13 July 2023
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Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 13-15 June 2023

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

1.1. Welcome and declarations of interest of members and experts

The Chair opened the meeting by welcoming all participants. 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 and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

Participants were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda for 13-15 June 2023 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 15-17 May 2023 were adopted with amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. rhizobium rhizogenes, lipopolysaccharide - EMA/OD/0000130058

Crazy Science & Business S.L.; Treatment of congenital diaphragmatic hernia (CDH)

COMP Rapporteur: Jana Mazelova

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

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of congenital diaphragmatic hernia, the sponsor should further elaborate on:

- the relevance of the non-clinical model used for the treatment of congenital diaphragmatic hernia, and the interpretation of the results obtained in the experiments,
- the methodology used in the non-clinical studies as well as the results from these studies and its relevance for the development of the product in the condition.

In the written response, and during an oral explanation before the Committee on 13 June 2023, the sponsor provided greater detail regarding the validity of the two models used to study the effects of the product in the condition. Extensive discussions were held regarding the methodology and results of the first non-clinical study which used the Nitrofen-induced non-clinical model . Of particular importance was the timing of the administration of the product to the study subjects and its meaningfulness and extrapolability to the human setting. The COMP was of the opinion that the methodology and time of the delivery of the product was not optimal and therefore the data could not be used to establish medical plausibility. It was, however, noted that the effect translated into improvement in lung development, characterised by an increase in number of respiratory bronchioles, alveolar ducts and alveoli.

Methodology and data from the second study were further elaborated. This study was conducted in the Wilm's tumour 1 conditional genetically deficient CDH non-clinical model. In all three treated mutants, the pleural cavities were completely closed, in stark contrast to the deficient knock-out controls. However, the diaphragm did not appear normal; it was thicker, more irregular, and exhibited less organised musculature. Despite these abnormalities, the diaphragm remained structurally intact. This also translated into improvement in lung development, characterised by an increase in number of respiratory bronchioles, alveolar ducts and alveoli.

The COMP concluded that the genetic model study was sufficient to support the medical plausibility for the purpose of an initial orphan designation and therefore recommended to grant the orphan designation.

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

The intention to treat the condition with the medicinal product containing rhizobium rhizogenes, lipopolysaccharide was considered justified based on non-clinical in vivo data showing an improvement in closure of the hernia as well as an increase in pulmonary bronchioles and alveoli.

The condition is life-threatening and chronically debilitating due to persistent pulmonary hypertension of the newborn and cardiac dysfunction. The overall survival has been reported as low as 50% in infants who are in need of extracorporeal membrane oxygenation.

The condition was estimated to be affecting approximately 2.3 in 10,000 persons in the European Union, at the time the application was made.

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 rhizobium rhizogenes, lipopolysaccharide, for treatment of congenital diaphragmatic hernia, was adopted by consensus.

2.1.2. bortezomib - EMA/OD/0000116655

Accord Healthcare S.L.; Treatment of patients with light chain (AL) amyloidosis

COMP Rapporteur: Enrico Costa

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 asked to further discuss the significant benefit of bortezomib over daratumumab in its approved indication: "Darzalex (daratumumab) is indicated in combination with cyclophosphamide, bortezomib and dexamethasone for the treatment of adult patients with newly diagnosed systemic AL amyloidosis".

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

In the written response, and during an oral explanation before the Committee on 13 June 2023, it was noted that daratumumab is authorised for use for the exact same patient population for which the sponsor seeks to have bortezomib designated as an orphan medicinal product.

For completeness, the authorised indication of daratumumab, as reflected in its Summary of Product Characteristics, states the following:

"Darzalex is indicated in combination with cyclophosphamide, bortezomib and dexamethasone for the treatment of adult patients with newly diagnosed systemic AL amyloidosis".

The sponsor seeks the designation of bortezomib in the following condition "Treatment of AL amyloidosis".

There is a full overlap between the authorised product daratumumab (Darzalex) and the candidate orphan product in terms of targeted patient populations. The sponsor has not claimed that the candidate orphan product would be intended for a subset of the patient population in AL amyloidosis not yet covered by the authorised use of daratumumab (Darzalex).

Further to the above, for bortezomib to be designated as an orphan medicinal product, the sponsor would need to establish the existence (of an assumption) of significant benefit of bortezomib over daratumumab (Darzalex).

To that effect, and in response to the question of the COMP, the sponsor responded in writing stating that a direct comparison to daratumumab would not be feasible (ethically or scientifically) as the two products should be used in combination and not separately.

The sponsor also argued for the positive benefits of bringing bortezomib on-label for AL amyloidosis. They argued that the existence of a continuity gap between bortezomib's licensed indications and current treatment recommendations by scientific societies represents a continuous conundrum to clinicians who wish to provide the best possible care to their patients but are forced to continue using bortezomib off-label. According to the sponsor, the absence of alignment between current guidelines and treatment algorithms creates inequalities in accessing the standard of care across the European territory as it

transfers the decision to approve bortezomib's use to institutions and local committees, which in turn look at regulatory authorities for guidance.

The sponsor stated that the pursued orphan drug designation intends to provide a robust foundation to existing clinical practice and would represent a step forward towards a new approved indication. Accordingly, the submission is to be considered an attempt at harmonising current practice and normalising access to an established therapy, and not to displace daratumumab; therefore, it is the sponsor's understanding that a direct comparison against daratumumab will be difficult if not impossible to undertake, will not provide any clinically meaningful data, and ultimately be detrimental to patients.

In this respect, COMP would like to note that there is no requirement for a medicinal product to be authorised as orphan in order to have an on-label therapeutic use. As a matter of fact, for a product to be designated (and subsequently authorised) as orphan in the presence of products already authorised for the same patient population, the (strict) criteria of significant benefit need to be met.

During the oral explanation, some scientific aspects were also discussed with the sponsor:

The COMP noted that the results presented by the sponsor on the Kimmich CR et al., 2020, study were not suitable to conclude on a better effect of Dara+bor+dex vs Dara+dex. The sponsor acknowledged this and explained that the trial was not planned to show a difference but was instead intended as a hypothesis generating trial. Other studies submitted show simply the benefit of using bortezomib in AL amyloidosis patients.

However, none of the submitted studies seek to establish, or may be relied upon for establishing, (any assumption of) significant benefit of bortezomib over daratumumab.

The sponsor's statement that "studies of daratumumab as monotherapy or in combination consistently show higher and deeper rates of haematologic response for combination treatment" was not supported by the COMP.

The published trials and retrospective series indicated that daratumumab is highly effective also in relapsed/refractory patients with AL amyloidosis, with apparently no remarkable differences between single-agent and combination therapies (Palladini et al. Cells, 2021).

The sponsor was not able to establish (the assumption of) a significant benefit of bortezomib over the one authorised product daratumumab in its approved indication, i.e. in combination with cyclophosphamide, bortezomib and dexamethasone for the treatment of adult patients with newly diagnosed systemic AL amyloidosis.

Without prejudice to the above and only for completeness, it bears noting that the sponsor did not claim (and, in any event, did not establish) the existence of an assumption of significant benefit of bortezomib over daratumumab used as a monotherapy.

The intention to treat the condition with the medicinal product containing bortezomib was considered justified based on published clinical data showing haematological responses in patients with the condition treated with bortezomib in combination with other products.

The condition is life-threatening and chronically debilitating due to the accumulation of fibril deposits which disrupt normal tissue structure and function, notably in the heart, kidneys, liver, peripheral nervous system, gastrointestinal tract, and soft tissues.

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 have been authorised in the European Union, the sponsor has not provided sufficient justification for the assumption that the medicinal product containing bortezomib will be of significant benefit to those affected by the condition. The sponsor was not able to show a significant benefit of bortezomib over the one authorised product daratumumab in its approved indication, i.e. in combination with cyclophosphamide, bortezomib and dexamethasone for the treatment of adult patients with newly diagnosed systemic AL amyloidosis.

A negative opinion for bortezomib, for treatment of patients with light chain amyloidosis, was adopted by consensus. The sponsor will have 90 days to appeal from the COMP decision.

2.1.3. vactosertib - EMA/OD/0000119470

Sirius Regulatory Consulting Eu Limited; Treatment of osteosarcoma

COMP Rapporteur: Frauke Naumann-Winter

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

- Number of people affected

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 was asked to justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition and the applicability for the whole of the EU/EEA. The sponsor was requested to describe and justify the methodology used for the prevalence calculation and also provide a prevalence calculation based on incidence times duration of disease.

- Significant benefit

The sponsor was asked to further discuss and substantiate the significant benefit over the approved products, including the future positioning of the product in the armamentarium of the treatments.

In the written response, and during an oral explanation before the Committee on 13 June 2023, the sponsor had done an additional literature search but not identified any new articles. According to a revised calculation based on the formula P=I*D, the data the max incidence was estimated to 0.12, resulting in a prevalence of 1.2 in 10,000 which is lower than the 1.6 in 10,000 proposed prevalence derived from the registries. The COMP acknowledged the calculation and proposal made by the sponsor but considered that a prevalence of less than 2 could be adopted, based on the NORDCAN data and the number is not far from what the sponsor proposed.

The sponsor proposed that the target patient population for vactosertib is in the adjuvant- and metastatic or recurrent disease setting, where available treatments have no or limited efficacy. During the oral explanation the non-clinical models and the results were further discussed. The models were considered supportive for the advanced osteosarcoma setting and the ability of vactosertib to reduce metastatic cancer burden, a clinical setting in which patients are highly treatment resistant, was considered justified by the COMP. The sponsor

also explained more in detail the results in the one patient who had been treated with the product. Even though this is insufficient, it was considered that the survival of this patient compared favourably with the natural history and literature data of patients with metastatic osteosarcoma.

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

The intention to treat the condition with the medicinal product containing vactosertib was considered justified based on non-clinical data in a valid model of the condition showing improved survival, regression of engrafted tumours and a reduction in lung metastases.

The condition is chronically debilitating in particular due to the potential of limb amputation and life-threatening with a less than a 20% long-term survival rate following recurrence.

The condition was estimated to be affecting less than 2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing vactosertib will be of significant benefit to those affected by the condition. The sponsor has provided strong non-clinical evidence of the ability of vactosertib to reduce metastatic cancer burden, a clinical setting in which patients are highly treatment resistant and supported the clinical relevance by clinical data after failure of standard of care. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for vactosertib, for treatment of osteosarcoma, was adopted by consensus.

2.1.4. omadacycline - EMA/OD/0000131821

Paratek Ireland Limited; Treatment of nontuberculous mycobacterial pulmonary disease (NTM-PD)

COMP Rapporteur: Eva Malikova

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

- Significant benefit

The arguments on significant benefit were based on a major contribution to patient care 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 study and any additional clinical data to justify the assumption of significant benefit either in combination with amikacin or in patients resistant to amikacin for the proposed orphan condition.

In the written response, the sponsor noted that amikacin is only authorised for use in non-tuberculous mycobacterial (NTM) lung infections caused by *Mycobacterium avium* Complex (MAC) in adults with limited treatment option. It is argued that there are no authorised antibiotics for *Mycobacterium abscessus*. In a retrospective study, sustained sputum culture conversion with omadacycline 300 mg/day-based combinations was achieved in 8 patients

out of 10 with resistant *M. abscessus* versus 1 out of 9 (p=0.006), versus comparators, respectively). This data was also supplemented with non-clinical in vivo data showing improved efficacy with the combination of omadacycline with linezolide, cefoxitin and azithromycin on the colony forming units (CFU). The COMP accepted the new justification and data that the sponsor provided in the written response and cancelled the oral explanation.

Following review of the application by the Committee, it was agreed to broaden/rename the indication to 'treatment of nontuberculous mycobacterial lung disease'.

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

The intention to treat the condition with the medicinal product containing omadacycline was considered justified based on non-clinical in vivo data showing a reduction in *Mycobacterium abscessus*.

The condition is life-threatening and chronically debilitating due to progressive lung damage in severe forms that respond poorly to treatment. Five-year mortality rates have been reported up to 40%.

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.

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 omadacycline will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data and preliminary clinical data demonstrating that omadacycline reduces pulmonary bacterial load of *Mycobacterium abscessus*, in patients who are resistant to prior treatment and for which there are no authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for omadacycline, for treatment of nontuberculous mycobacterial lung disease, was adopted by consensus.

2.1.5. - EMA/OD/0000125383

Treatment of cryopyrin associated periodic syndromes

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 26 May 2023, prior to responding to the list of issues.

2.1.6. - EMA/OD/0000124780

Treatment of pre-eclampsia

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 30 May 2023, prior to responding to the list of issues.

2.1.7. lusvertikimab - EMA/OD/0000130960

OSE Immunotherapeutics; Treatment of acute lymphoblastic leukaemia (ALL)

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 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 provide an adequate justification of a clinically relevant advantage of the proposed product over all approved products in patients with relapsed ALL.

In the written response, the sponsor presented one case of a patient, with T-cell ALL (T-ALL) refractory to nelarabine, showing a reduction in the malignant cell count. They highlighted that while they did have an on-going trial which included patients with both forms of ALL they had not been able to extract the additional clinical data in the short time given to answer the question.

The COMP also discussed the merits of the non-clinical in vivo xenograft model (PDX model) of the condition. Within this study the sponsor had used T-ALL cells that were resistant to treatment with nelarabine which were derived from patients who were resistant to prior lines of therapy. The effect of the sponsor's product on these T-ALL cells showed a reduction in cell count .

The COMP considered that the non-clinical in vivo data showing an effect in the reduction of nelarabine resistant T-ALL cells and the preliminary single patient showing a similar effect in cell count supported the significant benefit for the purpose of an orphan designation. The COMP cancelled the oral explanation.

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

The intention to treat the condition with the medicinal product containing lusvertikimab was considered justified based on an improvement in survival in the non-clinical in vivo setting either when used as a monotherapy or in combination with standard of care.

The condition is chronically debilitating and life-threatening depending on the response to treatment, with acute leukaemic forms being fatal in a few weeks if left untreated. Symptoms include persistent fever, infections, anaemia, fatigue, breathlessness, bone and joint pain. The invasion of tumour cells in the bloodstream, the bone marrow and/or the lymphatic system result in lack of normal blood cells, bone marrow failure, and organ damage.

The condition was estimated to be affecting approximately 1.7 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 lusvertikimab will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate efficacy

in models of T-ALL which were relapsed or refractory to authorised therapies. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for lusvertikimab, for treatment of acute lymphoblastic leukaemia, was adopted by consensus.

2.1.8. pemafibrate - EMA/OD/0000124931

Kowa Pharmaceutical Europe GmbH; Treatment of primary biliary cholangitis (PBC)

COMP Rapporteur: Joao Rocha

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 presented data regarding pemafibrate being potentially more potent than other fibrates. However, the significant benefit of added effect to obeticholic acid was not directly established for pemafibrate but for bezafibrate and fenofibrate. The sponsor was asked to clarify whether the significant benefit of pemafibrate is in combination with obeticholic acid and not when in comparison to obeticholic acid.

In the written response, the sponsor provided additional evidence based on a publication from Soret et al., 2021, investigated whether obeticholic (OCA) and fibrates (bezafibrate or fenofibrate), administered together in combination with ursodeoxycholic acid (UDCA), have additive beneficial effects in patients with difficult-to-treat PBC, i.e., who presented with an inadequate response to UDCA. 58 PBC patients were treated for ≥3 months (mean duration 11 months). Half of the patients received OCA as second line and fibrates as third-line therapy (Group OCA-Fibrate), while the other half had the inverse therapeutic sequence (Group Fibrate-OCA). Compared to dual therapy, the overall gain in alkaline phosphatase (ALP) reduction associated with triple therapy was 22% per year ($p < 0.001$). When assessed by group, the reduction in ALP was higher in the OCA-fibrate group (42% per year, $p< 0.001$), than in fibrate-OCA group (11% per year, $p= 0.1$). Compared to dual therapy, triple therapy on the entire population was also associated with a significant reduction gain in total bilirubin (12% per year; $p<0.01$). Particularly when the fibrates were added to OCA and UDCA therapy (Group OCA-Fibrate), the fibrates led to a significant improvement of pruritus, mirroring the known beneficial effect of fibrates on PBC-associated pruritus in combination with UDCA only.

Based on the above the COMP concluded that a significant benefit is justified and supported when pemafibrate is combined with obeticholic acid. Therefore, the COMP cancelled the oral explanation.

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

The intention to treat the condition with the medicinal product containing pemafibrate was considered justified based on preliminary clinical data which showed a reduction in alkaline phosphatase and total bilirubin in patients with primary biliary cholangitis.

The condition is chronically debilitating due to pruritus, fatigue, hyperlipidaemia, hypothyroidism, deficiency of fat-soluble vitamins and osteopenia and life-threatening due

to progressive hepatic dysfunction, with development of portal hypertension and hepatic failure, and the increased risk of developing hepatocellular carcinoma.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing pemafibrate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed a reduction in alkaline phosphatase and total bilirubin in patients with primary biliary cholangitis who did not respond to authorised medicinal products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for pemafibrate, for treatment of primary biliary cholangitis, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000077804

Treatment of non-traumatic spontaneous intracerebral haemorrhage

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

2.2.2. - EMA/OD/0000101423

Treatment of solid organ transplant

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

2.2.3. - EMA/OD/0000126381

Treatment in allogeneic haematopoietic 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 July 2023 meeting.

[Post-meeting note: The COMP adopted the list of questions by written procedure following its June 2023 meeting.]

2.2.4. humanised IgG1 monoclonal antibody against muscle specific kinase - EMA/OD/0000126406

Argenx; Treatment of congenital myasthenic syndromes

COMP Rapporteur: Elisabeth Penninga

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

The intention to treat the condition with the medicinal product containing humanised IgG1 monoclonal antibody against muscle specific kinase was considered justified based on non-

clinical data in a model of the condition showing a positive effect on survival, and the rescue of functional outcomes after disease relapse.

The condition is life-threatening and chronically debilitating due to muscle weakness which affects primarily respiratory function that can result in nocturnal or continual hypoventilation, apnoea, stridor, repeated respiratory crises, or respiratory failure. Mobility function is also affected resulting in significant motor delay.

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 humanised IgG1 monoclonal antibody against muscle specific kinase, for treatment of congenital myasthenic syndromes, was adopted by consensus.

2.2.5. cannabidiol - EMA/OD/0000129401

Universitat Autònoma De Barcelona; Treatment of Leigh syndrome

COMP Rapporteur: Elisabeth Penninga

The Committee agreed that the condition, Leigh syndrome, 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 non-clinical data in a model of the condition showing the delay in the appearance of impaired motor skills and neurological decline, the improvement in breathing abnormalities, and the increase in survival.

The condition is chronically debilitating due to neurological deficits, psychomotor delay, dysmorphic features, cardiac, renal and metabolic dysfunction, and life-threatening with most patients dying in early childhood.

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 cannabidiol, for treatment of Leigh syndrome, was adopted by consensus.

2.2.6. - EMA/OD/0000131231

Treatment of malaria

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

2.2.7. ilginatinib maleate - EMA/OD/0000131315

Syneos Health Netherlands B.V.; Treatment of myelofibrosis

COMP Rapporteur: Karri Penttila

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

The intention to treat the condition with the medicinal product containing ilginatinib maleate was considered justified based on preliminary clinical data showing reduction in spleen volume and total symptom score in affected patients.

The condition is chronically debilitating and life-threatening due to anaemia, splenomegaly, extramedullary haematopoiesis, constitutional symptoms such as fatigue, night sweats and fever, cachexia and leukaemic progression.

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.

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 ilginatinib maleate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data suggesting a positive trend in efficacy in patients intolerant or refractory to currently authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for ilginatinib maleate, for treatment of myelofibrosis, was adopted by consensus.

2.2.8. - EMA/OD/0000131435

Treatment of gastro-entero-pancreatic neuroendocrine tumours

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

2.2.9. ulviprubart - EMA/OD/0000133388

PHARA; Treatment of inclusion body myositis

COMP Rapporteur: Michel Hoffmann

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

The intention to treat the condition with the medicinal product containing ulviprubart was considered justified based on non-clinical in vivo data and preliminary clinical data in patients with the condition demonstrating significant reductions in the pathogenic cell population of cytotoxic T-cells expressing killer cell lectin-like receptor G1 and a possible trend towards improvement in functional parameters.

The condition is chronically debilitating and life-threatening due to the development of progressive weakness and atrophy of the distal and proximal muscles leading to disability, falls, and the development of dysphagia which can result in severe respiratory complications.

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 ulviprubart, for treatment of inclusion body myositis, was adopted by consensus.

2.2.10. zedenoleucel - EMA/OD/0000133659

Scendea (NL) B.V.; 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 zedenoleucel was considered justified based on preliminarily clinical data reporting complete responses in patients with acute myeloid leukaemia who had haematopoietic stem cell transplantation and were relapsed/refractory or at high risk for relapse.

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 zedenoleucel will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data which showed responses in patients with acute myeloid leukaemia who had haematopoietic stem cell transplantation and were relapsed/refractory or at high risk for relapse and for whom no authorised treatments exist. The Committee considered that this constitutes a clinically relevant advantage.

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

2.2.11. - EMA/OD/0000134159

Treatment of tuberculosis

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

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 20 June 2023.]

2.2.12. paclitaxel obaluronate - EMA/OD/0000134174

Fidia Farmaceutici S.p.A.; Treatment of malignant mesothelioma

COMP Rapporteur: Bozenna Dembowska-Baginska

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

The intention to treat the condition with the medicinal product containing paclitaxel obaluronate was considered justified based on in vivo non-clinical data which showed reduced tumour volume in valid models of the condition.

The condition is life-threatening due to the invasion of the pleura leading to pleural effusions, dyspnoea and malignant ascites. Patients with pleural mesothelioma usually die due to increasing tumour bulk that gradually fills the hemithorax causing progressive respiratory insufficiency, pneumonia, or myocardial dysfunction with arrhythmias.

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.

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 paclitaxel obaluronate will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data showing higher anti-tumour effects compared to authorised medicinal products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for paclitaxel obaluronate, for treatment of malignant mesothelioma, was adopted by consensus.

2.2.13. vonafexor - EMA/OD/0000134246

Enyo Pharma; Treatment of Alport syndrome

COMP Rapporteur: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing vonafexor was considered justified based on non-clinical data in a relevant model of the condition showing reduced inflammation, decreased renal fibrosis, and tubular and glomerular lesions.

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

The condition was estimated to be affecting less than 2 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for vonafexor, for treatment of Alport syndrome, was adopted by consensus.

2.2.14. - EMA/OD/0000134260

Treatment of amyotrophic lateral sclerosis (ALS)

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

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 22 June 2023.]

2.2.15. chimeric human-murine IgG1 kappa monoclonal antibody against TNF alfa - EMA/OD/0000134297

FGK Representative Service GmbH; Treatment of sarcoidosis

COMP Rapporteur: Joao Rocha

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

The intention to treat the condition with the medicinal product containing chimeric human-murine IgG1 kappa monoclonal antibody against TNF alfa was considered justified based on published clinical data with TNF alf inhibitors showing an improvement in forced vital capacity.

The condition is life-threatening and chronically debilitating due to progressive tissue damage from active inflammation. Common organs affected are the lungs, skin, eyes, cardiovascular and peripheral nervous system. Involvement of these diverse organ systems can lead to marked reduction in functional capacity and quality of life. Mortality is increased due mainly to pulmonary and cardiovascular failure.

The condition was estimated to be affecting approximately 3.8 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 human-murine IgG1 kappa monoclonal antibody against TNF alfa will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical that demonstrate an improvement in forced vital capacity and a reduction in the decline of lung function in patients who are corticosteroid resistant. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for chimeric human-murine IgG1 kappa monoclonal antibody against TNF alfa, for treatment of sarcoidosis, was adopted by consensus.

2.2.16. - EMA/OD/0000134554

Treatment of neurofibromatosis type 1 (NF1)

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

2.2.17. nomacopan - EMA/OD/0000134584

Akari Malta Limited; Treatment in haematopoietic stem cell transplantation

COMP Rapporteur: Karri Penttila

The Committee agreed that the condition, treatment in 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 nomacopan was considered justified based on clinical data in patients with the condition showing the inhibitory effect on terminal complement activation and a positive clinical effect in some of the clinical signs and symptoms associated with the condition.

The condition is life-threatening and chronically debilitating due to susceptibility to severe infections and complications such as graft-versus-host disease and thrombotic microangiopathy.

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 nomacopan will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in patients receiving allogenic haematopoietic stem cell transplantation and suffering from haematopoietic stem cell transplantation-associated thrombotic microangiopathy that demonstrate that nomacopan as add-on to standard of care could translate into a positive effect in symptom amelioration. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for nomacopan, for treatment in haematopoietic stem cell transplantation, was adopted by consensus.

2.2.18. relacorilant - EMA/OD/0000134682

Granzer Regulatory Consulting & Services GmbH; Treatment of ovarian cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

The intention to treat the condition with the medicinal product containing relacorilant was considered justified based on preliminary clinical data suggesting a positive effect in progression free survival and overall survival in patients with relapsed disease.

The condition is chronically debilitating due to pain, weight loss, ascites and vaginal bleeding, and life-threatening with reduced life expectancy.

The condition was estimated to be affecting approximately 4.9 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing relacorilant will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data demonstrating improved efficacy when the product was added to current standard of care therapy and preliminary clinical data suggesting a positive effect in progression free survival and overall survival in heavily pre-treated patients, including those who progressed after current standard of care therapy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for relacorilant, for treatment of ovarian cancer, was adopted by consensus.

2.2.19. messenger ribonucleic acid coding for coiled-coil domain-containing protein 40 - EMA/OD/0000135073

Ethris GmbH; Treatment of primary ciliary dyskinesia

COMP Rapporteur: Gloria Maria Palomo Carrasco

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

The intention to treat the condition with the medicinal product containing messenger ribonucleic acid coding for coiled-coil domain-containing protein 40 was considered justified based on non-clinical data showing an improvement in ciliary function.

The condition is chronically debilitating due to infertility in men, hearing loss, congenital heart disease, and recurrent and chronic infections of the upper and lower respiratory tracts leading to impaired lung function and respiratory failure.

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 messenger ribonucleic acid coding for coiled-coil domain-containing protein 40, for treatment of primary ciliary dyskinesia, was adopted by consensus.

2.2.20. taldefgrobep alfa - EMA/OD/0000135225

Biohaven Bioscience Ireland Limited; Treatment of spinal muscular atrophy

COMP Rapporteur: Robert Nistico

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

The intention to treat the condition with the medicinal product containing taldefgrobep alfa was considered justified based on non-clinical in vivo data using a valid model of the condition showing improvement in gastrocnemius muscle mass and function.

The condition is life-threatening due to respiratory failure and chronically debilitating due to muscle wasting, weakness, failure to thrive, and orthopaedic complications.

The condition was estimated to be affecting approximately 0.2 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 taldefgrobep alfa 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 muscle function, mass and fibres following the use in combination with a murine upregulator of SMN-C1 which mimics authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for aldefgrobep alfa, for treatment of spinal muscular atrophy, was adopted by consensus.

2.2.21. tarperprumig - EMA/OD/0000135270

Alexion Europe; Treatment of sickle cell disease

COMP Rapporteur: Enrico Costa

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

The intention to treat the condition with the medicinal product containing tarperprumig was considered justified based on non-clinical in vivo data in a valid model of the condition which showed a decrease in intravascular haemolysis and a reduction in vaso-occlusion at the level of blood vessels in vital organs.

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

The condition was estimated to be affecting approximately 2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing tarperprumig will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate that the product simultaneously improves several signs of the condition (vaso-occlusion and haemolysis) which cannot be expected from the currently authorised (single) medicinal products. The Committee considered that this could constitute a clinically relevant advantage.

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

2.2.22. - EMA/OD/0000135309

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 July 2023 meeting.

2.2.23. - EMA/OD/0000135389

Treatment of amyotrophic lateral sclerosis

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

2.2.24. allogeneic peripheral blood-derived haematopoietic stem and progenitor cells, regulatory T cells and conventional T cells - EMA/OD/0000135426

Phortas GmbH; Treatment in haematopoietic stem cell transplantation

COMP Rapporteur: Tim Leest

The Committee agreed that the condition, treatment in 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 allogeneic peripheral blood-derived haematopoietic stem and progenitor cells, regulatory T cells and conventional T cells was considered justified based on clinical data in patients receiving allogenic haematopoietic stem cell transplantation suggesting a positive trend in graft-versus-host disease-free and relapse-free survival, and in overall survival, when compared to matched historic control data.

The condition is life-threatening and chronically debilitating due to susceptibility to severe infections and complications such as graft-versus-host disease.

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 allogeneic peripheral blood-derived haematopoietic stem and progenitor cells, regulatory T cells and conventional T cells will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in patients receiving allogenic haematopoietic stem cell transplantation (HSCT) that demonstrate that the use of proposed product compares favourably with regards to overall survival vs matched historic control data (unmanipulated HSCT). The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for allogeneic peripheral blood-derived haematopoietic stem and progenitor cells, regulatory T cells and conventional T cells, for treatment in haematopoietic stem cell transplantation, was adopted by consensus.

2.2.25. rituximab - EMA/OD/0000135452

4p-Pharma; Treatment of primary membranous nephropathy

COMP Rapporteur: Elisabeth Johanne Rook

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

The intention to treat the condition with the medicinal product containing rituximab was considered justified based on bibliographical clinical data showing a reduction of proteinuria.

The condition is chronically debilitating due to chronic proteinuria or nephrotic syndrome, with symptoms of oedema, fatigue, hypertension, and an increased risk of infections and thrombosis. A third of patients progress to end-stage renal disease, which is life-threatening, and will require dialysis or a kidney transplantation.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing rituximab will be of significant benefit to those affected by the

condition. The sponsor has provided bibliographical clinical data that demonstrate that the treatment of corticosteroid resistant patients with rituximab was more effective than cyclosporine in the reduction of proteinuria, at long term follow-up after 24 months. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for rituximab, for treatment of primary membranous nephropathy, 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 21 applications.

2.7. Evaluation on-going

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

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of Duchenne muscular dystrophy

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 hypoparathyroidism

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

[Post-meeting note: The COMP adopted the proposed answer by written procedure following its June meeting.]

3.1.3. -

Treatment of sickle cell disease

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

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

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

None

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

4.2.1. - talquetamab - EMEA/H/C/005864/0000, EU/3/21/2486, EMA/OD/0000126657

Accelerated assessment

Janssen - Cilag International; Treatment of multiple myeloma

The status of the procedure at CHMP was noted.

4.2.2. - cedazuridine, decitabine - EMEA/H/C/005823/0000, EU/3/21/2548, EMA/OD/0000141337

Otsuka Pharmaceutical Netherlands B.V.; Treatment of acute myeloid leukaemia

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

[Post-meeting note: The sponsor formally withdrew the orphan designation on 28 June 2023.]

4.2.3. Bylvay - odevixibat - EMEA/H/C/004691/II/0011, EU/3/12/1040, EMA/OD/0000123138

Albireo AB; Treatment of Alagille syndrome

CHMP Rapporteur: Johann Lodewijk Hillege

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

4.2.4. - tislelizumab - EMEA/H/C/005919/0000, EU/3/20/2357, EMA/OD/0000129253

Novartis Europharm Limited; Treatment of oesophageal cancer

The status of the procedure at CHMP was noted.

4.2.5. - epcoritamab - EMEA/H/C/005985/0000, EU/3/22/2581, EMA/OD/0000104478

Abbvie Deutschland GmbH & Co. KG; Treatment of diffuse large B-cell lymphoma

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

4.3. Appeal

4.3.1. Jaypirca - pirtobrutinib - EMEA/H/C/005863, EU/3/21/2450,

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

The COMP noted the intent to appeal from the applicant. The appeal rapporteurs were appointed.

4.4. On-going procedures

COMP co-ordinators were appointed for 3 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. Prevymis – letermovir - EMEA/H/C/004536/II/0033/G, EU/3/11/849, EMA/OD/0000133054

Merck Sharp & Dohme B.V.; Prevention of cytomegalovirus disease in patients with impaired cell-mediated immunity deemed at risk

CHMP Rapporteur: Filip Josephson; CHMP Co-Rapporteur: Aaron Sosa Mejia

The status of the procedure at CHMP was noted.

5.3. Appeal

None

5.4. On-going procedures

None

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

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the COMP

7.1.1. COMP membership

None

7.1.2. Vote by proxy

Jana Mazelova gave a proxy to Cecile Dop to vote on behalf of Jana Mazelova during part of the meeting.

Lyubina Todorova gave a proxy to Elisabeth Johanne Rook to vote on behalf of Lyubina Todorova during the entire duration of meeting.

Dinko Vitezic gave a proxy to Enrico Costa to vote on behalf of Dinko Vitezic during the entire duration of meeting.

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

Brigitte Schwarzer-Daum gave a proxy to Frauke Naumann-Winter to vote on behalf of Brigitte Schwarzer-Daum 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 9 June 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)

None

7.3.2. Upcoming ITF meetings

The COMP noted the upcoming ITF meetings.

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

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. Discussion on Orphan Maintenance Assessment Reports (OMARs)

COMP discussed and agreed to restructure the positive OMARs slightly and not rewrite the document after the oral explanation but to include the information about the question in the running text and the conclusion of the oral explanation subsequently.

8.2. EMA Business Pipeline activity and Horizon scanning

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 13-15 June 2023 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Violeta Stoyanova-Beninska	Chair	Netherlands	No interests declared	
Armando Magrelli	Vice-Chair	Expert recommended by EMA	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	No restrictions applicable to this meeting	
Tim Leest	Member	Belgium	No interests declared	
Elli Loizidou	Member	Cyprus	No interests declared	
Jana Mazelova	Member	Czechia	No interests declared	
Elisabeth Penninga	Member	Denmark	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Ruta Mameniskiene	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-Baginska	Member	Poland	No participation in discussion, final deliberations and voting on:	2.2.25. rituximab - EMA/OD/0000135452 4p-Pharma
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	Expert - via WebEx*	Expert	No restrictions applicable to this meeting	
Maria Cavaller Bellaubi	Expert - via WebEx*	Patients' Organisation Representative	No restrictions applicable to this meeting	
Johann Lodewijk Hillege	Member (CHMP member) – via WebEx*	Netherlands	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/