



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

20 December 2023  
EMA/COMP/464039/2023 Rev.1  
Human Medicines Division

## Committee for Orphan Medicinal Products (COMP)

### Minutes for the meeting on 03-05 October 2023

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

#### Health & safety

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

#### Disclaimers

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

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

#### Note on access to documents

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

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## 1. Introduction

### 1.1. Welcome and declarations of interest of members and experts

The Chairperson opened the meeting by welcoming all participants. The meeting was held in-person. In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

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

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

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

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

### 1.2. Adoption of agenda

The agenda for 03-05 October 2023 was adopted with no amendments.

### 1.3. Adoption of the minutes

The minutes for 05-07 September 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. oregovomab - EMA/OD/0000143999

IQVIA RDS Spain S.L.; Treatment of ovarian cancer

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:

- Number of people affected

It appears that the sponsor provided an under-estimate of the prevalence for ovarian cancer. They were invited to re-calculate the estimate and were asked to justify the

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

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

In their written response, the sponsor submitted a revised estimate for the prevalence. An additional publication was used for the revised estimate by Clamp A.R., et al., Weekly dose-dense chemotherapy in first-line epithelial ovarian, fallopian tube, or primary peritoneal cancer treatment (ICON8): overall survival results from an open-label, randomised, controlled, phase 3 trial. *Lancet Oncol*, 23, 919-930. From this study the sponsor proposed results which showed women aged 18 years or older with newly diagnosed ovarian cancer treated with carboplatin and paclitaxel (standard of care) had a median overall survival varying between 47.4 and 54.8 months. It is proposed that the prevalence should be expected to range between 3.60 and 4.17 per 10,000 people.

The COMP acknowledged that establishing the prevalence can be difficult in ovarian cancer as there is not one median survival available for all ovarian patients. This additional study was not considered to reflect the overall ovarian cancer survival in Europe as it had a selected patient population. In addition, the Committee did not consider that the proposed survival reflected current understanding which in some orphan designations have been up to 5.38 years. As a result of these considerations the COMP considered that the prevalence is closer to the threshold at 4.9 in 10,000 and amended the final estimate to this later number.

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 oregovomab was considered justified based on preliminary clinical data showing improved progression free survival as well as overall survival when the product is used in combination with paclitaxel & carboplatin in front line therapy.

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 provided sufficient justification for the assumption that the medicinal product containing oregovomab will be of significant benefit to those affected by the condition. The sponsor provided preliminary clinical data that demonstrated that there was a better progression free survival as well as overall survival when the product was used in combination with paclitaxel and carboplatin as compared to paclitaxel and carboplatin alone. The Committee considered that this constitutes a clinically relevant advantage.

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

Calliditas Therapeutics France S.A.S.; Treatment of Alport syndrome

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:

- Intention to diagnose, prevent or treat

The sponsor was invited to discuss the expected clinical benefit of setanaxib in the treatment of Alport syndrome, considering that a positive additive effect of setanaxib was only observed on a single efficacy parameter (when used in combination with the SoC therapy ramipril) and that setanaxib on its own did not show relevant effects on any efficacy parameter.

In the written response, the sponsor presented new data from a recent paper (Tong et al., 2023). Tong and co-authors evaluated setanaxib in a non-clinical model which represents a more slowly progressive form of Alport syndrome (Col4a3 C1615Y transgenic model). The authors found that setanaxib treatment significantly and substantially decreased both the albumin-to-creatinine ratio and 24-hour proteinuria. Setanaxib is described to act in Alport syndrome through the inhibition of podocyte apoptosis.

Furthermore, the sponsor emphasised again the positive effect of setanaxib on reducing blood urea nitrogen (BUN) levels in a relevant model of the proposed condition (Col4a3 KO model), either when administered as monotherapy or when used in combination with the ACE-inhibitor ramipril (non-clinical studies CO26440 and CO29100). Moreover, setanaxib in combination with ramipril had an additional effect on albuminuria in both these non-clinical studies. Consistent results were observed on the urine albumin-creatinine ratio (UACR) at 8 weeks of age.

The sponsor noted that proteinuria reduction translates to longer term beneficial renal effects in IgA nephropathy (Thompson et al., 2019 and Inker et al., 2016).

The COMP considered that overall sufficient data was presented to support the medical plausibility of setanaxib in Alport syndrome, for the purpose of initial orphan designation. Therefore the oral explanation was cancelled. The Committee also noted that clinical trials are already planned by the sponsor to investigate the effect of setanaxib together with SoC in patients with Alport syndrome.

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 setanaxib was considered justified based on non-clinical data in a relevant model of the condition showing a further reduction in albuminuria when used in combination with an angiotensin-converting enzyme (ACE) inhibitor, as compared to the ACE-inhibitor alone.

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

The condition was estimated to be affecting less than 1.5 in 10,000 persons in the European Union, at the time the application was made.

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

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

### 2.1.3. rucosopasem manganese - EMA/OD/0000139099

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Agos Healthcare Limited; Treatment of pancreatic cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for the treatment of pancreatic cancer the sponsor was asked to further elaborate on the results from the non-clinical and clinical studies.

In particular, the sponsor was requested to elaborate on the non-clinical studies with the proposed product, and on the possibility of extrapolation from the analogue used in the clinical studies.

- Significant benefit

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

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

In writing and during the oral explanation the sponsor provided additional information with the proposed product (rucosopasem) on non-clinical studies using different tumour models. The rationale put forward by the sponsor is that the mechanism of action of the proposed product is neither species nor tumour type specific. While this statement was acknowledged, the Committee considered the results provided in the pancreatic non-clinical model to be the most relevant for the medical plausibility claims and the focus was placed on them.

The sponsor also elaborated on the clinical data from a pilot trial of a rucosopasem analogue in combination with stereotactic body radiation therapy (SBRT) versus SBRT alone following initial chemotherapy in patients with locally advanced pancreatic cancer (LAPC). In this case, no clinical data with rucosopasem was available. The sponsor argued that these are close analogues and therefore the available clinical data from the analogue would be supportive for the medical plausibility claim. In order to support the bridging, the sponsor presented non-clinical in vitro data, and non-clinical pharmacokinetic data across multiple species. In these studies, rucosopasem showed similar plasma exposure and excretion profiles. Clinically, in two Phase 1 studies the safety and plasma exposure were conducted compared to that of the analogue which showed the main difference to be related to the maximum tolerated dose (MTD), but which showed similar pharmacokinetics.

In the answers to the significant benefit, the sponsor clarified that SBRT use for locally advanced non-metastatic pancreatic cancer is additive to chemotherapy and not intended to

replace chemotherapy. Considering the intended development, significant benefit will need to be demonstrated between existing SBRT regimens with or without the proposed product. However, the available non-clinical and clinical data could be acceptable in the context of the applied initial orphan designation.

Overall, although preliminary, these non-clinical and clinical data can be supportive of a positive opinion. The COMP adopted a positive opinion after the oral explanation. The COMP advised the sponsor to request EMA protocol assistance for further development. The Committee agreed that the condition, pancreatic cancer, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing rucosopasem manganese was considered justified based on non-clinical data in models of the condition showing an effect on tumour volume and tumour growth when used in combination with stereotactic body radiation therapy (SBRT).

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

The condition was estimated to be affecting approximately 2 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 rucosopasem manganese will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data in two models of the condition that showed increased antitumour activity in combination with stereotactic body radiation therapy (SBRT), when compared to SBRT treatment alone. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for rucosopasem manganese, for treatment of pancreatic cancer, was adopted by consensus.

#### 2.1.4. [5-bromo-N-\(prop-2-yn-1-yl\)-2-\(1H-1,2,4-triazol-1-yl\)pyrimidine-4,6-diamine - EMA/OD/0000143251](#)

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Palo Biofarma S.L.; Treatment of Prader-Willi syndrome

COMP Rapporteur: Olimpia Neagu

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 data presented by the sponsor was not sufficient and conclusive to support the medical plausibility of the proposed product in the treatment of the proposed condition. To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of Prader-Willi syndrome the sponsor was asked to further elaborate on:

- the relevance of the non-clinical model presented by the sponsor for the treatment of Prader-Willi syndrome, and the interpretation of the results obtained in the experiment,

- the preliminary clinical data in cancer patients and its relevance for the extrapolation in the treatment of Prader-Willi syndrome patients.
- 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 elaborate on the prevalence calculation, and justify the figure of choice within the interval proposed.

- Significant benefit

The sponsor was invited to substantiate their claim on significant benefit with relevant data. In the absence of convincing data to support medical plausibility, significant benefit cannot be established.

In the written response and during an oral explanation before the Committee on 5 October 2023, the sponsor provided new information on an ongoing Phase 2, proof of concept (PoC) study to evaluate the efficacy, safety, and pharmacokinetics of the proposed product in patients with Prader-Willi syndrome. As part of this data, secondary endpoints are described including efficacy-related measures such as caregiver assessments of hyperphagia-related behaviours, using the HQ-CT total score and the CGIC score, body weight, metabolic parameters, caregiver assessment of behaviour, biomarker assessment, as well as the pharmacokinetic profile of the proposed product in the target population. While this data is limited, results could indicate an improvement in weight and hyperphagia-related behaviours as part of the open label phase when the treatment was administered.

In the answers to the prevalence question, the sponsor conducted an indirect calculation using the incidence and the disease duration. For this purpose, nine studies were identified across different geographical locations averaging a birth incidence of 1 in 21,000. Taking a conservative approach of 1 in 15,000, a prevalence of around 0.6 was proposed which is in line with previous orphan designations.

In the answers to the significant benefit question, the sponsor elaborated on the effects observed in the hyperphagia-related behaviours which is currently not addressed by existing treatments. This could be advantageous in addressing a different aspect of the disease where authorised treatments would not be effective.

Overall, although preliminary, these data can be supportive of a positive opinion. The COMP adopted a positive opinion after the oral explanation. The COMP advised the sponsor to request EMA protocol assistance for further development.

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

The intention to treat the condition with the medicinal product containing 5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine was considered justified based on clinical data in two patients with the condition showing a potential effect on weight loss and an improvement in hyperphagia as measured by the Hyperphagia Questionnaire (HQ-CT).

The condition is life-threatening and chronically debilitating, in particular due to cognitive impairment, maladaptive behaviour, hyperphagia and morbid obesity leading to increased cardiovascular morbidity and mortality.

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 5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in patients with the condition that could indicate that the product improved the signs of hyperphagia as measured by the Hyperphagia Questionnaire (HQ-CT). The product could be added to the currently used growth hormone treatment to address the clinically relevant aspect of the condition which is not treated by growth hormone alone. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 5-bromo-N-(prop-2-yn-1-yl)-2-(1H-1,2,4-triazol-1-yl)pyrimidine-4,6-diamine, for treatment of Prader-Willi syndrome, was adopted by consensus.

#### 2.1.5. [N-{\(2S,3R\)-4,4-difluoro-1-\(2-hydroxy-2-methylpropanoyl\)-2-\[\(2,3',5'-trifluoro\[1,1'-biphenyl\]-3-yl\)methyl\]pyrrolidin-3-yl}ethanesulfonamide - EMA/OD/0000137539](#)

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Takeda Pharma A/S; Treatment of narcolepsy

COMP Rapporteur: Elisabeth Penninga

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 asked to detail the results of any clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients. All authorised medicinal products should be considered including methylphenidate.

The sponsor provided a written response in which it was highlighted that the product is expected to be used as first line therapy in the target patient population, defined as those with excessive daytime sleepiness (EDS) and cataplexy. In this patient population sodium oxybate and pitolisant were used first but were not considered very effective in reducing the frequency of cataplexy. The sponsor provided indirect comparisons to both sodium oxybate and pitolisant. These indirect comparisons were based on reported rates in section 5.1 of the SmPC for sodium oxybate and the EPAR for pitolisant compared to the clinical trial results reported in the clinical trial submitted. Both show modest effects on EDS, while the proposed product leads to greater changes in Maintenance of Wakefulness Test (MWT) and the Epworth Sleepiness Scale (ESS).

Indirect comparison suggests the proposed product also shows improved efficacy in treating cataplexy.

Early clinical data for the proposed product suggests significant benefit of improved efficacy in treating NT1 patients over pitolisant and sodium oxybate and indicates a potential of the proposed product for normalising NT1 patients' symptoms.

In additional indirect comparisons the sponsor indicated that modafinil and solriamfetol show efficacy on EDS symptom only, while the proposed product demonstrated efficacy on both EDS and cataplexy in NT1 patients. Data sources for the comparison for modafinil was section 5.1 of the Sunosi SmPC in Europe and the FDA Clinical Assessment Report. For solriamfetol data was derived from the European EPAR.

The proposed product offers significant benefit of improved efficacy over modafinil and solriamfetol as indicated by indirect comparison of efficacy on EDS, and due to additional effect of the proposed product on cataplexy.

The sponsor noted that for methylphenidate and dexamphetamine efficacy is shown only for EDS. They highlight that in recent recommendations for use both have a low recommendation for use in EDS (Bassetti et al., 2021). The proposed product may offer a better efficacy in EDS but more importantly it offers an effect on cataplexy that is not seen with either of these products.

The COMP considered the sponsor's written response had adequately addressed the questions and cancelled the oral explanation.

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

The intention to treat the condition with the medicinal product containing N-{(2S,3R)-4,4-difluoro-1-(2-hydroxy-2-methylpropanoyl)-2-[(2,3',5'-trifluoro[1,1'-biphenyl]-3-yl)methyl]pyrrolidin-3-yl}ethanesulfonamide was considered justified based on preliminary clinical data showing an improvement in wakefulness time and cataplexy in narcolepsy type 1 patients.

The condition is chronically debilitating in particular due to excessive daytime sleepiness and cataplexy episodes, as well as life-threatening with a 1.5-fold excess mortality in narcolepsy patients relative to those without narcolepsy.

The condition was estimated to be affecting approximately 4.1 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 N-{(2S,3R)-4,4-difluoro-1-(2-hydroxy-2-methylpropanoyl)-2-[(2,3',5'-trifluoro[1,1'-biphenyl]-3-yl)methyl]pyrrolidin-3-yl}ethanesulfonamide will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that show an improvement in wakefulness as well as cataplexy in narcolepsy type 1 patients who are not adequately responding to currently authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for N-{(2S,3R)-4,4-difluoro-1-(2-hydroxy-2-methylpropanoyl)-2-[(2,3',5'-trifluoro[1,1'-biphenyl]-3-yl)methyl]pyrrolidin-3-yl}ethanesulfonamide, for treatment of narcolepsy, was adopted by consensus.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its October 2023 meeting.]*

### 2.1.6. - EMA/OD/0000140934

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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 20 September 2023, prior to responding to the list of issues.

## 2.2. For discussion / preparation for an opinion

### 2.2.1. ambroxol hydrochloride - EMA/OD/0000119656

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CATS Consultants GmbH; Treatment of Gaucher's disease

COMP Rapporteur: Joao Rocha

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

The intention to treat the condition with the medicinal product containing ambroxol hydrochloride was considered justified based on preliminary clinical data showing a reduction in epileptic seizures and neurocognitive decline.

The condition is chronically debilitating in particular due to hepatosplenomegaly, thrombocytopenia, anaemia, bone disease, as well as neurological manifestations in the neuronopathic form of the condition, and life-threatening with reduced life expectancy.

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 ambroxol hydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a reduction in epileptic seizures and improvement in neurocognitive function in patients whose symptoms cannot be treated with the currently authorised medicines for the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for ambroxol hydrochloride, for treatment of Gaucher disease, was adopted by consensus.

### 2.2.2. riboflavin - EMA/OD/0000140338

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iniuva GmbH; Treatment of medium-chain acyl-coenzyme A dehydrogenase deficiency

COMP Rapporteur: Armando Magrelli

The Committee agreed that the condition, medium-chain acyl-coenzyme A dehydrogenase deficiency, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing riboflavin was considered justified based on clinical data in patients with the condition showing the amelioration of biomarkers of the condition such as a decrease of acylcarnitine levels, an increase in enzyme activity in lymphocytes measured in vitro, as well as an increase in the in vivo medium-chain acyl-CoA dehydrogenase (MCAD) activity.

The condition is life-threatening due to risk of metabolic decompensation and chronically debilitating due to the occurrence of hypoketotic hypoglycaemia, myopathy, cardiomyopathy, arrhythmias, lethargy, vomiting and seizures.

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 riboflavin, for treatment of medium-chain acyl-coenzyme A dehydrogenase deficiency, was adopted by consensus.

### 2.2.3. [humanised IgG1 monoclonal antibody against \*CLDN6\* conjugated to monomethyl auristatin E via a cathepsin hydrolysable dipeptide VC linker - EMA/OD/0000142281](#)

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Insight Drug Regulatory; Treatment of ovarian cancer

COMP Rapporteur: Jana Mazelova

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 humanised IgG1 monoclonal antibody against *CLDN6* conjugated to monomethyl auristatin E via a cathepsin hydrolysable dipeptide VC linker was considered justified based on preliminary clinical data in *CLDN6+*, platinum resistant patients showing a partial response.

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 humanised IgG1 monoclonal antibody against *CLDN6* conjugated to monomethyl auristatin E via a cathepsin hydrolysable dipeptide VC linker will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a partial response in ovarian cancer patients with *CLDN6+* disease who were heavily pre-treated and platinum resistant following treatment with the sponsor's product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for humanised IgG1 monoclonal antibody against *CLDN6* conjugated to monomethyl auristatin E via a cathepsin hydrolysable dipeptide VC linker, for treatment of ovarian cancer, was adopted by consensus.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its October 2023 meeting.]*

### 2.2.4. [– EMA/OD/0000142974](#)

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Treatment of Duchenne muscular dystrophy

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 November 2023 meeting.

#### 2.2.5. – [EMA/OD/0000142982](#)

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Treatment of moderate to severe traumatic brain injury

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 November 2023 meeting.

#### 2.2.6. – [EMA/OD/0000143407](#)

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Treatment of follicular 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 November 2023 meeting.

#### 2.2.7. [messenger RNA encoding Cas9, single guide RNA targeting the human \*KLKB1\* gene](#) – [EMA/OD/0000143789](#)

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Pharma Gateway AB; Treatment of hereditary angioedema

COMP Rapporteur: Elisabeth Penninga

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

The intention to treat the condition with the medicinal product containing messenger RNA encoding Cas9, Single guide RNA targeting the human *KLKB1* gene was considered justified based on preliminary clinical data showing a significant reduction in attacks in patients with the condition.

The condition is life-threatening and chronically debilitating due to recurrent attacks of oedema in various parts of the body that may cause airway obstruction leading to asphyxia.

The condition was estimated to be affecting less than 0.5 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing messenger RNA encoding Cas9, single guide RNA targeting the human *KLKB1* gene will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing a significant reduction in attacks in patients with the condition which compares favourably to authorised treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for messenger RNA encoding Cas9, single guide RNA targeting the human *KLKB1* gene, for treatment of hereditary angioedema, was adopted by consensus.

#### 2.2.8. [elesclomol-copper](#) – [EMA/OD/0000144266](#)

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Veristat Spain S.L.; Treatment of Menkes disease

COMP Rapporteur: Joao Rocha

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

The intention to treat the condition with the medicinal product containing elesclomol-copper was considered justified based on non-clinical in vivo data in a valid model of the condition showing improved survival and neuromotor function and preliminary clinical data in one patient with severe Menkes disease showing improvement in several neurodevelopmental parameters.

The condition is chronically debilitating in particular due to progressive neurodegeneration and marked connective tissue dysfunction with vascular, urogenital, and skeletal abnormalities. The condition is also life-threatening with death before the third year of life in the most severe cases.

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 elesclomol-copper, for treatment of Menkes disease, was adopted by consensus.

#### 2.2.9. [adeno-associated viral vector serotype rh10 encoding miRNA against SOD1 mRNA – EMA/OD/0000144510](#)

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uniQure Biopharma B.V; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Armando Magrelli

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 adeno-associated viral vector serotype rh10 encoding miRNA against *SOD1* mRNA was considered justified based on non-clinical data in models of the condition showing improvement in motor function, muscle strength, and survival.

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 1.1 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 adeno-associated viral vector serotype rh10 encoding miRNA against *SOD1* mRNA will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that demonstrate that the proposed product could have disease-modifying effect by targeting the pathogenic mechanism in *SOD1* amyotrophic lateral sclerosis possibly attenuating the decline in motor function. This would not be

expected from the currently authorised treatment for the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated viral vector serotype rh10 encoding miRNA against *SOD1* mRNA, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

#### **2.2.10. – EMA/OD/0000145792**

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Treatment of haemophilia B

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 November 2023 meeting.

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

#### **2.2.11. – EMA/OD/0000146696**

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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 November 2023 meeting.

### **2.3. Revision of the COMP opinions**

None

### **2.4. Amendment of existing orphan designations**

None

### **2.5. Appeal**

#### **2.5.1. bortezomib - EMA/OD/0000116655**

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Accord Healthcare, SLU; Treatment of patients with light chain (AL) amyloidosis

COMP appeal rapporteur: Elisabeth Johanne Rook

As part of the opinion of 15 June 2023, no significant benefit was demonstrated versus Darzalex (daratumumab), which is authorised for the first line treatment of AL amyloidosis in combination with a regimen also containing bortezomib. As part of the appeal, the sponsor positions the use of bortezomib in patients with relapsed or refractory (R/R) disease.

The sponsor claimed the medical plausibility/significant benefit of bortezomib in the later line treatment setting, by reference to published uncontrolled observational studies. Although uncontrolled, the studies can support medical plausibility in the context of an initial OD. Complete Response (CR) ranged between approximately 20-40% in the larger scaled studies in this patient population. Overall, there is a lack of data from randomised trials to inform the optimal second line treatment setting of AL amyloidosis. Nevertheless, the sponsor claims superiority of bortezomib-based regimens versus SoC in R/R disease.

In addition, the sponsor indirectly compared the outcomes from these observational studies with a reference population of R/R AL amyloidosis patients. No matchings were applied. However, it is not understood why only a single reference was chosen, given that multiple studies are available. Moreover, multiple different treatment regimens were used making the interpretation versus the diverse comparators challenging. In addition, no data were presented of second line bortezomib treatment from patients who failed on previous daratumumab + bortezomib (+ dexamethasone) treatment, the only authorised treatment option.

Despite the caveats regarding methodology, it is acknowledged that some of the available treatments are poorly tolerated in AL amyloidosis patients with and therefore tolerability does also guide the choice of treatment.

On balance, the efficacy of bortezomib in the R/R patient population has been shown for the purpose of establishing the claim of medical plausibility in the context of an initial orphan designation and consequently significant benefit could be plausible in a R/R patient population. On this basis, the COMP decided to adopt a positive opinion with a recommendation to request protocol assistance in order to overcome the uncertainties raised during the initial discussion.

For the purpose of orphan designation, the Committee for Orphan Medicinal Products considered that the condition originally proposed by the sponsor should be renamed as "AL amyloidosis". The Committee agreed that the condition, AL amyloidosis, is a distinct medical entity and meets the criteria for orphan designation.

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 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 has provided bibliographic clinical data that showed responses in patients with relapsed or refractory (R/R) disease, a patient population for which no treatments are currently authorised. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for bortezomib, for treatment of AL amyloidosis, was adopted by majority (24 out of 25 votes). The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

The divergent position (Irena Rogovska) was appended to this opinion.

## **2.6. Nominations**

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

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COMP rapporteurs were appointed for 14 applications.

## **2.7. Evaluation on-going**

The Committee noted that evaluation was on-going for 19 applications for orphan designation.

## **3. Requests for protocol assistance with significant benefit question**

### **3.1. Ongoing procedures**

#### **3.1.1. -**

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Treatment of soft tissue sarcoma

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

#### **3.1.2. -**

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Treatment of tuberous sclerosis

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

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

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

#### **4.1.1. Zilbrysq - zilucoplan - EMEA/H/C/005450/0000, EU/3/22/2650, EMA/OD/0000120845**

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UCB Pharma S.A.; Treatment of myasthenia gravis

A list of issues was adopted on 7 September 2023.

An oral explanation was held on 3 October 2023.

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 4 October 2023, prior to final opinion.

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

#### **4.1.2. Yorvipath – teriparatide - EMEA/H/C/005934, EU/3/20/2350, EMA/OD/0000140073**

Ascendis Pharma Bone Diseases A/S; Treatment of hypoparathyroidism

A list of issues was adopted on 7 September 2023.

An opinion recommending not to remove Yorvipath, teriparatide, EU/3/20/2350 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

*[Post-meeting note: The COMP adopted the opinion by written procedure following its October 2023 meeting].*

#### **4.1.3. Finlee – dabrafenib - EMEA/H/C/005885/0000, EU/3/20/2372, EMA/OD/0000134197**

Novartis Europharm Limited; Treatment of glioma

COMP Rapporteur: Frauke Naumann-Winter; COMP Co-Rapporteur: Bozenna Dembowska-Baginska

An opinion recommending not to remove Finlee, dabrafenib, EU/3/20/2372 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

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

#### **4.2.1. Albriozza – sodium phenylbutyrate / ursodoxicoltaurine - EMEA/H/C/005901, EU/3/20/2284, EMA/OD/0000096503**

Amylyx Pharmaceuticals EMEA; Treatment of amyotrophic lateral sclerosis

The status of the procedure at CHMP was noted.

#### **4.2.2. – rezafungin - EMEA/H/C/005900/0000, EU/3/20/2385, EMA/OD/0000140230**

Mundipharma GmbH; Treatment of invasive candidiasis

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 November 2023 meeting.

#### **4.2.3. Agamree – vamorolone - EMEA/H/C/005679/0000, EU/3/14/1309, EMA/OD/0000141144**

Santhera Pharmaceuticals (Deutschland) GmbH; Treatment of Duchenne muscular dystrophy

COMP Rapporteur: Elisabeth Penninga; COMP Co-Rapporteur: Armando Magrelli

An opinion recommending not to remove Agamree, vamorolone, EU/3/14/1309 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

*[Post-meeting note: The COMP adopted the opinion by written procedure following its October 2023 meeting].*

#### **4.2.4. – elranatamab - EMEA/H/C/005908, EU/3/21/2471, EMA/OD/0000147440**

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Pfizer Europe MA EEIG; Treatment of multiple myeloma

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

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

#### **4.2.5. Loargys – pegzilarginase - EMEA/H/C/005484, EU/3/16/1701, EMA/OD/0000140263**

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Immedica Pharma AB; Treatment of hyperargininemia

COMP Rapporteur: Elisabeth Johanne Rook; COMP Co-Rapporteur: Ingeborg Barisic

An opinion recommending not to remove Loargys, pegzilarginase, EU/3/16/1701 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

*[Post-meeting note: The COMP adopted the opinion by written procedure following its October 2023 meeting].*

### **4.3. Appeal**

#### **4.3.1. Bylvay - odevixibat - EMEA/H/C/004691/II/0011, EU/3/12/1040, EMA/OD/0000152080**

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Albireo AB; Treatment of Alagille syndrome

COMP appeal Rapporteur: Elisabeth Johanne Rook; COMP appeal Co-Rapporteur: Ines Alves; CHMP Rapporteur: Johann Lodewijk Hillege

In the grounds for appeal, and during an oral explanation before the Committee on 3 October 2023, the sponsor aimed to address the main issues which led to the negative opinion.

The COMP upheld the negative view and an opinion recommending removing Bylvay, odevixibat, EU/3/12/1040 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

**4.5. On-going procedures**

COMP co-ordinators were appointed for 2 applications.

**4.6. 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. Prevmis – Ietermovir – EMEA/H/C/004536/II/0033/G, EU/3/11/849, EMA/OD/0000133054

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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 An opinion recommending not to remove Prevmis, Ietermovir, EU/3/11/849 from the EC Register of Orphan Medicinal Products was adopted by consensus.

The Orphan Maintenance Assessment Report will be publicly available on the EMA website.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its October 2023 meeting.]*

**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**

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None

#### **7.1.2. Vote by proxy**

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Armando Magrelli gave a proxy to Frauke Naumann-Winter to vote on behalf of Armando Magrelli during the entire duration of meeting.

Brigitte Schwarzer Daum gave a proxy to Tim Leest to vote on behalf of Brigitte Schwarzer Daum during part of the meeting.

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

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

Pauline Evers gave a proxy to Elisabeth Johanne Rook to vote on behalf of Pauline Evers during part of the meeting.

#### **7.1.3. Strategic Review & Learning meetings**

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SRLM meeting in Madrid under the Spanish Presidency of the Council of the EU

The COMP noted the upcoming meeting and the topics to be discussed.

#### **7.1.4. Protocol Assistance Working Group (PAWG)**

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The working group on Protocol Assistance met remotely on 2 October 2023.

#### **7.1.5. COMP Decisions Database**

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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**

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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)**

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None

### 7.3.2. Upcoming ITF meetings

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The COMP noted the upcoming ITF meetings.

## 7.4. Cooperation within the EU regulatory network

### 7.4.1. European Commission

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None

## 7.5. Cooperation with International Regulators

### 7.5.1. Food and Drug Administration (FDA)

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None

### 7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

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None

### 7.5.3. Therapeutic Goods Administration (TGA), Australia

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None

### 7.5.4. Health Canada

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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

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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

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

## 8. Any other business

### 8.1. Quarterly update on Real World Evidence, including DARWIN EU®

EMA provided an update of ongoing and planned studies via DARWIN EU as well as on the plans for onboarding of new data partners for year 2. The objectives of the study on multiple myeloma (patient characterisation, treatment patterns and survival in the period 2012-2022) were introduced. While this study is conducted as a use case of health technology assessment bodies and payer organisations, COMP expressed an interest for the results to be shared once available.

EMA furthermore presented a research project intending to explore alternative sources and prevalence estimates.

COMP asked for the proposals to be circulated after the meeting for further input by the members.

### 8.2. Nomination of COMP representative for ENCePP Steering Group 2024-2026

The COMP noted the information. The call was circulated and it was agreed to come back to this topic at the November COMP plenary.

## 9. List of participants

including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 03-05 October 2023 COMP meeting, which was held in-person.

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

| Name                       | Role    | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|----------------------------|---------|-----------------------------|---|---|
| Violeta Stoyanova-Beninska | Chair   | Netherlands                 | No interests declared                             |   |
| Brigitte Schwarzer-Daum    | Member* | Austria                     | No restrictions applicable to this meeting        |   |
| Tim Leest                  | Member  | Belgium                     | No interests declared                             |   |
| Dinko Vitezic              | Member  | Croatia                     | No interests declared                             |   |
| Ioannis Kkolos             | 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 restrictions applicable to this meeting        |   |
| Joao Rocha                   | Member  | Portugal                    | No restrictions applicable to this meeting        |   |
| Olimpia Neagu                | Member* | Romania                     | No interests declared                             |   |
| Eva Malikova                 | Member  | Slovak Republic             | No interests declared                             |   |
| Gloria Maria Palomo Carrasco | Member  | Spain                       | No interests declared                             |   |

| Name   | Role                    | Member State or affiliation           | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|--|-------------------------|---------------------------------------|---|---|
| Darius Matusевичius  | Member                  | Sweden                                | No restrictions applicable to this meeting        |   |
| Pauline Evers  | Member                  | Patients' Organisation Representative | No interests declared                             |   |
| Julian Isla  | Member                  | Patients' Organisation Representative | No interests declared                             |   |
| Ines Alves   | Member                  | Patients' Organisation Representative | No restrictions applicable to this meeting        |   |
| Ingeborg Barisic   | Member                  | Expert recommended by EMA             | No restrictions applicable to this meeting        |   |
| Judit Molnar   | Member                  | Expert recommended by EMA             | No restrictions applicable to this meeting        |   |
| Maria Cavaller Bellaubi  | Expert                  | Patients' Organisation Representative | No restrictions applicable to this meeting        |   |
|  | Patient representative* | Germany                               | No interests declared                             |   |
|  | Patient representative* | France                                | No interests declared                             |   |
| A representative from the European Commission attended the meeting |                         |                                       |   |   |
| Meeting run with support from relevant EMA staff                   |                         |                                       |   |   |

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

## 10. Explanatory notes

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

### Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

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

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

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

**Sponsor**

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

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

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

More detailed information on the above terms can be found on the EMA website:

[www.ema.europa.eu/](http://www.ema.europa.eu/)