05 December 2024
EMA/COMP/545264/2024
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 05-07 November 2024

Chair: Tim Leest – Vice-Chair: Frauke Naumann-Winter

Health and safety information

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).

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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 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 meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions, as included in the pre-meeting list of participants and restrictions.

Participants were asked to declare any changes, omissions or errors to their declared interests 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 Chair welcomed the new member to the Committee.

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 November 2024 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 08-10 October 2024 were adopted with no amendments and will be published on EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. EMA/OD/0000182883

Treatment of AL amyloidosis

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 18 October 2024, prior to responding to the list of issues.

2.1.2. EMA/OD/0000175842

Treatment of Duchenne muscular dystrophy

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 provide additional arguments and data to substantiate the significant benefit of their product vs current satisfactory methods in Duchenne muscular dystrophy (DMD), in particular vamorolone and deflazacort.

In the written response, and during an oral explanation before the Committee on 05 November 2024, the sponsor was invited to further substantiate the significant benefit of their product vis a vis the relevant satisfactory methods, i.e. the glucocorticoids deflazacort and vamorolone. The sponsor did not include a glucocorticoid control in their non-clinical studies, neither in the ones conducted in the severe nor the intermediate DMD models and no preclinical data are publicly available regarding the effect of corticosteroids on muscle function and survival in these specific DMD models. The sponsor refers to a study published by Sali et al., 2012, which reports that in a milder DMD model the translatability of long-term corticosteroid treatment to the human situation has been questioned. However, the COMP noted that glucocorticoids are known as effective treatment for patients with DMD and several studies are describing effects of glucocorticoid treatment on functional endpoints in non-clinical models of DMD.

The sponsor further re-emphasised that their product is unlikely to replace corticosteroids. Instead, based on the clinical development plan, it will be studied as an adjunctive therapy to these treatments. However, no data was presented by the sponsor to support this approach, neither in a valid disease model nor through (preliminary) clinical data.

Considering the above, the COMP did not consider the significant benefit of the sponsor's product over currently authorised treatment options established.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 06 November 2024, prior to final opinion.

2.1.3. EMA/OD/0000183952

Treatment of Duchenne muscular dystrophy

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

- Significant benefit

The arguments on significant benefit are based on 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 any indirect comparisons to the use of corticosteroids or potential benefits of use on top of corticosteroids to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

In the written response, and during an oral explanation before the Committee on 05 November 2024, the sponsor explained that a combination with vamorolone during the first stages of the proposed medicinal product treatment is foreseen. Thereby the proposed medicinal product will offer a durable, long-term effect in comparison with corticosteroids that cannot modify disease progression.

The proposed medicinal product will not cure the disease, but is expected to modify its progression by providing short but functional dystrophin. The sponsor also emphasised the corticosteroid-sparing effect (reduction or elimination) of the proposed medicinal product. Safety claims could not be considered acceptable by the COMP at this stage of initial OD (only non-clinical data is available for the proposed medicinal product and no comparison in this sense can be made to established treatment regimens with corticosteroids).

Given that a majority of Duchenne muscular dystrophy (DMD) patients are on corticosteroids treatment, it can be expected that unless the effect of the proposed medicinal product is fully maximised, the patients will remain on the current standard of care (SoC). In this sense, transition to a Becker MD phenotype will depend on the efficacy at the molecular level of the product, which remains uncertain since the threshold for efficacy (in cells and tissues) remains unknown in patients. No comparison with corticosteroids has been provided.

The sponsor was not able to provide additional data or clarification regarding the potential therapeutic impact. The COMP considered they could not conclude whether significant benefit had been established or not and therefore, they 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 05 November 2024, prior to final opinion.

2.1.4. EMA/OD/0000222362

Treatment of pulmonary arterial hypertension

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 18 October 2024, prior to responding to the list of issues.

2.1.5. mitapivat sulfate - EMA/OD/0000182940

Agios Netherlands B.V.; Treatment of sickle cell disease

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:

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of sickle cell disease the sponsor was asked to build upon the exploratory findings from the clinical development regarding vaso-occlusive crises (VOCs). The sponsor was requested to clarify any potential correlation between the primary and secondary endpoints in the sponsor-conducted study and the occurrence or

management of VOCs. Additionally, if data on the proportion of haemoglobin types at baseline and at the end of the study is available, this information should be provided.

In the written response, the sponsor addressed the questions raised by the COMP regarding the development of mitapivat for the treatment of sickle cell disease (SCD). The focus was on the potential benefits of mitapivat in addressing both anaemia and VOCs - two major challenges faced by SCD patients.

Sickle cell disease presents with a mix of complications, including organ damage from chronic anaemia and acute pain crises due to blood vessel blockages (VOCs). Lower haemoglobin levels are linked to increased risks of complications and early mortality. VOCs, in particular, are a significant cause of hospital visits and reduced quality of life.

The sponsor provided evidence from earlier clinical studies showing that mitapivat may help improve haemoglobin levels, reduce haemolysis, and decrease the occurrence of VOCs. In a Phase 2 study, patients treated with mitapivat experienced fewer pain crises and showed improvements in haemoglobin levels and red blood cell health. Another study indicated that mitapivat might improve oxygen delivery without increasing the risk of blood thickening.

Additionally, the sponsor clarified that mitapivat does not appear to change the proportions of different haemoglobin types, which is supported by the data from the ongoing clinical trials.

Based on the data provided, COMP accepted the sponsor’s response and issued a positive opinion for the purpose of an initial orphan designation. Therefore, the oral hearing was cancelled. The sponsor was advised to seek further guidance via protocol assistance given the complexity of the treatment landscape in this condition.

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 mitapivat sulfate was considered justified based on clinical data in patients with the condition demonstrating haemoglobin responses, reduction in haemolysis markers, and a lower annualised sickle cell pain crises rates compared to placebo.

The condition is chronically debilitating in particular due to vaso-occlusive crises, haemolytic anaemia, acute chest syndrome, chronic kidney disease, pulmonary hypertension and susceptibility to infections, and life-threatening with reduced survival.

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 mitapivat sulfate will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in patients with the condition showing haemoglobin and haemolysis responses regardless of hydroxyurea background use. In addition, based on the available clinical data, mitapivat has the potential to target a patient population across varying disease severities. The Committee considered that this constitutes a clinically relevant advantage.

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

2.1.6. colistimethate sodium - EMA/OD/0000177828

PureIMS B.V.; Treatment of cystic fibrosis

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 elaborate on the methodology used to investigate patient-reported outcomes. The differences between the previous and new versions of the two products studied should be clarified.

The sponsor has provided explanations on the potential use of the new product over existing treatments however, they were asked to further substantiate the rationale of significant benefit.

Further explanation regarding potential bias in interpretation of the retrospective observational analysis, the robustness and reliability of the information provided by both the survey and pharmacist-led follow-up, and the clinical impact of such data on the claimed clinically relevant advantage and major contribution to patient care.

In the written response, and during an oral explanation before the Committee on 06 November 2024, the sponsor explained that Colistin Cyclops was developed upon the manufacturing experience, performance data, and user feedback gained with its predecessor Colistin Twincer. Cyclops enables the use of a scaled-up semi-automatic powder-filling process and results in better usability, patient satisfaction, and slightly better dispersion performance than Colistin Twincer.

With regard to cough, the chance of its occurrence is theoretically lower with Colistin Cyclops than with Colistin Twincer, due to its finer aerosol and slightly higher resistance (theoretically resulting in a lower inhalation flow rate and lower mouth-throat deposition). In addition, because dose emission from Cyclops is more robust at lower inhalation flow rates, patients can often mitigate cough by inhaling less forcefully with Cyclops, whereas this was not possible with Twincer. This means that any data on the occurrence of cough with the use of Colistin Twincer will be similar if not better with Colistin Cyclops (i.e. the Twincer data will present a worst-case scenario).

Inhaled mannitol does not have an antibiotic effect against *Pseudomonas aeruginosa*. Therefore, the significant benefit of Colistin Cyclops over Bronchitol is a clinically relevant advantage in the treatment of pulmonary *Pseudomonas aeruginosa* infections in cystic fibrosis (CF).

The sponsor highlighted that neither Colobreathe nor Tobipodhaler, both dry powder inhalers, were currently used much in Europe and this was supported by a recent publication ("Inhaled antimicrobial prescribing for *Pseudomonas aeruginosa* infections in Europe" by Sloan C et al., 2024).

The COMP accepted that the dry powder inhalers are very rarely used in the EU.

Colistin Cyclops offers a major contribution to patient care by significantly impacting ease-of-use, and hence, substantially reducing treatment burden and by that significantly improving adherence to treatment. It was additionally noted that nebulisation is often

identified as (one of) the most burdensome aspects to CF treatment as inhalation takes a lot of time (3 to 15 minutes, excluding cleaning). The nebulisers need to be cleaned and nebulisers are bulky, require power from the mains, and hence, severely impair freedom of movement. To support this, the sponsor cited data from "Colistin dry powder inhalation with the Twincer™: An effective and more patient friendly alternative to nebulization" by Akkerman-Nijland AM et al., 2020.

The COMP accepted that Colistin Cyclops may be of major contribution to patient care over nebulised formulations. The COMP agreed to recommend granting the orphan designation.

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

The intention to treat the condition with the medicinal product containing colistimethate sodium was considered justified based on preliminary clinical data showing similar values to nebulised colistimethate regarding forced expiratory volume and pulmonary exacerbations.

The condition is chronically debilitating and life-threatening due to the recurrent and resistant respiratory infections with development of bronchiectasis and terminal 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.

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 colistimethate sodium will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a significant reduction in cough versus other dry power formulations of authorised medicines and patient reported outcomes which support better convenience to nebulised delivery of authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for colistimethate sodium, for treatment of cystic fibrosis, was adopted by majority (26 out of 29).

The COMP member of Norway agreed with the above-mentioned recommendation of the COMP. The COMP member of Iceland is vacant, and the COMP member of Liechtenstein did not participate in the meeting.

The divergent positions (Ines Alves, Jana Mazelova, Elisabeth Johanne Rook) were appended to this opinion.

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

2.1.7. EMA/OD/0000175548

Treatment of focal segmental glomerulosclerosis

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

- Intention to diagnose, prevent or treat

The sponsor was requested to provide a more comprehensive outline of the two non-clinical studies that were provided as evidence for medical plausibility (unilateral ureteral obstruction (UUO) and in vitro glomerulus-on-a-chip model). Histopathology data from the UUO model on glomerular podocyte preservation would be helpful. For the in vitro model, the sponsor was asked to explain what cell-lines are used, how the study was designed and to what extent the data are translatable to the clinic. Study reports were requested as well.

- Significant benefit

It was noted that cyclosporine is authorised for the treatment of "steroid-dependent and steroid-resistant nephrotic syndrome, due to primary glomerular diseases such as minimal change nephropathy, focal and segmental glomerulosclerosis, or membranous glomerulonephritis".

The sponsor was invited to provide arguments and available data to substantiate the significant benefit of their product vis a vis cyclosporine.

Furthermore, the sponsor was asked to provide a justification on whether their product could be of benefit in patients who are not eligible for cyclosporine (e.g. in first-line, or not meeting criteria of nephrotic syndrome, intolerance to calcineurin inhibitors (CNI) like cyclosporine) and if these patients are eligible for the Phase II trial.

In the written response, and during an oral explanation before the Committee on 06 November 2024, the sponsor submitted additional information from the in-vitro glomerulus on a chip model, which used non-patient derived primary human podocytes and glomerular endothelial cells, to further support the medical plausibility. As regards the use of non-clinical in vivo models, the sponsor clarified that while drug-target specific disease models are described in the literature (e.g. Krall et al., 2010), their attempts to generate such a model have failed. Furthermore, the sponsor emphasised the existence of species differences in the glomerular expression of the drug target and its family members between rodents and humans. Other non-clinical in vivo models displaying podocyte injury and proteinuria have not been considered by the sponsor.

To address the COMPs question on the significant benefit of their product vs the authorised product cyclosporine, the sponsor considered that their product may be used as an add-on to standard of care, including cyclosporine, as the mechanism of action is different. However, no data has been submitted by the sponsor to support such an approach.

The COMP concluded that based on the non-clinical in vitro and in vivo models chosen by the sponsor, it was not possible to have reassurance on the efficacy of the sponsors product in focal segmental glomerulosclerosis, which is a disease characterised by podocyte injury and proteinuria. Furthermore, no data has been provided to support the sponsors claim of a significant benefit of their product over CNIs such as cyclosporine.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 06 November 2024, prior to final opinion.

2.1.8. EMA/OD/0000222517

Treatment of autoimmune haemolytic anaemia

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 17 October 2024, prior to responding to the list of issues.

2.1.9. EMA/OD/0000179368

Treatment of soft tissue sarcoma

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 21 October 2024, prior to responding to the list of issues.

2.1.10. felzartamab - EMA/OD/0000222144

Human Immunology Biosciences Ireland Limited; Treatment in solid organ transplantation

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 complement the data on incidence of solid organ transplantation with the prevalence of patients living with a transplanted organ, possibly based on indirect methods. The sponsor was requested to re-estimate the prevalence based on relevant epidemiological studies and registers for the proposed orphan condition and given the uncertainty about many of the assumptions regarding indirect estimation of prevalence, the sponsor should perform sensitivity analyses.

In the written response, the sponsor provided an updated prevalence estimate of the target patient population which was based on the number of transplants per year, patient survival rates, and incidence numbers of antibody-mediated rejection in the EU.

The COMP accepted the argumentation that the sponsor had provided and proposed a prevalence of approximately 1 in 10,000. The Committee then recommended that the orphan designation could be granted.

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

The intention to treat the condition with the medicinal product containing felzartamab was considered justified based on preliminary clinical data showing a reduction in biopsy-proven antibody-mediated rejection in patients with renal transplants.

The condition is chronically debilitating and life-threatening due to delayed graft function following transplantation and risk of graft loss as well as loss of function of the transplanted organ.

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 felzartamab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a reduction in antibody-mediated rejection which is currently not treated with authorised medicines.

A positive opinion for felzartamab, for treatment of solid organ transplantation, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. divesiran - EMA/OD/0000166372

Silence Therapeutics GmbH; Treatment of polycythaemia vera

COMP Rapporteur: Karri Penttila

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

The intention to treat the condition with the medicinal product containing divesiran was considered justified based on preliminary clinical data in polycythaemia vera patients showing a reduction in the number of phlebotomies.

The condition is life-threatening and chronically debilitating due to thromboembolic and haemorrhagic complications, splenomegaly and myelofibrotic, myelodysplastic or leukaemic transformation.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing divesiran will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed a reduction in the number of phlebotomies in patients at low risk for thromboembolic complications with the product as a monotherapy. The clinical data also support use of divesiran as an add-on to authorised cytoreductive treatment in high-risk patients with a continued need for phlebotomy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for divesiran, for treatment of polycythaemia vera, was adopted by consensus.

2.2.2. vosoritide - EMA/OD/0000182637

Biomarin International Limited; Treatment of hypochondroplasia

COMP Rapporteur: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing vosoritide was considered justified based on preliminary clinical data which showed an increase in growth velocity in children with hypochondroplasia.

The condition is chronically debilitating due to manifestations such as epilepsy, neurocognitive issues, spinal stenosis, conductive hearing loss and life-threatening with shorter 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 vosoritide, for treatment of hypochondroplasia, was adopted by consensus.

2.2.3. roginolisib - EMA/OD/0000183015

Transcrip Ireland Limited; Treatment of uveal melanoma

COMP Rapporteur: Dinko Vitezic

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

The intention to treat the condition with the medicinal product containing roginolisib was considered justified based on preliminary clinical data which showed tumour control in patients with metastatic uveal melanoma.

The condition is life-threatening with a reduced survival in relapsed/refractory disease and chronically debilitating especially due to enucleation and in metastatic disease due to pain, organ failure, and treatment burden.

The condition was estimated to be affecting approximately 0.9 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 roginolisib will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data which demonstrate that the proposed product showed responses in relapsed or refractory uveal melanoma patients across different HLA genotypes which cannot be achieved with the current available treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for roginolisib, for treatment of uveal melanoma, was adopted by consensus.

2.2.4. votoplam - EMA/OD/0000184238

PTC Therapeutics International Limited; Treatment of Huntington’s disease

COMP Rapporteur: Ruta Mameniskiene

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

The intention to treat the condition with the medicinal product containing votoplam was considered justified based on preliminary clinical data showing a reduction in mutant huntingtin protein levels and a trend toward improvement in a clinical composite endpoint which includes motor and cognitive function parameters.

The condition is life-threatening and chronically debilitating due to severe behavioural and cognitive disturbances and progressive motor dysfunction.

The condition was estimated to be affecting approximately 1.1 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 votoplam will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing a reduction in mutant huntingtin protein levels and a trend toward improvement in a clinical composite endpoint which includes motor and cognitive function parameters. This cannot be expected from currently authorised treatments which only address the symptom of Huntington's chorea. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for votoplam, for treatment of Huntington's disease, was adopted by consensus.

2.2.5. allogeneic cardiosphere-derived cells - EMA/OD/0000222656

Adoh B.V.; Treatment of Duchenne muscular dystrophy

COMP Rapporteur: Darius Matusevicius

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

The intention to treat the condition with the medicinal product containing allogeneic cardiosphere-derived cells was considered justified based on non-clinical data showing improved survival, improved skeletal and cardiac muscle function as well as decreased cardiac fibrosis, and early-phase clinical studies which demonstrate improvements in motor function.

The condition is life-threatening and chronically debilitating due to progressive muscle weakness eventually affecting all voluntary muscles; this is followed by dilated cardiomyopathy and cardiac output decrease, leading to terminal respiratory or cardiac failure.

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 allogeneic cardiosphere-derived cells will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data which showed the protective effect in muscle strength of the proposed product when used as an add-on treatment to corticosteroid treatment. The Committee considered that this constitutes a clinically relevant advantage or major contribution to patient care.

A positive opinion for allogeneic cardiosphere-derived cells, for treatment of Duchenne muscular dystrophy, was adopted by consensus.

2.2.6. EMA/OD/0000223155

Treatment of pancreatic cancer

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 December meeting.

2.2.7. EMA/OD/0000223853

Treatment of primary biliary cholangitis (PBC)

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 December meeting.

2.2.8. monepantel - EMA/OD/0000224328

Regenold GmbH; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Michel Hoffmann

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 monepantel was considered justified based on preliminary clinical data which showed 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 monepantel will be of significant benefit to those affected by the condition. The sponsor has presented preliminary clinical data demonstrating that the proposed product attenuates motor function decline, a benefit that is not anticipated with the currently authorised medicinal product, riluzole. Furthermore, the clinical data suggests that the proposed product may be applicable to a broader patient population than tofersen, which is specifically indicated for the treatment of amyotrophic lateral sclerosis (ALS) patients with mutations in the superoxide dismutase 1 (*SOD1*) gene. The Committee considered that this constitutes a clinically relevant advantage.

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

2.2.9. 4-(4-(2-(diethylamino)ethoxy)phenyl)-1-(4-methoxybenzyl)-1H-1,2,3-triazol-5-amine - EMA/OD/0000224413

Opis S.r.l.; Treatment of neurofibromatosis type 2

COMP Rapporteur: Maria Judit Molnar

The Committee agreed that the condition, neurofibromatosis type 2, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing 4-(4-(2-(diethylamino)ethoxy)phenyl)-1-(4-methoxybenzyl)-1H-1,2,3-triazol-5-amine was considered justified based on non-clinical data in a valid model which showed a reduction of tumour growth.

The condition is chronically debilitating due to the development of central nervous system tumours. The development of bilateral vestibular nerve schwannomas frequently leads to hearing loss. The condition is life-threatening due to possible malignant transformation of the tumours and compression of vital neurological structures in the brain stem.

The condition was estimated to be affecting approximately 0.17 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 4-(4-(2-(diethylamino)ethoxy)phenyl)-1-(4-methoxybenzyl)-1H-1,2,3-triazol-5-amine, for treatment of neurofibromatosis type 2, was adopted by consensus.

2.2.10. EMA/OD/0000224798

Treatment of congenital alpha-1 antitrypsin deficiency

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 December meeting.

2.2.11. adeno-associated virus serotype 5 containing the human *RORA* gene - EMA/OD/0000225406

Ocugen Limited; Treatment of inherited retinal dystrophies due to dysfunction in the *ABCA4* gene

COMP Rapporteur: Fernando Mendez Hermida

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

The intention to treat the condition with the medicinal product containing adeno-associated virus serotype 5 containing the human *RORA* gene was considered justified based on in vivo data which showed improvement in retinal function.

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

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

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

A positive opinion for adeno-associated virus serotype 5 containing the human *RORA* gene, for treatment of inherited retinal dystrophies due to dysfunction in the *ABCA4* gene, was adopted by consensus.

2.2.12. davunetide - EMA/OD/0000226175

AdRes EU B.V.; Treatment of activity-dependent neuroprotective protein (ADNP) syndrome

COMP Rapporteur: Gloria Maria Palomo Carrasco

The Committee agreed that the condition, activity-dependent neuroprotective protein (ADNP) syndrome, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing davunetide was considered justified based on non-clinical data in relevant models of the condition showing the amelioration of synaptic, motor, and cognitive deficits.

The condition can be life-threatening and is chronically debilitating due to the disruption in essential processes in brain and organ development, leading to severe neurodevelopmental impairments, organ dysfunction including the heart, and a high risk of comorbidities such as seizures, heart disease, and tauopathy, which collectively compromise overall health and quality of life.

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.

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 davunetide, for treatment of activity-dependent neuroprotective protein (ADNP) syndrome, was adopted by consensus.

2.2.13. diazoxide choline - EMA/OD/0000226273

Soleno Therapeutics Europe Limited; Treatment of glycogen storage disease type I

COMP Rapporteur: Cécile Dop

The Committee agreed that the condition, glycogen storage disease type I, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing diazoxide choline was considered justified based on case histories showing an improvement glucose homeostasis and normalisation of hepatic function.

The condition is life-threatening due to complications arising from hypoglycaemic events and chronically debilitating due to the risk of such events, the need for regular consumption of meals throughout the night, and organ dysfunction due to substrate accumulation.

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 diazoxide choline, for treatment of glycogen storage disease type I, was adopted by consensus.

2.2.14. EMA/OD/0000226506

Treatment of inherited retinal dystrophy due to defects in the *RPE65* gene

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 December meeting.

2.2.15. EMA/OD/0000226832

Treatment of chronic pancreatitis

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 December meeting.

2.2.16. EMA/OD/0000227422

Treatment of non-traumatic osteonecrosis

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 December meeting.

2.2.17. 2'-O-4'-C-(S)-ethyl-P-thioadenylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thioguanylyl-(3'-O->5'-O)-2'-O-methyl-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thioadenylyl-(3'-O->5'-O)-2'-fluoro-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thiouridylyl-(3'-O->5'-O)-2'-O-methyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-adenosine - EMA/OD/0000227727

Regintel Limited; Treatment of autosomal dominant polycystic kidney disease

COMP Rapporteur: Joao Rocha

The Committee agreed that the condition, autosomal dominant polycystic kidney disease, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing 2'-O-4'-C-(S)-ethyl-P-thioadenylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thioguanylyl-(3'-O->5'-O)-2'-O-methyl-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thioadenylyl-(3'-O->5'-O)-2'-fluoro-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thiouridylyl-(3'-O->5'-O)-2'-O-methyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-adenosine was considered justified based on beneficial effects on kidney weight/body weight ratio and kidney fibrosis score in valid non-clinical in vivo models of the disease and on preliminary clinical data in patients with the condition achieving an improvement in kidney function, as assessed by the reduction in the total kidney volume.

The condition is chronically debilitating and potentially life-threatening due to renal manifestations such as renal cyst infection, nephrolithiasis, and kidney failure requiring dialysis.

The condition was estimated to be affecting approximately 4.0 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 2'-O-4'-C-(S)-ethyl-P-thioadenylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thioguanylyl-(3'-O->5'-O)-2'-O-methyl-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thioadenylyl-(3'-O->5'-O)-2'-fluoro-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thiouridylyl-(3'-O->5'-O)-2'-O-methyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-adenosine will be of significant benefit to those affected by the condition. The sponsor has provided in vivo non-clinical data that showed that the proposed product has an additive effect when combined with the authorised medicinal product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 2'-O-4'-C-(S)-ethyl-P-thioadenylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thioguanylyl-(3'-O->5'-O)-2'-O-methyl-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thioadenylyl-(3'-O->5'-O)-2'-fluoro-P-thiocytidylyl-(3'-O->5'-O)-2'-fluoro-P-thiouridylyl-(3'-O->5'-O)-2'-O-methyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-P-thiouridylyl-(3'-O->5'-O)-2'-O-4'-C-(S)-ethyl-adenosine, for treatment of autosomal dominant polycystic kidney disease, was adopted by consensus.

2.2.18. elebsiran - EMA/OD/0000227741

FGK Representative Service GmbH; Treatment of hepatitis delta virus infection

COMP Rapporteur: Enrico Costa

The Committee agreed that the condition, hepatitis delta virus infection, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing elebsiran was considered justified based on non-clinical data in models of the disease and clinical data in patients with the condition demonstrating dose-dependent, sustained virologic responses.

The condition is chronically debilitating and life-threatening due to the development of cirrhosis, portal hypertension, liver insufficiency and hepatocellular carcinoma.

The condition was estimated to be affecting approximately 4 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing elebsiran will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate a virological response in patients with chronic hepatitis delta virus who were either non-responders or experienced tolerability issues with the currently authorised treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for elebsiran, for treatment of hepatitis delta virus infection, was adopted by consensus.

2.2.19. autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 - EMA/OD/0000227841

PharmaLex GmbH; Treatment of myasthenia gravis

COMP Rapporteur: Evangelia Giannaki

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

The intention to treat the condition with the medicinal product containing autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 was considered justified based on preliminary clinical data showing an improvement in mobility and validated myasthenia measures.

The condition is life-threatening and chronically debilitating due to muscle weakness affecting in particular muscles that control eye and eyelid movement, facial expressions, chewing, talking, and swallowing. Recurrent myasthenic crisis can also affect muscles that control breathing, resulting in life-threatening respiratory impairment.

The condition was estimated to be affecting approximately 3.6 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate an improvement in mobility and validated myasthenia gravis parameters in patients who are refractory to authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19, for treatment of myasthenia gravis, was adopted by consensus.

2.2.20. tobevibart - EMA/OD/0000227852

FGK Representative Service GmbH; Treatment of hepatitis delta virus infection

COMP Rapporteur: Enrico Costa

The Committee agreed that the condition, hepatitis delta virus infection, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing tobevibart was considered justified based on non-clinical data in models of the disease and clinical data in patients with the condition demonstrating dose-dependent, sustained virologic responses.

The condition is chronically debilitating and life-threatening due to the development of cirrhosis, portal hypertension, liver insufficiency and hepatocellular carcinoma.

The condition was estimated to be affecting approximately 4 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing tobevibart will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate a virological response in patients with chronic hepatitis delta virus who were either non-responders or experienced tolerability issues with the currently authorised treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for tobevibart, for treatment of hepatitis delta virus infection, was adopted by consensus.

2.2.21. EMA/OD/0000227928

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 December meeting.

2.2.22. mRNA encoding Cas9-deaminase, single guide RNA against the human *TGM1* gene - EMA/OD/0000228058

Charite Universitaetsmedizin Berlin KöR; Treatment of autosomal recessive congenital ichthyosis (ARCI)

COMP Rapporteur: Fernando Mendez Hermida

The Committee agreed that the condition, autosomal recessive congenital ichthyosis (ARCI), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing mRNA encoding Cas9-deaminase, single guide RNA against the human *TGM1* gene was considered justified based non-clinical data in a model of the condition demonstrating the correction of the disease-causing mutation and the partial restoration of the TGase-1 enzyme activity addressing the root cause of the disease. The observed increase in TGase-1 activity would exceed the critical threshold needed to potentially improve patient symptoms.

The condition can be life-threatening and is chronically debilitating in particular due to manifestations such as collodion babies, the development of scales, an impairment of the epidermal barrier resulting in infections and trans epithelial water loss, hyperkeratosis interfering with sweat gland function, ectropion, conductive hearing loss, hair loss, palmoplantar and nail abnormalities, as well as the development of skin malignancies.

The condition was estimated to be affecting approximately 0.1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing mRNA encoding Cas9-deaminase, single guide RNA against the human *TGM1* gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data in a model of the disease indicating that the proposed product has disease modifying potential that could provide long-term disease stabilisation rather than just alleviating symptoms. This could expand treatment options to a wider patient population, including those ineligible for existing therapies due to disease

severity or contraindications. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for mRNA encoding Cas9-deaminase, single guide RNA against the human *TGM1* gene, for treatment of autosomal recessive congenital ichthyosis (ARCI), was adopted by consensus.

2.2.23. arsenic trioxide - EMA/OD/0000228105

Pharma IT ApS; Treatment of acute promyelocytic leukaemia

COMP Rapporteur: Frauke Naumann-Winter

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

The intention to treat the condition with the medicinal product containing arsenic trioxide was considered justified based on clinical data which showed responses in patients with acute promyelocytic leukaemia.

The condition is chronically debilitating and life-threatening due to the severe coagulopathies and a high mortality rate of relapsed/refractory disease.

The condition was estimated to be affecting approximately 2.9 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 arsenic trioxide will be of significant benefit to those affected by the condition. The oral formulation might reduce the treatment burden compared to the authorised intravenous therapy. The Committee considered that this constitutes a major contribution to patient care.

A positive opinion for arsenic trioxide, for treatment of acute promyelocytic leukaemia, 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 9 upcoming applications.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 2 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

None

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. Wainzua - eplontersen - EMEA/H/C/006295, EU/3/23/2828, EMA/OD/0000177780

AstraZeneca AB; Treatment of transthyretin-mediated amyloidosis

COMP Rapporteur: Joao Rocha; COMP Co-Rapporteur: Maria Judit Molnar

A list of issues was adopted on 08 October 2024.

An oral explanation was held on 05 November 2024.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the orphan designation from the register of orphan medicinal products, on 06 November 2024, prior to final opinion.

The orphan designation withdrawal 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. - imetelstat - EMEA/H/C/006105, EU/3/20/2305, EMA/OD/0000225798

Geron Netherlands B.V.; Treatment of myelodysplastic syndromes

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor requested a deferral to January 2025 and will be invited to an oral explanation before the Committee at the January meeting.

4.2.2. Pemazyre - pemigatinib - EMEA/H/C/005266/II/0015, EU/3/19/2216, EMA/OD/0000167021

Incyte Biosciences; Treatment of myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2

CHMP Rapporteur: Alexandre Moreau; CHMP Co-Rapporteur: Janet Koenig

The status of the procedure at CHMP was noted.

4.2.3. - garadacimab - EMEA/H/C/006116, EU/3/21/2532, EMA/OD/0000133460

CSL Behring GmbH; Treatment of hereditary angioedema

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 December meeting.

4.2.4. - beremagene geperpavec - EMEA/H/C/006330, EU/3/18/2012, EMA/OD/0000233504

Krystal Biotech Netherlands; Treatment of epidermolysis bullosa

The status of the procedure at CHMP was noted.

4.2.5. - seladelpar lysine dihydrate - EMEA/H/C/004692, EU/3/17/1930, EMA/OD/0000170646

Cymabay Ireland Limited; Treatment of primary biliary cholangitis

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

4.2.6. - tiratricol - EMEA/H/C/005220, EU/3/17/1945, EMA/OD/0000168628

Rare Thyroid Therapeutics; Treatment of monocarboxylate transporter 8 (MCT8) deficiency

The status of the procedure at CHMP was noted.

4.2.7. - acoramidis - EMEA/H/C/006333, EU/3/18/2081, EMA/OD/0000224696

BridgeBio Europe B.V.; 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 December meeting.

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 2 applications.

4.5. Orphan Maintenance Reports

None

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

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

None

5.3. Appeal

None

5.4. On-going procedures

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

The Chair welcomed Jana Schweigertova, as the new member for Slovakia.

7.1.2. Vote by proxy

Boje Kvorning Ehmsen gave a proxy to Birgitte Schwarzer-Daum to vote on behalf of Boje Kvorning Ehmsen during the entire meeting.

Fernando Mendez Hermida gave a proxy to Joao Rocha to vote on behalf of Fernando Mendez Hermida during the entire meeting.

Ioannis Kkolos gave a proxy to Evangelia Giannaki to vote on behalf of Ioannis Kkolos during the entire meeting.

Maria Driessens gave a proxy to Ines Alves to vote on behalf of Maria Driessens during part of the meeting.

Karri Penttila gave a proxy to Vallo Tillmann to vote on behalf of Karri Penttila during part of the meeting.

Frauke Naumann-Winter gave a proxy to Elisabeth Rook to vote on behalf of Frauke Naumann-Winter during part of the meeting.

Judit Molnar gave a proxy to Zsofia Gyulai to vote on behalf of Judit Molnar during part of the meeting.

Julian Isla gave a proxy to Gloria Palomo Carrasco to vote on behalf of Julian Isla during part of the meeting.

7.1.3. Strategic Review & Learning meetings

Preliminary feedback was noted from the COMP SRLM under the Hungarian Presidency of the Council of the EU held in person on 29-30 October 2024 in Budapest, Hungary.

7.1.4. Protocol Assistance Working Group (PAWG)

None

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)

João Rocha and Inês Alves were appointed as COMP representative for respectively HCPWP and PCWP.

7.3.2. Innovation Task Force (ITF) meetings

Documents were tabled for information.

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

7.7.1. Draft COMP Work Plan for 2025

COMP Chair: Tim Leest

Documents were circulated.

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2024

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2024 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. Patient engagement methodologies

The topic was postponed to January 2025.

9. List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 05-07 November 2024 COMP meeting, which was held in-person.

An asterisk (*) after the role, in the second column, signals that the member 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
Tim Leest	Chair	Belgium	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	No restrictions applicable to this meeting	
Dinko Vitezic	Member	Croatia	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 (Vice-Chair)	Germany	No interests declared	
Evangelia Giannaki	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	
Luana Mifsud Buhagiar	Member	Malta	No interests declared	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Jana Schweigertova	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	
Julian Isla	Member	Patients' Organisation Representative	No interests declared	
Ines Alves	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Mariette Driessens	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Fernando Mendez Hermida	Member*	Expert recommended by EMA	No interests declared	
Ingeborg Barisic	Member	Expert recommended by EMA	No interests declared	
Maria Judit Molnar	Member	Expert recommended by EMA	No participation in discussion, final deliberations and voting on:	2.1.2. EMA/OD/0000175842 2.1.3. EMA/OD/0000183952 2.2.4. votoplam - EMA/OD/0000184238 2.2.5. allogeneic cardiosphere-derived cells - EMA/OD/0000222656

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				2.2.19. autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 - EMA/OD/0000227841
Maria Cavaller Bellaubi	Expert	Patients' Organisation Representative	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

Experts' declared interests 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/