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Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Final minutes for the meeting on 16-18 June 2020

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

16 June 2020, 09:00-19:30, remote virtual meeting

17 June 2020, 08:30-20:10, remote virtual meeting

18 June 2020, 08:30-17:20, 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.

Further information with relevant explanatory notes can be found at the end of this document.

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

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. 21 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

Dr. Giuseppe Capovilla and Dr. Ingeborg Barisic were re-appointed as COMP members nominated by the European Commission on the EMA's recommendation.

1.2. Adoption of agenda

The agenda for 16-18 June 2020 was adopted with the following topic under A.O.B:

- Strategic Review & Learning meeting – 24-25 September 2019, Germany,

- EMA Business Pipeline activity and Horizon scanning.

1.3. Adoption of the minutes

The minutes for 18-20 May 2020 were adopted with no amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. - EMA/OD/0000030023

Treatment of peripheral T-cell lymphoma (PTCL)

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 29 May 2020, prior to responding to the list of issues.

2.1.2. pegylated adrenomedullin - EMA/OD/0000029989

Bayer AG; Treatment of acute respiratory distress syndrome (ARDS)

COMP Rapporteur: Martin Mozina

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

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of acute respiratory distress syndrome (ARDS) the sponsor was asked to provide details of the methodology used in the non-clinical studies, especially regarding the administration of the product in relation to the timing of the ARDS-inducing challenges, as well as numbers and figures of the results.

- 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 Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

The sponsor was invited to provide estimates of the incidence of ARDS based also on more recent literature than up to 2013 as currently presented.

In addition, the sponsor justified how the changes introduced with the Berlin classification that merged ALI and ARDS into the same ARDS clinical entity were taken into account

- Significant benefit

In order to justify the significant benefit of the proposed product the sponsor was requested to discuss any potential clinical advantage over corticosteroids or any other medicinal product authorized for the treatment of the condition in EU/EEA countries.

In the written response, and during an oral explanation before the Committee on 16 June 2020, the sponsor presented details of the non-clinical proof of concept studies supporting the medical plausibility, including studies in valid models of the condition. The two studies showed positive results in extravascular lung water and the PaO2/FiO2 ratio, two parameters considered clinically relevant. The COMP found this data supportive of the medical plausibility.

The COMP also considered that the revised incidence calculations were satisfactory, since the sponsor properly addressed the potential impact of the changes in the definition of ARDS introduced with the Berlin classification. The proposed estimate of 3.2 in 10,000 was accepted.

In relation to the significant benefit, the sponsor performed an extensive search in national formularies and identified those countries where corticosteroids are authorized. The COMP acknowledged that while corticosteroids are authorized for the condition in some EU member states, they are however contraindicated in other member states. The sponsor discussed the non-clinical results of the proposed product and especially the effects on extravascular water and the PaO2/FiO2 ratio in the models, which are clinically relevant outcomes and in which the effects of corticosteroids are not established.

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 pegylated adrenomedullin was considered justified based on non-clinical data in valid models of the condition, showing beneficial effects on relevant endpoints reflecting lung oedema and lung function.

The condition is life-threatening due to hypoxia and alveolar oedema, with mortality up to 50%, and chronically debilitating due to the potential of persistent functional and cognitive impairment.

The condition was estimated to be occurring in approximately 3.2 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 pegylated adrenomedullin will be of significant benefit to those affected by the condition. This is based on non-clinical data showing relevant effects on different components of the condition, including extravascular lung water and parameters of lung oxygenation and function. The Committee considered that this constitutes a clinically relevant advantage for the patients affected by the condition.

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

2.1.3. adeno-associated viral vector expressing acid alpha-glucosidase gene - EMA/OD/0000030112

Audentes Therapeutics Netherlands B.V.; Treatment of glycogen storage disease type II (Pompe's disease)

COMP Rapporteur: Lyubina Racheva Todorova

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 data in an in vivo non-clinical model of the condition. Improvements in glycogen levels were found in muscles but not in the nervous system. Consequently, muscle strength improvement was observed. The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition. However, no comparative data to alglucosidase alfa was presented and the information on durability of treatment effect was limited.

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 the authorised medicinal product for the proposed orphan condition. In particular, a discussion of effects observed with the proposed gene therapy vis-à-vis the authorised ERT product would be helpful.

In the written response, the sponsor provided an account of published data with other gene therapies in this and other conditions, which all indicate the durability of effects and durability of genetic change induced by gene therapy products. The committee accepted the

notion of a potential single treatment using gene therapy technology and considered that this would constitute a clinically relevant advantage. In addition, the sponsor provided comparative data on the efficacy of an analogous gene therapy product compared to alglucosidase alpha in a model of the condition, which indicated at least comparable reductions of glycogen in muscles with both products and a restoration of the enzyme production by muscle cells only in case of the gene therapy. The committee accepted these arguments as supportive of the assumption of significant benefit over existing enzyme replacement therapy.

The Committee agreed that the condition, glycogen storage disease type II (Pompe's disease), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing adeno-associated viral vector expressing acid alpha-glucosidase gene was considered justified based on non-clinical data in a model of the condition demonstrating improved glycogen metabolism in muscles as well as improved grip strength.

The condition is life-threatening and chronically debilitating due to accumulation of glycogen in muscle and nerve cells resulting in progressive skeletal myopathy, cardiomyopathy, and respiratory insufficiency. This leads to death within the first two years of life in the infantile forms, and in the fourth decade of life in forms with later onset.

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 adeno-associated viral vector expressing acid alpha-glucosidase gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that allows to assume that the treatment would sustain its effect over a long period of time compared to frequently administered enzyme replacement therapy which is currently the only authorised treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated viral vector expressing acid alpha-glucosidase gene, for treatment of glycogen storage disease type II (Pompe's disease), was adopted by consensus.

2.1.4. - EMA/OD/0000030089

Treatment of GM1-gangliosidosis

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

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of GM1-gangliosidosis the sponsor was asked to further elaborate on:

  - the relevance of the non-clinical model used for the treatment of GM1-gangliosidosis, and the interpretation of the results obtained in the experiments,

- the methodology used in the non-clinical study as well as the results from the study and its relevance for the development of the product in the condition.

In the written response, and during an oral explanation before the Committee on 18 June 2020, the sponsor tried to justify the limited data that was available on the non-clinical in vivo model used to determine the potential efficacy. The sponsor claimed that the product was sufficiently safe to justify the Phase II study they were planning to launch soon. The COMP did not question the safety of the product as it was acknowledged that the product had been available in other countries for some time. The COMP questioned the variability seen in the response in the data submitted and the lack of a second confirmatory study in another non-clinical in vivo model of the condition. The sponsor acknowledged that the efficacy data was not robust enough to justify medical plausibility and that a second study in a validated non-clinical in vivo model would help establish the proof of concept. The COMP considered that the medical plausibility had not been sufficiently supported by data.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 18 June 2020, prior to final opinion.

2.1.5. - EMA/OD/0000030352

Treatment of hypertrophic cardiomyopathy

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

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of hypertrophic cardiomyopathy 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;
  - the relevance of the outcomes studied;
  - the bridging between the analogue used in some non-clinical studies and the active substance proposed for designation.

- 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 indicate on which population the prevalence calculation is based on. The COMP noted that literature reports high prevalence rates of the condition (Elliot et al, Eur Heart J 2014; 35:2733-2779).

- Significant benefit

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

The sponsor was requested to provide a list of authorised products and standard of care in the proposed condition and a data-driven comparative discussion to justify a clinically relevant advantage or major contribution to patient care.

In the written response, and during an oral explanation before the Committee on 16 June 2020, the sponsor included new data in a model of the condition, which had the additional feature of outflow tract obstruction. In that model, data with the product as applied for designation reduced left ventricular outflow tract (LVOT) peak pressure, as well as contractility through as measured by fractional shortening. It was considered that such additional data in a new relevant outcome measure may be accepted for the intention to treat the condition. With regards to the issue of prevalence, the sponsor refuted the validity of the references with higher prevalence rates. In particular, the references used in the ESC guideline were rejected, arguing that "none used the modern imaging and diagnostic criteria that are currently ESC guideline-recommendations" (Rapezzi 2013; Elliott 2014). The sponsor also referred to a Chinese population study by Zhou et al, (Am J Med, 116 (2004), pp. 14-18) that reported a 0.16% prevalence and argued that if "applying current diagnostic criteria to the Zou results yields a prevalence of 0.09%, which is likely an overestimate". The sponsor used instead the studies of Magnusson 2017, Pujades-Rodriguez 2018, Husser et 2018, and argued with a 4 to 5 per 10,000 estimate. The COMP noted that even when using the Husser et al reference, the reported prevalence rates challenge the threshold, and the sponsor had to apply post-hoc corrections leading to a lower estimate. It was also considered that given that a plethora of publications pointing to hypertrophic cardiomyopathy (HCM) being a non-rare condition, and with an apparent increasing trend over time, it was not possible to conclude that the condition affects less than 5 per 10,000 at the time of application.

Moreover, for the issue of significant benefit, no specific list of authorized products was produced as requested, but the novel mechanism of action of the proposed compound was juxtaposed to the three classes of drugs used in the condition. The sponsor argued that none of available treatments were designed to treat the progressive pathologic ventricular hypertrophy and hypercontractility that characterize HCM, and none of the used agents were specifically designed to reduce inotropy. It was also argued that currently available products serve as a pharmacologic "bridge" to invasive septal reduction therapies rather than being a successful long-term strategy. The COMP noted that a) products are authorised in the EU for the proposed condition (such as propranolol in Sweden with a label for hypertrophic obstructive cardiomyopathy) and that b) in the models and endpoints examined, the effects might be comparable to those of the authorised products in the same settings. In the absence of data supporting a comparative discussion, and to support a clinically relevant advantage or major contribution to patient care, the significant benefit could not be considered justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 18 June 2020, prior to final opinion.

2.1.6. - EMA/OD/0000029210

Treatment of amyotrophic lateral sclerosis

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 non-clinical data in a model of the condition and preliminary clinical data that are difficult to interpret in terms of functional improvement and survival benefit. The assumptions of efficacy were based on extrapolation to a different group of products.

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of amyotrophic lateral sclerosis the sponsor was requested to further elaborate on:

- the results obtained in the non-clinical models used, and the interpretation of the results obtained in the experiments,
- the bridging of the data from different groups of products to the proposed product in non-clinical and clinical studies,
- the data obtained with the proposed product in patients and the interpretation of the results,
- the relevance of clinical data obtained with the use of Treg transfusions for the development of the proposed product.

- Significant benefit

The arguments on significant benefit were based on the new mechanism of action and the potential improved efficacy in the condition. However, no evidence of improvements in ALS model or patients were presented to suggest improved efficacy over riluzole.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the non-clinical and clinical studies to justify the assumption of significant benefit over the authorised medicinal product for the proposed orphan condition.

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

In the written response, and during an oral explanation before the Committee on 17 June 2020, the sponsor provided additional explanation of the data presented in the application. It was also clarified that an ongoing academic clinical study with the product may provide, in the near future, some answers to the questions posed by the committee. The COMP considered that the non-clinical and clinical evidence provided so far with the use of the product was not sufficient to make an assumption of medical plausibility in the condition. It was also considered that bridging efficacy data from another product with a similar mode of action in ALS is not appropriate, because the two products exert their effects in a different way and may ultimately have different characteristics and activity.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 18 June 2020, prior to final opinion.

2.1.7. triheptanoin - EMA/OD/0000030109

Ultragenyx Germany GmbH; Treatment of long-chain fatty acid oxidation disorders (LC-FAOD)

COMP Rapporteur: Dinah Duarte

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:

- Proposed condition

The sponsor was invited to compare and contrast the different types of long-chain Fatty acid oxidation disorders (LC-FAOD), with reference to the aetiology, pathophysiological, histopathological and clinical characteristics. Any international classification systems would be helpful in that regard.

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of long-chain fatty acid oxidation disorders (LC-FAOD) the sponsor was requested further elaborate on the effects of the product in (carnitine palmitoyl transferase 1) CPTI and (carnitine-acylcarnitine translocase) CACT deficiency.

- Prevalence

The sponsor was requested to further elaborate on the case definition and the methodology including the model used for survival and considerations regarding the birth rate.

In the written response, and during an oral explanation before the Committee on 17 June 2020*,* the sponsor focused on the commonality of the early metabolic crises in all long chain fatty acid oxidation disorders, including a reference to ICD-10 codes, to justify the grouping of these conditions.

As regards the medical plausibility, the sponsor included more clinical data. The sponsor provided the clinical narratives from individual patients, reporting a trend for improvement in the frequencies of metabolic crises.

As for prevalence, the sponsor provided an approximately 0.071 per 10,000 estimates using a flow incidence-to-prevalence- forecast model for all FAODs.

In evaluation of the above justifications, the COMP considered that the enzyme deficiencies would have to be designated separately in line with the different aetiology and previous regulatory practice. Moreover, it was considered that despite the paucity of data and uncontrolled nature of observations, there was a trend in favour of the product, showing a reduction in metabolic crises incidence in particular in the CACT subtype.

The Committee communicated the outcome of the discussion to the sponsor, who acknowledged the intention to designate CACT, and provided a recalculation of the prevalence for this specific subtype.

Following review of the application by the Committee, it was agreed to rename the indication to treatment of carnitine-acylcarnitine translocase deficiency.

The Committee agreed that the condition, carnitine-acylcarnitine translocase 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 observations in treated patients showing a reduction in the frequency of metabolic crises.

The condition is chronically debilitating due to fatigue, hypoglycaemia, muscle wasting, rhabdomyolysis and life-threatening in particular due to cardiomyopathy.

The condition was estimated to be affecting significantly 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-acylcarnitine translocase deficiency, was adopted by consensus.

2.1.8. - EMA/OD/0000023895

Treatment of pulmonary arterial hypertension (PAH)

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

- Number of people affected

The sponsor was requested to provide a specific prevalence estimate as number of PAH patients over 10,000 population in the EU, based on up-to-date information.

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

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

- Significant benefit

In order to justify the significant benefit of the proposed product the sponsor was invited to further discuss the data from non-clinical studies in comparison with ambrisentan, since the overall effect of the proposed product appears comparable to that of ambrisentan across the studies.

The sponsor was asked to provide a discussion in relation to the medicinal products other than endothelin receptor antagonists that are used for the treatment of pulmonary arterial hypertension.

Claims of major contribution to patient care were considered preliminary at that stage in absence of data on the efficacy and safety of the proposed product.

In the written response, and during an oral explanation before the Committee on 17 June 2020, the sponsor presented the revised prevalence calculations. Additional sources were consulted compared to the initial application, including published articles, and registries from 4 different European countries. The revised proposed prevalence of 1.2. in 10,000 was considered acceptable and it is also not dissimilar from previous applications, which concluded with a prevalence of approximately 1.5 in 10,000.

Regarding significant benefit, the sponsor re-discussed the previously proposed grounds, mainly based on the mechanism of action and the longer-half life than the currently authorized treatments. However, the product was considered having similar mechanism of action to that of products currently on the market. The non-clinical studies performed so far by sponsor showed similar effects of the proposed product on pulmonary arterial pressure and right ventricular pressure as ambrisentan, currently authorized for the condition. Any claim of major contribution to patient care linked to the longer half-life of the product is also

premature at this stage, in absence of a demonstration of at least comparable safety and efficacy of the proposed product to the currently authorized ones.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 17 June 2020, prior to final opinion.

2.1.9. - EMA/OD/0000030276

Treatment of gestational hypermethioninemia

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 3 June 2020, prior to responding to the list of issues.

2.1.10. - EMA/OD/0000026421

Treatment of hematopoietic stem cell transplantation

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:

- Proposed condition

From the data presented so far, the eligible population for treatment appears to be broader than the proposed population. The applicant was invited to justify the proposed orphan condition as applied for designation.

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of hematopoietic stem cell transplantation (HSCT) the sponsor was asked to further elaborate on:

  - the effects in the population covered by the HSCT indication as proposed for designation,
  - the absence of effects in the primary endpoint and across the subgroups studied,
  - the validity of the post-hoc analysis presented

- Significant benefit

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 a clinically relevant advantage or major contribution to patient care.

In the written response, and during an oral explanation before the Committee on 16 June 2020, the sponsor addressed the indication applied for, and stressed that parainfluenza infections can cause significant morbidity and mortality especially in high risk immunocompromised individuals including HSCT recipients. However, it was acknowledged that parainfluenza infections are also an issue in other immunocompromised settings, as well as in paediatric patients.

The COMP discussed that a possible target indication could have been parainfluenza infections as a whole, and that the sponsor had not justified the proposed indication for the purpose of orphan designation.

With regards to the medical plausibility, the sponsor further elaborated on the available clinical observations. The COMP considered that the main study did not succeed to establish a clear effect, as it relied on a post hoc analysis to identify possible target populations. Even in such a setting, most of the argued trends were not statistically significant. In the absence of robust data, and notwithstanding the issue of the proposed condition, it was considered that the medical plausibility and significant benefit could not be considered justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 17 June 2020, prior to final opinion.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000016117

Prevention of bronchopulmonary dysplasia

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 July meeting.

2.2.2. - EMA/OD/0000019700

Treatment of metastatic pancreatic ductal adenocarcinoma (PDAC)

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 July meeting.

2.2.3. - EMA/OD/0000023667

Treatment of idiopathic pulmonary fibrosis

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 July meeting.

2.2.4. - EMA/OD/0000024640

Treatment of retinitis pigmentosa

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 July meeting.

2.2.5. - EMA/OD/0000028003

Treatment of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

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 July meeting.

2.2.6. - EMA/OD/0000028006

Treatment of myoclonic epilepsy with Ragged-Red Fibres

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 July meeting.

2.2.7. hemopexin, human - EMA/OD/0000028172

CSL Behring GmbH; 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 hemopexin was considered justified based on data generated in non-clinical in vivo models of the condition showing a reduction in vascular stasis associated with a reduction in vaso-occlusive crisis.

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 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 hemopexin, human will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that targets the release of heme in acute crisis for which there is no treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for hemopexin, human, for treatment of sickle cell disease, was adopted by consensus.

2.2.8. - EMA/OD/0000029026

Treatment of follicular lymphoma

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

2.2.9. C-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker - EMA/OD/0000029070

Ascendis Pharma Growth Disorders A/S; Treatment of achondroplasia

COMP Rapporteur: Ausra Matuleviciene

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

The intention to treat the condition with the medicinal product containing C-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker was considered justified based on improvements in long bone growth in a model of the condition.

The condition is chronically debilitating due to manifestations such as otolaryngeal system dysfunction, and rhizomelic short stature, thoracolumbar kyphosis, spinal stenosis, and foramen magnum stenosis and life-threatening with approximately 10 years shorter life expectancy compared to the general population.

The condition was estimated to be affecting approximately 0.6 in 10,000 persons in the European Union, at the time the application was made.

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 C-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker, for treatment of achondroplasia, was adopted by consensus.

2.2.10. - EMA/OD/0000029150

Diagnosis of progressive supranuclear palsy (PSP)

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 July meeting.

2.2.11. - EMA/OD/0000029282

Treatment in solid organ transplant

The sponsor withdrew the application for orphan designation on 17 May 2020 prior to the COMP discussion.

2.2.12. fasudil hydrochloride - EMA/OD/0000029906

Aneuryst (Ireland) Limited; Treatment of non-traumatic subarachnoid haemorrhage

COMP Rapporteur: Martin Mozina

The Committee agreed that the condition, non-traumatic subarachnoid haemorrhage, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing fasudil hydrochloride was considered justified based on published clinical data demonstrating favourable outcomes and reduced vasospasm in patients affected by the condition.

The condition is life-threatening and chronically debilitating due to cerebral ischemia, hydrocephalus, intracerebral haemorrhage, interventricular haemorrhage, subdural hematoma, seizures, increased intracranial pressure, left ventricular systolic dysfunction or myocardial infarction. The condition has a high mortality rate which, at 5 years, is between 65-70%.

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 fasudil hydrochloride will be of significant benefit to those affected by the condition. The sponsor provided published clinical data that demonstrate that patients who were treated with the proposed product achieved reduced vasospasm incidence and lower disability scores post-treatment compared to patients treated with nimodipine. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for fasudil hydrochloride, for treatment of non-traumatic subarachnoid haemorrhage, was adopted by consensus.

2.2.13. maralixibat chloride - EMA/OD/0000030237

Granzer Regulatory Consulting & Services; Treatment of biliary atresia

COMP Rapporteur: Zsofia Gyulai

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

The intention to treat the condition with the medicinal product containing maralixibat chloride was considered justified based on non-clinical data showing reduced serum bile acid levels and reduced liver inflammation.

The condition is life-threatening and chronically debilitating due to the development of portal hypertension, cholangitis, portal fibrosis and biliary cirrhosis.

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

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

A positive opinion for maralixibat chloride, for treatment of biliary atresia, was adopted by consensus.

2.2.14. - EMA/OD/0000030305

Treatment of primary sclerosing cholangitis

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

2.2.15. - EMA/OD/0000031667

Prevention of haemolytic uraemic 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 July meeting.

2.2.16. - EMA/OD/0000031867

Treatment of haematopoietic stem cell transplantation

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 July meeting.

2.2.17. - EMA/OD/0000031911

Treatment of inherited disorders of oxidative phosphorylation

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 July meeting.

2.2.18. imetelstat sodium - EMA/OD/0000031951

Parexel International GmbH; Treatment of myelodysplastic syndromes

COMP Rapporteur: Karri Penttila

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

The intention to treat the condition with the medicinal product containing imetelstat sodium was considered justified based on early clinical data demonstrating achievement of transfusion independence in a proportion of patients with low risk myelodysplastic syndromes.

The condition is life-threatening and chronically debilitating in particular due to anaemia, thrombocytopenia, and neutropenia, as well as transformation into acute myeloid leukemia.

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 provided sufficient justification for the assumption that the medicinal product containing imetelstat sodium will be of significant benefit to those affected by the condition. The sponsor provided clinical data that demonstrate that patients with low risk condition who were transfusion dependent even after pre-treatment with erythropoiesis stimulating agents and who are ineligible for treatment with lenalidomide did achieve either transfusion independence or reduction of transfusion frequency. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for imetelstat sodium, for treatment of myelodysplastic syndromes, was adopted by consensus.

2.2.19. - EMA/OD/0000031991

Prevention of retinopathy of prematurity

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 July meeting.

2.2.20. retinol palmitate - EMA/OD/0000032007

Provepharm S.A.S.; Prevention of bronchopulmonary dysplasia

COMP Rapporteur: Eva Malikova

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

The intention to prevent the condition with the medicinal product containing retinol palmitate was considered justified based on bibliographic clinical data showing reduced incidence of bronchopulmonary dysplasia with the proposed product.

The condition is life-threatening and chronically debilitating due to inflammation and scarring in the lungs, resulting in necrotizing bronchiolitis and alveolar septal injury, which compromises the oxygenation of blood.

The population of patients eligible for prevention of the condition was estimated to be less than 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 prevention in the European Union for the population at risk of developing the condition.

A positive opinion for retinol palmitate, for prevention of bronchopulmonary dysplasia, was adopted by majority (23 out of 26 votes).

The divergent positions (*Brigitte Blöchl-Daum; Armando Magrelli; Tim Leest)* were appended to this opinion.

2.2.21. tinostamustine - EMA/OD/0000032028

Mundipharma Corporation (Ireland) Limited; Treatment of T-cell prolymphocytic leukaemia

COMP Rapporteur: Karri Penttila

The Committee agreed that the condition, T-cell prolymphocytic leukaemia, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing tinostamustine was considered justified based on non-clinical in vivo data in a model of the condition, where treatment with the proposed product resulted in reduction in leukocyte burden and spleen size.

The condition is life-threatening with approximately 5% of patients surviving for 5 years and chronically debilitating in particular due to manifestations such as hepatosplenomegaly and generalized lymphadenopathy, skin infiltration and serous effusions, as well as bone marrow failure, manifesting as anaemia and/or thrombocytopenia.

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

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

A positive opinion for tinostamustine, for treatment of T-cell prolymphocytic leukaemia, was adopted by consensus.

2.2.22. - EMA/OD/0000032154

Treatment of amyotrophic lateral sclerosis

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 July meeting.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

2.5.1. benzyl benzoate, beta-caryophyllene, cineole, cinnamaldehyde, cinnamyl acetate, linalool, trans-2-methoxycinnamaldehyde - EMA/OD/0000036241

Septeos S.A.S.; Treatment of eumycetoma

In the grounds for appeal, and during an oral explanation before the Committee on 17 June 2020, the sponsor discussed the unsatisfactory cure rates with the available medicinal products for the treatment of eumycetoma, pointing out that the best published cure rates are around 50% and these are achieved with long term anti-fungal treatment. Disease control is achieved in up to 80% of cases with surgery and antifungal treatment. The COMP acknowledged that there are unmet needs in the treatment of eumycetoma and indeed significant benefit is assumed to show what the advantages of a new product would be as compared to products that are already authorized, which, based on the legislation, are considered satisfactory. However, the sponsor failed to demonstrate this during the orphan designation procedure. In addition, when medicinal products are authorized, a positive benefit/risk is established by the regulators based on clinical benefits and detrimental effect, and this is at the base of such products being considered satisfactory. This applies to all medicinal products for which clinical benefits have been demonstrated to outweigh the risk and are relevant for the patients, whether such products are curative of the whole disease, curing some of its manifestations, control symptoms, or any other outcome that has been considered relevant in the assessment of the benefits.

The sponsor then remarked that there are no medicinal products for the treatment of mycetoma that can be considered satisfactory when looking at authorized indications as reported in the Summary of Product Characteristics (SmPCs) of antifungal treatments. The COMP responded that the fact that posaconazole has an authorized indication for the treatment of eumycetoma was acknowledged by the sponsor in the initial application, and in the grounds of the appeal. In addition, it was noted that in some European countries (e.g. Sweden and Germany) itraconazole has a broad range of indications in the SmPC, which include skin fungal infections. Such broad indications would allow the use in the treatment of eumycetoma as fungal infection of the skin (eumycetoma affects skin and connective tissue). Amphotericin B is listed in the UK SmPC as indicated for eumycetoma. It was therefore confirmed by the COMP, in line with what previously stated, that satisfactory methods for the treatment of eumycetoma exist according to the definition of satisfactory methods applied to medicinal products (i.e. authorised products) in Regulation (EC) No 141/2000, and subsequent applications and guidance from the European Commission. Based on this, data to demonstrate significant benefit of the proposed product was requested.

In conclusion, the grounds of the appeal were based on challenging the definition of satisfactory methods and its application by the COMP. No scientific considerations or justifications to the purpose of significant benefit were presented by the sponsor in the written appeal and during the oral explanation. The COMP confirmed the previous negative grounds based on the lack of demonstration of significant benefit.

The COMP therefore adopted a negative opinion by consensus and recommends the refusal of the granting of the designation of benzyl benzoate, beta-caryophyllene, cineole, cinnamaldehyde, cinnamyl acetate, linalool, trans-2-methoxycinnamaldehyde as an orphan medicinal product for orphan condition: treatment of eumycetoma.

Having examined the grounds for appeal and the additional considerations provided during the oral explanation the COMP considered that:

The intention to treat the condition was considered justified based on non-clinical data in a model of the condition showing a small improvement in survival upon treatment with the proposed product as compared to either vehicle or the standard first line treatment, itraconazole.

Eumycetoma was estimated to be affecting approximately 0.01 in 10,000 persons in the European Union, at the time the application was made.

The sponsor has established that the condition is chronically debilitating and/or life-threatening.

Thus, the requirements under Article 3(1)(a) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has not provided sufficient justification for the assumption that the medicinal product containing benzyl benzoate, beta-caryophyllene, cineole, cinnamaldehyde, cinnamyl acetate, linalool, trans-2-methoxycinnamaldehyde will be of significant benefit to those affected by the condition. Although the non-clinical model used was considered as valid for the purpose of supporting medical plausibility in eumycetoma, the data produced in this model were not found sufficient to support the significant benefit. The sponsor has shown that the treatment with the proposed product leads to a marginal improvement in survival in the non-clinical model when compared to the treatment with itraconazole. However, the sponsor failed to support the claim that such improvement is clinically relevant. In addition, the sponsor has not established the significant benefit over other authorised, satisfactory methods of treatment - amphotericin B and posaconazole.

Thus, the requirement under Article 3(1)(b) of Regulation (EC) No 141/2000 on orphan medicinal products is not fulfilled.

The COMP concludes that the requirements laid down in Article (3)(1) (a) and (b) of Regulation (EC) No 141/2000 on orphan medicinal products are not fulfilled. The COMP therefore recommends the refusal of the granting of the designation of benzyl benzoate, beta-caryophyllene, cineole, cinnamaldehyde, cinnamyl acetate, linalool, trans-2-methoxycinnamaldehyde as an orphan medicinal product for orphan condition: treatment of eumycetoma.

2.5.2. melatonin - EMA/OD/0000036026

Worphmed S.r.l.; Treatment of intracerebral hemorrhage

In the grounds for appeal, the sponsor proposed intracerebral haemorrhage (ICH) as a distinct medical entity and wished to clarify that this is the condition and that they do not intend to use the condition interchangeably with haemorrhagic stroke. This being the case the focus of the assessment was on intracerebral haemorrhage.

ICH is caused by bleeding, primarily into parenchymal brain tissue and is responsible for 9% to 27% of all strokes worldwide (Steiner T et al, World Stroke Organisation, Vol 9, October 2014, 840-855). The haematoma locations are deep or ganglionic, lobar, cerebellar, and

brain stem in descending order of frequency. Intracerebral haemorrhage occurs twice as common as SAH and is equally deadly.

ICH is defined by its location within the brain parenchyma with "deep" ICH being located within the basal ganglia and internal capsule (35%-70%), brain stem (5%-10%), and cerebellum (5%-10%). In contrast, "lobar" ICH (15%-30%) refers to haemorrhages located in the cortical-subcortical areas and follows a "lobar" pattern across one or less often multiple lobes of the brain. Deep ICH accounts for about two thirds of spontaneous ICH cases and lobar ICH accounts for the remaining third.

Risk factors for ICH include hypertension, cerebral amyloid angiopathy, advanced age, antithrombotic therapy and history of cerebrovascular disease.

Two types of ICH are described; these are traumatic ICH and spontaneous nontraumatic ICH the latter entailing bleeding that occurs without trauma or known bleeding causes such as an arteriovenous malformation, cerebral aneurysm or tumour.

ICH mortality is about 40% at 30 days making it one of the deadliest acute medical events, similar to SAH in acute mortality. At 1yr the mortality is 50%. Half the deaths take place in the first 48 to 73 hrs and are related to neurological complications. Deaths after the first month are usually the result of medical complications (i.e. pulmonary embolism, aspiration pneumonia, sepsis, and gastrointestinal bleeding).

The sponsor has opted to apply for the broad term ICH which would include the traumatic forms of ICH as well as the rarer spontaneous nontraumatic forms for the purpose of the prevalence calculation.

Further to the clarifications of the sponsor in the grounds of appeal, the COMP considered that ICH qualified as a distinct medical entity. This entails that the sponsor would not need to provide data to support the specificity of melatonin to ICH.

The sponsor based its prevalence for the condition of ICH estimate on two publications: Jolink et al 20015 and Sundboll et al 2016. The prevalence estimate based on these publications did not exceed 2.45 in 10,000 persons in the EU. However, the two publications only covered prevalence calculations for spontaneous non-traumatic ICH and not for the broader condition of ICH. Accordingly, the sponsor did not provide evidence capable of establishing the prevalence of the applied-for condition in the EU (which, as noted above, covers both traumatic ICH and spontaneous non-traumatic ICH).

Instead, the COMP considered that the prevalence of ICH in the EU would be well above 5 in 10,000.

The COMP therefore adopted a negative opinion by consensus and recommends the refusal of the granting of the designation of melatonin as an orphan medicinal product for orphan condition: treatment of intracerebral haemorrhage.

Having examined the grounds for appeal and the additional considerations provided during the appeal procedure, the COMP considered that:

The sponsor proposed that 'intracerebral haemorrhage' is a distinct medical condition. The COMP accepted that ICH was a distinct medical condition.

The sponsor has not provided a comprehensive estimation of the prevalence of the proposed orphan condition and therefore has not established that the condition affects not

more than 5 in 10,000 persons in the European Union at the time the application was made.

The sponsor has established that the condition is chronically debilitating and life-threatening.

Thus, the requirements under Article 3(1)(a) of Regulation (EC) No 141/2000 on orphan medicinal products are not fulfilled.

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

The COMP concludes that the requirements laid down in Article (3)(1) (a) and (b) of Regulation (EC) No 141/2000 on orphan medicinal products are not cumulatively fulfilled. The COMP therefore recommends the refusal of the granting of the designation of melatonin as an orphan medicinal product for the orphan condition: treatment of intracerebral haemorrhage.

2.6. Nominations

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

COMP coordinators were appointed for 24 applications

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 5 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of ß-thalassaemia intermedia and major

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 June meeting.]

3.1.2. -

Treatment of amyotrophic lateral sclerosis

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 June meeting.]

3.2. Finalised letters

3.2.1. -

Treatment of mucopolysaccharidosis type II (Hunter syndrome)

The finalised letter was circulated for information.

3.2.2. -

Treatment of hepatocellular carcinoma

The finalised letter was circulated for information.

3.2.3. -

Treatment of Duchenne muscular dystrophy

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment of short bowel syndrome

The new request was noted.

3.3.2. -

Treatment of Philadelphia chromosome-positive chronic myelogenous leukaemia in chronic phase

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. Idefirix – imlifidase - EMEA/H/C/004849, EMA/OD/237/16, EU/3/16/1826, EMA/OD/0000005755

Hansa Biopharma AB; Prevention of graft rejection following solid organ transplantation

An opinion recommending not to remove Idefirix, imlifidase, EU/3/16/1826 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 June meeting.]

4.2.2. - elexacaftor/tezacaftor/ivacaftor - EMEA/H/C/005269, EU/3/18/2116, EMA/OD/0000020155

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

The status of the procedure at CHMP was noted.

4.2.3. – tagraxofusp - EMEA/H/C/005031, EMA/OD/064/15, EU/3/15/1567, EMA/OD/0000004627

TMC Pharma (EU) Limited; Treatment of blastic plasmacytoid dendritic cell neoplasm

The status of the procedure at CHMP was noted.

4.2.4. – crizanlizumab - EMEA/H/C/004874, EMA/OD/026/12, EU/3/12/1034, EMA/OD/0000009984

Novartis Europharm Limited; Treatment of sickle cell 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 September meeting.

[Post-meeting note: The COMP adopted a list of issues by written procedure following its June meeting.]

4.2.5. – avapritinib - EMA/OD/037/17, EU/3/17/1889, EMA/OD/0000030630

Blueprint Medicines (Netherlands) B.V.; Treatment of gastrointestinal stromal tumours

The COMP adopted a list of issues that will be sent to the sponsor.

4.2.6. – amikacin - EMEA/H/C/005264, EMA/OD/191/13, EU/3/14/1259, EMA/OD/0000030955

Insmed Netherlands B.V.; Treatment of nontuberculous mycobacterial lung

The status of the procedure at CHMP was noted.

4.2.7. – deferiprone - EMEA/H/C/005004, EMA/OD/006/18, EU/3/18/2034, EMA/OD/0000011266

Apotex B.V.; Treatment of neurodegeneration with brain iron accumulation

The status of the procedure at CHMP was noted.

4.2.8. – belantamab mafodotin - EMEA/H/C/004935/0000, EMA/OD/077/17, EU/3/17/1925, EMA/OD/0000028779

Accelerated assessment

GlaxoSmithKline (Ireland) Limited; Treatment of multiple myeloma

The status of the procedure at CHMP was noted.

4.2.9. – pexidartinib - EMEA/H/C/004832, EMA/OD/279/14, EU/3/15/1457, EMA/OD/0000021360

Daiichi Sankyo Europe GmbH; Treatment of tenosynovial giant cell tumour, localised and diffuse type

CHMP negative opinion was noted.

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 2 applications.

4.5. Orphan Maintenance Reports

Documents were tabled for information.

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

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

5.2.1. Kalydeco – ivacaftor - Type II variation - EMEA/H/C/002494/II/0085, EMA/OD/010/08, EU/3/08/556, EMA/OD/0000036247

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.

5.2.2. Kalydeco – ivacaftor- Type II variation - EMEA/H/C/002494/II/0086, EMA/OD/010/08, EU/3/08/556, EMA/OD/0000036251

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

CHMP rapporteur: Maria Concepcion Prieto Yerro

The status of the procedure at CHMP was noted.

5.3. Appeal

None

5.4. On-going procedures

COMP co-ordinators were appointed for 2 applications.

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 meetings

None

7.1.2. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 16 June 2020.

7.1.3.

None

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.

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

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

The COMP representatives on the PCWP presented the discussion paper for patients and consumers on secondary use of data for medicines and public health purposes. COMP members were invited to send comments by the 9th of July.

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

None

7.3.3. Guideline on registry-based studies - Consultation with EMA Committees

The COMP received an introduction of the guideline on registry-based studies in advance of the written consultation planned in June-July 2020. COMP members were invited to send comments by 31 July 2020.

7.3.4.

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. EMA Business Pipeline activity and Horizon scanning

The document was tabled for information.

8.2. Strategic Review & Learning meeting – 24-25 September 2020, Germany

The COMP discussed the organisational matters of the SRLM to be host by Germany in September 2020. Further discussion is expected next month.

8.3. 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/

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 June 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 Kovarova	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	
Nikolas Sypsas	Member	Greece	No restrictions applicable to this meeting	
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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No interests declared	
Elisabeth 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	
Angelo Loris Brunetta	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Julian Isla	Member	Patients' Organisation Representative	No interests declared	
Bruno Sepodes	Member	Expert recommended by EMA	No interests declared	
Ingeborg Barisic	Expert	Croatia	No restrictions applicable to this meeting	
Giuseppe Capovilla	Expert	Italy	No interests declared	
Virginie Hivert	Expert	Patients' Organisation Representative	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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.