19 January 2023
EMA/COMP/946245/2022
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 06-08 December 2022

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

Disclaimers

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

Of note, the minutes are 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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Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members and experts

The Chair opened the meeting by welcoming all participants. Due to the coronavirus (COVID-19) pandemic, 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 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 for agenda topics was identified.

Participants 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.

Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda for 6-8 December 2022 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 8-10 November 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. nanatinostat, valganciclovir - EMA/OD/0000105219

Pharma Gateway AB; Treatment of diffuse large B-cell lymphoma (DLBCL)

COMP Rapporteur: Frauke Naumann-Winter

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

- Significant benefit

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

The sponsor was asked to further elaborate on the use of products authorised for DLBCL independently from the Epstein-Barr virus (EBV) status and on the outcome of patients with EBV^+ DLBCL when treated with such products.

Additional information on patients with EBV^+DLBCL who benefitted from the targeted approach were required to support either a clinically relevant advantage or a major contribution to patient care claim (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:JOC_2016_424_R_0003&from=EN).

In the written response, the sponsor highlighted the poor outcome of EBV^+ DLBCL patients compared to EBV^- patients (as described by Castillo 2018, Bourbon 2021, Lu 2015, Sato 2014, Juul 2018, and several earlier publications). In addition, the sponsor claimed that since there are no specific therapies that have demonstrated improved outcomes in relapsed/refractory EBV^+ DLBCL (Di 2021), the international treatment guidelines recommend the same treatment modality for DLBCL regardless of EBV subtype. Before being recognized as a distinct subtype in the WHO 2020 classification, in WHO 2016 the entity was called EBV^+ DLBCL of the elderly. Furthermore, the sponsor provided updated data of the ongoing study based on a more recent data cut-off (September 2022) which included in total 9 EBV^+ DLBCL patients. The overall response rate (ORR) is 67% (6/9), including 3 patients with complete response (CR) and 3 with partial response (PR). The duration of the reported responses was 30 and 35 months for the PR and CR retrospectively.

The data provided for the proposed product are derived from a study which recruited patients who were not eligible for HSCT or CAR-T and almost half of the patients studied were treated in second line.

The COMP acknowledged that it is difficult to justify significant benefit over authorized products, especially due to the lack of knowledge /reporting on this rare subtype EBV^+ DLBCL. In the absence of knowledge of the specific position of the proposed oral fixed dose combination of a molecularly targeted treatment restricted to EBV positivity, data of durable anti-tumour effects in patients with relapsed or primary refractory disease in patients who received more than 2 lines of treatment and who are not eligible for HSCT or CAR-T are considered sufficient to justify the assumption of significant benefit at the time of initial orphan designation. Therefore, the oral explanation was cancelled.

The Committee agreed that the condition, diffuse large B-cell lymphoma, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing nanatinostat, valganciclovir was considered justified based on preliminary clinical data which showed responses in patients with relapsed/refractory Epstein-Barr virus positive diffuse large B-cell lymphoma.

The condition is chronically debilitating due to constitutional symptoms, local symptoms of lymphadenopathy, end-organ damage from disease involvement, and bone marrow failure that may lead to infections, anaemia, and thrombocytopenia and life-threatening in patients not responding to treatment.

The condition was estimated to be affecting approximately 4.3 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 nanatinostat, valganciclovir will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that pre-treated patients with relapsed/refractory Epstein-Barr virus positive diffuse large B-cell lymphoma, who have limited treatment options, responded to treatment with the proposed product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for nanatinostat, valganciclovir, for treatment of diffuse large B-cell lymphoma, was adopted by consensus.

2.1.2. - EMA/OD/0000103787

Treatment of primary sclerosing cholangitis (PSC)

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 primary sclerosing cholangitis the sponsor was asked to further elaborate on:

  - the interpretation of the results obtained in the non-clinical in vivo experiments showing the complementary action of the proposed product with ursodeoxycholic acid (UDCA);
  - the results obtained in the clinical study in previously treated UDCA patients. The sponsor was asked to further discuss the added benefit of this product when compared to UDCA alone.

- Significant benefit

The sponsor was asked to further elaborate the results of any clinical data to support the significant benefit assumption in the context of the current therapeutic management of patients. In particular, evidence from the particular study that shows an improvement in clinical benefit in patients with prior UDCA treatment should be further elaborated. The sponsor was asked to present a more thorough analysis on the beneficial effect of the proposed product in patients with prior UDCA treatment, specifically providing a descriptive (time/exposure) analysis of the clinical course of biomarker evolution during UDCA treatment and comparison with the treatment of proposed product. The sponsor was also asked to further discuss the added benefit in this product when compared to UDCA alone.

In the written response, and during an oral explanation before the Committee on 6 December 2022, the COMP considered that the addition of the proposed product into UDCA can be accepted. Also the nature of the molecular product was discussed.

The COMP therefore was not of the opinion that this was a single new chemical entity.

Regarding significant benefit, the sponsor failed to demonstrate a clear effect of the proposed product in patients with prior UDCA treatment. The sponsor did not present additional data compared to the previous one that convinced the COMP that patients who switched from UDCA to the proposed product performed better in the relevant biomarkers. For gamma-glutamyl transferase (GGT) and aspartate aminotransferase/alanine aminotransferase (AST/ALT) the difference was small and the relevance in PSC is not as important as for example alkaline phosphatase (ALP). Of the four subjects with prior UDCA usage (the only data relevant for significant benefit analysis) included in the study the earliest start of UDCA was approximately1 year prior to study initiation. This was the one clear case that provided the additional effect to UDCA because it lasted more than 6 months which would be enough for a stable effect, however, similar data for the other 3 patients regarding the start of UDCA prior to the switch was not as clear cut and the additional benefit difficult to establish. For example, one patient stopped UDCA 1 month prior to the proposed product which showed a worsening of biomarkers and thus could not be excluded.

The COMP noted a publication (1st November 2022) with more complete data from the same trial. Some of the main characteristics of the trial are present and a graph that showed a clear absence of effect of ALP levels, the most important biomarker in PSC (Kowdley et al 2022). The publication reported the maintenance of ALP values in patients taking UDCA prior to the proposed product. 22 patients were on prior UDCA and stopped. Of these 8 were on placebo, 6 on 500 mg/kg and 8 on 1000 mg/kg of the proposed product. 6/22 started 500mg/kg and 8/22 on 1000 mg/kg for the intention-to-treat group. Of these only 1/8 patients stopped taking 1 month earlier, all others did so a 1 day before switching.

The COMP considered that the sponsor's considerations on significant benefit were insufficient to support the additional benefit of using the proposed product in patients who had had prior use of UDCA and where there might be a need due to lack of response.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 7 December 2022, prior to final opinion.

2.1.3. - EMA/OD/0000103269

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 was asked to clarify the following issues:

- Medical plausibility

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

  - the clinical relevance of the observed tumour growth inhibition compared to no treatment. The sponsor was requested to elaborate on the indirect comparison of the proposed product versus chemotherapy of independently performed in vivo experiments (different cell lines, different models) and the extent of tumour growth inhibition observed in active control in the published model.

- Number of people affected

Applying the PTCL/NHL proportion to partial prevalence instead of incidence is not correct, as NHL (non-Hodgkin's lymphoma) is a very heterogenous umbrella term and covers subtypes which vary greatly in their prognosis and thus, disease duration.

The sponsor was asked to re-estimate prevalence taking into considerations the recommendation given in the guideline "Points to Consider on the Estimation and Reporting of a Prevalence of a Condition for Orphan Designation".

- Significant benefit

The arguments on significant benefit were based on the potential improved efficacy of the proposed product versus the authorised treatments in the applied condition.

The sponsor was asked to further justify significant benefit of the proposed product over authorised standard of care in view that neither in vitro data alone nor the indirect comparison of independently performed experiments support the assumption of significant benefit over broadly authorised systemic chemotherapeutic agents.

The sponsor was asked to elaborate on the expected use of the proposed product within the treatment algorithm of PTCL and to provide more information on the planned clinical development.

In the written response, and during an oral explanation before the Committee on 6 December 2022, the sponsor replied on the clinical relevance of the observed tumour growth inhibition compared to no treatment by arguing that theoretically the reduction on the time to progression could be translated clinically into improvement of progression-free survival. Furthermore, regarding the indirect comparison of the proposed product versus chemotherapy, the sponsor highlighted the publication by Magni et al., which reports a statistically significant tumour growth inhibition of 77% in cyclophosphamide, doxorubicin, etoposide, vincristine and prednisone (CHOEP)-treated subjects when compared to untreated subjects in HD-MAR-2, and in OCI-Ly12 models (HD-MAR-2 is comparable to sponsor's model, even though different cell line). However, the sponsor did not elaborate on the limitations of the indirect comparisons in view of the different models and different cell lines used.

Regarding the calculation of the prevalence the new proposed figure of <1/10,000 is in line with recent designations, however, the sponsor again did not perform a calculation based on applying a PTCL/NHL ratio to reported NHL incidence but by using PTCL incidence, partial prevalence and relative survival (national registries in FR, BE, NL, UK, IE).

Finally, for the justification of the significant benefit, the sponsor argued that in a relapsed/ refractory setting, given the biological heterogeneity within the various PTCL subtypes a high unmet medical need still exists. According to the sponsor, the proposed product is expected to be first used as monotherapy in PTCL not otherwise specified (PTCL NOS), angioimmunoblastic T-cell lymphoma (AITL), enteropathy-associated T-cell lymphoma (EATL) patients who have relapsed or are refractory after at least one line of chemotherapy. Finally, the sponsor's considerations on the significant benefit over broadly authorised chemotherapy remain theoretical and are not supported by further direct or indirect comparisons.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 6 December 2022, prior to final opinion.

2.1.4. - EMA/OD/0000089519

Treatment of soft tissue sarcoma (STS)

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 21 November 2022, prior to responding to the list of issues.

2.1.5. - EMA/OD/0000104107

Treatment of glioma

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

- 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 the assumption of significant benefit over authorised medicinal products for the proposed orphan condition. The sponsor was requested to detail the clinical protocol and the treatment regimens.

In the written response, and during an oral explanation before the Committee on 6 December 2022, the sponsor provided additional information regarding the clinical protocol. Clinical data stems from a Phase I dose escalation study to determine safety, tolerability and maximal tolerated dose of the proposed product in combination to standard of care treatment for the applied orphan condition.

The sponsor argued that a key medical challenge for the intended patient population is treatment-related lymphopenia (TRL), which would be associated with reduced survival. It is then indicated that treatments that can address such drug adverse reaction by increasing lymphocyte counts may provide an opportunity to alleviate this negative and improve patient survival. To build on such argument, the sponsor compared historical data to the Phase I study. While this information was discussed in detail, limitations were acknowledged which hamper the interpretability of the results such as the small number of patients and the dose escalation nature of the study, with patients receiving lower doses than the recommended phase 2 dose.

The COMP agreed with the sponsor that it is difficult to conclude based on the outcome from the limited data available and considered the totality of evidence provided to be not sufficient to fulfil the criterion for an initial orphan designation in the applied condition.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 7 December 2022, prior to final opinion.

2.1.6. - EMA/OD/0000096050

Treatment of Duchenne muscular dystrophy

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 2 December 2022, prior to responding to the list of issues.

2.1.7. - EMA/OD/0000099774

Prevention of tuberculosis

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 COMP noted that the sponsor is targeting a patient population who are already infected with tuberculosis bacillus. The data submitted is for post-exposure prophylaxis, which is considered by the COMP as secondary prevention and therefore a treatment. For this reason, the proposed orphan condition is not "prevention of tuberculosis" but "treatment of tuberculosis". As the sponsor holds a marketing authorisation for the treatment of tuberculosis for this product, the current submission is not considered valid. (ref. Article 5.1 of Regulation (EC) No 141/2000).

In the written response, and during an oral explanation before the Committee on 7 December 2022, the sponsor highlighted the case that their product is a different medicinal product as it is an intramuscular (IM) as well as long-acting formulation.

The COMP accepted that this was a different medicinal product and therefore accepted that the product qualified for an orphan designation.

The sponsor then proceeded to claim that their medicinal product was for the prevention of tuberculosis disease. They indicated that they were not targeting patients who had active tuberculosis infection but those who had latent tuberculosis disease, claiming that this is different to tuberculosis infection. The sponsor was aiming to prevent the switch from latent to active tuberculosis.

The sponsor agreed that both tuberculosis infection and disease are part of the spectrum of terms used for tuberculosis. The sponsor had accepted in their written response that they were targeting secondary prevention of tuberculosis and as they could not establish that tuberculosis disease was a different condition to tuberculosis, the COMP concluded that as this was treatment of the bacillus, the correct condition following the orphan regulation was concluded to be treatment of tuberculosis. The sponsor accepted this conclusion. The prevalence will include the latent forms and the active forms, resulting in a figure of 3.7 in 10,000. This was accepted by the COMP.

The next part of the discussion was to establish if significant benefit could be ascertained with the data submitted. Sirturo (oral product) has the following indication: Sirturo is indicated for use as part of an appropriate combination regimen for pulmonary multidrug-resistant tuberculosis (MDR-TB) in adult and paediatric patients (5 years to less than 18 years of age and weighing at least 15 kg) when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

The target patient population for this application was defined by the sponsor as:

According to Standards 18 and 19 in the ESTC, the following groups are considered at high risk of having been infected and/or developing (severe) active TB disease if infected and should therefore be tested for latent TB infection (LTBI) [ECDC, 2018]:

- contacts of an infectious TB patient, which include household and family members as well as contacts outside the household, i.e., individuals with intensive or

prolonged contact in congregate settings like prisons, homeless or migrant shelters, and indoor spaces like schools or offices;

- persons with HIV infection;
- patients initiating anti-tumour necrosis factor (TNF) treatment;
- patients receiving dialysis;
- patients preparing for organ or haematological transplantation;
- patients with silicosis.

As this patient population was considered different to that defined by the current indication of Sirturo, the significant benefit over Sirturo would be that it treated a different patient population. The COMP asked what data the sponsor had to establish if there was a clinically relevant advantage to using their product over the recommended approved standard of care in Europe which consists of isoniazid and ethambutol or isoniazid and rifampicin used in combination. The sponsor could only provide very preliminary comparative pharmacokinetic data in a non-clinical model of the condition showing similarity in effect in reducing tuberculous colony forming units. This data showed that the same effect could be achieved with the IM formulation at a lower dose to that needed with the oral dose. The assumption is that this would offer better safety for the IM formulation as compared to the oral formulations. This might be the case but with only PK data and no functional or clinical data to support this claim, it was not accepted by the COMP. The sponsor also argued a major contribution to patient care based on the better compliance with the IM formulation versus the oral formulations. The COMP acknowledged that there are problems with adherence to oral treatment but noted that no data was submitted and thus could not recommend granting the designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 8 December 2022, prior to final opinion.

2.1.8. - EMA/OD/0000106875

Treatment of narcolepsy

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 18 November 2022, prior to responding to the list of issues.

2.1.9. octreotide acetate - EMA/OD/0000095228

Amryt Pharmaceuticals Designated Activity Company; Treatment of carcinoid syndrome (CS)

COMP Rapporteur: Bozenna Dembowska-Baginska

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 assumptions of potential efficacy, safety and a major contribution to patient care of a new route of administration. However, no data was provided to support the assumptions.

Without clinical experience, the sponsor was asked to justify the relevance of clinical data from patients with a different medical condition in the applied condition.

Furthermore, the sponsor was invited to provide significant benefit justifications versus injectable somatostatin analogues, currently authorised for patients with carcinoid syndrome.

In written responses the sponsor claimed the significant benefit based on improved safety. Based on a recent study of patient satisfaction with long-acting somatostatin receptor ligands (SRLs) in 202 neuroendocrine tumour (NET) patients, including 181 patients with CS, showed that over one-third (36%) of patients reported injection site pain or discomfort of moderate severity or worse within 5 days of their most recent injection and 30% reported pain of the same severity 14 and 28 days after injection [Darden 2021]. Of note, 68.8% (n = 139) of patients said that their monthly injections differed based on the nursing staff/person administering the injection. Among 86 patients (43%) who reported experiencing any amount of anxiety prior to their last injection, the most commonly reported reasons included injection site reactions (e.g., pain, swelling, bruising, soreness).

The sponsor also claimed the significant benefit based on the major contribution to patient care referring to the data available for acromegaly patients. Since the route and frequency of administration of injectable somatostatin receptor ligands (iSRLs) is the same in both acromegaly and CS the sponsor argued similar benefit would be expected in CS patients. The need for monthly clinic visits to receive SRL injections must be considered a major burden for patients. At an emotional level anxiety, frustration, and loss of independence due to assistance required in receiving injections compound the physical impact. Work time is lost in scheduling and traveling for injections, and from adverse effects associated with injections. These concerns are independent of the nature of the underlying condition.

The COMP considered that the sponsor provided literature data to support that there are serious and documented difficulties with the formulation or route of administration of the currently authorized octreotide products that are administered via intramuscular or subcutaneous route, e.g. pain and local reactions at the injection site. In addition, there is the need for the authorized products to be administered by healthcare professionals, requiring monthly visits to the hospital. The COMP agreed that the significant benefit can be considered justified at this stage. The COMP, on the other hand, strongly recommended that the sponsor will focus on an appropriate study design and seek protocol assistance in order to prove these assumptions. The COMP considered that the responses were satisfactory, and the oral explanation was cancelled.

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

The intention to treat the condition with the medicinal product containing octreotide acetate was considered justified based on the reduction of flushing and diarrhoea which has been observed with the subcutaneous form of administration and pharmacokinetic data showing that the exposure achieved with the oral formulation is equivalent to the exposure achieved with the parenteral authorised formulations.

The condition is chronically debilitating due to flushing and diarrhoea, and life-threatening due to heart failure and bronchoconstriction.

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 octreotide acetate will be of significant benefit to those affected by the condition. The sponsor provided data to support that there are serious and documented difficulties with the formulation or route of administration of the currently authorized octreotide products that are administered via intramuscular or subcutaneous route, such as pain and local reactions at the injection site. The Committee considered that this constitutes a clinically relevant advantage. In addition, the Committee considered that the possibility of having an oral formulation of octreotide in alternative to the available parenteral formulations could reduce hospital visits which constitutes a major contribution to patient care for the patients affected by the condition.

A positive opinion for octreotide acetate, for treatment of carcinoid syndrome, was adopted by consensus.

2.1.10. 3-(1-(2',3'-dimethoxy-[1,1'-biphenyl]-4-yl)-1H-1,2,3-triazol-4-yl)benzoic acid - EMA/OD/0000097397

Chemicare S.r.l.; Treatment of Duchenne muscular dystrophy (DMD)

COMP Rapporteur: Armando Magrelli

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 the treatment of Duchenne muscular dystrophy the sponsor was asked to further elaborate on the interpretation of the results obtained in the experiments and justify the relevance of these results to functional outcomes.

In the written response, and during an oral explanation before the Committee on 7 December 2022, the sponsor elaborated on the evaluation on serum creatine kinase (CK) levels, the performance on grip test and the apoptosis and necrosis in muscle fibres using Evans Blue dye at specific time-points. The sponsor argued that these pharmacological parameters, are representative of muscle damage in the pathophysiological pathway of DMD, but they are also parameters evaluated in humans both for the diagnosis, and for the effectiveness of new drugs. The sponsor also explained that the smaller difference observed in the muscle strength by the end of Day 27 is related to the age of the mice since the older the mice get the more difficult it becomes to identify changes in the weight and the performance. The COMP considered that the improvement of the maximal muscle strength supported by the effect on serum CK levels and on the reduction of the % of Evans Blue dye positive cells can justify the medical plausibility.

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

The intention to treat the condition with the medicinal product containing 3-(1-(2',3'-dimethoxy-[1,1'-biphenyl]-4-yl)-1H-1,2,3-triazol-4-yl)benzoic acid was considered justified based on non-clinical data in a model of the condition which showed an improvement of the maximal muscle strength.

The condition is life-threatening and chronically debilitating due to progressive muscle weakness eventually affecting all voluntary muscles; this is followed by dilated cardiomyopathy and cardiac output decrease, leading to terminal respiratory or cardiac failure.

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.

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 3-(1-(2',3'-dimethoxy-[1,1'-biphenyl]-4-yl)-1H-1,2,3-triazol-4-yl)benzoic acid will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data suggesting effects in a broader patient population which is not covered by the currently authorised product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 3-(1-(2',3'-dimethoxy-[1,1'-biphenyl]-4-yl)-1H-1,2,3-triazol-4-yl)benzoic acid, for treatment of Duchenne muscular dystrophy, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000070986

Treatment of megacystis microcolon intestinal hypoperistalsis 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 January 2023 meeting.

2.2.2. vorasidenib hemicitrate hemihydrate - EMA/OD/0000086832

Les Laboratoires Servier; Treatment of glioma

COMP Rapporteur: Dinko Vitezic

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 vorasidenib hemicitrate hemihydrate was considered justified based on non-clinical studies in a valid model of the condition showing reduction in tumour growth as well as preliminary clinical data, in patients with glioma responding to treatment.

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

The condition was estimated to be affecting approximately 2.6 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 vorasidenib hemicitrate hemihydrate will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that showed responses in relapsed patients previously treated with temozolomide and/or radiotherapy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for vorasidenib hemicitrate hemihydrate, for treatment of glioma, was adopted by consensus.

2.2.3. N1,N14-diethyl-3S,12S-dihydroxyhomospermine tetrahydrochloride - EMA/OD/0000100767

PPD Bulgaria EOOD; Treatment of pancreatic cancer

COMP Rapporteur: Brigitte Schwarzer-Daum

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

The intention to treat the condition with the medicinal product containing N1,N14-diethyl-3S,12S-dihydroxyhomospermine tetrahydrochloride was considered justified based on inhibition of tumour growth and improvement in survival in non-clinical in vivo models of the condition.

The condition is chronically debilitating due to pain in the upper abdomen, loss of appetite, nausea, vomiting, weight loss, jaundice, fatigue, weakness and depression and life-threatening with a markedly reduced life expectancy.

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 N1,N14-diethyl-3S,12S-dihydroxyhomospermine tetrahydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided data in non-clinical in vivo models of the condition supporting improved effects in inhibition of tumour growth in combination with available treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for N1,N14-diethyl-3S,12S-dihydroxyhomospermine tetrahydrochloride, for treatment of pancreatic cancer, was adopted by consensus.

2.2.4. - EMA/OD/0000102985

Treatment of hereditary cerebral amyloid angiopathies

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 January 2023 meeting.

2.2.5. autologous hematopoietic cells genetically modified with a lentiviral vector containing the human RAG2 gene - EMA/OD/0000104665

Leiden University Medical Center; Treatment of recombination activating gene 2 deficient – severe combined immunodeficiency (RAG2-SCID)

COMP Rapporteur: Elisabeth Johanne Rook

The Committee agreed that the condition, recombination-activating gene 2 deficient 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 hematopoietic cells genetically modified with a lentiviral vector containing the human *RAG2 gene* was considered justified based on non-clinical data in a valid model of the condition demonstrating restoration of B- and T-cell formation, leading to an adequate adaptative immune response upon challenge.

The condition is chronically debilitating and life-threatening due to serious infections, chronic diarrhoea, interstitial lung disease, and failure to thrive.

The condition was estimated to be affecting less than 0.03 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 autologous hematopoietic cells genetically modified with a lentiviral vector containing the human *RAG2 gene*, for treatment of recombination-activating gene 2 deficient severe combined immunodeficiency, was adopted by consensus.

2.2.6. - EMA/OD/0000104730

Treatment of congenital alpha-1 antitrypsin deficiency

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 January 2023 meeting.

2.2.7. - EMA/OD/0000105270

Diagnosis of glioma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the January 2023 meeting.

2.2.8. - EMA/OD/0000105836

Treatment of pancreatic cancer

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 January 2023 meeting.

2.2.9. - EMA/OD/0000108995

Treatment of autosomal dominant polycystic kidney 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 January 2023 meeting.

2.2.10. retifanlimab - EMA/OD/0000110129

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

COMP Rapporteurs: Jana Mazelova, Bozenna Dembowska-Baginska

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

The intention to treat the condition with the medicinal product containing retifanlimab was considered justified based on preliminary clinical data showing responses in patients with Merkel cell carcinoma.

The condition is chronically debilitating due to aggressive skin lesions and neuroendocrine features and life-threatening with limited life expectancy in patients with advanced disease.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing retifanlimab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary data indicating that the proposed product has higher responses compared with the authorised treatment based on indirect comparisons. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for retifanlimab, for treatment of Merkel cell carcinoma, was adopted by consensus.

2.2.11. efzofitimod - EMA/OD/0000110207

FGK Representative Service GmbH; Treatment of sarcoidosis

COMP Rapporteur: Irena Rogovska

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

The intention to treat the condition with the medicinal product containing efzofitimod was considered justified based on preliminary clinical data showing an improvement in Forced Vital Capacity percentage, reduction in steroid use (or steroid sparing effect) and improvement in pulmonary sarcoidosis-symptom specific and non-specific scores.

The condition is life-threatening and chronically debilitating due to progressive tissue damage from active inflammation. Common organs affected are the lungs, skin, eyes, cardiovascular and peripheral nervous system. Involvement of these diverse organ systems can lead to marked reduction in functional capacity and quality of life. Mortality is increased due mainly to pulmonary and cardiovascular failure.

The condition was estimated to be affecting approximately 3.8 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 efzofitimod will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a dose dependent effect in the reduction of corticosteroid use in patients with pulmonary sarcoidosis. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for efzofitimod, for treatment of sarcoidosis, was adopted by consensus.

2.2.12. opelconazole - EMA/OD/0000111633

Tmc Pharma (EU) Limited; Treatment of invasive aspergillosis

COMP Rapporteur: Zsofia Gyulai

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

The intention to treat the condition with the medicinal product containing opelconazole was considered justified based on non-clinical studies in models of the condition showing clearance of *Aspergillus fumigatus* infection and improved survival, as well as preliminary clinical data in patients with invasive aspergillosis responding to treatment.

The condition is life-threatening and chronically debilitating due to progressive dyspnoea, chest pain, haemoptysis, and dissemination of the infection to several organs including the brain. Mortality rates are up to 70–95% in recipients of bone marrow transplant.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing opelconazole will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data in patients who are unable to receive standard of care antifungal therapy due to lack of clinical response or due to safety reasons who responded to treatment via inhalation with the proposed product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for opelconazole, for treatment of invasive aspergillosis, was adopted by consensus.

2.2.13. adeno-associated viral vector serotype 2 containing the human *SLC6A3* gene - EMA/OD/0000111754

FGK Representative Service GmbH; Treatment of dopamine transporter deficiency syndrome

COMP Rapporteur: Robert Nistico

The Committee agreed that the condition, dopamine transporter deficiency 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 viral vector serotype 2 containing the human *SLC6A3* gene was considered justified based on non-clinical in vivo data in a valid disease model demonstrating improved survival and motor function.

The condition is chronically debilitating due to dystonia, parkinsonism, dyskinesia and difficulty with swallowing and life-threatening due to respiratory complications often leading to premature death.

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

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

A positive opinion for adeno-associated viral vector serotype 2 containing the human *SLC6A3* gene, for treatment of dopamine transporter deficiency syndrome, was adopted by consensus.

2.2.14. - EMA/OD/0000111992

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 January 2023 meeting.

2.2.15. autologous CD34+ cells transduced with a lentiviral vector encoding the human *NCF1* gene - EMA/OD/0000112174

3R Pharma Consulting GmbH; Treatment of chronic granulomatous disease type I

COMP Rapporteur: Zsofia Gyulai

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of chronic granulomatous disease.

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

The intention to treat the condition with the medicinal product containing autologous CD34+ cells transduced with a lentiviral vector encoding the human *NCF1* gene was considered justified based on non-clinical data in an in vivo model of chronic granulomatous disease type 1, where treatment showed restoration of superoxide production in myeloid cells.

The condition is life-threatening due to recurrent infections and chronically debilitating in particular due to infectious, inflammatory and granulomatous complications of the lungs, skin, lymph nodes, gastro-intestinal tract and liver.

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

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

A positive opinion for autologous CD34+ cells transduced with a lentiviral vector encoding the human *NCF1* gene, for treatment of chronic granulomatous disease, was adopted by consensus.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

None

2.6. Nominations

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

COMP rapporteurs were appointed for 22 applications.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 15 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of respiratory distress syndrome

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

3.1.2. -

Treatment of myelodysplastic syndrome (MDS)

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

3.1.3. -

Treatment of paroxysmal nocturnal haemoglobinuria

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

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

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

None

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

4.2.1. Fintepla – fenfluramine hydrochloride - EMEA/H/C/003933/II/0012, EU/3/17/1836, EMA/OD/0000075867

Zogenix ROI Limited; Treatment of Lennox-Gastaut syndrome

COMP Rapporteur: Elisabeth Johanne Rook; COMP Co-Rapporteur: Joao Rocha; CHMP Rapporteur: Thalia Marie Estrup Blicher; CHMP Co-Rapporteur: Johann Lodewijk Hillege

An opinion recommending not to remove fintepla, fenfluramine hydrochloride, EU/3/17/1836 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 December 2022 meeting.]

4.2.2. Hemgenix – etranacogene dezaparvovec - EMEA/H/C/004827, EU/3/18/1999, EMA/OD/0000087180

CLS Behring GmbH; Treatment of haemophilia B

COMP Rapporteur: Karri Penttila; COMP Co-Rapporteur: Enrico Costa

An opinion recommending not to remove hemgenix, etranacogene dezaparvovec, EU/3/18/1999 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 December 2022 meeting.]

4.2.3. – cipaglucosidase alfa - EMEA/H/C/005703, EU/3/18/2000, EMA/OD/0000098435

Amicus Therapeutics Europe Limited; Treatment of glycogen storage disease type II (Pompe'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 January 2023 meeting.

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. Reblozyl – luspatercept - EMEA/H/C/004444/II/0009, EU/3/14/1300, EMA/OD/0000072540

Bristol-Myers Squibb Pharma EEIG; Treatment of beta-thalassaemia intermedia and major

CHMP Rapporteur: Daniela Philadelphy; CHMP Co-Rapporteur: Ewa Balkowiec Iskra

Action: For discussion/adoption

The status of the procedure at CHMP was noted.

5.3. Appeal

None

5.4. On-going procedures

None

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

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the COMP

7.1.1. COMP membership

The Chair thanked Dimitrios Filippou for his contribution as a member for Greece.

7.1.2. Vote by proxy

Eva Malikova gave a proxy to Michel Hoffmann to vote on behalf of Eva Malikova during part of the meeting.

Frauke Naumann-Winter gave a proxy to Elisabeth Johanne Rook to vote on behalf of Frauke Naumann-Winter during part of the meeting.

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

7.1.3. Strategic Review & Learning meetings

None

7.1.4. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 1 December 2022.

7.1.5. Principal Decisions Database

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

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendation on eligibility to PRIME – report

Documents were tabled for information

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

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

The COMP noted the feedback from PCWP/HCPWP annual meeting with all eligible organisations.

7.3.2. Upcoming ITF meetings

The COMP noted the upcoming ITF meetings.

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

COMP noted the discussion on the draft work plan

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2022

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2022 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. Preparation of EMA Regulatory & Scientific Conference on RNA-based medicines

COMP noted the presentation on Regulatory and scientific virtual conference on RNA-based medicines to be held on 2nd February 2023.

8.2. Review of orphan designation criteria and OMAR preparation

COMP noted the guidance document, which outlines the interaction between the EMA Coordinator and the Rapp/Co-Rapp at the different stages of the procedure and defines timelines for this interaction.

8.3. EMA Business Pipeline activity and Horizon scanning

The COMP noted the documents.

8.4. Feedback from the ENCePP Plenary

The COMP noted the feedback from ENCePP Plenary.

8.5. ICH M11 Public Consultation

The purpose of the new harmonised Guideline on Clinical electronic Structured Harmonised Protocol (CeSHarP) is to introduce the clinical protocol template and the technical specification to ensure that protocols are prepared in a consistent fashion and provided in a harmonised data exchange format acceptable to the regulatory authorities.

The ICH M11 Clinical Electronic Structured Harmonised Protocol Template provides comprehensive clinical protocol organization with standardized content with both required and optional components.

The Technical Specification presents the conformance, cardinality, and other technical attributes that enable the interoperable electronic exchange of protocol content with a view to develop an open, non-proprietary standard to enable electronic exchange of clinical protocol information.

Further information can be found on the ICH M11 page, including the three aforementioned documents available for download. The public consultation was initiated on 26th October 2022 and is open until 26 February 2023.

Furthermore, members were invited to review the draft M11 template (general review, but also specific with respect to other guidelines such as ICH E9(R1)) during the public consultation period and to submit comments before 26 February 2023: https://www.ema.europa.eu/en/ich-m11-guideline-clinical-study-protocol-template-technical-specifications-scientific-guideline

8.6. Methodology Working Party

The COMP noted the introduction of MWP to the Committees.

9. List of participants

including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 6-8 December 2022 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	Vice-Chair	Expert recommended by EMA	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	No restrictions applicable to this meeting	
Tim Leest	Member	Belgium	No interests declared	
Lyubina Racheva Todorova	Member	Bulgaria	No interests declared	
Dinko Vitezic	Member	Croatia	No interests declared	
Elli Loizidou	Member	Cyprus	No interests declared	
Jana Mazelova	Member	Czechia	No interests declared	
Elisabeth Penninga	Member	Denmark	No interests declared	
Vallo Tillmann	Member	Estonia	No interests declared	
Karri Penttilä	Member	Finland	No interests declared	
Cecile Dop	Member	France	No interests declared	
Frauke Naumann-Winter	Member	Germany	No interests declared	
Zsofia Gyulai	Member	Hungary	No interests declared	
Enrico Costa	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No restrictions applicable to this meeting	
Michel Hoffmann	Member	Luxembourg	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Robert Nistico	Member	Malta	No restrictions applicable to this meeting	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland	No restrictions applicable to this meeting	
Joao Rocha	Member	Portugal	No restrictions applicable to this meeting	
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	Slovak Republic	No interests declared	
Gloria Maria Palomo Carrasco	Member	Spain	No interests declared	
Darius Matusevicius	Member	Sweden	No restrictions applicable to this meeting	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Julian Isla	Member	Patients' Organisation Representative	No interests declared	
Ines Alves	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Maria Cavaller Bellaubi	Expert - via Webex *	Patients' Organisation Representative	No restrictions applicable to this meeting	
Kristin Karlsson	MWP Vice-Chair - via WebEx*	Sweden	No restrictions applicable to this meeting	
Meeting run with support from relevant EMA staff				

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

10. Explanatory notes

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

Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

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

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

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

Sponsor

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

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

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

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