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SCIENCE MEDICINES HEALTH

14 March 2024  
EMA/COMP/87308/2024  
Human Medicines Division

## Committee for Orphan Medicinal Products (COMP)

### Minutes for the meeting on 13-15 February 2024

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

#### 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 Committee members for concerned agenda topics.

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.

### 1.2. Adoption of agenda

The agenda for 13-15 February 2024 was adopted with no amendments.

### 1.3. Adoption of the minutes

The minutes for 16-18 January 2024 were adopted with no amendments and will be published on the EMA website.

## 2. Applications for orphan medicinal product designation

### 2.1. For opinion

#### 2.1.1. mibavademab - EMA/OD/0000146222

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Regeneron Ireland Designated Activity Company; Treatment of Berardinelli-Seip syndrome (congenital generalised lipodystrophy)

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

Berardinelli-Seip syndrome (congenital generalised lipodystrophy) appears to belong to part of a broader group of disorders called congenital lipodystrophy syndromes. The sponsor was

requested to discuss if this condition could be qualified under treatment of congenital lipodystrophy syndromes as well as any other causes of these syndromes. Note that this was for the purposes of orphan medicinal product designation. The sponsor's attention was drawn to the orphan regulations and relevant guidelines (especially section A of [2022/C 440/02](#)).

- Number of people affected

The Committee noted that there is the possibility of grouping the condition under the term congenital lipodystrophy syndromes. The sponsor was requested to propose a revised prevalence estimate with the assumptions for congenital lipodystrophy syndromes.

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

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

In the written response, and during an oral explanation before the Committee on 13 February 2024, the sponsor noted that to characterise lipodystrophies based on aetiology alone, rather than on a set of signs and symptoms would inappropriately group together two very distinct syndromes (partial and generalised lipodystrophy) with different signs and symptoms, disease onset, and severity. To support this claim, the sponsor highlighted the classification system as presented in Brown et al., 2016.

The COMP accepted the arguments proposed by the sponsor regarding the current nomenclature and differences highlighted.

The original prevalence estimate submitted was accepted for the Berardinelli-Seip syndrome which was 0.0051 cases per 10,000.

The COMP believed the questions had been addressed adequately and that they could recommend granting the orphan designation.

The Committee agreed that the condition, Berardinelli-Seip syndrome (congenital generalised lipodystrophy), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing mibavademab was considered justified based on non-clinical in vivo data as well as preliminary clinical data showing treatment with the high dose regimen resulted in clinically meaningful reductions in HbA1c and triglycerides compared to baseline.

The condition is chronically debilitating due to the consequences of uncontrolled diabetes mellitus, hypertriglyceridemia, and steatohepatitis (e.g. risk of accelerated micro- and macrovascular complication, liver cirrhosis). The severity of metabolic abnormalities can lead to acute complications that can be debilitating such as painful eruptive xanthomas and life-threatening due to repeating bouts of acute pancreatitis.

The condition was estimated to be affecting approximately 0.005 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 mibavademab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a reduction in HbA1c and triglycerides in patients that are resistant to metreleptin treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for mibavademab, for treatment of Berardinelli-Seip syndrome (congenital generalised lipodystrophy), was adopted by consensus.

### 2.1.2. mibavademab - EMA/OD/0000147895

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Regeneron Ireland Designated Activity Company; Treatment of Lawrence syndrome (acquired generalised lipodystrophy)

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

Lawrence syndrome (acquired generalised lipodystrophy) appears to belong to part of a broader group of disorders called acquired lipodystrophy syndromes. The sponsor was requested to discuss if this condition could be qualified under treatment of acquired lipodystrophy syndromes as well as any other causes of these syndromes. The COMP considered that iatrogenic acquired lipodystrophies were not considered as part of the umbrella term (J Clin Endocrinol Metab. 2016 Dec; 101(12): 4500–4511). Note that this was for the purposes of orphan medicinal product designation. The sponsor's attention was drawn to the orphan regulations and relevant guidelines (especially section A of [2022/C 440/02](#)).

- Number of people affected

The Committee noted that there is the possibility of grouping the condition under the umbrella term acquired lipodystrophy syndromes. The sponsor was requested to propose a revised prevalence estimate with the assumptions for acquired lipodystrophy syndromes.

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

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

In the written response, and during an oral explanation before the Committee on 13 February 2024, the sponsor noted that to characterise lipodystrophies based on aetiology alone, rather than on a set of signs and symptoms would inappropriately group together two very distinct syndromes (partial and generalised lipodystrophy) with different signs and symptoms, disease onset, and severity. To support this claim, the sponsor highlighted the classification system as presented in Brown et al., 2016.

The COMP accepted the arguments proposed by the sponsor regarding the current nomenclature and differences highlighted.

The original prevalence estimate submitted was accepted for the Lawrence syndrome which was 0.0007 in 10,000 was rounded off to 0.001 in 10,000.

The COMP was of the opinion that the questions had been addressed adequately and that they could recommend granting the orphan designation.

The Committee agreed that the condition, Lawrence syndrome (acquired generalised lipodystrophy), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing mibavademab was considered justified based on non-clinical in vivo data as well as preliminary clinical data showing treatment with the high dose regimen resulted in clinically meaningful reductions in HbA1c and triglycerides compared to baseline.

The condition is chronically debilitating due to diabetes mellitus and its long-term complications. Patients develop recurrent episodes of acute pancreatitis from extreme hypertriglyceridemia; end stage liver disease resulting from progressive cirrhosis secondary to hepatic steatosis and/or steatohepatitis; end-stage renal disease due to chronic kidney diseases related to diabetes or associated with the syndrome; cardiomyopathy and accelerated atherosclerotic vascular disease. The disease is often associated with fatality at a young age typically from cardiovascular, renal, or hepatic causes.

The condition was estimated to be affecting approximately 0.001 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 mibavademab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a reduction in HbA1c and triglycerides in patients that are resistant to metreleptin treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for mibavademab, for treatment of Lawrence syndrome (acquired generalised lipodystrophy), was adopted by consensus.

### 2.1.3. - EMA/OD/0000156633

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 24 January 2024, prior to responding to the list of issues.

### 2.1.4. - EMA/OD/0000150709

Treatment of Pilonidal disease

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 2 February 2024, prior to responding to the list of issues.



## 2.1.5. alrefimotide acetate, riletamotide acetate, tapderimotide acetate - EMA/OD/0000142006

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ULTIMOVACS ASA; Treatment of mesothelioma

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:

- 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 mesothelioma the sponsor was requested to further elaborate on:

- the results obtained in the preliminary clinical data and provide additional follow-up data which could clarify the impact of the add on therapy,
- results observed in the control arm compared to published results.
- Number of people affected

The Committee has noted that the incidence of the condition has been declining over time and that it could be lower than the proposed worst-case estimate. The sponsor was therefore requested to provide a more realistic estimate using more current data and a less conservative assumption of the duration of the condition. The sponsor was requested 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 was advised to refer to the ["Points to Consider on the Estimation and Reporting of a Prevalence of a Condition for Orphan Designation"](#).

In the written response, the sponsor defended their position.

Regarding prevalence it was noted that median survival of mesothelioma patients varies based on several factors which include the type of mesothelioma, the stage of the disease at diagnosis, the individual general health, and the efficacy of therapy. A realistic duration of pleural mesothelioma was estimated to be between 18 and 29 months.

Using an incidence of 1.8 the sponsor estimated the prevalence to 0.43 in 10,000. It was noted that the prevalence has dropped in recent years and a revised final estimate of 0.4 in 10,000 was accepted by the COMP.

Updated survival data from the investigator-initiated trial in patients failing first-line therapy could not be provided. The sponsor, however, submitted favourable progression free survival data from the local assessment which helps to contextualise the outcomes of trials in the setting targeted. In view of the valid second line target patient population for this cancer vaccination approach and the adequately justified combination treatment (nivolumab/ipilimumab), the favourable overall survival data in this comparative proof of concept study, although immature and not consistently supported by secondary endpoints, can be accepted for medical plausibility for initial orphan designation.

The data therefore support treatment in the second line setting where currently no authorised medicines exist to support significant benefit based on a clinically relevant advantage. The COMP considered that the written response adequately addressed the concerns of the COMP and cancelled the oral explanation. The Committee recommended granting the orphan designation.

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

The intention to treat the condition with the medicinal product containing alrefimotide acetate, riletamotide acetate, tapderimotide acetate was considered justified based on preliminary clinical data showing an improvement in overall survival.

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

The condition was estimated to be affecting approximately 0.4 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 alrefimotide acetate, riletamotide acetate, tapderimotide acetate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate an improvement in overall survival when the product is used in combination in second line treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for alrefimotide acetate, riletamotide acetate, tapderimotide acetate, for treatment of mesothelioma, was adopted by consensus.

## **2.2. For discussion / preparation for an opinion**

### **2.2.1. autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent - EMA/OD/0000152958**

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Raremoon Consulting Esp S.L.; Treatment of multiple myeloma

COMP Rapporteur: Evangelia Giannaki

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

The intention to treat the condition with the medicinal product containing autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent was considered justified based on the preliminary clinical data showing that patients with relapsed or refractory multiple myeloma achieved partial or complete responses.

The condition is chronically debilitating due to development of hypercalcemia, renal insufficiency, anaemia and/or bleeding, frequent infections, and bone lesions, and life-threatening due to poor survival of patients with relapsed and refractory disease.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data which showed that patients with relapsed and refractory multiple myeloma previously treated with the authorised medicinal products achieved partial, complete or stringent complete responses. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent, for treatment of multiple myeloma, was adopted by consensus.

#### 2.2.2. - EMA/OD/0000155985

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Treatment of traumatic spinal cord 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 March 2024 meeting.

#### 2.2.3. zatolmilast - EMA/OD/0000157446

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Shionogi B.V.; Treatment of fragile X syndrome

COMP Rapporteur: Cécile Dop

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

The intention to treat the condition with the medicinal product containing zatolmilast was considered justified based on non-clinical in vivo data in a model of the condition showing improvement in behavioural outcome measures and preliminary clinical data showing an improvement in communication and language use.

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

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

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

A positive opinion for zatolmilast, for treatment of fragile X syndrome, was adopted by consensus.

#### 2.2.4. sevasemten - EMA/OD/0000158128

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FGK Representative Service GmbH; Treatment of Becker muscular dystrophy

COMP Rapporteur: Maria Judit Molnar

The Committee agreed that the condition, Becker 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 sevasemten was considered justified based on non-clinical data in a model of the condition showing an improvement in functional outcomes and biomarkers of the disease, in combination with preliminary clinical data indicating a reduction in biomarkers of muscle damage and the improvement in functional outcomes when compared with natural history data from individuals with Becker muscular dystrophy and a similar level of function.

The condition is chronically debilitating due to decline in muscle strength and ambulation, and increased risk of cardiomyopathy. It can be life-threatening due to the progressive decline in respiratory and cardiac function.

The condition was estimated to be affecting approximately 0.2 in 10,000 persons in the European Union, at the time the application was made.

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 sevasemten, for treatment of Becker muscular dystrophy, was adopted by consensus.

#### 2.2.5. - EMA/OD/0000158137

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Treatment of Duchenne muscular dystrophy (DMD)

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 March 2024 meeting.

#### 2.2.6. 4-(4-methyl-piperazin-1-yl)-N-{6-[2-(4-trifluoromethyl-benzyloxy)-ethoxy]-1H-indazol-3-yl}-benzamide hemioxalate - EMA/OD/0000158813

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Nerviano Medical Sciences S.r.l.; Treatment of acute myeloid leukaemia

COMP Rapporteur: Jana Mazelova

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

The intention to treat the condition with the medicinal product containing 4-(4-methyl-piperazin-1-yl)-N-{6-[2-(4-trifluoromethyl-benzyloxy)-ethoxy]-1H-indazol-3-yl}-benzamide hemioxalate was considered justified based on non-clinical data in models of the condition supporting inhibition of tumour growth and increased survival, as well as preliminarily clinical data showing responses in relapsed/refractory patients.

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

The condition was estimated to be affecting approximately 1.5 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 4-(4-methyl-piperazin-1-yl)-N-{6-[2-(4-trifluoromethyl-benzyloxy)-ethoxy]-1H-indazol-3-yl}-benzamide hemioxalate will be of significant benefit to

those affected by the condition. The sponsor has provided preliminary clinical data which showed responses in heavily pretreated patients with acute myeloid leukaemia including those who have failed treatment with the currently authorised medicinal product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 4-(4-methyl-piperazin-1-yl)-N-{6-[2-(4-trifluoromethyl-benzyloxy)-ethoxy]-1H-indazol-3-yl}-benzamide hemioxalate, for treatment of acute myeloid leukaemia, was adopted by consensus.

#### **2.2.7. - EMA/OD/0000158981**

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Treatment of congenital pseudarthrosis of long bones

The COMP adopted a list of issues that will be sent to the sponsor. The Committee will discuss the submitted answers to the list of issues at the March 2024 meeting.

#### **2.2.8. - EMA/OD/0000159738**

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Treatment of ataxia-oculomotor apraxia-4

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 March 2024 meeting.

### **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**

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COMP rapporteurs were appointed for 17 applications.

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

The Committee noted that evaluation was on-going for 4 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 Fabry disease

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 sickle cell disease

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

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

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

None

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

##### **4.2.1. Filspari - sparsentan - EMEA/H/C/005783, EU/3/20/2345, EMA/OD/0000110380**

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Vifor France; Treatment of primary IgA nephropathy

COMP Rapporteur: Armando Magrelli; COMP Co-Rapporteur: Elisabeth Johanne Rook

An opinion recommending not to remove Filspari, sparsentan, EU/3/20/2345 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 February 2024 meeting.]*

##### **4.2.2. - danicopan - EMEA/H/C/005517, EU/3/17/1946, EMA/OD/0000136076**

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Alexion Europe SAS; Treatment of paroxysmal nocturnal haemoglobinuria

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 March 2024 meeting.

#### 4.2.3. Qalsody – tofersen - EMEA/H/C/005493, EU/3/16/1732, EMA/OD/0000137554

Biogen Netherlands B.V.; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Darius Matusevicius; COMP Co-Rapporteur: Robert Nistico

An opinion recommending not to remove Qalsody, tofersen, EU/3/16/1732 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 February 2024 meeting.]*

#### 4.2.4. Zynyz – retifanlimab - EMEA/H/C/006194, EU/3/22/2743, EMA/OD/0000152395

Incyte Biosciences Distribution B.V.; Treatment of Merkel cell carcinoma

COMP Rapporteur: Elisabeth Johanne Rook; COMP Co-Rapporteur: Dinko Vitezic

An opinion recommending not to remove Zynyz, retifanlimab, EU/3/22/2743 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 February 2024 meeting.]*

#### 4.2.5. – iptacopan - EMEA/H/C/005764, EU/3/20/2281, EMA/OD/0000141229

Novartis Europharm Limited; Treatment of paroxysmal nocturnal haemoglobinuria

The status of the procedure at CHMP was noted.

#### 4.2.6. – dantrolene sodium, hemiheptahydrate - EMEA/H/C/006009, EU/3/21/2443, EMA/OD/0000102465

Norgine B.V.; Treatment of malignant hyperthermia

The status of the procedure at CHMP was noted.

### **4.3. Appeal**

None

### **4.4. On-going procedures**

COMP co-ordinators were appointed for 5 applications.

### **4.5. Orphan Maintenance Reports**

Documents were tabled for information.

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

### **5.1. After adoption of CHMP opinion**

#### **5.1.1. Aspaveli – pegcetacoplan - EMEA/H/C/005553/II/0011, EU/3/17/1873, EMA/OD/0000140083**

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Swedish Orphan Biovitrum AB (publ); Treatment of paroxysmal nocturnal haemoglobinuria

CHMP Rapporteur: Alexandre Moreau; CHMP Co-Rapporteur: Selma Arapovic

As agreed during the previous meeting, a list of issues was sent to the sponsor for response.

In the written response, and during an oral explanation before the Committee on 14 February 2024 the sponsor defended their position.

The Committee agreed that the proposed therapeutic indication falls entirely within the scope of the orphan condition of the designated orphan medicinal product.

The prevalence of paroxysmal nocturnal haemoglobinuria (hereinafter referred to as “the condition”) was estimated to remain below 5 in 10,000 and was concluded to be 0.4 in 10,000 persons in the European Union, at the time of the review of the designation criteria.

The condition is life-threatening and chronically debilitating due to the complications of chronic haemolysis, such as abdominal pain, cytopenia, and kidney malfunction, and due to occurrence of thrombosis and haemorrhage in various organs. Vascular complications in the central nervous system are the most common cause of death.

The sponsor’s claim that Aspaveli is of significant benefit to those affected by the orphan condition was not established.

The COMP, having considered the information submitted by the sponsor and on the basis of Article 5(12)(b) of Regulation (EC) No 141/2000, is of the opinion that the criteria for designation as set out in the first paragraph of Article 3(1)(a) are satisfied and the criteria for designation as set out in Article 3(1)(b) are not satisfied.

An opinion recommending the removal of Aspaveli, pegcetacoplan, EU/3/17/1873 from the EC Register of Orphan Medicinal Products was adopted as COMP did not reach the two-third-majority position in favour of the designation of the medicinal product as an orphan medicinal product. The divergent positions were appended to this opinion. The sponsor will have 90 days to appeal from the COMP decision.

### **5.2. Prior to adoption of CHMP opinion**

#### **5.2.1. Carvykti - ciltacabtagene autoleucel - EMEA/H/C/005095/II/0021, EU/3/20/2252, EMA/OD/0000141581**

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Janssen - Cilag International; Treatment of multiple myeloma

COMP Rapporteur: Maria Elisabeth Kalland; COMP Co-Rapporteur: Karri Penttila; CHMP Rapporteur: Jan Mueller-Berghaus



An opinion recommending not to remove Carvykti, ciltacabtagene autoleucel, EU/3/20/2252 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

*[Post-meeting note: The COMP adopted the opinion by written procedure following its February 2024 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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The Chair welcomed Emma Fagan, as the new member for Ireland.

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

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None

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

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The Committee was updated about the next strategic review and learning meeting to be held in person on 27-28 March 2024 in Leuven, Belgium.

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

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The working group on Protocol Assistance met face-to-face on 13 February 2024.

#### **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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Documents were tabled for information.

#### **7.3.2. Innovation Task Force (ITF) meetings**

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The COMP noted the upcoming ITF meetings and the presentation of an overview of ITF activities in 2023.

#### **7.3.1. Revision of EMA guideline on epileptic disorders**

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[Clinical investigation of medicinal products in the treatment of epileptic disorders - Scientific guideline](#)

The COMP noted the presentation on the revision of EMA guideline on epileptic disorders.

### **7.4. Cooperation within the EU regulatory network**

#### **7.4.1. European Commission**

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None

#### **7.4.2. Feedback from the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Plenary**

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The COMP noted the presentation of ENCePP activities in 2023 and feedback of the ENCePP plenary held in December 2023.

#### **7.4.3. EURORDIS update on Rare Diseases Day events**

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The COMP received an update of the upcoming rare disease day and other events in 2024.

### **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 2024

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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

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

### 8. **Any other business**

#### 8.1. **New tool for searching scientific advice - Scientific Explorer**

The COMP received a demonstration of the new tool for searching CHMP scientific advices.

#### 8.2. **Overview of the relevant case-law of the Court of Justice of the European Union**

The COMP discussed the principles from the case-law of the Court of Justice of the European Union that are relevant for the drafting of COMP assessment reports.

### 9. **List of participants**

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 13-15 February 2024 COMP meeting, which was held in-person.

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

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Violeta Stoyanova-Beninska	Chair	Netherlands	No interests declared	
Armando Magrelli	Vice-Chair	Expert recommended by EMA	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	No restrictions applicable to this meeting	
Tim Leest	Member	Belgium	No interests declared	
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	
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	
Emma Fagan	Member	Ireland	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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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 participation in final deliberations and voting on:	4.2.3. Qalsody – tofersen - EMEA/H/C/005493, EU/3/16/1732, EMA/OD/000013755 4
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	Slovak Republic	No interests declared	
Gloria Maria Palomo Carrasco	Member	Spain	No interests declared	
Darius Matusevicius	Member	Sweden	No restrictions applicable to this meeting	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Julian Isla	Member	Patients' Organisation Representative	No interests declared	
Ines Alves	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Judit Molnar	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Maria Cavaller Bellaubi	Expert	Patients' Organisation Representative	No restrictions applicable to this meeting	
Loes den Otter	Expert	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
André Elferink	Expert	Netherlands	No interests declared	
Meeting run with support from relevant EMA staff				

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

## 10. Explanatory notes

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

### Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

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

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

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

Sponsor

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

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

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

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