11 May 2021
EMA/COMP/222143/2021
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 13-15 April 2021

Chair: Violeta Stoyanova-Beninska

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

1.1. Welcome and declarations of interest of members and experts

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

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

The COMP noted that Armando Magrelli's mandate as COMP member representing Italy has ended.

Giuseppe Capovilla gave a proxy to Angelo Loris Brunetta to vote on behalf of Giuseppe Capovilla during part of April 2021 COMP meeting.

1.2. Adoption of agenda

The agenda for 13-15 April 2021 was adopted with the following topic under 7.7:

- COMP work plan.

1.3. Adoption of the minutes

The minutes for 16-18 March 2021 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/0000049059

Treatment of generalised pustular psoriasis (GPP)

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

Generalised Pustular Psoriasis (GPP) was requested to 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 was drawn to the Orphan regulations and relevant guidelines (especially section A of ENTR/6283/00).

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

a) the unique features of GPP allowing to differentiate from other types of psoriasis (e.g. palmoplantar pustulosis),

b) the overlaps in triggers, pathophysiology, clinical presentation and treatment approaches between GPP and other types of psoriasis,

c) the expected efficacy of the proposed product in other forms of psoriasis.

- 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 provide a prevalence calculation of the final proposed condition.

- Significant benefit

Products authorised broadly for the treatment of psoriasis could be considered for the treatment of GPP. The sponsor was requested to provide a full list of such products authorised in the EU (centrally or nationally).

Further, the sponsor was requested 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.

The sponsor was asked to provide details of the intended clinical use of the product in the treatment algorithm to support the significant benefit assumption in the context of the current therapeutic management of patients.

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

In the written response, and during an oral explanation before the Committee on 13 April 2021, the sponsor tried to further justify the condition and elaborated on the clinical and histopathological differences between plaque and pustular psoriasis. In addition, the sponsor clarified their belief that there is no continuity between different types of psoriasis and the genetic predisposition, albeit complex, seems to speak in favour of distinguishing psoriasis subtypes as distinct conditions. For example, IL36RN mutations are associated with GPP but not with plaque psoriasis or palmoplantar pustulosis. The sponsor admitted however, that IL36 overactivation plays a role in other types of psoriasis independent of the mutation status. Also, one patient may present with more than one form of psoriasis consecutively or at the same time. The sponsor admitted that there are overlaps in the inflammatory

pathways involved in plaque and pustular psoriasis types. Due to these overlaps and the potential blurred lines between diagnoses given to patients, the COMP considered that the most appropriate term for an orphan designation would be 'treatment of psoriasis'. This condition does not, however, meet the orphan prevalence criterion. In addition, the sponsor discussed indirectly the expected benefits of the product over the standard of care (e.g., acitretin and ciclosporin), which has limited efficacy in the condition. No comparative data supporting the notion that the proposed product offers an improved efficacy was presented. Thus, the data submitted in support of significant benefit over medicines used in treatment of GPP were considered insufficient.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 13 April 2021, prior to final opinion.

2.1.2. adeno-associated viral vector serotype 2.5T encoding the human cystic fibrosis transmembrane conductance regulator with a partial deletion in the R domain - EMA/OD/0000049823

Raremoon Consulting Esp S.L.; Treatment of cystic fibrosis (CF)

COMP Rapporteur: Eva Malikova

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 cystic fibrosis the sponsor was requested to further elaborate on:

a) the results obtained in in-vitro data regarding the clinical use in the treatment of cystic fibrosis,

b) the relevance of the non-clinical model used for the treatment of cystic fibrosis, and the interpretation of the results obtained in the experiments, and why other valid non-clinical in-vivo models were not feasible,

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

- Significant benefit

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

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

The sponsor was asked to detail the results of any clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients.

In the written response, the sponsor submitted new data produced in a non-clinical in vivo model.

The COMP noted that nasal inhalation of the product resulted in the expression of human cystic fibrosis transmembrane conductance regulator (CFTR) in the respiratory tract of model. Although the data only represent a proof of concept, the whole package is acceptable to support the medical plausibility.

The target for the proposed product is approximately 20% of CF patients who do not benefit from any of the four approved CFTR modulators (ivacaftor, lumacaftor/ivacaftor, tezacaftor/ivacaftor, and elexacaftor/ivacaftor/tezacaftor).

Thus, the argumentation for significant benefit was based on the fact that approximately 20% of CF patients do not have a disease modifying therapy available. Additionally, the sponsor has shown with in vitro data that the proposed product seems to restore the functionality of CFTR more profoundly than Orkambi. Since there is still a proportion of patients that are not covered by the current therapy, and since the product has shown some benefit over Orkambi, the COMP concluded that the assumptions of significant benefit are acceptable.

The planned oral explanation was therefore cancelled.

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

The intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 2.5T encoding the human cystic fibrosis transmembrane conductance regulator with a partial deletion in the R domain was considered justified based on data showing expression of CFTR in a non-clinical in vivo model of the condition.

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

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing adeno-associated viral vector serotype 2.5T encoding the human cystic fibrosis transmembrane conductance regulator with a partial deletion in the R domain will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate a restoration of CFTR expression which could target all patients with the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated viral vector serotype 2.5T encoding the human cystic fibrosis transmembrane conductance regulator with a partial deletion in the R domain, for treatment of cystic fibrosis, was adopted by consensus.

2.1.3. 6-Amino-5-chloro-N-((1R)-1-(5-(((5-chloro-4-(trifluoromethyl)-2-pyridinyl)amino)carbonyl)-2-thiazolyl)ethyl)-4-pyrimidinecarboxamide - EMA/OD/0000050198

Parexel International (Irl) Limited; Treatment of glioma

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 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 updated results from clinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

In the written response to the raised issue on the significant benefit the sponsor presented the updated results from the ongoing study. The five patients who achieved a response (5 out of 9 responses; overall response rate (ORR) = 56%) have completed the study outlined 24 months of therapy without progression or discontinuation of therapy due to adverse events. Furthermore, a total of 16 additional patients have been enrolled into the study (as of 31 January 2021). Of the 16 patients, 11 are patients with a low-grade glioma harbouring a RAF alteration. No patient enrolled in the 420mg/m2 cohort has had a dose-limiting toxicity (DLT). Based on investigator review, of the 13 patients evaluable for response, 5 out of 13 have responded. Three of 13 have withdrawn for toxicity, 1 of 13 had stable disease and withdrew, 4 of 13 had progressive disease. Independent review is planned, but not yet completed.

The COMP considered that the updated results confirmed the responses observed and that the preliminary clinical data demonstrate that patients with refractory low-grade glioma responded to treatment. The planned oral explanation was therefore cancelled.

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

The intention to treat the condition with the medicinal product containing 6-Amino-5-chloro-N-((1R)-1-(5-(((5-chloro-4-(trifluoromethyl)-2-pyridinyl)amino)carbonyl)-2-thiazolyl)ethyl)-4-pyrimidinecarboxamide was considered justified based on preliminary clinical data showing confirmed responses in a few paediatric low grade glioma patients.

The condition is chronically debilitating due to symptoms caused the tumour compressing the surrounding brain tissue including headache, anorexia, nausea, vomiting, seizures, neurological deficits, personality and cognitive impairment. The condition is also life-threatening, with poor 5-year survival of less than 5% for glioblastoma multiforme patients.

The condition was estimated to be affecting approximately 2.3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing 6-Amino-5-chloro-N-((1R)-1-(5-(((5-chloro-4-(trifluoromethyl)-2-pyridinyl)amino)carbonyl)-2-thiazolyl)ethyl)-4-pyrimidinecarboxamide will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that patients with refractory low-grade glioma responded to treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 6-Amino-5-chloro-N-((1R)-1-(5-(((5-chloro-4-(trifluoromethyl)-2-pyridinyl)amino)carbonyl)-2-thiazolyl)ethyl)-4-pyrimidinecarboxamide, for treatment of glioma, was adopted by consensus.

2.1.4. human IgG1 monoclonal antibody against alpha-synuclein - EMA/OD/0000047784

H. Lundbeck A/S; Treatment of multiple system atrophy (MSA)

COMP Rapporteur: Michel Hoffmann

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 multiple system atrophy the sponsor was asked to further elaborate on:

a) the relevance of the non-clinical model used for the treatment of multiple system atrophy, and the interpretation of the results obtained in the experiments,

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

In the written response, the sponsor explained that the product is an immunotherapy with an antibody targeting alpha-synuclein by inhibiting transmission of alpha-synuclein seeds. The main mechanism of action of the product is blocking of neuronal and oligodendrocyte alpha-synuclein seed uptake. Antibodies used for immunotherapy do not penetrate cells, and therefore the sponsor uses in vitro data and a non-clinical model for in vivo studies which allow to prove the potential extracellular effect of their product.

It was noted that viral alpha-synuclein transgenic expression of alpha synuclein in oligodendrocytes has been used in different non-clinical models of MSA. The sponsor argued that these models could be useful to determine the mechanisms of alpha-synuclein-induced intracellular toxicity in oligodendroglial cells. However, these models do not allow the prion-like behaviour of alpha-synuclein because there is no, or very little, transmission of pathology in these models from one cell to another.

In summary the sponsor`s explanation allowed a better understanding of the data presented in the original application. The models used are relevant to prove a potential effect of the product in reducing the extracellular seeding of alpha synuclein. The written responses were considered satisfactory and the oral explanation was cancelled.

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

The intention to treat the condition with the medicinal product containing human IgG1 monoclonal antibody against alpha-synuclein was considered justified based on data from a non-clinical in vivo model of the condition which shows reduction in the propagation of alpha-synuclein.

The condition can be severely debilitating due to progressive motor and or cerebellar dysfunction, autonomic failure, and gait disorders, or life threatening due to recurrent infections or pulmonary embolism.

The condition was estimated to be affecting approximately 0.4 in 10,000 persons in the European Union, at the time the application was made.

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 human IgG1 monoclonal antibody against alpha-synuclein, for treatment of multiple system atrophy, was adopted by consensus.

2.1.5. - EMA/OD/0000047579

Treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL)

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

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 address the following issues:

a) Clarify whether SLL was included in the calculations.

b) The prevalence should be recalculated with data on EU-27 only.

c) The prevalence should be re-calculated by using complete prevalence reported by national registries e.g. NORDCAN.

d) In view of the uncertainties of the indirect estimation of prevalence and the fact that the prevalence of CLL/SLL is very close to the threshold, a sensitivity analyses of the estimate of prevalence should be provided.

- Significant benefit

The arguments on significant benefit were based on the comparison of the mechanism of action versus other kinase inhibitors, on the efficacy and on the safety.

The sponsor was requested to detail the population enrolled in the submitted studies and describe with more details the previous treatments.

Contextualization of the efficacy and safety results against approved CLL therapies, including venetoclax, were missing. The sponsor was requested to provide adequate justification of significant benefit against venetoclax.

In the written response, and during an oral explanation before the Committee on 14 April 2021, the sponsor argued that SLL is a disease with low incidence and the majority of the public domain databases that the sponsor identified did not list SLL as a separate category for data reporting. An updated prevalence calculation was presented with a data on EU-27 only and by using the relative proportions of patients in each Binet stage group, based on recent literature sources. The COMP concluded that since the indirect calculations introduced many variables (the proportion of patients in each Binet stage group and the median survival) and the fact that the prevalence of CLL/SLL is very close to the threshold, a direct prevalence figure would be necessary to ascertain certainty on the prevalence calculation.

For the demonstration of significant benefit, the sponsor argued mainly on indirect efficacy and safety comparisons of the proposed combination therapy against acalabrutinib for the treatment of naïve patients and on indirect efficacy and safety comparisons of the proposed combination therapy against approved treatments (mainly ibrutinib and venetoclax + rituximab) for relapsed/refractory patients.

The COMP noted that in the treatment naïve patients, it seems that the efficacy of the proposed combination therapy is comparable with acalabrutinib. However, at the same time the number of treatment discontinuations is considerable higher with the proposed combination therapy compared to acalabrutinib. In addition, the COMP considered that it is not possible to conclude on better or comparable efficacy and safety of the proposed product in relapsed CLL patients based on the data presented. In addition, regarding the comparison with venetoclax, based on the summary of prior systemic therapy only 2 patients that had received venetoclax as prior treatment received the proposed product (1 received the proposed combination therapy and 1 received the proposed product only). However, the sponsor did not provide any specific efficacy data of these patients so no conclusion on efficacy comparison with venetoclax could be drawn.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 14 April 2021, prior to final opinion.

2.1.6. - EMA/OD/0000037733

Treatment of systemic sclerosis

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 March 2021, prior to responding to the list of issues.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000037664

Treatment of cystinuria

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 May meeting.

2.2.2. begelomab - EMA/OD/0000037706

Adienne S.r.l.; Treatment of dermatomyositis

COMP Rapporteur: Olimpia Neagu

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

The intention to treat the condition with the medicinal product containing begelomab was considered justified based on preliminary clinical data demonstrating remission of cutaneous manifestations of the disease and reduced muscle inflammation.

The condition is life-threatening and chronically debilitating due to skin lesions, cardiac impairment, progressively debilitating muscle weakness and increased risk of malignancy.

The condition was estimated to be affecting approximately 1.4 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing begelomab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that patients who were not adequately managed using corticosteroids, immunoglobulin infusions and immunosuppressive therapy achieved remission with improvement of skin, muscle and other disease manifestations. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for begelomab, for treatment of dermatomyositis, was adopted by consensus.

2.2.3. macitentan - EMA/OD/0000042650

Janssen-Cilag International N.V.; Treatment of functional single ventricle heart disease

COMP Rapporteur: Lyubina Racheva Todorova

Following review of the application by the Committee, it was agreed to rename the indication to treatment of functional single ventricle congenital heart disease.

The Committee agreed that the condition, functional single ventricle congenital heart disease, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing macitentan was considered justified based on clinical cases in the literature showing improved exercise capacity, decreased pulmonary vascular resistance, improved patients' New York Heart Association functional class and increased cardiac index.

The condition is chronically debilitating due to impaired cardiac ventricular function, atrial arrhythmias and thrombotic events. Some patients also develop neuropsychological, psychiatric, and behavioural deficits. The condition is also life-threatening with an estimate of 30-year survival in approximately 85% of patients after surgical Fontan completion.

The condition was estimated to be affecting approximately 0.4 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for macitentan, for treatment of functional single ventricle congenital heart disease, was adopted by consensus.

2.2.4. eflornithine - EMA/OD/0000044418

Brancaster Pharma Ireland Limited; Treatment of neuroblastoma

COMP Rapporteur: Bozenna Dembowska-Baginska

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

The intention to treat the condition with the medicinal product containing eflornithine was considered justified based on non-clinical data in a model of the condition supporting an increase in tumour-free survival, as well as clinical responses in relapsed or refractory patients treated with eflornithine.

The condition is life threatening and chronically debilitating due to its aggressive nature and frequency of metastatic disease. It accounts for almost 15% of childhood cancer fatalities.

The condition was estimated to be affecting approximately 1.1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing eflornithine will be of significant benefit to those affected by the condition. The sponsor has referred to clinical studies in relapsed or refractory patients who responded to treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for eflornithine, for treatment of neuroblastoma, was adopted by consensus.

2.2.5. elamipretide - EMA/OD/0000046486

Scendea (NL) B.V.; Treatment of Barth syndrome

COMP Rapporteur: Elisabeth Johanne Rook

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

The intention to treat the condition with the medicinal product containing elamipretide was considered justified based on preliminary clinical data showing improvements in 6 minutes walking test as well as in heart function.

The condition is life-threatening due to heart failure and chronically debilitating due to cardiomyopathy, ventricular arrhythmia, growth retardation, fatigue and exercise intolerance, motor delay, poor appetite, neutropenia, hypoglycaemia, lactic acidosis and hyperammonaemia.

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.

A positive opinion for elamipretide, for treatment of Barth syndrome, was adopted by consensus.

2.2.6. 2-[4-[3-(methylamino)-1-phenylpropoxy]phenyl]ethanol hydrochloride - EMA/OD/0000048861

Connecta Therapeutics S.L.; Treatment of fragile X syndrome

COMP Rapporteur: Dinah Duarte

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

The intention to treat the condition with the medicinal product containing 2-[4-[3-(methylamino)-1-phenylpropoxy]phenyl]ethanol hydrochloride was considered justified based on non-clinical data in a valid model of the condition showing improvements in social recognition.

The condition is chronically debilitating due to developmental delay, a range of neurobehavioral and neurocognitive complications.

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

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

A positive opinion for 2-[4-[3-(methylamino)-1-phenylpropoxy]phenyl]ethanol hydrochloride, for treatment of fragile X syndrome, was adopted by consensus.

2.2.7. - EMA/OD/0000049844

Treatment of solid organ 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 May meeting.

2.2.8. - EMA/OD/0000051199

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 May meeting.

2.2.9. 2-amino-6-[(2S)-2-hydroxypropanoyl]-7,8-dihydro-1H-pteridin-4-one - EMA/OD/0000051718

Ptc Therapeutics International Limited; Treatment of hyperphenylalaninemia

COMP Rapporteur: Julian Isla

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

The intention to treat the condition with the medicinal product containing 2-amino-6-[(2S)-2-hydroxypropanoyl]-7,8-dihydro-1H-pteridin-4-one was considered justified based on preliminary clinical data showing reduction of elevated blood phenylalanine levels.

The condition is chronically debilitating (if untreated) due to high blood phenylalanine levels which cause cognitive impairment.

The condition was estimated to be affecting approximately 1.9 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the

medicinal product containing 2-amino-6-[(2S)-2-hydroxypropanoyl]-7,8-dihydro-1H-pteridin-4-one will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate reduction of elevated blood phenylalanine levels that cannot be achieved with the currently authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 2-amino-6-[(2S)-2-hydroxypropanoyl]-7,8-dihydro-1H-pteridin-4-one, for treatment of hyperphenylalaninemia, was adopted by consensus.

2.2.10. - EMA/OD/0000051869

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 May meeting.

2.2.11. trehalose - EMA/OD/0000052176

FGK Representative Service GmbH; Treatment of amyotrophic lateral sclerosis (ALS)

COMP Rapporteur: Gloria Maria Palomo Carrasco

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 trehalose was considered justified based on bibliographical non-clinical in vivo data in models of the condition showing beneficial effects on survival, motor function and delay of disease progression.

The condition is life-threatening and chronically debilitating due to progressive degeneration of motor neurons, ultimately leading to paralysis and respiratory failure. The survival of the patients is usually limited to 2-3 years.

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 trehalose will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate beneficial effects on survival, motor function and delay of disease progression which is not expected with the currently authorised medicine. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for trehalose, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

2.2.12. synthetic 2′-O-(2-methoxyethyl)-modified antisense oligonucleotide linked to a triantennary cluster of N-acetyl galactosamine sugars targeting transmembrane protease, serine 6 mRNA - EMA/OD/0000052224

Ionis Development (Ireland) Limited; Treatment of beta thalassemia intermedia and major

COMP Rapporteur: Angelo Loris Brunetta

The Committee agreed that the condition, beta thalassemia intermedia and major, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing synthetic 2′ -O-(2-methoxyethyl)-modified antisense oligonucleotide linked to a triantennary cluster of N-acetyl galactosamine sugars targeting transmembrane protease, serine 6 mRNA was considered justified based on non-clinical in vivo data in models of the condition showing an improvement in iron serum levels and haemoglobin levels.

The condition is life-threatening and chronically debilitating due to the severe anaemia, the need for blood transfusions, and the complications related to these, in particular in beta-thalassaemia major patients.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing synthetic 2'-O-(2-methoxyethyl)-modified antisense oligonucleotide linked to a triantennary cluster of N-acetyl galactosamine sugars targeting transmembrane protease, serine 6 mRNA will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate an improvement in erythropoiesis which does not occur with iron chelators administration. In addition, it is assumed that it could target a different patient population to other authorised medicines. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for synthetic 2'-O-(2-methoxyethyl)-modified antisense oligonucleotide linked to a triantennary cluster of N-acetyl galactosamine sugars targeting transmembrane protease, serine 6 mRNA, for treatment of beta thalassemia intermedia and major, was adopted by consensus.

2.2.13. zanubrutinib - EMA/OD/0000052449

BeiGene Ireland Limited; Treatment of marginal zone lymphoma

COMP Rapporteur: Maria Elisabeth Kalland

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

The intention to treat the condition with the medicinal product containing zanubrutinib was considered justified based on preliminary clinical data in relapsed or refractory marginal zone lymphoma patients who responded to the product with high and durable overall response rates.

The condition is chronically debilitating and life-threatening due to lymphadenopathy, splenomegaly, mucosa and bone-marrow involvement with development of pancytopenia and increased risk of opportunistic infections. Five-year survival ranges from 30% to up to 90%.

The condition was estimated to be affecting approximately 1.6 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the

medicinal product containing zanubrutinib will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in a relapsed/refractory population that responded to treatment with the proposed product. The Committee considered that this constitutes a clinically relevant advantage or major contribution to patient care.

A positive opinion for zanubrutinib, for treatment of marginal zone lymphoma, was adopted by consensus.

2.2.14. melatonin - EMA/OD/0000052825

Worphmed S.r.l.; 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 melatonin was considered justified based on non-clinical data in models of the condition showing photoreceptor preservation and improved retinal function.

The condition is chronically debilitating due to progressive loss of vision inevitably leading to blindness.

The condition was estimated to be affecting approximately 3.5 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 melatonin will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that demonstrate that the product has a broader mechanism of action and would treat variants of the condition which are not covered by the only authorised product, Luxturna. The Committee considered that this could constitute a clinically relevant advantage.

A positive opinion for melatonin, for treatment of retinitis pigmentosa, was adopted by consensus.

2.2.15. autologous mobilised peripheral blood-derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral vector containing a normal version of the coding region of the *IL2RG* gene - EMA/OD/0000052862

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

COMP Rapporteur: Lyubina Racheva Todorova

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 0.04 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 mobilised peripheral blood-derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral vector containing a normal version of the coding region of the *IL2RG* gene, for treatment of X-linked severe combined immunodeficiency, was adopted by consensus.

2.2.16. - EMA/OD/0000052866

Treatment of essential thrombocythaemia

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 May meeting.

2.2.17. adeno-associated viral vector serotype 5 expressing the human Cone-Rod Homeobox gene - EMA/OD/0000052925

Variant; Treatment of Leber's congenital amaurosis

COMP Rapporteur: Tim Leest

The Committee agreed that the condition, Leber's congenital amaurosis, 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 5 expressing the human Cone-Rod Homeobox gene was considered justified based on non-clinical in vivo data in models of the condition showing a partial restoration of visual function.

The condition is chronically debilitating due to the development of progressive and irreversible loss of sight over time.

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 has provided sufficient justification for the assumption that the medicinal product containing adeno-associated viral vector serotype 5 expressing the human Cone-Rod Homeobox gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate an improvement in visual function. The model is representative of a patient population affected

by a different mutation as compared to the one targeted by the currently authorised medicine. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated viral vector serotype 5 expressing the human Cone-Rod Homeobox gene, for treatment of Leber's congenital amaurosis, was adopted by consensus.

2.2.18. adeno-associated virus serotype 9 expressing the cDNA for human MECP2 - EMA/OD/0000053087

Novartis Gene Therapies EU Limited; Treatment of Rett syndrome

COMP Rapporteur: Giuseppe Capovilla

The Committee agreed that the condition, Rett syndrome, 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 virus serotype 9 expressing the cDNA for human *MECP2* was considered justified based on non-clinical in vivo data which showed improvement in survival, body weight and behaviour.

The condition is life-threatening and chronically debilitating due to severe locomotor disability, severe intellectual disability, sleep disturbances, seizures, respiratory complications and development of arrhythmias resulting in decreased life-expectancy.

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

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

A positive opinion for adeno-associated virus serotype 9 expressing the cDNA for human *MECP2*, for treatment of Rett syndrome, was adopted by consensus.

2.2.19. dantrolene sodium, hemiheptahydrate - EMA/OD/0000056143

Norgine B.V.; Treatment of malignant hyperthermia

COMP Rapporteur: Michel Hoffmann

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

The intention to treat the condition with the medicinal product containing dantrolene sodium was considered justified based on literature data showing that the active substance can effectively prevent death in around 90% of treated patients.

The condition is life-threatening due to tachycardia and other arrhythmias, acidosis, muscle rigidity, and hyperkalaemia. If untreated, the condition is fatal in more than 90% of cases.

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.

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 dantrolene sodium, hemiheptahydrate will be of significant

benefit to those affected by the condition. The sponsor has provided nonclinical data that demonstrate that the proposed product is easily dissolved in smaller infusion volume, which would enable a much shorter administration time of the proposed product compared the currently authorized formulation of dantrolene, offering the potential to reduce the morbidity and mortality associated with treatment delay. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for dantrolene sodium, hemiheptahydrate, for treatment of malignant hyperthermia, was adopted by consensus.

2.2.20. - EMA/OD/0000045928

Treatment of nasopharyngeal cancer

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

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

None

2.6. Nominations

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

COMP coordinators were appointed for 26 applications.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 21 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of mucopolysaccharidosis type I

The discussion was postponed.

3.1.2. -

Treatment of glioma

The discussion was postponed.

3.1.3. -

Diagnosis of AL amyloidosis

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

3.1.4. -

Treatment of Gaucher disease

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

3.2. Finalised letters

3.2.1. -

Treatment of pancreatic cancer

The finalised letter was circulated for information.

3.2.2. -

Treatment of growth hormone deficiency

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment of transthyretin-mediated amyloidosis in patients with cardiomyopathy

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

4.1.1. Efmody (previously: Cirkrono) - hydrocortisone - EMEA/H/C/005105/0000, EU/3/05/296, EMA/OD/0000032128

Diurnal Europe B.V.; Treatment of congenital adrenal hyperplasia

COMP Rapporteurs: Elisabeth Johanne Rook; Lenka Gaidadzi

A list of issues was adopted on 18 February 2021.

An oral explanation was held on 14 April 2021.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the orphan designation from the register of orphan medicinal products, on 15 April 2021, prior to final opinion.

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

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

4.2.1. Enspryng – satralizumab - EMEA/H/C/004788, EMA/OD/014/16, EU/3/16/1680, EMA/OD/0000016001

Roche Registration GmbH; Treatment of neuromyelitis optica spectrum disorders

COMP Rapporteur: Tim Leest; Expert: Armando Magrelli

An opinion recommending not to remove Enspryng, satralizumab, EU/3/16/1680 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 April 2021 meeting.]

4.2.2. Koselugo – selumetinib - EMEA/H/C/005244/0000, EMA/OD/045/18, EU/3/18/2050, EMA/OD/0000033877

AstraZeneca AB; Treatment of neurofibromatosis type 1

COMP Rapporteurs: Bozenna Dembowska-Baginska; Elisabeth Johanne Rook

An opinion recommending not to remove Koselugo, selumetinib, EU/3/18/2050 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 April 2021 meeting.]

4.2.3. – elivaldogene autotemcel - EMEA/H/C/003690/0000, EMA/OD/009/12, EU/3/12/1003, EMA/OD/0000044429

Accelerated Assessment

bluebird bio (Netherlands) B.V; Treatment of adrenoleukodystrophy

The status of the procedure at CHMP was noted.

4.2.4. – odevixibat - EMEA/H/C/004691/0000, EMA/OD/022/12, EU/3/12/1028, EMA/OD/0000048989

Accelerated Assessment

Albireo; Treatment of progressive familial intrahepatic cholestasis

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 May meeting.

4.3. Appeal

None

4.4. On-going procedures

None

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

None

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 meetings

None

7.1.2. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 9 April 2021.

7.1.3. Election of COMP Vice-Chairperson

Postponed

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendation on eligibility to PRIME – report

Documents were tabled for information.

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

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

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

The COMP discussed and noted the updates on the progression of COMP 2021 Work Plan topics.

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2021

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2021 was 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. Inter-Committee SAG Oncology

The COMP noted that EMA scientific committee members can propose experts for appointment as core members in the Inter-committee Scientific Advisory Group for Oncology.

8.2. Data Standards Strategy survey and workshop

The COMP noted the Data Standards Strategy, its development, goals, objectives and communication plan. EMA has launched this initiative to develop a data standards strategy, with a view to addressing the HMA/EMA Big Data Task Force recommendation to engage in international initiatives related to data standardisation.

The strategy will enable the European medicines regulatory network to leverage data more effectively to deliver evidence in support of benefit-risk decision-making on the development, authorisation and use of medicines. The intention is to optimise the processing of such data by different stakeholders through improved submission formats tailored to their needs, while ensuring data security.

EMA plans to consult a wide range of stakeholders to understand their data standardisation needs related to the submission, receipt, use and re-use of scientific data at each stage of the medicinal product lifecycle. Therefore, a survey will be launched to gather input regarding the application and use of Data Standards within the EU Regulatory Network. Data collected in this survey will not be published, but aggregated survey results will be presented in the Data Standards Strategy workshop, taking place on May 18, 2021.

8.3.

9. List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 13-15 April 2021 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	
Brigitte Schwarzer-Daum	Member	Austria	No restrictions applicable to this meeting	
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	Czechia	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	
Zsofia Gyulai	Member	Hungary	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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 restrictions applicable to this meeting	
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	Slovak Republic	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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Angelo Loris Brunetta	Member	Patients' Organisation Representative	No interests declared	
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Giuseppe Capovilla	Member	Expert recommended by EMA	No interests declared	
Virginie Hivert*	Expert - via WebEx	Patients' Organisation Representative	No restrictions applicable to this meeting	
Armando Magrelli*	Expert - via WebEx	Italy	No interests declared	
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.

10. Explanatory notes

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

Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

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

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

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

Sponsor

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

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

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

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