7 October 2020
EMA/COMP/486363/2020
Human Medicines Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 08-10 September 2020

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

08 September 2020, 08:30-19:30, remote virtual meeting

09 September 2020, 08:30-19:30, remote virtual meeting

10 September 2020, 08:30-18:20, remote virtual meeting

Disclaimers

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

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

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

Note on access to documents

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

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1. Introduction

1.1. Welcome and declarations of interest of members and experts

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the COMP plenary session to be held 8-10 September 2020.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the pre-meeting list of participants and restrictions.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. The following additional interests and/or restrictions were declared at the start or during the meeting:

Brigitte Schwarzer-Daum has voluntarily refrained from any participation in the EMA/OD/0000030250 procedure.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

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

1.2. Adoption of agenda

The agenda for 8-10 September 2020 was adopted with the following topic under A.O.B:

- Letter from sponsor.

1.3. Adoption of the minutes

The minutes for 14-16 July 2020 were adopted with no amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. decitabine, tetrahydrouridine - EMA/OD/0000034330

Novo Nordisk A/S; Treatment of sickle cell disease

COMP Rapporteur: Angelo Loris Brunetta

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

- Number of people affected

The sponsor provided an older estimate of the prevalence in Europe of the condition. The sponsor was requested to provide an updated estimate and justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor was requested to describe and justify the methodology used for the prevalence calculation and re-estimate the prevalence for the European Union.

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

In the written response, the sponsor provided a revised prevalence calculation in their written procedure which highlighted the difficulties in obtaining data on the current migration from Africa to Europe. In addition, the COMP had a general discussion on the difficulties in establishing the prevalence in this condition noting the wide variability in previous prevalence submissions. The COMP concluded that in general a prevalence of less than 2 in 10,000 should be accepted in this case as it will help reflect the variability noted and that the submission should be amended to reflect this in the grounds.

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

The intention to treat the condition with the medicinal product containing decitabine, tetrahydrouridine was considered justified based on preliminary clinical data which showed an increase in the serum levels of foetal haemoglobin.

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

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing decitabine, tetrahydrouridine will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate an increase in foetal haemoglobin in patients who were resistant to hydroxyurea. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for decitabine, tetrahydrouridine, for treatment of sickle cell disease, was adopted by consensus.

2.1.2. autologous CD34+ cells transduced with a lentiviral vector encoding galactosidase alpha - EMA/OD/0000035407

Clinical Technology Centre (Ireland) Limited; Treatment of Fabry Disease

COMP Rapporteur: Geraldine O'Dea

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

- Number of people affected

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

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

In the written response, the sponsor submitted a revised prevalence estimate which included both incidence and duration proposing a final calculation of less than 2 in 10,000. The COMP accepted this revised prevalence estimate and recommended granting the Orphan Designation.

The Committee agreed that the condition, Fabry 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 galactosidase alpha was considered justified based on preliminary clinical data showing normalisation and sustained levels of alpha galactosidase.

The condition is chronically debilitating due to recurrent episodes of severe pain that do not respond to standard analgesics, and life-threatening due to renal failure, cardiovascular and cerebrovascular complications.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous CD34+ cells transduced with a lentiviral vector encoding galactosidase alpha could be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that enzyme replacement therapy can be reduced or stopped following use of the sponsor's product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous CD34+ cells transduced with a lentiviral vector encoding galactosidase alpha, for treatment of Fabry disease, was adopted by consensus.

2.1.3. - EMA/OD/0000035212

Treatment of Graft versus Host Disease (GvHD)

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

- Medical plausibility

The sponsor was invited to elaborate on the settings of the non-clinical studies, in particular with regard to whether the settings reflect prevention or treatment.

- 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 the available clinical study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

In the written response, and during an oral explanation before the Committee on 8 September 2020, the sponsor further discussed the raised issues.

With regards to the medical plausibility, the sponsor explained in further details the particulars of the model used and the assessments performed. In the model used, it is reported that there is significant GvHD-associated loss of intestinal stem cells as early as 3 days post bone marrow transplant, and substantial donor T-cell infiltration and gastrointestinal GvHD histology by day 7. The COMP considered that the medical plausibility would be acceptable for designation.

As regards the significant benefit issue, the sponsor performed an indirect comparison of the available clinical data versus the results of a study of treatment a GvHD with corticosteroids alone as well as studies with mycophenolate mofetil and sirolimus.

Overall, the indirect nature of comparisons, the older data used, the paucity of data and overlapping results, made it difficult to draw any comparative assumption. The COMP considered therefore that the significant benefit was not justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 10 September 2020, prior to final opinion.

2.1.4. - EMA/OD/0000031078

Treatment of soft tissue sarcomas

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

- Number of people affected

The sponsor presented the calculation of prevalence based on RARECARE database. The methodology and inclusion of other sources of prevalence were however not clearly presented.

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

The sponsor was requested to justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor was requested to describe and justify the methodology used for the prevalence calculation and provide an updated calculation based on the most up to date and comprehensive sources found.

- Significant benefit

The sponsor discussed assumptions of significant benefit over doxorubicin and ifosfamide in non-clinical models by indirectly comparing published studies to the results of the sponsor with the proposed product. Based on clinical data, however, where at best stable disease was observed, it was difficult to understand the benefit over these products. Moreover, a thorough discussion of benefit over the later line treatments such as pazopanib or trabectedin was needed.

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

In the written response, and during an oral explanation before the Committee on 8 September 2020, the sponsor provided a renewed calculation of soft tissue sarcoma in the EU. The sponsor did not discuss the inclusion details of this calculation but the methodology and sources were accepted by the COMP. However, based on the sponsor's calculation, the condition 'soft tissue sarcoma' appeared to exceed 5 in 10,000 cases in the EU. This could be potentially explained by the inclusion of gastrointestinal stromal tumours, which were previously excluded by the COMP as a separate orphan condition. In consequence, the sponsor proposed a new orphan condition, treatment of synovial sarcoma, as a condition that meets the prevalence criterion. The COMP rejected this proposal, which was not sufficiently justified in the sponsor's position.

In addition, the sponsor did not provide sufficient data with the proposed product, which would indicate efficacy greater than the one achieved with the currently authorised products for treatment of soft tissue sarcoma. The data presented by the sponsor with the use of the proposed product was considered very old and the COMP believed more data would be required to substantiate the assumption of significant benefit over the standard of care.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 11 September 2020, prior to final opinion.

2.1.5. (S)-1-(5-((2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)sulfonyl)-3,4,5,6-tetrahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-3-hydroxy-2-phenylpropan-1-one - EMA/OD/0000033107

Clinipace GmbH; Treatment of sickle cell disease

COMP Rapporteur: Angelo Loris Brunetta

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 sickle cell disease (SCD) the sponsor should further elaborate on:

- the methodology used in the non-clinical studies as well as the results from these studies and their relevance for the development of the product in the condition,
- the available clinical observations in SCD patients,

- number of affected individuals.

The sponsor appears to have provided an older estimate of the prevalence in Europe of the condition. The sponsor was requested to provide an updated estimate and justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor was asked to describe and justify the methodology used for the prevalence calculation and re-estimate the prevalence for the European Union.

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"

- Significant benefit

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

As regards the safety argument, it is well known that extrapolation from non-clinical or early clinical studies cannot fully predict the safety of a product in its clinical setting, thus other relevant data is required to justify safety arguments in most cases.

The sponsor was also requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the ongoing clinical study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition. Potential effects in patients non-responsive to or intolerant to hydroxyurea may be discussed.

In the written response, and during an oral explanation before the Committee on 8 September 2020, the sponsor further elaborated on the mechanism of action and included some new in vivo data.

The sponsor also discussed in more detail the available clinical observations with a single dose of the active substance administered in 5 patients and 2 patients serving as controls.

For the issue of prevalence, the sponsor performed a review of recent literature and the current prevalence for SCD in the EU-27 was recalculated to be 1.65 up to a conservative estimate of 2.2. The COMP acknowledged the difficulties with the prevalence calculation and considered that in accordance with the data above, a less than 2 per 10,000 may be considered acceptable.

With regards to Significant Benefit, the sponsor submitted a comparative discussion versus hydroxyurea. The 5 treated patients were already receiving hydroxyurea, and as such an add-on effect can be assumed. The COMP considered the arguments provided acceptable as justification of clinically relevant advantage.

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

The intention to treat the condition with the medicinal product containing (S)-1-(5-((2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)sulfonyl)-3,4,5,6-tetrahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-3-hydroxy-2-phenylpropan-1-one was considered justified based on non-clinical data in models of the condition as well as preliminary clinical observations supporting improvements in haemoglobin levels in affected patients.

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

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 (S)-1-(5-((2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)sulfonyl)-3,4,5,6-tetrahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-3-hydroxy-2-phenylpropan-1-one will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical observations supporting add-on effects on increasing haemoglobin in treated patients also receiving hydroxyurea. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for (S)-1-(5-((2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)sulfonyl)-3,4,5,6-tetrahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-3-hydroxy-2-phenylpropan-1-one, for treatment of sickle cell disease, was adopted by consensus.

2.1.6. tebentafusp - EMA/OD/0000030272

Pharma Gateway AB; Treatment of uveal melanoma

COMP Rapporteur: Martin Mozina

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

- Intention to diagnose, prevent or treat

The sponsor was requested to further justify uveal melanoma as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the orphan regulations and relevant guidelines (especially section A of ENTR/6283/00).

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of uveal melanoma the sponsor should further elaborate on the newly added data and arguments in support of the claim that the condition is a distinct medical entity, as compared to the previous application in November 2019.

In the written response, and during an oral explanation before the Committee on 8 September 2020, the sponsor provided extensive and detailed discussion of the individual aspects of uveal melanoma such as clinical characteristics, histopathology, pathophysiology and classification of uveal melanoma, as opposed to other subtypes of melanoma. The sponsor also referred to the unmet need in this treatment resistant population of patients.

The COMP questioned the delineation of uveal melanoma based on several commonalities between this and other melanoma types. The sponsor accepted the statement that uveal melanoma and meningeal melanoma share similar characteristics and that their descriptions are still a subject of ongoing research. There is also a genetic overlap between uveal and blue nevus melanoma. The sponsor referred to the excessive rarity of meningeal melanomas and melanomas of blue nevi so that they should not drive the discussion on

distinctive characteristics of different types of melanoma. However, a rarity of the condition was not considered a sufficient argument.

The COMP discussed also the WHO classifications systems, which distinguish conditions based on defined criteria serving another purpose than the purpose of the orphan regulation. For example, ICD-10 classification recognises uveal melanoma based on its anatomical site, rather than a set of distinct characteristics. The WHO Classification of Skin Tumours (2018) also distinguishes uveal melanoma, but based on aetiology, which is not linked to UV radiation. Based on the wording of other entities delineated in this classification, the criteria used did not include the totality of disease characteristics. The sponsor concurred that the classification systems are not up-to-date and behind the advances in understanding the diseases from a scientific point of view.

The COMP considered that for the purpose of the European orphan designation, the arguments presented were not sufficient to consider uveal melanoma a separate condition. Instead, the COMP considered that uveal melanoma is a subset of a non-rare condition, namely of melanoma, and that the validity of this subset cannot be substantiated. This is because the proposed product is not specific to this condition and could be used also in cutaneous melanoma. Its potential efficacy was exemplified in the clinical trial presented by the sponsor, where 5% of cutaneous melanoma patients achieved objective responses.

Uveal melanoma is not accepted as a distinct medical entity for the purpose of an orphan designation. This was considered on the basis of commonalities between the different melanoma subtypes and the lack of applicability of classifications. Therefore, melanoma should have been considered as the condition for the purpose of orphan designation.

The intention to treat melanoma with the medicinal product containing tebentafusp was considered justified based on objective responses in patients with relapsed/refractory uveal and cutaneous melanoma.

The condition is life-threatening with a reduced survival in relapsed/refractory disease and chronically debilitating especially in metastatic disease due to pain, organ failure and treatment burden.

The sponsor has not justified that melanoma affects less than 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 tebentafusp will be of significant benefit to those affected by the condition. The sponsor has provided data that show objective responses in patients with relapsed/ refractory disease. The Committee considered that this constitutes a clinically relevant advantage.

A negative opinion for tebentafusp, for treatment of uveal melanoma, was adopted as COMP did not reached the two-third-majority position in favour of the designation of the medicinal product as an orphan medicinal product. The divergent positions were appended to this opinion. The sponsor will have 90 days to appeal from the COMP decision.

(Note: This is in line with the COMP Rules of Procedure which states that: "In the absence of a two-third-majority position in favour of the designation of a medicinal product as an orphan medicinal product, the Committee's opinion is deemed to be negative.")

[Post-meeting note: *The COMP adopted the divergent position by written procedure following its September meeting.]*

2.1.7. retigabine - EMA/OD/0000030264

FGK Representative Service GmbH; Treatment of KCNQ2 encephalopathy

COMP Rapporteur: Giuseppe Capovilla

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". A point estimate for the complete prevalence is expected, rather than birth prevalence which is supplied by the sponsor.

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

- Significant benefit

The arguments on significant benefit were based on the new mechanism of action and the potential improved efficacy in the condition. The sponsor was requested to further discuss the arguments in particular with regards to the previous and concomitant therapies of patients and the effects of the product proposed for designation.

In the written response, and during an oral explanation before the Committee on 8 September 2020, the sponsor further elaborated on the raised issues.

The prevalence issue was considered to be resolved.

The non-clinical data were discussed again and an improved efficacy over phenobarbital was argued, however there was no statistical certainty to support this.

With regards to the available clinical observations, the sponsor outcomes were discussed. It was stressed that 13 out of 17 subjects demonstrated improvements in seizures and or neurodevelopmental/behavioural outcomes. Seizure response improved in 11/13 subjects and neurodevelopmental/behaviour outcomes improved in 12/13 subjects. Given that most of these patients are purported to be refractory to previous treatment, an improved efficacy of the product was assumed. Following review of the application by the Committee, it was agreed to rename the indication to treatment of KCNQ2 developmental and epileptic encephalopathy.

The Committee agreed that the condition, KCNQ2 developmental and epileptic encephalopathy, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing retigabine was considered justified based on non-clinical models and clinical observations in affected patients, who responded to treatment with a reduction in seizures.

The condition is chronically debilitating due to epileptic seizures, diffuse hypotonia, limb spasticity, lack of visual fixation and tracking and mild to moderate intellectual deficiency. The condition is also life-threatening due to the risk of sudden unexpected death in epilepsy.

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 retigabine will be of significant benefit to those affected by the condition. The sponsor has discussed clinical narratives with the product reducing seizure frequency in previously treatment refractory cases. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for retigabine, for treatment of KCNQ2 developmental and epileptic encephalopathy, was adopted by consensus.

2.1.8. - EMA/OD/0000032059

Treatment of Charcot-Marie-Tooth disease

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

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of Charcot-Marie-Tooth (CMT) disease the sponsor was asked to further elaborate on:

- the relevance of the results in non-clinical models of CNS diseases, such as the ones presented to support the medical plausibility, to CMT, which is a peripheral nerve disorder,
- the lack of effect on the primary endpoint in the majority (4/5) patients with CMT in the clinical study,
- the clinical relevance of the positive trends described by the sponsor in the primary and secondary endpoints of the study.

In the written response, and during an oral explanation before the Committee on 8 September 2020, the sponsor acknowledged that the non-clinical data submitted with this application, while supporting the hypothesized mechanism of action in CNS disorders involving demyelination and axonal degeneration, were not directly relevant for the medical plausibility in the proposed condition CMT.

In relation to the clinical data, the sponsor remarked that there are no established endpoints for studies in the proposed condition and the main purpose of the clinical study was to identify endpoints that could be used in a future pivotal placebo-controlled trial. The sponsor also commented that the primary endpoint was a new exploratory composite electrophysiological endpoint never used in previous trials and that it may be too stringent, since only one patient responded. The trends and the variability of the results of the secondary endpoints were also discussed. The COMP considered that the fact that the clinical responses were inconsistent across patients and across endpoints did not allow

concluding on the medical plausibility at the current stage, and this small clinical study did not support the proof of concept. Studies on larger patient populations will be needed.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 8 September 2020, prior to final opinion.

2.1.9. teclistamab - EMA/OD/0000028614

Janssen-Cilag International N.V.; Treatment of multiple myeloma

COMP Rapporteur: Karri Penttila

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".

Taking into consideration that the target condition is an incurable disease with increasing relapses, the sponsor is invited to provide a complete prevalence estimate. Indirect methods may also be used towards this end, that would refer to both the available incidence supplied by the European Cancer Information System, as well as an updated duration of the condition/longer survival of patients in the EU.

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

- Significant benefit

The arguments on significant benefit were based on the new mechanism of action and the potential improved efficacy in the condition. The sponsor was requested to further discuss the comparison of the effects observed with the products versus all the existing authorised treatments in the relapsed/ refractory setting.

Based on the written response, the COMP considered that this level of evidence was sufficient to support the assumption of significant benefit for the purpose of initial orphan designation, and the oral explanation was cancelled.

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

The intention to treat the condition with the medicinal product containing teclistamab was considered justified based on preliminary clinical observations showing responses in heavily pretreated relapsed/refractory patients.

The condition is chronically debilitating and life-threatening in particular due to the development of hypercalcemia, renal insufficiency, anaemia and bone lesions.

The condition was estimated to be affecting approximately 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 teclistamab will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that support higher response rates in last line multiple myeloma patients compared to the expectations with the currently authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for teclistamab, for treatment of multiple myeloma, was adopted by consensus.

2.1.10. retifanlimab - EMA/OD/0000035563

Incyte Biosciences Distribution B.V.; Treatment of anal cancer

COMP Rapporteur: Elisabeth Johanne Rook

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

- Intention to diagnose, prevent or treat

The sponsor provided preliminary data from an ongoing clinical study. However, the durability of achieved responses was not possible to assess in a proportion of patients.

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of anal cancer the sponsor was asked to provide an updated analysis of data from the ongoing clinical study. Particularly, the durability of the responses obtained would be of interest in addition to any update regarding the response rate to treatment.

- Number of people affected

The sponsor provided a calculation of prevalence assuming 5-year disease duration. Given that the reported 5-year survival of patients affected by squamous cell carcinoma reaches 80%, this assumption may be an underestimate. The sponsor was invited to discuss the survival of patients affected by anal cancer and to provide a sensitivity analysis assuming longer disease duration as per most recent literature/registry data.

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".

- Significant benefit

The sponsor claimed that no satisfactory methods of treatment exist for treatment of anal cancer. The sponsor was reminded that it is his responsibility to check in central but also national registries if this is indeed the case. For example, mitomycin-C is authorised for treatment of anal cancer in several member states. The sponsor was requested to provide a comprehensive list of products authorised for treatment of anal cancer in the EU.

The sponsor presented data from a clinical study in patients who have progressed on or after a standard-of-care platinum-based chemotherapy regimen. The medical history of patients (e.g. the list of medicines they were refractory to or the stage of the disease), was not clearly specified.

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

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

Based on the written response, the COMP considered that this level of evidence was sufficient to support the assumption of significant benefit for the purpose of initial orphan designation, and the oral explanation was cancelled.

The Committee agreed that the condition, anal cancer, 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 clinical data in patients progressing after platinum-based chemotherapy who achieved durable partial or complete responses.

The condition is chronically debilitating due to any combination of a mass, non-healing ulcer, pain, bleeding, itching, discharge, faecal incontinence and fistulae and life-threatening due to a 5-year survival around 80%.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing retifanlimab will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that patients with advanced and metastatic anal cancer who relapsed following standard platinum-based chemotherapy regimen achieved durable responses. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for retifanlimab, for treatment of anal cancer, was adopted by consensus.

2.1.11. - EMA/OD/0000030250

Treatment of solid organ transplantation

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

- 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 solid organ transplantation the sponsor was asked to provide more information on baseline characteristics and details of the treatment and further elaborate on:

- the results obtained from the investigator-initiated trials (IIT) and to contextualise it within the long-term outcome of patients undergoing renal transplantation.

In the written response, and during an oral explanation before the Committee on 9 September 2020, the sponsor provided a response to the concerns raised regarding the medical plausibility. The sponsor acknowledged the limitations of the preliminary data from the open-label IIT that was presented in the application but could not present the requested further information as the trial is still ongoing.

Instead, the sponsor presented data from another study recently completed, a randomized, placebo-controlled, Phase 2 pilot study to evaluate the safety and efficacy of the proposed product in subjects with late antibody-mediated rejection (ABMR).

Compared to other orphan drug desigations in the setting of antibody mediated rejection, the information provided by the sponsor was more limited. In addition, there is no preclinical in vivo data with the proposed product to complement the clinical observation in few patients.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 9 September 2020, prior to final opinion.

2.1.12. 1-(3-methylbutanoyl)-l-aspartyl-l-threonyl-l-histidyl-l-phenylalanyl-l-prolyl-(l-cystinyl-l-isoleucyl-[(n6-(s)-4-carboxy-4-palmitamidobutanoyl)-l-lysinyl]-l-phenylalanyl-l-glutamyl-l-prolyl-l-arginyl-l-serinyl-l-lysinyl-l-glycinyl-l-cystinyl)-l-lysinamide, disulfide, acetate - EMA/OD/0000009949

Scendea (NL) B.V.; Treatment of polycythaemia vera

COMP Rapporteur: Karri Penttila

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:

- Prevalence

The sponsor was invited to provide the most plausible point estimate for the number of affected persons, instead of proposing a wide range of possible estimates.

- Significant benefit

The arguments on significant benefit were based on the new mechanism of action.

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

In the written response, and during an oral explanation before the Committee on 9 September 2020, the sponsor recalculated prevalence to approximately 3.3 per 10,000 by using an assumption of 0.22 /10,000 yearly incidence rate and 15 years of duration.

With regards to the significant benefit, updated clinical observations were put forward from the available studies. The sponsor argued that the patients maintain haematocrit below 45% in treated with phlebotomy alone, as well as in patients treated with phlebotomy plus cytoreductive therapy. It was also argued that all patients dosed in the ongoing Phase 2 study to date achieved doses that were able to control their haematocrit without a phlebotomy.

The COMP considered that the assumption of significant benefit would be considered justified based on a) data that support reduction of haematocrit and the need of phlebotomy in patients at low risk for thromboembolic complications with the product as a monotherapy and b) data supporting effects in high risk patients as an add-on to other available treatments.

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

The intention to treat the condition with the medicinal product containing 1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate was considered justified based on preliminary clinical observations in affected patients where treatment with the product resulted in reduction of haematocrit and the need for venesections.

The condition is life-threatening with a survival of approximately 15 years, and chronically debilitating due to thromboembolic and haemorrhagic complications, splenomegaly and myelofibrotic, myelodysplastic or leukaemic transformation.

The condition was estimated to be affecting approximately 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 1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that support reduction of haematocrit and the need of phlebotomy in patients at low risk for thromboembolic complications with the product as a monotherapy. The clinical data also support effects in high risk patients as an add-on to other available treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate, for treatment of polycythaemia vera, was adopted by consensus.

2.1.13. - EMA/OD/0000034496

reatment of COVID-19 related ARDS

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:

- COVID-19 -related ARDS (acute respiratory distress syndrome) should be justified as a distinct medical entity or a valid subset.

Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the Orphan regulations and relevant guidelines (especially section A of ENTR/6283/00). This includes demonstrating that ARDS in COVID-19 has unique pathophysiological and clinical characteristics that differentiate it from the broader condition, and also justify that the mechanism of action and effects of the proposed product are such that they are expected to work only in the proposed subset and not in the broader condition outside the subset.

Notwithstanding the condition, to establish correctly whether there exists a scientific rationale for the development of the proposed product the sponsor was asked to further elaborate on a number of aspects of the study from Castillo et al, 2020, including: the clinical status of the COVID-19 positive patients receiving the propose product who did not have ARDS, and the baseline characteristics of the external control group (age, comorbidities, respiratory support status, background therapy).

The use of various doses of the proposed product together with variable time of initiation in the study and its potential impact on the results, and the extrapolation of the data of this study with oral administration to the proposed parenteral administration needed also to be clarified.

- 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 prevalence estimate (incidence in this case) to the purpose of orphan designation needs to correspond to the one at the time of the submission of the application. For this reason, the applicant's calculations related to an average of the whole year were not acceptable.

The sponsor was requested therefore to re-calculate the prevalence estimate based on the above. Relevant epidemiological studies and literature should be used. The sponsor was asked to further justify the use of ICU admission as proxy of ARDS.

In the written response, and during an oral explanation before the Committee on 9 September 2020, the sponsor discussed the available data in relation to COVID-19 related ARDS and also in relation to ARDS in general, since from the written response it appeared that the final intention was to apply for ARDS. The COMP highlighted that the data presented so far would not support a designation in ARDS because the medical plausibility could not be established based on the non-clinical data, as no valid model of ARDS were presented, nor on the clinical data provided. The clinical data presented in support of the plausibility included a study in respiratory distress syndrome in the newborns, which is different from ARDS; a study in patients admitted in ICU but without knowledge whether they were admitted for ARDS; and a study in patients with confirmed or suspected COVID-19, among whom only a handful had ARDS.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 10 September 2020, prior to final opinion.

2.1.14. (4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1h-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)) - EMA/OD/0000033552

Novartis Europharm Limited; Treatment of IgA nephropathy

COMP Rapporteur: Martin Mozina

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

- Proposed condition

The sponsor was invited to justify the scope of the proposed condition in particular with regards to the exclusion of secondary IgA nephropathy cases.

- 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 IgA nephropathy the sponsor was asked to further elaborate on the effects of the proposed treatment on the renal function, as per the available clinical observations.

- Number of people affected

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

The sponsor was asked to re-calculate the prevalence estimate based on up to date epidemiological studies and registers relevant for the proposed orphan condition in the EU27 +UK, and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor was requested to perform a sensitivity analysis of the reported calculations.

The sponsor was also invited to elaborate on the number of primary and secondary cases of IgA nephropathy.

In the written response, and during an oral explanation before the Committee on 10 September 2020, the sponsor confirmed that primary IgA nephropathy (IgAN) is the sought indication, on the basis that the complement AP is only of pathogenic significance in the development of primary IgAN. The COMP considered that primary IgAN can be delineated as a separate entity on the basis of poorly galactosylated IgA1 which eventually discloses a "cryptic" epitope in the IgA1 hinge-region. The previous designations were also taken into consideration in that regard. The condition was re-articulated accordingly to refer only to primary IgAN.

With regards to the intention to treat the condition, the sponsor provided a general discussion on the relevance of UPCR (urine protein/creatinine ratio) as a relevant endpoint. The improvement was acknowledged, taking into consideration the short follow-up of patients.

As for the prevalence issue it was literature based and calculated from incidence multiplied by an assumed duration of up to 38.2 years according to different sensitivity analyses. The sponsor proposed an overall (primary and secondary) prevalence of 4.71 per 10,000 (sensitivity range 4.8-6.5 per 10,000). However, by assuming that 20% of prevalent cases were secondary IgAN cases the prevalence of primary IgAN in EU27+UK can be estimated as 3.77 in 10,000 population (range from sensitivity analyses: 3.84-5.20 in 10,000. The COMP considered an estimate of approximately 4 in 10,000 to be in line with the above and acceptable for the amended indication.

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of primary IgA nephropathy.

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

The intention to treat the condition with the medicinal product containing (4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1h-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)) was considered justified based on a reduction in urine protein to creatinine ratio in treated patients.

The condition is life-threatening and chronically debilitating due to progressive loss of kidney function leading to kidney failure requiring dialysis and transplantation.

The condition was estimated to be affecting approximately 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 (4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1h-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)), for treatment of primary IgA nephropathy, was adopted by consensus.

2.1.15. autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - EMA/OD/0000035618

Kite Pharma EU B.V.; Treatment of acute lymphoblastic leukaemia

COMP Rapporteur: Maria Elisabeth Kalland

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

- Number of people affected

The sponsor provided a calculation of prevalence based on 2017 data. The estimate was lower that what was expected for the proposed condition at this point in time. The sponsor was invited to provide an updated calculation, considering most recent data sources such as HMRN or ECIS database.

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".

- Significant benefit

The arguments on significant benefit were based on the potential improved efficacy in the condition. The sponsor provided a comparative discussion in relation to some of the later line treatments authorised at the time the application was made.

However, comparative discussion vs. inotuzumab and tisagenlecleucel needed elaboration, in order to assume clinically relevant advantage over these products.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the clinical studies to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition, and in particular the above-mentioned products. In addition, further information on the ongoing and planned clinical development would be of interest for the Committee.

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

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

The intention to treat the condition with the medicinal product containing autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured was considered justified based on clinical data in heavily pre-treated patients showing high rate of durable responses.

The condition is chronically debilitating and life-threatening depending on the response to treatment, with acute leukaemic forms being fatal in a few weeks if left untreated. Symptoms include persistent fever, infections, anaemia, fatigue, breathlessness, bone and joint pain. The invasion of the bloodstream, the bone marrow and/or the lymphatic system result in lack of normal blood cells, bone marrow failure, and organ damage.

The condition was estimated to be affecting less than 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 autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that patients who were relapsed/refractory to the standard of care achieved a high rate of complete and durable responses. This compared favourably to all products authorised in the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured, for treatment of acute lymphoblastic leukaemia, was adopted by consensus.

2.1.16. 2-(2-(^{18}F)fluoropyridin-4-yl)-9h-pyrrolo[2,3-b:4,5-c']dipyridine - EMA/OD/0000035180

Life Molecular Imaging GmbH; Diagnosis of corticobasal degeneration

COMP Rapporteur: Darius Matusevicius

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

- Number of people affected

The sponsor provided a calculation of prevalence, which differs in approach and methodology to the recently accepted calculation in relation to a sister application from the sponsor (Case EMA/OD/0000029150).

The sponsor was requested to provide a new calculation of the number of patients who would undergo the proposed diagnostic test, which would be methodologically in line with the previous application.

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

In the written response, the sponsor provided a recalculation of the prevalence of the condition, taking into consideration published information about the incidence of the condition as applied for. The calculation was aligned with the sister application for diagnosis of PSP (progressive supranuclear palsy) as requested and was found acceptable by the COMP. The proposed prevalence of the condition is 0.9 in 10,000 persons in the EU.

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

The intention to diagnose the condition with the medicinal product containing 2-(2-(^{18}F)fluoropyridin-4-yl)-9H-pyrrolo[2,3-b:4,5-c']dipyridine was considered justified based on early clinical data where the qualitative assessment showed a significant sensitivity and specificity for the detection of tau deposition in the globus pallidus and putamen, and the ventral midbrain as well as the central, parietal, and frontal cortex region of corticobasal degeneration patients when compared to other tauopathy patients, alpha-synucleopathy patients and healthy controls. This could facilitate an earlier and more reliable diagnosis of corticobasal degeneration and could assist in the differentiation of the condition from other neurodegenerative diseases.

The condition is chronically debilitating due to akinesia, rigidity, dystonia, and myoclonus. During the disease course, most patients develop rigid immobility in just a few years and require care. The condition is also life-threatening due to poor prognosis, and a mean disease duration of 6.6 years, ranging from 2.0 to 12.5 years.

The condition was estimated to be affecting approximately 0.9 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 diagnosis in the European Union for patients affected by the condition.

A positive opinion for 2-(2-(^{18}F)fluoropyridin-4-yl)-9H-pyrrolo[2,3-b:4,5-c']dipyridine, for diagnosis of corticobasal degeneration, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/0000030636

Treatment of unclassifiable interstitial lung 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 October meeting.

2.2.2. adeno-associated viral vector serotype 9 encoding a codon-optimised human aspartylglucosaminidase transgene - EMA/OD/0000031910

Real Regulatory Limited; Treatment of aspartylglucosaminuria

COMP Rapporteur: Dinah Duarte

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

The intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 9 encoding a codon-optimised human aspartylglucosaminidase transgene was considered justified based on data in a non-clinical model of the condition, showing increase in levels of glycosylasparaginase, and improvements in mobility in the treated subjects.

The condition is chronically debilitating in particular due to progressive intellectual and physical disability and life-threatening with death usually occurring before the age of 50 years.

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 viral vector serotype 9 encoding a codon-optimised human aspartylglucosaminidase transgene, for treatment of aspartylglucosaminuria, was adopted by consensus.

2.2.3. - EMA/OD/0000032268

Treatment of gastric 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 October meeting.

2.2.4. ribitol - EMA/OD/0000033863

Premier Research Group S.L.; Treatment of limb-girdle muscular dystrophy

COMP Rapporteur: Dinah Duarte

The Committee agreed that the condition, limb-girdle 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 ribitol was considered justified based on non-clinical data in a valid model of the condition demonstrating improvements in cardiac and motor function.

The condition is chronically debilitating due to muscle wasting, consequent reduced mobility and debilitating fatigue and potentially life threatening due to respiratory complications;

The condition was estimated to be affecting approximately 0.2 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for ribitol, for treatment of limb-girdle muscular dystrophy, was adopted by consensus.

2.2.5. - EMA/OD/0000034572

Treatment of hereditary angioedema

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 October meeting.

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 22 September 2020.]

2.2.6. - EMA/OD/0000034870

Treatment of pancreatic 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 October meeting.

2.2.7. leniolisib - EMA/OD/0000034892

Pharming Group N.V.; Treatment of activated phosphoinositide 3-kinase delta syndrome

COMP Rapporteur: Lyubina Racheva Todorova

The Committee agreed that the condition, activated phosphoinositide 3-kinase delta syndrome, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing leniolisib was considered justified based on preliminary clinical observations showing restoration of lymphocyte population frequencies and reduction of spleen and lymph nodes sizes.

The condition is life-threatening and chronically debilitating due to recurrent respiratory infections, leading to bronchiectasis, progressive lymphopenia, and defective antibody production.

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

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 leniolisib, for treatment of activated phosphoinositide 3-kinase delta syndrome, was adopted by consensus.

2.2.8. highly branched poly(beta-amino ester) complexed with a nanoplasmid containing the human *COL7A1* gene - EMA/OD/0000035451

Amryt Genetics Limited; Treatment of epidermolysis bullosa (EB)

COMP Rapporteur: Armando Magrelli

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

The intention to treat the condition with the medicinal product containing highly branched poly(beta-amino ester) complexed with a nanoplasmid containing the human *COL7A1* gene was considered justified based on non-clinical data in a model of the condition showing

expression of *COL7a* in dermal-epidermal junctions and improved histology of the treated skin.

The condition is chronically debilitating and life-threatening due to blister formation in response to minor friction or trauma, leading to the development of multiple complications including life-threatening infections, failure to thrive, and predisposition to the development of squamous cell carcinoma.

The condition was estimated to be affecting approximately 0.8 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 highly branched poly(beta-amino ester) complexed with a nanoplasmid containing the human *COL7A1* gene, for treatment of epidermolysis bullosa, was adopted by consensus.

2.2.9. - EMA/OD/0000036055

Treatment of oesophageal 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 October meeting.

2.2.10. sparsentan - EMA/OD/0000036435

Retrophin Europe Limited; Treatment of primary immunoglobulin A nephropathy

COMP Rapporteur: Martin Mozina

Following review of the application by the Committee, it was agreed to broaden/rename the indication to treatment of primary IgA nephropathy.

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

The intention to treat the condition with the medicinal product containing sparsentan was considered justified based on non-clinical in vivo data showing a normalisation of creatinaemia and proteinuria.

The condition is life-threatening and chronically debilitating due to progressive loss of kidney function leading to kidney failure requiring dialysis and transplantation.

The condition was estimated to be affecting approximately 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/for the population at risk of developing the condition.

A positive opinion for sparsentan, for treatment of primary IgA nephropathy, was adopted by consensus.

2.2.11. adeno-associated virus serotype hu68 containing the human *GLB1* gene - EMA/OD/0000037095

Pharma Gateway AB; Treatment of GM1 gangliosidosis

COMP Rapporteur: Elisabeth Johanne Rook

The Committee agreed that the condition, GM1 gangliosidosis, 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 hu68 containing the human *GLB1* gene was considered justified based on non-clinical in vivo data which showed improvements in survival as well as motor and neurological function.

The condition is life-threatening due to a reduced life expectancy in the moderate to severe forms of the condition which makes up to 90% of those affected and chronically debilitating due to neurodegeneration associated with cognitive decline, seizures, hepatomegaly, splenomegaly, skeletal irregularities, joint stiffness, muscle weakness and problems with gait.

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

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

A positive opinion for adeno-associated virus serotype hu68 containing the human *GLB1* gene, for treatment of GM1 gangliosidosis, was adopted by consensus.

2.2.12. trehalose - EMA/OD/0000037166

Theranexus S.A.S.; Treatment of neuronal ceroid lipofuscinosis

COMP Rapporteur: Darius Matusevicius

The Committee agreed that the condition, neuronal ceroid lipofuscinosis, 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 non-clinical in vivo data in a model of the condition which shows a reduction in neuronal cell death, functional outcomes and survival.

The condition is life-threatening and chronically debilitating due to visual, cognitive, and motor skills decline, speech impediment, behavioural problems, seizures, cerebral atrophy which lead to early death.

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 trehalose will be of significant benefit to those affected by the condition. The sponsor has provided in non-clinical in vivo data that demonstrate trehalose can reduce neuronal cell death and protect hearing in neuronal ceroidal lipofucinosis type 3

where no authorised medicines exist. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for trehalose, for treatment of neuronal ceroid lipofuscinosis, was adopted by consensus.

2.2.13. poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-methoxy-, amide with cystathionine γ-lyase [pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer - EMA/OD/0000037386

Aeglea Biotherapeutics UK Limited; Treatment of homocystinuria

COMP Rapporteur: Geraldine O'Dea

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

The intention to treat the condition with the medicinal product containing poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [Pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer was considered justified based on non-clinical data in a model of the condition showing reduced total homocysteine levels, reduced kyphosis and improved survival.

The condition is life-threatening and chronically debilitating due to mental retardation, osteoporosis, stroke, myocardial infarction, and pulmonary embolism. The principal contributors of premature death are cardiovascular complications, in particular arterial and venous thrombosis.

The condition was estimated to be affecting less than 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 poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [Pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that demonstrate that the use of the product in addition to milk-derived betaine in the model of the condition improved survival. In addition, the product could be potentially used in large proportion of patients who do not respond to treatment with pyridoxine or cobalamin. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [Pyridoxal 5'-phosphate cofactor] (synthetic engineered human), for treatment of homocystinuria, was adopted by consensus.

2.2.14. - EMA/OD/0000037416

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

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 October meeting.

[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 18 September 2020.]

2.2.15. miglustat - EMA/OD/0000037799

Theranexus S.A.S.; Treatment of neuronal ceroid lipofuscinosis

COMP Rapporteur: Giuseppe Capovilla

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

The intention to treat the condition with the medicinal product containing miglustat was considered justified based on non-clinical in vivo data showing a reduction in neuronal death.

The condition is life-threatening and chronically debilitating due to visual, cognitive, and motor skills decline, speech impediment, behavioural problems, seizures, cerebral atrophy which lead to early death.

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 miglustat will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that demonstrate miglustat can reduce neuronal cell death in neuronal ceroidal lipofucinosis type 3 where no authorised medicines exist. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for miglustat, for treatment of neuronal ceroid lipofuscinosis, was adopted by consensus.

2.2.16. - EMA/OD/0000037822

Treatment of frontotemporal dementia (FTD)

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 October meeting.

2.2.17. poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1) - EMA/OD/0000037830

Ascendis Pharma Bone Diseases A/S; Treatment of hypoparathyroidism

COMP Rapporteur: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1) was

considered justified based on clinical data in patients with the condition which showed sustained normalisation of calcium and phosphate serum levels.

The condition is chronically debilitating due to neuromuscular symptoms, cognitive impairment, abnormal calcium and phosphate metabolism, and reduced bone turnover. The condition may be life-threatening due to risk of hypocalcaemia that may lead to seizures, cardiac arrhythmias, cardiomyopathy and laryngeal spasm if untreated.

The condition was estimated to be affecting approximately 3.2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1) will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate a reduction or elimination of standard of care involving the use of vitamin D supplementation. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1), for treatment of hypoparathyroidism, was adopted by consensus.

2.2.18. - EMA/OD/0000037899

Treatment of congenital pulmonary hypoplasia in infancy

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 October meeting.

2.2.19. adeno-associated virus serotype 5 containing the human *RDH12* gene - EMA/OD/0000038026

MeiraGTx B.V.; Treatment of *RDH12* mutation associated retinal dystrophy

COMP Rapporteur: Tim Leest

The Committee agreed that the condition, *RDH12* mutation associated retinal dystrophy, 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 5 containing the human *RDH12* gene was considered justified based on the totality of the evidence in the non-clinical in vivo data including improvement in electroretinogram values.

The condition is chronically debilitating due to loss of visual acuity.

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 containing adeno-associated virus serotype 5 containing the human *RDH12* gene, for treatment of *RDH12* mutation associated retinal dystrophy, was adopted by consensus.

2.2.20. tipifarnib - EMA/OD/0000030309

TMC Pharma (EU) Limited; Treatment of angioimmunoblastic T-cell lymphoma (AITL) and other nodal T-cell lymphomas of follicular helper T-cell (TFH) origin

COMP Rapporteur: Karri Penttila

Following review of the application by the Committee, it was agreed to rename the indication to treatment of peripheral T-cell lymphoma.

The Committee agreed that the condition, peripheral T-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 tipifarnib was considered justified based on preliminary clinical observations in relapsed/refractory patients who responded to treatment with tipifarnib monotherapy.

The condition is life-threatening and chronically debilitating due to poor response to therapy and high rate of relapses. Clinical presentation and course vary from an indolent clinical behaviour for years in milder subtypes, to fulminant disease in aggressive sub-types.

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 tipifarnib will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical observations supporting objective responses with the product in monotherapy, in a population that has relapsed or was refractory to existing treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for tipifarnib, for treatment of peripheral T-cell lymphoma, was adopted by consensus.

2.2.21. - EMA/OD/0000031771

Treatment of traumatic brain injury with development of oedema

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 October 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 42 applications submitted.

2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 16 applications for orphan designation.

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of bullous pemphigoid

The Committee was briefed on the significant benefit issues.

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

3.1.2. -

Treatment of amyotrophic lateral sclerosis

The Committee was briefed on the significant benefit issues.

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

3.2. Finalised letters

3.2.1. -

Treatment of short bowel syndrome

The finalised letter was circulated for information.

3.2.2. -

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

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment of systemic mastocytosis

The new request was noted.

3.3.2. -

Treatment of neuroblastoma

The new request was noted.

3.3.3. -

Treatment of immune thrombocytopenia

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. Calquence – acalabrutinib - EMEA/H/C/005299, EMA/OD/196/15, EU/3/16/1624, EMA/OD/0000021547

AstraZeneca AB; Treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma

COMP Rapporteurs: Karri Penttilä; Frauke Naumann-Winter

A list of issues was adopted on 16 July 2020.

An oral explanation was held on 8 September 2020.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the orphan designation from the EC register of orphan medicinal products, on 10 September 2020, prior to final opinion.

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

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

Novartis Europharm Limited; Treatment of sickle cell disease

COMP Rapporteurs: Armando Magrelli; Angelo Loris Brunetta

The oral explanation with the sponsor was cancelled.

An opinion recommending not to remove Adakveo, crizanlizumab, EU/3/12/1034 from the EC Register of Orphan Medicinal Products was adopted by consensus.

4.1.3. The orphan maintenance assessment report will be publicly available on the EMA website.Arikayce liposomal - amikacin - EMEA/H/C/005264/0000, EU/3/14/1259, EMA/OD/0000030955

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

COMP Rapporteurs: Nikolaos Sypsas; Eva Malikova

An opinion recommending not to remove Arikayce liposomal, amikacin, EU/3/14/1259 from the EC Register of Orphan Medicinal Products was adopted by consensus.

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

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

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

Zogenix ROI Limited; Treatment of Dravet syndrome

The status of the procedure at CHMP was noted.

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

Accelerated assessment

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

The status of the procedure at CHMP was noted.

4.3.3. - obiltoxaximab - EMEA/H/C/005169/0000, EU/3/18/2065, EMA/OD/0000037218

SFL Pharmaceuticals Deutschland GmbH; Treatment of anthrax

An opinion recommending not to remove Obiltoxaximab SFL, obiltoxaximab, EU/3/18/2065 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 September meeting.]

4.3.4. - valoctocogene roxaparvovec - EMEA/H/C/004749/0000, EU/3/16/1622, EMA/OD/0000024177

Accelerated assessment

BioMarin International Limited; Treatment of haemophilia A

The status of the procedure at CHMP was noted.

4.3.5. UPKANZ - deferiprone - EMEA/H/C/005004/0000, EU/3/18/2034, EMA/OD/0000011266

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

The discussion was cancelled as the Marketing Authorisation Application had been withdrawn after the CHMP July meeting.

4.3.6. - somapacitan - EMEA/H/C/005030/0000, EU/3/18/2068, EMA/OD/0000033719

Novo Nordisk A/S; Treatment of growth hormone deficiency

The status of the procedure at CHMP was noted.

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

Accelerated assessment

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

The status of the procedure at CHMP was noted.

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

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

The status of the procedure at CHMP was noted.

4.4. Appeal

None

4.5. On-going procedures

COMP co-ordinators were appointed for 3 applications.

4.6. Orphan Maintenance Reports

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

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

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

GlaxoSmithKline (Ireland) Limited; Treatment of ovarian cancer

CHMP Rapporteur: Bjorg Bolstad; CHMP Co-Rapporteur: Alexandre Moreau

The COMP discussed 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 October meeting.

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

5.2.2. Deltyba - delamanid - EMEA/H/C/002552/X/0046/G, EMA/OD/094/07, EU/3/07/524

Otsuka Novel Products GmbH; Treatment of tuberculosis

The COMP agreed that a formal review of the maintenance of the orphan designation for the applied indication is not needed.

5.3. Appeal

None

5.4. On-going procedures

COMP co-ordinators were appointed for 3 applications.

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

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the COMP

7.1.1. Strategic Review & Learning Meeting – COMP, 24-25 September 2020, Germany

The final agenda and details for the SRLM meeting was presented by German member. The meeting will be held virtually on 24-25 September 2020.

7.1.2. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 4 September 2020.

7.1.3. COMP Workshop 2020 on support for orphan medicines development

The COMP discussed the details and organisation of the upcoming COMP Workshop that will take place Monday the 30th November 2020. It will be held virtually. There will be IRIS training session held in the afternoon.

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendation on eligibility to PRIME – report from CHMP

Documents were tabled for information.

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

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

Documents were tabled for information.

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. Therapeutic Goods Administration (TGA), Australia

None

7.5.4. Health Canada

None

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

None

7.7. COMP work plan

None

7.8. Planning and reporting

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

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2020 were circulated.

7.8.2. Overview of orphan marketing authorisations/applications

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

8. Any other business

8.1. Reactivation of EMA Working parties

The reply letter to EMA was tabled for information.

8.2. EMA Business Pipeline activity and Horizon scanning

The document was tabled for information.

8.3. Letter from sponsor

The COMP noted the letter from the sponsor and decided to draft a response letter to explain COMP position.

9. Explanatory notes

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

Abbreviations / Acronyms

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

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

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

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

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

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

Sponsor

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

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

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

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

List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 8-10 September meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Violeta Stoyanova-Beninska	Chair	Netherlands	No interests declared	
Armando Magrelli	Member (Vice-Chair)	Italy	No interests declared	
Brigitte Schwarzer-Daum	Member	Austria	Brigitte Schwarzer-Daum has voluntarily refrained from taking part in discussions, final deliberations and voting in the EMA/OD/0000030250 procedure.	2.1.11. - EMA/OD/0000030250
Tim Leest	Member	Belgium	No interests declared	
Dinko Vitezic	Member	Croatia	No interests declared	
Vasileios Loutas	Member	Cyprus	No interests declared	
Lenka Gaidadzi	Member	Czech Republic	No interests declared	
Elisabeth Penninga	Member	Denmark	No interests declared	
Vallo Tillmann	Member	Estonia	No interests declared	
Karri Penttilä	Member	Finland	No interests declared	
Cecile Dop	Member	France	No interests declared	
Frauke Naumann-Winter	Member	Germany	No interests declared	
Zsofia Gyulai	Member	Hungary	No interests declared	
Geraldine O'Dea	Member	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Irena Rogovska	Member	Latvia	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No interests declared	
Elisabeth Johanne Rook	Member	Netherlands	No interests declared	
Maria Elisabeth Kalland	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland	No restrictions applicable to this meeting	
Dinah Duarte	Member	Portugal	No interests declared	
Olimpia Neagu	Member	Romania	No interests declared	
Eva Malikova	Member	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	
Angelo Loris Brunetta	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Julian Isla	Member	Patients' Organisation Representative	No interests declared	
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Bruno Sepodes	Member	Expert recommended by EMA	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Giuseppe Capovilla	Member	Expert recommended by EMA	No interests declared	
Virginie Hivert	Expert - via AC	Patients' Organisation Representative	No restrictions applicable to this meeting	
Meeting run with support from relevant EMA staff				

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