



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 February 2024
EMA/COMP/47120/2024
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 16-18 January 2024

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

Disclaimers

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

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

Note on access to documents

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

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us

Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

An agency of the European
Union



Table of contents

1.	Introduction	5
1.1.	Welcome and declarations of interest of members and experts.....	5
1.2.	Adoption of agenda.....	5
1.3.	Adoption of the minutes	5
2.	Applications for orphan medicinal product designation	5
2.1.	For opinion	5
2.1.1.	mRNA encoding the human <i>CFTR</i> gene - EMA/OD/0000149117	5
2.1.2.	- EMA/OD/0000139765	7
2.1.3.	carboplatin - EMA/OD/0000144999.....	8
2.1.4.	human IgG1 monoclonal antibody targeting amyloid transthyretin - EMA/OD/0000154242 .	9
2.1.5.	tinengotinib - EMA/OD/0000149156.....	11
2.2.	For discussion / preparation for an opinion.....	12
2.2.1.	raludotatug deruxtecan - EMA/OD/0000140382.....	12
2.2.2.	- EMA/OD/0000142006	13
2.2.3.	ifinatumab deruxtecan - EMA/OD/0000145757	13
2.2.4.	- EMA/OD/0000146222	14
2.2.5.	paclitaxel - EMA/OD/0000147176	14
2.2.6.	- EMA/OD/0000147895	14
2.2.7.	- EMA/OD/0000150709	14
2.2.8.	repagermanium - EMA/OD/0000155761	15
2.2.9.	donidalorsen - EMA/OD/0000156328	15
2.2.10.	- EMA/OD/0000156633	16
2.2.11.	plerixafor - EMA/OD/0000156752	16
2.2.12.	autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent - EMA/OD/0000157053	16
2.2.13.	andecaliximab - EMA/OD/0000157307	17
2.3.	Revision of the COMP opinions	18
2.4.	Amendment of existing orphan designations.....	18
2.5.	Appeal	18
2.6.	Nominations	18
2.6.1.	New applications for orphan medicinal product designation - Appointment of COMP rapporteurs.....	18
2.7.	Evaluation on-going.....	18
3.	Requests for protocol assistance with significant benefit question	18
3.1.	Ongoing procedures	18
3.1.1.	-	18

4.	Review of orphan designation for orphan medicinal products at time of initial marketing authorisation	18
4.1.	Orphan designated products for which CHMP opinions have been adopted	18
4.2.	Orphan designated products for discussion prior to adoption of CHMP opinion	19
4.2.1.	Nezglyal – leriglitazone - EMEA/H/C/005757, EU/3/16/1770, EMA/OD/0000144315.....	19
4.2.2.	– danicopan - EMEA/H/C/005517, EU/3/17/1946, EMA/OD/0000136076	19
4.3.	Appeal	19
4.4.	On-going procedures	19
4.5.	Orphan Maintenance Reports.....	19
5.	Review of orphan designation for authorised orphan medicinal products at time marketing authorisation extension	19
5.1.	After adoption of CHMP opinion	19
5.2.	Prior to adoption of CHMP opinion	19
5.2.1.	Abecma – idecabtagene vicleucel - EMEA/H/C/004662/II/0031, EU/3/17/1863, EMA/OD/0000132929	19
5.2.2.	Aspaveli – pegcetacoplan - EMEA/H/C/005553/II/0011, EU/3/17/1873, EMA/OD/0000140083	20
5.3.	Appeal	20
5.4.	On-going procedures	20
6.	Application of Article 8(2) of the Orphan Regulation	20
7.	Organisational, regulatory and methodological matters	20
7.1.	Mandate and organisation of the COMP	20
7.1.1.	COMP membership.....	20
7.1.2.	Vote by proxy	20
7.1.3.	Strategic Review & Learning meetings.....	20
7.1.4.	Protocol Assistance Working Group (PAWG)	20
7.1.5.	COMP Decisions Database.....	20
7.2.	Coordination with EMA Scientific Committees or CMDh-v	21
7.2.1.	Recommendation on eligibility to PRIME – report.....	21
7.3.	Coordination with EMA Working Parties/Working Groups/Drafting Groups	21
7.3.1.	Working Party with Patients’ and Consumers’ Organisations (PCWP) and Working Party with Healthcare Professionals’ Organisations (HCPWP)	21
7.3.2.	Upcoming Innovation Task Force (ITF) meetings	21
7.4.	Cooperation within the EU regulatory network.....	21
7.4.1.	European Commission.....	21
7.4.2.	Feedback from the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Plenary	21
7.5.	Cooperation with International Regulators.....	21
7.5.1.	Food and Drug Administration (FDA).....	21

7.5.2.	Japanese Pharmaceuticals and Medical Devices Agency (PMDA).....	21
7.5.3.	Therapeutic Goods Administration (TGA), Australia	21
7.5.4.	Health Canada.....	21
7.6.	Contacts of the COMP with external parties and interaction with the Interested Parties to the Committee	21
7.7.	COMP work plan	22
7.7.1.	Work plan for 2024	22
7.8.	Planning and reporting	22
7.8.1.	List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2024	22
7.8.2.	Overview of orphan marketing authorisations/applications.....	22
8.	Any other business	22
8.1.	New tool for searching scientific advice - Scientific Explorer.....	22
8.2.	Ultra-rare diseases project	22
9.	List of participants	22
10.	Explanatory notes	24

1. Introduction

1.1. Welcome and declarations of interest of members and experts

The Chair opened the meeting by welcoming all participants. The meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members and experts and based on the topics in the agenda of the 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.

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

The Chair announced the start of the Belgian presidency of the Council of the European Union (EU).

1.2. Adoption of agenda

The agenda for 16-18 January 2024 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 05-07 December 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. mRNA encoding the human *CFTR* gene - EMA/OD/0000149117

Arcturus Therapeutics Europe B.V.; Treatment of cystic fibrosis

COMP Rapporteur: Enrico Costa

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

- Significant benefit

The sponsor was invited to submit the actual efficacy/activity data with the proposed medicinal product in the:

- a) human bronchial epithelial (HBE) cells derived from a cystic fibrosis (CF) patient with the G542X/R1162X (*CFTR*-null) mutation and
- b) the murine *CFTR* G542X mutation (Class I null mutation, i.e., *CFTR* functional knockout) model.

Furthermore, the sponsor was asked to clarify if patients with *CFTR* null mutations are included in part 2 of the currently ongoing exploratory study (ARCT-032-01).

Lastly, with regards to the efficacy data in the non-murine in vivo model following the fourth dose, it would be helpful for the COMP to understand possible reasons for the observed efficacy response (increase in mucociliary clearance (MCC)) in the vehicle (LUNAR-TdT) treated group.

In the written response, the sponsor provided non-clinical in vitro data showing restoration of the activity of the cystic fibrosis transmembrane conductance regulator (*CFTR*) in cells from patients with *CFTR* null mutations (G542X/R1162X). Furthermore, the sponsor submitted non-clinical in vivo data in models with *CFTR* null mutations showing restoration of *CFTR* function as measured through the surrogate parameter of nasal potential difference (NPD). The preferable efficacy parameter of mucus clearance could not be used in this murine CF model due to significant anatomical differences of the respiratory tract and the lack of producing excess mucus. Nevertheless, NPD is a measure of voltage across the nasal epithelium which results from transepithelial ion transport and reflects in part *CFTR* function.

Lastly, the sponsor stated that the MCC observed in the vehicle (LUNAR-TdT) treated group was considered overall rather minimal. Except for one outlier. The reduced efficacy after the fourth dose of the proposed medicinal product and any non-specific effects warrant further refinement of the sponsors' newly developed non-clinical in vivo CF model-based MCC technique which requires frequent intubation.

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

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

The intention to treat the condition with the medicinal product containing mRNA encoding the human *CFTR* gene was considered justified based on non-clinical in vitro data showing increase/restoration of *CFTR* activity in cells from patients with cystic fibrosis carrying various *CFTR* mutations and non-clinical in vivo data in two models carrying mutations in the *CFTR* gene showing restoration of *CFTR* function and improvement in mucociliary clearance.

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

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing mRNA encoding the human *CFTR* gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vitro data showing restoration of the activity of the CFTR also in cells from patients with *CFTR* null mutations and non-clinical in vivo data in a model carrying a *CFTR* null mutation showing restoration of CFTR function. Efficacy in patients with *CFTR* null mutations cannot be expected with currently authorised medicinal products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for mRNA encoding the human *CFTR* gene, for treatment of cystic fibrosis, was adopted by consensus.

2.1.2. - EMA/OD/0000139765

Treatment of glioma

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 glioma the sponsor should further elaborate on:

- the relevance of the non-clinical model used for the treatment of the condition, the methodology followed, and the interpretation of the results obtained in the experiments,
 - the clinical data in patients with the condition and its relevance for the development of the product in the condition.
- Significant benefit

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

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

In the written response, and during an oral explanation before the Committee on 16 January 2024, the sponsor defended their position. As part of the response, the sponsor clarified the available non-clinical and clinical data.

The non-clinical models used for studying the anti-tumour effect on glioma included were thoroughly described as well as the results of the experiments which would indicate that the proposed product showed a dose-dependent inhibitory effect on tumour growth. In addition, the combination of the product with temozolomide (TMZ) showed synergistic effects suggesting the potential use in combination therapy.

Additionally, further information was provided on the initial Phase I dose-finding and pharmacokinetic study C-0401 in which 54 patients with recurrent or refractory glioma were enrolled. The majority of patients had a diagnosis of glioblastoma multiforme. All 54

patients had previously undergone surgery for their brain tumours and all of them received prior TMZ. Of these patients 12.0% had a response to therapy.

In addressing the significant benefit question, the sponsor provided information on prior lines of treatment for the patient population illustrating the relapse or refractory nature of these patients to authorised treatments such as temozolomide. In addition, a detailed description was provided for the patient with a complete response who is still in remission.

Overall, at this point in time the responses from the sponsor addressing the medical plausibility concerns were considered satisfactory by the COMP based on the totality of evidence from non-clinical and clinical data showing responses upon treatment, however, the arguments on significant benefit were not considered as sufficient given the lack of information on the clinical study, and the absence of a cohesive response as part of the non-clinical studies in comparison with authorised treatments. As part of the discussion the sponsor indicated potential new clinical data that could become available. As a result, the sponsor was advised to resubmit the application as soon as this information is available as it could help dispel the existing doubts for granting an initial orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 16 January 2024, prior to final opinion.

2.1.3. carboplatin - EMA/OD/0000144999

Carthera; Treatment of glioma

COMP Rapporteur: Jana Mazelova

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of glioma the sponsor should further elaborate on:

- the process of selection of the product based on in vitro results (sensitivity in patient-derived and commercially available cell lines),
 - the relevance of the non-clinical model used for the treatment of glioma, and the interpretation of the results obtained in the experiments between the different treatment groups,
 - the methodology used in the clinical studies as well as the results from these studies and their relevance for the development of the product in the condition. Additional data on the advantages of the medical device compared to the medicinal product alone.
- Significant benefit

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the clinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition. Comparative data to authorised treatments should be provided.

In the written response, the sponsor clarified the mechanism of the medical device used in the delivery of the proposed product carboplatin. Once implanted, the device is activated on demand to aid the delivery of the proposed product into the target area.

In support of the arguments for medical plausibility, the sponsor elaborated on the rationale behind the selection of the active substance carboplatin. This was sustained by bibliographic and proprietary non-clinical and clinical data. Overall, information was provided on the methodology of the studies and the outcomes observed which overall supported the activity of the proposed product having an effect on tumour volume and survival.

In responding to the significant benefit question the sponsor elaborated on the available clinical data from study SC9-GBM-01, with patients at first or second recurrence of the disease after they received standard first line therapy (surgery followed by radio-chemotherapy and maintenance treatment with temozolomide). The median survival was indirectly compared to authorised treatments as reported in the literature. Although interpretation of these results was limited due to the small cohorts, the findings in a relapse or refractory population would support the assumption of a significant benefit.

Overall, at this point in time the responses from the sponsor were considered satisfactory by the COMP, and a positive opinion was adopted prior to the oral explanation. The sponsor was advised to request protocol assistance for the next steps in the development.

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

The intention to treat the condition with the medicinal product containing carboplatin using an implantable ultrasound medical device was considered justified based on non-clinical data in models of the condition showing a positive effect on survival and tumour growth, as well as preliminary clinical data which showed an effect on tumour volume and increased survival in pre-treated glioblastoma patients.

The condition is chronically debilitating due to symptoms caused by the tumour compressing the surrounding brain tissue including headache, anorexia, nausea, vomiting, seizures, neurological deficits, personality changes and cognitive decline. The condition is also life-threatening, with a limited median overall survival.

The condition was estimated to be affecting approximately 2.7 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing carboplatin will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that indicate tumour stabilisation with the proposed product in high-grade glioma patients pre-treated with standard of care treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for carboplatin, for treatment of glioma, was adopted by consensus.

2.1.4. [human IgG1 monoclonal antibody targeting amyloid transthyretin - EMA/OD/0000154242](#)

Alexion Europe; Treatment of transthyretin-mediated amyloidosis

COMP Rapporteur: Zsofia Gyulai

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 issue:

- 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"](#).

Due to improved recognition and early diagnosis of deposits of misfolded transthyretin (TTR) amyloid in patients with heart failure in recent years, the sponsor should reinforce the prevalence calculation based on up-to-date relevant epidemiological studies and registers for the proposed orphan condition. The sponsor should also perform a sensitivity analysis of the reported calculations clustered by aetiology - ATTRv and ATTRwt.

In the written response, and during an oral explanation before the Committee on 17 January 2024, the sponsor discussed the most up-to-date relevant epidemiological data. A comprehensive literature review was conducted to estimate the prevalence and incidence of ATTR, including the two main presentations of cardiomyopathy (ATTR-CM) and polyneuropathy (ATTR-PN) as well as the hereditary (ATTRv) and wildtype (ATTRwt) forms, in the European Union (EU) using data from published literature up to 2023.

This literature search yielded 265 articles. Of these, studies reporting incidence/prevalence of ATTR overall or an ATTR subtype (clinical or aetiology) in Europe were included both from non-endemic and endemic countries. These studies measured ATTR incidence/prevalence in 20 of the EU-27 member states, and 4 other European countries.

In addition, in lieu of a sensitivity analysis – given the uncertainty of the parameters needed to indirectly derive the prevalence – the sponsor assessed the prevalence growth of ATTR-CM in the last 5 years, with projection for the next 5 years. As part of this analysis the sponsor relied on studies published in more recent years, thereby covering a period where the advances in diagnosis were already in place. Furthermore, while multiple sources were identified, emphasis was put on nationwide studies, using high-quality national registers, and reporting annual prevalence of ATTR-CM specifically.

As a result, even when considering the highest estimates available, the findings would demonstrate that the prevalence of ATTR falls below the established EU threshold for orphan drug designation.

Overall, at this point in time the prevalence calculation can be supportive of a positive opinion. The COMP adopted a positive opinion after the oral explanation.

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

The intention to treat the condition with the medicinal product containing human IgG1 monoclonal antibody targeting amyloid transthyretin was considered justified based on preliminary clinical data suggesting a reduction in cardiac tracer uptake and an improvement in biomarkers in patients with cardiomyopathy manifestations of the condition, in combination with exploratory functional data that could indicate the stabilisation of the disease progression.

The condition is life-threatening and chronically debilitating in particular due to the development of neuropathy and cardiomyopathy.

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 human IgG1 monoclonal antibody targeting amyloid transthyretin will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data suggesting improvements in the deposits of misfolded transthyretin (TTR) amyloid with the proposed product in combination with standard of care indicating a disease modifying potential. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for human IgG1 monoclonal antibody targeting amyloid transthyretin, for treatment of ATTR amyloidosis, was adopted by consensus.

2.1.5. [tinengotinib - EMA/OD/0000149156](#)

Parexel International (IRL) Limited; Treatment of biliary tract 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:

- Condition

The COMP considered that the appropriate condition for orphan designation is the overarching condition of biliary tract cancer (BTC).

- Number of people affected

The sponsor was asked to provide a revised prevalence calculation and final estimate for the overarching disease entity/orphan condition of biliary tract cancer (comprising intra- and extrahepatic cholangiocarcinoma, gallbladder cancer and ampulla of Vater cancer). European epidemiologic data sources should be considered as much as possible.

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 updated the proposed condition to biliary tract cancer (BTC), in line with the COMP's request.

The sponsor proposed a new complete prevalence estimate of 0.73 per 10,000 in line with the broader condition of BTC. This estimate comprised the cumulative incidence values of the condition subsets of intra- and extrahepatic cholangiocarcinoma (CCA), gallbladder cancer (GBC) and ampulla of Vater cancer (AVC) mainly based on GLOBOCAN for 2020 data (i.e. 0.68), and multiplied by a median survival of 12.7 months (1.06 years), based on median survival figures of GBC (6.1 months: de Savornin Lohman E et al., 2020), CCA (13.9 months: Strijker et al., 2019; Mavros et al., 2014) and AVC (18.3 months: De Jong et al., 2021).

While the COMP agreed with the incidence rate of around 0.68 for BTC, a more conservative disease duration was preferred, in view of the heterogeneity of the disease and the proportion of patients with long-term benefit. In this regard, the COMP also referred to survival data of BTC patients from the German Centre for Cancer Registry 2022 (ZfDK). One year after diagnosis, less than half of the patients are still alive. After more than 5 years, the survival rate is rather stable, indicating that about 10% of patients have been permanently cured. In recent literature, similar survival rates were reported for populations in Belgium (Gilliaux et al., 2021), Finland (Koppatz et al., 2021) and Sweden (Strijker et al., 2019).

In conclusion, the COMP accepted a prevalence estimate of approximately 1.5 per 10,000. This estimate was based on an up-rounded value of the sponsor's incidence rate of 0.68 per 10,000 multiplied by an average disease duration of 2 years.

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

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

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

The intention to treat the condition with the medicinal product containing tinengotinib was considered justified based on preliminary clinical data showing tumour responses in patients with advanced cholangiocarcinoma carrying an FGFR alteration.

The condition is chronically debilitating due to development of hepatic insufficiency, progressive biliary obstruction followed by complications such as infections, and life-threatening with a low overall survival following diagnosis.

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 tinengotinib will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed responses with the product in patients with advanced cholangiocarcinoma carrying an FGFR alteration and who have been previously treated with currently authorised therapies including FGFR inhibitors. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for tinengotinib, for treatment of biliary tract cancer, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. [raludotatug deruxtecan - EMA/OD/0000140382](#)

Daiichi Sankyo Europe GmbH; Treatment of ovarian cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

The intention to treat the condition with the medicinal product containing raludotatug deruxtecan was considered justified based on preliminary clinical data showing a partial response in mostly platinum-resistant patients.

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 raludotatug deruxtecan will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate partial responses in heavily pre-treated and platinum-resistant ovarian cancer patients, following treatment with the sponsor's product. The COMP considered that this constitutes a clinically relevant advantage.

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

2.2.2. - EMA/OD/0000142006

Treatment of mesothelioma

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 February 2024 meeting.

2.2.3. ifinatamab deruxtecan - EMA/OD/0000145757

Daiichi Sankyo Europe GmbH; Treatment of small cell lung cancer

COMP Rapporteur: Frauke Naumann-Winter

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

The intention to treat the condition with the medicinal product containing ifinatamab deruxtecan was considered justified based on non-clinical data showing an inhibition of tumour growth, and preliminary clinical data showing durable responses in patients affected by the condition and whose disease progressed after two prior lines of treatment.

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

The condition was estimated to be affecting approximately 1.3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing ifinatamab deruxtecan will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data in relapsed or refractory patients with small cell lung cancer who had progressed after a median of two prior lines of treatment, and who responded to treatment with the proposed product. The Committee considered that this constitutes a clinically relevant advantage.

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

2.2.4. - EMA/OD/0000146222

Treatment of Berardinelli-Seip syndrome (congenital generalised lipodystrophy)

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 February 2024 meeting.

2.2.5. paclitaxel - EMA/OD/0000147176

Woodley Bioreg S.r.l.; Treatment of gastric cancer

COMP Rapporteur: Frauke Naumann-Winter

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

The intention to treat the condition with the medicinal product containing paclitaxel was considered justified based on non-clinical data in models of the condition which showed antitumour activity and clinical data which showed responses in patients with recurrent or metastatic gastric cancer.

The condition is chronically debilitating due to dysphagia, weight loss and gastric bleeding, and life threatening with poor overall survival.

The condition was estimated to be affecting approximately 3.3 in 10,000 persons in the European Union, at the time the application was made.

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

The sponsor has provided non-clinical data that demonstrate that paclitaxel as monotherapy and in combination with anti-tumour agents showed superior responses than ramucirumab both as monotherapy and in combination. In addition, the sponsor has provided clinical data with paclitaxel as a single agent showing responses in patients with gastric tumours that have progressed upon prior systemic therapy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for paclitaxel, for treatment of gastric cancer, was adopted by consensus.

2.2.6. - EMA/OD/0000147895

Treatment of Lawrence syndrome (acquired generalised lipodystrophy)

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 February 2024 meeting.

2.2.7. - EMA/OD/0000150709

Treatment of pilonidal disease

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 February 2024 meeting.

2.2.8. repagermanium - EMA/OD/0000155761

Scendea (NL) B.V.; Treatment of focal segmental glomerulosclerosis

COMP Rapporteur: Elisabeth Johanne Rook

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

The intention to treat the condition with the medicinal product containing repagermanium was considered justified based on preliminary non-clinical data in a model of the condition which showed a reduction in the number of podocytes lost and an improvement in proteinuria.

The condition is life-threatening and chronically debilitating due to the development of end-stage kidney disease.

The condition was estimated to be affecting approximately 2.6 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 repagermanium will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that demonstrate the product could offer an alternative in patients who are refractory to cyclosporin. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for repagermanium, for treatment of focal segmental glomerulosclerosis, was adopted by consensus.

2.2.9. donidalorsen - EMA/OD/0000156328

Ionis Ireland Limited; Treatment of hereditary angioedema

COMP Rapporteur: Elisabeth Penninga

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

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 donidalorsen 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 donidalorsen 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 donidalorsen, for treatment of hereditary angioedema, was adopted by consensus.

2.2.10. - EMA/OD/0000156633

Treatment of soft tissue sarcoma

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 February 2024 meeting.

2.2.11. plerixafor - EMA/OD/0000156752

4p-Pharma; Treatment of acute respiratory distress syndrome

COMP Rapporteur: Joao Rocha

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

The intention to treat the condition with the medicinal product containing plerixafor was considered justified based on non-clinical data, showing beneficial effects on relevant endpoints reflecting lung function.

The condition is life-threatening with mortality up to approximately 50% and chronically debilitating due to persistent functional respiratory impairment.

The condition was estimated to be affecting approximately 3.2 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 plerixafor will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data which showed a potential non-immunosuppressant effect in the condition, where the use of steroids is not established. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for plerixafor, for treatment of acute respiratory distress syndrome, was adopted by consensus.

2.2.12. autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent - EMA/OD/0000157053

Raremoon Consulting Esp S.L.; Treatment of AL amyloidosis

COMP Rapporteur: Darius Matusevicius

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 autologous CD3-positive T-cells expressing a chimeric antigen receptor against B cell maturation agent was considered justified based on preliminary clinical data in patients with immunoglobulin light chain amyloidosis showing a high haematological response rate and organ responses.

The condition is chronically debilitating and life-threatening 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 1.3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing 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 clinical data that demonstrate that pre-treated patients with relapsed/refractory immunoglobulin light chain amyloidosis and with organ involvement who failed several lines of treatment including currently authorised therapy achieved 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 AL amyloidosis, was adopted by consensus.

2.2.13. andecaliximab - EMA/OD/0000157307

Regulatory Pharma Net S.r.l.; Treatment of fibrodysplasia ossificans progressiva

COMP Rapporteur: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing andecaliximab was considered justified based on non-clinical data in valid models of the condition showing reduction in heterotopic ossification.

The condition is chronically debilitating due to episodes of painful tumour-like soft-tissue swellings followed by the development of heterotopic ossification throughout the body and across joints causing progressive impairment of movement. The condition is life-threatening due to complications of thoracic insufficiency syndrome as a consequence of ankyloses in the thorax that lead to premature death.

The condition was estimated to be affecting less than 0.02 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for andecaliximab, for treatment of fibrodysplasia ossificans progressiva, was adopted by consensus.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

None

2.6. Nominations

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

COMP rapporteurs were appointed for 7 applications.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 8 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of malignant mesothelioma

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. Nezglyal – Ieriglitazone - EMEA/H/C/005757, EU/3/16/1770, EMA/OD/0000144315

Minoryx Therapeutics S.L.; Treatment of adrenoleukodystrophy

The status of the procedure at CHMP was noted.

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

Alexion Europe SAS; Treatment of paroxysmal nocturnal haemoglobinuria

The status of the procedure at CHMP was noted.

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 1 application.

4.5. Orphan Maintenance Reports

Documents were tabled for information.

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

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

5.2.1. Abecma – idecabtagene vicleucel - EMEA/H/C/004662/II/0031, EU/3/17/1863, EMA/OD/0000132929

Bristol-Myers Squibb; Treatment of multiple myeloma

COMP Rapporteur: Maria Elisabeth Kalland; COMP Co-Rapporteur: Karri Penttila; CAT Rapporteur: Rune Kjekken; CAT Co-Rapporteur: Heli Suila

An opinion recommending not to remove Abecma, idecabtagene vicleucel, EU/3/17/1863 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 January 2024 meeting.]

5.2.2. [Aspaveli – pegcetacoplan - EMEA/H/C/005553/II/0011, EU/3/17/1873, EMA/OD/0000140083](#)

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

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

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 February 2024 meeting.

5.3. **Appeal**

None

5.4. **On-going procedures**

COMP co-ordinators were appointed for 1 application.

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

None

7. **Organisational, regulatory and methodological matters**

7.1. **Mandate and organisation of the COMP**

7.1.1. **COMP membership**

None

7.1.2. **Vote by proxy**

None

7.1.3. **Strategic Review & Learning meetings**

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)**

The working group on Protocol Assistance met remotely on 15 January 2024.

7.1.5. **COMP Decisions Database**

The COMP acknowledged the importance of adding further topics to the database.

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendation on eligibility to PRIME – report

Documents were tabled for information.

7.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

7.3.1. Working Party with Patients’ and Consumers’ Organisations (PCWP) and Working Party with Healthcare Professionals’ Organisations (HCPWP)

None

7.3.2. Upcoming Innovation Task Force (ITF) meetings

The COMP noted the upcoming ITF meetings.

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

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

The discussion was postponed.

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. Therapeutic Goods Administration (TGA), Australia

None

7.5.4. Health Canada

None

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

None

7.7. COMP work plan

7.7.1. Work plan for 2024

The COMP work plan for 2024 was adopted and has been [published](#).

7.8. Planning and reporting

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

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2024 were circulated.

7.8.2. Overview of orphan marketing authorisations/applications

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

8. Any other business

8.1. New tool for searching scientific advice - Scientific Explorer

The discussion was postponed.

8.2. Ultra-rare diseases project

The COMP noted the presentation on the ultra-rare diseases project.

9. List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 16-18 January 2024 COMP meeting, which was held 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	
Tim Leest	Member	Belgium	No interests declared	
Dinko Vitezic	Member	Croatia	No interests declared	
Ioannis Kkolos	Member	Cyprus	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Enrico Costa	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No restrictions applicable to this meeting	
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 participation in final deliberations and voting on:	4.2.1. Nezglyal – leriglitazone - EMEA/H/C/005757, EU/3/16/1770, EMA/OD/0000144315
Maria Cavaller Bellaubi	Expert	Patients' Organisation Representative	No restrictions applicable to this meeting	
Clemens Mittmann	Expert	Germany	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.

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/