health Canada

None

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

None

7.7. COMP work plan

None

7.8. Planning and reporting

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

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

7.8.2. Overview of orphan marketing authorisations/applications

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

8. Any other business

8.1. Update on the patient experience data - major contribution to patient care project

The COMP noted the presentation on the major contribution to patient care (MCPC) project. The current challenges and benefits of the tool were discussed. A pilot will run for 3 months and if the project is considered successful further implementation in a broader level will be explored.

8.2. EMA business Pipeline activity

Documents were tabled for information.

9. List of participants

including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 05-07 December 2023 COMP meeting, which was held in-person.

An asterisk (*) after the role, in the second column, signals that the member / alternate attended remotely. Additional experts participated in (part of) the meeting, either in-person or remotely.

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	
Ioannis Kkolos	Member	Cyprus	No interests declared	
Jana Mazelova	Member	Czechia	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	
Evangelia Yannaki	Member	Greece	No restrictions applicable to this meeting	
Zsofia Gyulai	Member	Hungary	No interests declared	
Enrico Costa	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No restrictions applicable to this meeting	
Michel Hoffmann	Member	Luxembourg	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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-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	
Judit Molnar	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Maria Cavaller Bellaubi	Expert	Patients' Organisation Representative	No restrictions applicable to this meeting	
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.

For a list of acronyms and abbreviations, see:

Abbreviations used in EMA scientific committees & CMD documents and in relation to EMA's regulatory activities

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