4 November 2020
EMA/COMP/556648/2020
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 06-08 October 2020

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

06 October 2020, 08:30-18:45, remote virtual meeting

07 October 2020, 08:30-18:45, remote virtual meeting

08 October 2020, 08:30-12:45, remote virtual 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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the minutes for the COMP plenary session held 06-08 October 2020.

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, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the pre-meeting list of participants and restrictions.

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

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 and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

Bruno Sepodes gave a proxy to Dinah Duarte to vote on behalf of Bruno Sepodes during the October 2020 COMP meeting.

Giuseppe Capovilla gave a proxy to Armando Magrelli to vote on behalf of Giuseppe Capovilla during the October 2020 COMP meeting.

1.2. Adoption of agenda

The agenda for 06-08 October 2020 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 08-10 September 2020 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. - EMA/OD/0000037416

Treatment of non-small cell lung cancer with EGFR and MET alterations

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 18 September 2020, prior to responding to the list of issues.

2.1.2. - EMA/OD/0000031771

Treatment of traumatic brain injury with development of oedema

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

Traumatic brain injury (TBI) with development of oedema should be justified as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the Orphan regulations and relevant guidelines (especially section A of ENTR/6283/00).

Moreover, it appears that the sponsor defines the population on the basis of Marshall CT classification of brain injury, thereby excluding patients with diffuse type I disease. The sponsor was invited to justify any pharmacodynamic effects in patients without visible neuroimaging findings. This was also to be considered on the basis of the incompletely understood mechanism of action of the product.

- Intention to treat the condition

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of traumatic brain injury with development of oedema, the sponsor was asked to further elaborate on the relevance of the non-clinical models used for the treatment of traumatic brain injury with development of oedema, and the interpretation of the results obtained in the experiments, including statistical considerations thereof.

- Number of people affected

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

The sponsor was requested to re-calculate the prevalence estimate based on relevant epidemiological studies and registers for the proposed orphan condition and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

- Significant benefit

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

The sponsor was invited to provide data showing the effects of the products in settings of TBI-oedema where the blood brain barrier has been compromised. The sponsor was also invited to provide a justification of significant benefit versus cerebrolysin, which is authorised nationally in the EU.

In the written response, and during an oral explanation before the Committee on 06 October 2020, the sponsor further discussed the following issues. Regarding the proposed condition, this was argued to be a valid subset of TBI, on the grounds of clinical considerations and because there was "no evidence from the non-clinical or clinical assessments of any effects on coagulation, haemodynamic or blood pressure parameters". The COMP remained guarded concerning the definition of the population, counterarguing that different imaging techniques could detect oedematous signs with different sensitivity

and at different points in time (for example after initial admission). It was also considered that the proposal could be viewed as a severity grade, and that the broader TBI indication should have been considered. This was also in line with a mechanism of action of the product that was not fully elucidated, and as such broader pharmacodynamic effects could not be excluded.

As for the non-clinical models used, the fluid percussion injury and controlled cortical impact models were described in more detail, and statistically significant effects with regards to reduction of oedema, improved motor function and learning and ICP (intracranial pressure) reduction were noted. The COMP accepted that there was a rationale to treat the condition based on this data, but this was notwithstanding the need to justify the proposed indication as a valid indication for the purpose of orphan designation in Europe.

For the prevalence issue, the main assumption used was a 8.7% ratio versus all TBIs in order to calculate the proposed estimate of 2.5 per 10.000. The COMP noted that the broader TBI population should have been considered, as the proposed condition would not be acceptable for the purpose of orphan designation. Nevertheless, the broader indication was considered not rare and therefore not designatable.

As for the criterion of significant benefit, it was clarified based on literature that both models used have impaired blood-brain barrier function, while the argument versus cerebrolysin revolved around different mechanism of actions. The COMP accepted the argument that the non-clinical models would have the blood-brain-barrier impaired, and as such the product could have a broader application compared to mannitol. This consideration however was notwithstanding the need to justify the proposed condition as valid for the purpose of orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 08 October 2020, prior to final opinion.

2.1.3. zanidatamab - EMA/OD/0000032268

Voisin Consulting S.A.R.L.; Treatment of gastric cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

- Significant benefit

The sponsor presented clinical data from a study in which patients with locally advanced (unresectable) and/or metastatic HER2-expressing cancers were recruited and treated with zanidatamab monotherapy or in combination with capecitabine and paclitaxel. It was unclear which patients in the study had gastric cancer and what was their medical history (in addition to HER2 directed therapy).

The arguments on significant benefit were based on the potential improved efficacy in the condition.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the clinical study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition. In particular the following details would be helpful:

- Medical history of patients including chemotherapy agents used prior to study enrolment;
- Discussion of currently used second line therapies such as ramucirumab;
- Updated clinical data from the ongoing Phase 1 study, which would indicate the durability of the responses observed.

Furthermore, it was considered to be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 06 October 2020, the sponsor provided updated and a slightly more mature clinical dataset. The medical history was discussed in greater detail revealing that patients with HER-2 expressing gastric cancer enrolled in the study were relapsed not only to HER2 directed therapy (including trastuzumab) but also various chemotherapy regimens and ramucirumab. The sponsor presented promising overall response rates, especially in the study arm where the proposed product was used in combination with chemotherapy. The overall response rates in the presented study were indirectly compared to published studies with other treatment options in late line treatment (such as Lonsurf). Although the data was not mature enough to conclude on the overall survival yet, the initial data indicated a potential for durable responses in heavily pre-treated patients. The committee considered that this would be enough to assume the clinically relevant advantage at this initial designation stage.

The sponsor was strongly encouraged to seek protocol assistance when planning the pivotal study of the proposed product.

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 zanidatamab was considered justified based on clinical data in heavily pre-treated patients showing a significant proportion of objective responses, some of which were durable.

The condition is chronically debilitating due to symptoms associated with the tumour burden and life-threatening with median overall survival of 16 months.

The condition was estimated to be affecting approximately 2.4 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 had provided sufficient justification for the assumption that the medicinal product containing zanidatamab will be of significant benefit to those affected by the condition. The sponsor had provided clinical data that demonstrated that patients who were relapsed/refractory to trastuzumab, chemotherapy and ramucirumab achieved objective, and in some cases of the ongoing study, durable responses. Indirect comparisons to available treatment options in late line treatment indicated a significantly higher overall response rate. The Committee considered that would constitute a clinically relevant advantage.

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

2.1.4. adeno-associated viral vector serotype 9 expressing codon-optimized human *GRN* gene - EMA/OD/0000037822

PPD Bulgaria EOOD; Treatment of frontotemporal dementia (FTD)

COMP Rapporteur: Robert Nistico

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

- Intention to diagnose, prevent or treat

The sponsor presented data in a non-clinical model of the condition showing reduced neuropathological defects and neuroinflammation. No functional endpoints were presented, which would support a potential clinical effect of the proposed product in the condition.

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of frontotemporal dementia the sponsor was asked to further elaborate on:

- The methodology used in the non-clinical studies as well as the results from these studies and their relevance for the development of the product in the condition and;
- Any functional improvements observed in the non-clinical model used.

- Number of people affected

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

The sponsor was asked to re-calculate the prevalence taking into consideration all variants of FTD included in the proposed 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 should describe and justify the methodology used for the prevalence calculation.

In the written response, and during an oral explanation before the Committee on 06 October 2020, the sponsor provided additional explanation of the data generated in the genetic model of the condition. In this model, behavioural phenotypes are inconsistent and variable and therefore, the measurement of potential functional improvement upon treatment may be impossible. In view of this limitation of the existing model and the fact that clinical development of a gene therapy will benefit from protocol assistance, the COMP considered the provided surrogate measurements sufficient for the assumption of medical plausibility at this point in time. The sponsor was advised to seek protocol assistance on the further development of the product.

In addition, the sponsor provided a discussion on the calculated prevalence based on available sources and proposed the overall prevalence of FTD to be 2.2. in 10,000. This estimate was considered acceptable.

The Committee agreed that the condition, treatment of frontotemporal dementia, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 9 expressing codon-optimized human *GRN* gene was considered

justified based on non-clinical data showing reduction in neuropathological defects and neuroinflammation.

The condition is life-threatening and chronically debilitating due to neurological and cognitive impairment and limited life-expectancy.

The condition was estimated to be affecting approximately 2.2 in 10,000 persons in the European Union, at the time the application was made.

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

The COMP therefore recommended the designation of this medicinal product, containing adeno-associated viral vector serotype 9 expressing codon-optimized human GRN gene as an orphan medicinal product for the orphan condition: treatment of frontotemporal dementia.

A positive opinion for adeno-associated viral vector serotype 9 expressing codon-optimized human *GRN* gene, for treatment of frontotemporal dementia, was adopted by majority (26 out of 27 votes).

The divergent position (*Darius Matusevicius*) was appended to this opinion.

The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

2.1.5. tislelizumab - EMA/OD/0000036055

BeiGene Ireland Limited; Treatment of oesophageal cancer

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:

- Medical plausibility

The sponsor was asked to elaborate on the robustness of the conclusion of an add-on activity of the proposed product in the setting of combination therapy.

- Number of people affected

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

The sponsor was invited to provide an estimate for complete prevalence taking into consideration the duration of the condition and the crude incidence rates from European Cancer Information System.

- Significant Benefit

The sponsor was requested to further elaborate on the issue of significant benefit, by discussing the previous therapies of the studied populations and the results of the studies. A comparative discussion of the effects with the product versus the current standard of care in the EU was expected in that regard.

In the written response, and during an oral explanation before the Committee on 07 October 2020, the sponsor elaborated on the issues. Regarding the medical plausibility issues, an indirect comparison with available clinical data was performed with the product in combination with chemotherapy, comparing survival outcomes to the published control arm of a phase 3 study with an authorised product added to chemotherapy in a similar population. The sponsor also performed indirect comparison observations versus selected phase 2 studies from the literature arguing improved efficacy. The COMP however, considered that the comparability issues were not clear regarding the add-on benefits.

Regarding the request on the prevalence estimate, the sponsor proposed a median survival of less than a year, and an incidence rate of 0.68/10,000 with reference to European Cancer Information System (ECIS), to supporting the rarity of the condition. It was also pointed out that based on GLOBOCAN 5-year prevalence would be approximately twice numerically compared to incidence, thereby leading to a 1.5 per 10,000 revised estimate. The COMP referred to their previous opinions and agreed that the condition was estimated to be affecting less than 1 in 10,000 persons in the European Union.

Regarding significant benefit, the sponsor also elaborated on the population in the clinical studies submitted. It was noted that over 56% had received at least 2 prior lines of therapy (including docetaxel). An observed mOS of up to 6 months and with remission rates of approximately 10% with the product as a monotherapy were reported. The COMP considered that the preliminary clinical observations in relapsed/refractory patients, who responded to treatment with the product as a monotherapy would suffice for the assumption of a clinically relevant advantage of improved efficacy.

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

The intention to treat the condition with the medicinal product containing tislelizumab was considered justified based on preliminary clinical observations in relapsed/refractory patients, who responded to treatment with the product.

The condition is chronically debilitating due to dysphagia, regurgitation, odynophagia, upper gastrointestinal bleeding, acid indigestion and life-threatening with 5- year survival reported in the range of 15%-25%.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor had provided sufficient justification for the assumption that the medicinal product containing tislelizumab would be of significant benefit to those affected by the condition. The sponsor had provided preliminary clinical observations in relapsed/refractory patients, who responded to treatment with the product as a monotherapy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for tislelizumab, for treatment of oesophageal cancer, was adopted by consensus.

2.1.6. anti-(pancreatic adenocarcinoma upregulated factor) IgG1 humanised monoclonal antibody - EMA/OD/0000034870

Prestige Biopharma Belgium; Treatment of pancreatic cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

- Significant benefit

The sponsor presented non-clinical data to support the improved efficacy of the proposed product when added to gemcitabine. The sponsor proposed to develop the product in advanced stage and/or metastatic pancreatic cancer. In this setting other products and combination regimens can be used, which were not sufficiently discussed by the sponsor.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the non-clinical study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition. Any assumption with regards to significant benefit over regimens such as FOLFORINOX or gemcitabine + nab-paclitaxel should be supported by data.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 07 October 2020, the sponsor provided an additional discussion of the non-clinical data available to date. The sponsor reiterated that the intent is to develop the product as an add on to the standard of care. The committee enquired about the data in a model where a group had been treated with a combination of gemcitabine and nab-paclitaxel and were informed that such data was not generated yet. The COMP acknowledged a clear add-on effect of the proposed product in combination with gemcitabine, which could offer an advantage to some patients who were not eligible to combination regiment treatment options. Although the product is early in development, the COMP considered sufficient limited evidence had been submitted and support the assumption of significant benefit based on the currently available data. The sponsor was however strongly encouraged to seek protocol assistance in planning further development of the product.

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

The intention to treat the condition with the medicinal product containing anti-(pancreatic adenocarcinoma upregulated factor) IgG1 humanised monoclonal antibody was considered justified based on non-clinical data in a model of the condition showing add-on effect of the proposed product when used in combination with gemcitabine.

The condition is chronically debilitating because of pain, loss of appetite, nausea, vomiting, weight loss, jaundice, fatigue, weakness and depression and life-threatening with a median survival of about 6 months.

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 had provided sufficient justification for the assumption that the medicinal product containing anti-(pancreatic adenocarcinoma upregulated factor) IgG1 humanised monoclonal antibody will be of significant benefit to those affected by the condition. The sponsor had provided non-clinical data that demonstrate that the product may be of significant benefit when used in combination with gemcitabine in treatment of pancreatic cancer. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for anti-(pancreatic adenocarcinoma upregulated factor) IgG1 humanised monoclonal antibody, for treatment of pancreatic cancer, was adopted by majority (27 out of 28 votes).

The divergent position (*Brigitte Schwarzer-Daum*) was appended to this opinion.

The Norwegian COMP member agreed with the above-mentioned recommendation of the COMP.

2.1.7. perflubron - EMA/OD/0000037899

Boyd Consultants Limited; Treatment of congenital pulmonary hypoplasia in infancy

COMP Rapporteur: Irena Rogovska

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 congenital pulmonary hypoplasia, the sponsor should further justify that the results of the clinical studies in congenital diaphragmatic hernia-related hypoplasia can be translated to other types of congenital pulmonary hypoplasia.

- Number of people affected

The sponsor should revise the prevalence calculations taking into account all potential causes of secondary congenital pulmonary hypoplasia.

- Significant benefit

The sponsor should discuss the significant benefit of the proposed product in relation to the current standard of care of the condition.

The sponsor explained that the proposed perfluorooctyl-bromide (PFOB) mainly acts to support the slow, within-lung growth of an infant's hypoplastic lung via its physicochemical attributes while simultaneously functioning as a breathable medium. In this regard, PFOB essentially functions as a within-lung stent to extend the hypoplastic lung regardless of its cause, increasing the capacity of physiologic gas exchange. This aspect of its mechanism of action, which is focused on helping the hypoplastic lung to grow, rather than one which induces an effect via traditional receptor-based pharmacology, is independent of the underlying condition that has resulted in the hypoplastic lung. Therefore, it could be acceptable to extrapolate data on the efficacy of PFOB in patients with congenital diaphragmatic hernia-related hypoplasia (the most common underlying cause of pulmonary hypoplasia) to the other, much more rare conditions that can result in its development.

The sponsor acknowledged an error in the initial calculations and provided an updated table on incidence of congenital conditions known to cause secondary congenital pulmonary hypoplasia. The updated estimate is 0.17 cases per 10,000 persons. The updated estimate does however not include conditions where pulmonary hypoplasia is present e.g. Fetal akinesia deformation sequence (Arthrogryposis multiplex congenita-pulmonary hypoplasia syndrome), Matthew-Wood syndrome (Anophthalmia-pulmonary hypoplasia syndrome), NEK9-related lethal skeletal dysplasia (Lethal skeletal dysplasia-fetal akinesia-contractures-thoracic dysplasia-pulmonary hypoplasia syndrome) and PAGOD syndrome (Pulmonary hypoplasia-agonadism-dextrocardia-diaphragmatic hernia syndrome). In addition, summing up incidence rates (17.5) is not correct as the denominator is different in different cases of primary estimation. Despite this, the updated estimate is in line with what is reported in literature and can be accepted for the orphan designation. At the time of MA it is important that the sponsor makes sure also these underlying conditions are included in the prevalence estimate.

The sponsor's claim that "any treatment that can remove the need for, or reduce the duration of, mechanical ventilation/ECMO and reduce inflammation would represent a significant therapeutic benefit for patients" was supported by the COMP.

In the written response, the sponsor presented a sufficient level of evidence to support the assumption of significant benefit for the purpose of initial orphan designation, and the oral explanation was cancelled.

The Committee agreed that the condition, congenital pulmonary hypoplasia in infancy, is a distinct medical entity and meets the criteria for orphan designation.

For the purpose of orphan designation, the Committee considered that the condition originally proposed by the sponsor should be renamed as "treatment of congenital pulmonary hypoplasia" (hereinafter referred to as "the condition") based on the delineation of "infancy" not being needed.

The intention to treat the condition with the medicinal product containing perflubron was considered justified based on clinical data showing improvements in oxygenation and ventilation as well as improved survival.

The condition is life-threatening due to high mortality and for the few patients surviving, chronically debilitating due to chronic lung problems including reduced lung capacity and susceptibility to lung infections.

The condition was estimated to be occurring in approximately 0.17 in 10,000 persons per year 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 perflubron will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that perflubron can remove the need for, or reduce the duration of, mechanical ventilation/extracorporeal membrane oxygenation and promote lung growth. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for perflubron, for treatment of congenital pulmonary hypoplasia, was adopted by consensus.

2.1.8. - EMA/OD/0000034572

Treatment of hereditary angioedema

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 22 September 2020, prior to responding to the list of issues.

2.1.9. - EMA/OD/0000030636

Treatment of unclassifiable interstitial lung disease

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

- Intention to diagnose, prevent or treat

The sponsor should justify unclassifiable interstitial lung disease (UILD) as a distinct medical entity or a valid subset, i.e. a disease entity with specific aetiology, pathophysiology and clinical characteristics. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the orphan regulations and relevant guidelines (especially section A of ENTR/6283/00).

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of UILD the sponsor should further discuss the clinical study, including:

- The primary and secondary study endpoints, including the reliability of using home spirometry to measure the primary endpoint;
- The clinical significance of group median analysis as a measure of forced vital capacity (FVC) change in the study, and whether this analysis was pre-planned or decided after seeing the study results;
- The meaning of 'predicted' FVC changes, and how such prediction was performed/modelled;
- The differences between home and on-site FVC measurements;
- The clinical relevance of the results of the secondary endpoints.

- Number of people affected

Depending on the definition of the condition, the sponsor should re-calculate the prevalence estimate based on relevant epidemiological studies and registers and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

- Significant benefit

The sponsor was asked to further elaborate on the significant benefit of the proposed product in relation to the current standard of care for interstitial lung diseases (ILD).

In the written response, and during an oral explanation before the Committee on 06 October 2020, the sponsor referred again to the updated classification from 2013 but also to a publication from 2020 by Wijsenbeek and Cottin. While emphasizing the commonalities in pathophysiological features, clinical manifestations, and diagnostic features, as well as the

similarly progressive nature of many of these diseases, the review highlights the fact that most often clinicians see patients with connective tissue disease (CTD–ILD), idiopathic pulmonary fibrosis (IPF), chronic hypersensitivity pneumonias (CHP), sarcoidosis, or unclassifiable fibrotic ILD as a separate entity with specific characteristics. However, it is also mentioned that UILD has "non-specific" features. Moreover, the authors mention that the proposed product "reduces disease progression in patients with progressive, unclassifiable, fibrotic ILD." This is another reason why the condition does not represent distinct medical entity. In summary, it is still not clear how the UILD differentiates from pathophysiological point from other types of ILD other than it is "unclassifiable".

The sponsor admitted that there was a higher variability introduced with using the handheld spirometry but also thinks that the various analyses performed on both handheld and site spirometry show a consistent and clinically meaningful result in favour of the proposed product vs placebo. The group median analysis was retrospectively introduced, after failure of the primary analysis and was not pre-planned, i.e. introduced after the study results were seen and after un-blinding of the study.

The secondary endpoints seem to have been selected based on acceptable endpoints for the more established idiopathic pulmonary fibrosis studies and the sponsor argues for why they are also relevant for UILD. As not many studies have been done in this patient population so far it seems reasonable to use established endpoint even though they might not be the most relevant for this particular patient population.

However, this failed clinical study was not considered supportive of the medical plausibility by the COMP.

Regarding the prevalence the sponsor maintains that the condition UILD is valid but has updated the estimate with two approaches. As well as using the incidence times duration approach, using a mean duration of 7 years establishes a prevalence which is 1.5 in 10,000. This could per se have been accepted if the condition would have been accepted.

With regards to significant benefit, nintedanib is currently the only product centrally approved for the treatment of chronic fibrosing ILDs including UILD. However, as the medical plausibility has not been established the significant benefit remains questionable.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 07 October 2020, prior to final opinion.

2.2. For discussion / preparation for an opinion

2.2.1. (R)-tetrahydrofuran-3-yl 4-(6-(5-(4-ethoxy-1-isopropylpiperidin-4-yl)pyridin-2-yl)pyrrolo[1,2-b]pyridazin-4-yl)piperazine-1-carboxylate sesquisuccinate - EMA/OD/0000028397

Ipsen Pharma; Treatment of fibrodysplasia ossificans progressiva

COMP Rapporteur: Ingeborg Barisic

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 (R)-tetrahydrofuran-3-yl 4-(6-(5-(4-ethoxy-1-isopropylpiperidin-4-yl)pyridin-2-yl)pyrrolo[1,2-b]pyridazin-4-yl)piperazine-1-carboxylate sesquisuccinate was considered justified based on

non-clinical data in a model of the condition showing reduction in oedema and heterotopic ossification post injury.

The condition is chronically debilitating due to episodes of painful tumour-like soft-tissue swellings followed by the development of extra bone 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 around 50 years of age.

The condition was estimated to be affecting less than 0.01 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 (R)-tetrahydrofuran-3-yl 4-(6-(5-(4-ethoxy-1-isopropylpiperidin-4-yl)pyridin-2-yl)pyrrolo[1,2-b]pyridazin-4-yl)piperazine-1-carboxylate sesquisuccinate, for treatment of fibrodysplasia ossificans progressiva, was adopted by consensus.

2.2.2. alisitol, retinol palmitate, zinc gluconate - EMA/OD/0000033691

Vanessa Research Magyarorszag Kft.; Treatment of microvillus inclusion disease

COMP Rapporteur: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing alisitol, retinol palmitate, zinc gluconate was considered justified based on non-clinical data in a model of the condition showing improved survival and on preliminary clinical data in a patient showing reduction in stool output.

The condition is life-threatening and chronically debilitating due to persistent and treatment resistant diarrhoea.

The condition was estimated to be affecting less than 0.01 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 alisitol, retinol palmitate, zinc gluconate, for treatment of microvillus inclusion disease, was adopted by consensus.

2.2.3. - EMA/OD/0000034375

Treatment of multiple myeloma

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 November meeting.

2.2.4. autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene - EMA/OD/0000035302

Clinical Technology Centre (Ireland) Limited; Treatment of sickle cell disease

COMP Rapporteur: Angelo Loris Brunetta

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

The intention to treat the condition with the medicinal product containing autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene was considered justified based on preliminary clinical data showing significant reduction in the rate of vaso-occlusive crises.

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

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that patients who are not adequately managed with the use of hydroxyurea achieved significant improvements in the rate of vaso-occlusive crises when treated with the proposed product. In addition, it is expected that a single administration of the product will obviate the need for the current chronic standard of care. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene, for treatment of sickle cell disease, was adopted by consensus.

2.2.5. - EMA/OD/0000035896

Treatment of glioma

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

2.2.6. - EMA/OD/0000036404

Treatment of relapsed refractory myelodysplastic syndrome

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

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 09 October 2020.]

2.2.7. L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide - EMA/OD/0000037176

Neuropath Therapeutics Limited; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Zsofia Gyulai

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

The intention to treat the condition with the medicinal product containing L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide was considered justified based on delay in motor function decline in a non-clinical model of the proposed condition.

The condition is life-threatening and chronically debilitating due to progressive degeneration of motor neurons, ultimately leading to paralysis and respiratory failure.

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

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 L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide will be of significant benefit to those affected by the condition. The sponsor has provided data showing a delay in motor function decline in a non-clinical model of the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

2.2.8. - EMA/OD/0000037744

Treatment of pulmonary arterial hypertension

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

2.2.9. triheptanoin - EMA/OD/0000037871

Ultragenyx Germany GmbH; Treatment of carnitine palmitoyltransferase I deficiency

COMP Rapporteur: Dinah Duarte

The Committee agreed that the condition, carnitine palmitoyltransferase I deficiency, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing triheptanoin was considered justified based on preliminary clinical data showing a reduction in rhabdomyolysis events over time.

The condition is chronically debilitating due to cardiomyopathy, liver dysfunction, severe hypoglycaemia, and rhabdomyolysis. Sudden death may occur from arrhythmia or hypoglycaemia.

The condition was estimated to be affecting less than 0.01 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 triheptanoin, for treatment of carnitine palmitoyltransferase I deficiency, was adopted by consensus.

2.2.10. - EMA/OD/0000038040

Treatment of hepatocellular carcinoma

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

2.2.11. - EMA/OD/0000038423

Treatment of Huntington's 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 November meeting.

2.2.12. autologous CD34+ cells (bone marrow-derived) transduced ex vivo with the self-inactivating (sin) lentiviral vector CL20-4i-EF1a-hyc-OPT containing a normal version of the coding region of the *IL2RG* gene - EMA/OD/0000038481

Real Regulatory Limited; Treatment of X-linked severe combined immunodeficiency (X-SCID)

COMP Rapporteur: Tim Leest

The Committee agreed that the condition, X-linked severe combined immunodeficiency, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing autologous bone marrow derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral vector containing a normal version of the coding region of the *IL2RG* gene was considered justified based on preliminary clinical observations in treated patients showing immune reconstitution.

The condition is chronically debilitating due to recurrent infections and failure to thrive, and life-threatening with death within the first two years for untreated patients.

The condition was estimated to be affecting approximately 0.01 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 bone marrow derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral vector containing a normal version of the coding region of the IL2RG gene will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical observations supporting immune reconstitution and obviation of regular IVIG supplementation. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous CD34+ cells (bone marrow-derived) transduced ex vivo with the self-inactivating (sin) lentiviral vector CL20-4i-EF1a-hyc-OPT containing a normal

version of the coding region of the *IL2RG* gene, for treatment of X-linked severe combined immunodeficiency, was adopted by consensus.

2.2.13. - EMA/OD/0000038634

Treatment of progressive multifocal leukoencephalopathy

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

2.2.14. 3,5-diamino-6-chloro-n-(n-(4-(4-(2-(hexyl((2s,3r,4r,5r)-2,3,4,5,6-pentahydroxyhexyl)amino)ethoxy)phenyl)butyl)-carbamimidoyl)pyrazine-2-carboxamide, sodium chloride solution 4.2% (w/v) - EMA/OD/0000039164

EUDRAC GmbH; Treatment of primary ciliary dyskinesia (PCD)

COMP Rapporteur: Irena Rogovska

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

The intention to treat the condition with the medicinal product containing 3,5-diamino-6-chloro-N-(N-(4-(4-(2-(hexyl((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)ethoxy)phenyl)butyl)-carbamimidoyl)pyrazine-2-carboxamide, sodium chloride solution 4.2% (w/v) was considered justified based on preliminary clinical data showing an improvement in predicted forced expiratory volume in one second.

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

The condition was estimated to be affecting approximately 2.2 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 3,5-diamino-6-chloro-N-(N-(4-(4-(2-(hexyl((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)ethoxy)phenyl)butyl)-carbamimidoyl)pyrazine-2-carboxamide, sodium chloride solution 4.2% (w/v), for treatment of primary ciliary dyskinesia, was adopted by consensus.

2.2.15. - EMA/OD/0000039198

Treatment of peripheral artery disease in patients with end-stage kidney disease receiving haemodialysis

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

2.2.16. DNA plasmid encoding human transferrin gene - EMA/OD/0000039389

Eyevensys S.A.S.; Treatment of retinitis pigmentosa

COMP Rapporteur: Tim Leest

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

The intention to treat the condition with the medicinal product containing DNA plasmid encoding human transferrin gene was considered justified based on preliminary non-clinical in vivo data which showed visual function as measured by electroretinogram measurements was maintained.

The condition is chronically debilitating due to the development of nyctalopia (night blindness) and tunnel vision that progresses to total blindness.

The condition was estimated to be affecting approximately 2.5 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 DNA plasmid encoding human transferrin gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate that the product can be used for a broader group of patients with retinitis pigmentosa than voretigene neparvovec. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for DNA plasmid encoding human transferrin gene, for treatment of retinitis pigmentosa, 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 coordinators were appointed for 25 applications submitted.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 27 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of systemic mastocytosis

The Committee was briefed on the significant benefit issues.

[Post-meeting note: The COMP adopted the proposed answers on the significant benefit issues by written procedure following its October meeting.]

3.1.2. -

Treatment of neuroblastoma

The Committee was briefed on the significant benefit issues.

[Post-meeting note: The COMP adopted the proposed answers on the significant benefit issues by written procedure following its October meeting.]

3.1.3. -

Treatment of immune thrombocytopenia

The Committee was briefed on the significant benefit issues.

[Post-meeting note: The COMP adopted the proposed answers on the significant benefit issues by written procedure following its October meeting.]

3.1.4. -

Treatment of non-infectious uveitis

The Committee was briefed on the significant benefit issues.

[Post-meeting note: The COMP adopted the proposed answers on the significant benefit issues by written procedure following its October meeting.]

3.2. Finalised letters

3.2.1. -

Treatment of bullous pemphigoid

The finalised letter was circulated for information.

3.2.2. -

Treatment of amyotrophic lateral sclerosis

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment of desmoid tumours

The new request was noted.

3.3.2. -

Treatment of marginal zone lymphoma

The new request was noted.

3.3.3. -

Treatment of glioblastoma

The new request was noted.

3.3.4. -

Treatment of ornithine transcarbamylase deficiency

The new request was noted.

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. Fintepla - fenfluramine hydrochloride - EMEA/H/C/003933/0000, EU/3/13/1219, EMA/OD/0000024920

Zogenix ROI Limited; Treatment of Dravet syndrome

COMP Rapporteurs: Dinah Duarte; Giuseppe Capovilla

An opinion recommending not to remove Fintepla, fenfluramine hydrochloride (EU/3/13/1219) from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

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

4.2.2. Epidyolex - cannabidiol - EMEA/H/C/004675/II/0005, EMA/OD/165/17, EU/3/17/1959, EMA/OD/0000033940

GW Pharma (International) B.V.; Treatment of tuberous sclerosis

CHMP Rapporteur: Mark Ainsworth; CHMP Co-Rapporteur: Ondřej Slanař

The status of the procedure at CHMP was noted.

4.2.3. Libmeldy - autologous CD34+ cell enriched population that contains hematopoietic stem and progenitor cells transduced ex vivo using a lentiviral vector encoding the human arylsulfatase A gene - EMEA/H/C/005321/0000, EU/3/07/446, EMA/OD/0000023359

Accelerated assessment

Orchard Therapeutics (Netherlands) B.V.; Treatment of metachromatic leukodystrophy

COMP Rapporteurs: Armando Magrelli; Elisabeth Johanne Rook

An opinion recommending not to remove Libmeldy, autologous CD34+ cells transfected with lentiviral vector containing the human arylsulfatase A cDNA, (EU/3/07/446) from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

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

4.2.4. Oxlumo - lumasiran - EMEA/H/C/005040/0000, EU/3/16/1637, EMA/OD/0000034914

Accelerated assessment

Alnylam Netherlands B.V.; Treatment of primary hyperoxaluria type 1

COMP Rapporteurs: Dinah Duarte; Vallo Tillmann

An opinion recommending not to remove Oxlumo, lumasiran, (EU/3/16/1637) from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

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

4.2.5. Tecartus - Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102/0000, EU/3/19/2220, EMA/OD/0000026061

Accelerated assessment

Kite Pharma EU B.V.; Treatment of mantle cell lymphoma

COMP Rapporteurs: Maria Elisabeth Kalland; Frauke Naumann-Winter

An opinion recommending not to remove Tecartus, autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing

anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured, (EU/3/19/2220) from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

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

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 2 applications.

4.5. Orphan Maintenance Reports

4.5.1. Kaftrio Orphan Maintenance Assessment Report

Document was tabled for information.

4.5.2. Kalydeco Orphan Maintenance Assessment Report

Document was tabled for information.

4.5.3. Ayvakyt Orphan Maintenance Assessment Report

Document was tabled for information.

4.5.4. Pretomanid FGK Orphan Maintenance Assessment Report

Corrigendum

The document was adopted.

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

5.1. After adoption of CHMP opinion

5.1.1. Zejula - niraparib - EMEA/H/C/004249/II/0019, EU/3/10/760, EMA/OD/0000031233

GlaxoSmithKline (Ireland) Limited; Treatment of ovarian cancer

COMP Rapporteurs: Brigitte Schwarzer-Daum; Frauke Naumann-Winter; CHMP Rapporteur: Bjorg Bolstad; CHMP Co-Rapporteur: Alexandre MoreauA list of issues was adopted on 10 September 2020.

An oral explanation to be held on 07 October 2020, was cancelled.

The Committee confirmed that all issues previously identified in this application had been addressed.

An opinion recommending not to remove Zejula, niraparib (EU/3/10/760) 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.

5.2. Prior to adoption of CHMP opinion

5.2.1. Kaftrio - ivacaftor/tezacaftor/elexacaftor - EMEA/H/C/005269/II/0001, EMA/OD/0000001208, EU/3/18/2116, EMA/OD/0000042077

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

CHMP Rapporteur: Johann Lodewijk Hillege

The COMP agreed that a formal review of the maintenance of the orphan designation for the applied indication is needed.

5.2.2. Kalydeco - ivacaftor - EMEA/H/C/002494/II/0089, EMA/OD/010/08, EU/3/08/556, EMA/OD/0000042076

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

CHMP Rapporteur: Maria Concepcion Prieto Yerro

The COMP agreed that a formal review of the maintenance of the orphan designation for the applied indication is needed.

5.2.3. Blincyto – blinatumomab - EMEA/H/C/003731/II/0030, EMA/OD/029/09, EU/3/09/650, EMA/OD/00000016144

Amgen Europe B.V.; Treatment of acute lymphoblastic leukaemia

CHMP Rapporteur: Alexandre Moreau; CHMP Co-Rapporteur: Armando Genazzani

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the November 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. Strategic Review & Learning Meeting – COMP, 24-25 September 2020, Germany

The COMP noted the report from the meeting presented by German member.

7.1.2. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 2 October 2020.

7.1.3. COMP Workshop 2020 on support for orphan medicines development

The COMP noted the details and organisation of the upcoming COMP Workshop that will take place Monday the 30th November 2020.

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendation on eligibility to PRIME – report from CHMP

Documents were tabled for information.

7.2.1. COMP-CAT Working Group

The COMP-CAT Working Group meeting took place on 5 October 2020 by teleconference.

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

7.3.1. Working Party with Patients' and Consumers' Organisations (PCWP)

None

7.3.2. Working Party with Healthcare Professionals' Organisations (HCPWP)

None

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. Therapeutic Goods Administration (TGA), Australia

None

7.5.4. Health Canada

None

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

None

7.7. COMP work plan

None

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2020

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2020 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. COMP meeting schedule (2022-2024)

Committee meeting dates (2022-2024) were adopted.

9. Explanatory notes

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

Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

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

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

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

Sponsor

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

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

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

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/

10. List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 06-08 October 2020 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Violeta Stoyanova-Beninska	Chair	Netherlands	No interests declared	
Armando Magrelli	Member (Vice-Chair)	Italy	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	No interests declared	
Tim Leest	Member	Belgium	No interests declared	
Lyubina Racheva - Todorova	Member	Bulgaria	No interests declared	
Dinko Vitezic	Member	Croatia	No interests declared	
Vasileios Loutas	Member	Cyprus	No interests declared	
Lenka Gaidadzi	Member	Czech Republic	No interests declared	
Elisabeth Penninga	Member	Denmark	No interests declared	
Vallo Tillmann	Member	Estonia	No interests declared	
Karri Penttilä	Member	Finland	No interests declared	
Cecile Dop	Member	France	No interests declared	
Frauke Naumann-Winter	Member	Germany	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Zsofia Gyulai	Member	Hungary	No interests declared	
Geraldine O'Dea	Member	Ireland	No interests declared	
Irena Rogovska	Member	Latvia	No interests declared	
Aušra Matulevičienė	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No interests declared	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland	No restrictions applicable to this meeting	
Dinah Duarte	Member	Portugal	No interests declared	
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	Slovakia	No interests declared	
Martin Mozina	Member	Slovenia	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	
Angelo Loris Brunetta	Member	Patients' Organisation Representative	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Virginie Hivert	Expert*	Patients' Organisation Representative	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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