25 January 2018
EMA/COMP/375607/2017 Corr.[1]
Inspections, Human Medicines Pharmacovigilance and Committees

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 13-15 June 2017

Chair: Bruno Sepodes – Vice-Chair: Lesley Greene

13 June 2017, 09:00-18:30, room 2F

14 June 2017, 08:30-18:30, room 2F

15 June 2017, 08:30-12:00, room 2F

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).

[1] Correction of the of the agenda point number for which restriction applied

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members and experts

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions.

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

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 21 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda for 13-15 June 2017 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 10-12 May 2017 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. Oxymetazoline hydrochloride - EMA/OD/325/16

RDD Pharma Limited; Treatment of spinal cord injury

COMP coordinator: Dinah Duarte; Patient expert: Simon Pinnell

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

- Significant benefit

The sponsor is invited to discuss the significant benefit of the proposed product in the perspective of the current methods to relieve faecal incontinence. Significant benefit may be based on clinically relevant advantages and/or major contribution to patient care. Assumptions of significant benefit need to be supported with any available data. In the absence of data the significant benefit cannot be justified.

In the written response, and during an oral explanation before the Committee on 13 June 2017, the sponsor clarified the proposed grounds of significant benefit in the treatment of faecal incontinence in patient with spinal cord injury. The clinical data that were presented in this application were with topical oxymetazoline used in addition to the existing treatment methods; therefore the significant benefit can be justified based on a clinically relevant advantage when the product is used on top of standard of care for faecal incontinence in spinal cord injury.

In the present case a designation for the whole condition was considered justified, since all patients with spinal cord injury, irrespective of the aetiology of the spinal cord injury, may benefit from the product.

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

The intention to treat the condition with the medicinal product containing oxymetazoline hydrochloride was considered justified based on preliminary clinical data showing reduction of faecal incontinence episodes in patients affected by the condition.

The condition is life-threatening and chronically debilitating due to sensory and motor loss of function in the limbs, with reduced life expectancy.

The condition was estimated to be affecting approximately 4.2 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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing oxymetazoline hydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing reduction of faecal incontinence episodes in patients already treated with standard of care methods. The Committee considered that this constitutes a clinically relevant advantage for the patients affected by the condition.

A positive opinion for oxymetazoline hydrochloride, for treatment of spinal cord injury, was adopted by consensus.

2.1.2. Recombinant human antibody directed against misfolded human superoxide dismutase 1 - EMA/OD/030/17

The Medical & Regulatory Partnership Limited; Treatment of amyotrophic lateral sclerosis

COMP coordinator: Violeta Stoyanova/Robert Nistico

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

- Intention to diagnose, prevent or treat

The sponsor presented non-clinical data in prophylactic (pre-symptomatic) setting. No data to demonstrate the product's efficacy in symptomatic amyotrophic lateral sclerosis was shown.

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of amyotrophic lateral sclerosis, the sponsor should further elaborate on:

– the relevance of the preclinical models used for the treatment of amyotrophic lateral sclerosis, and the interpretation of the results obtained in the experiments,

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

- Significant benefit

The arguments on significant benefit are based on the new mechanism of action and the potential improved efficacy in the condition. The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the non-clinical study to justify the translatability of these observations to the clinical setting.

In the written response, and during an oral explanation before the Committee on 13 June 2017, the sponsor described in detail the non-clinical model of amyotrophic lateral sclerosis used. The sponsor argued that the product was used in treatment of early manifestations of the disease. The COMP discussed with the sponsor about the future development from a clinical point of view, where patients are often diagnosed well after the onset of symptoms. The COMP considered the arguments presented by the sponsor acceptable at the stage of initial orphan drug designation to support the assumption of medical plausibility and, consequently, significant benefit.

Following review of the application by the Committee, it was agreed to broaden/rename the active substance to recombinant human antibody directed against misfolded human superoxide dismutase 1.

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

The intention to treat the condition with the medicinal product containing recombinant human antibody directed against misfolded human superoxide dismutase 1 was considered justified based on non-clinical data demonstrating a delay in motor function deterioration in early stages of the condition.

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

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

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing recombinant human antibody directed against misfolded human superoxide dismutase 1 will be of significant benefit to those affected by the condition. The sponsor has provided preclinical data that demonstrate that the product delays the development of motor abnormalities and body weight loss (attributed to muscle mass loss) in a model of the condition when applied early in the disease. This compared favourably to authorised products that are not shown to have any effect on motor function. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for recombinant human antibody directed against misfolded human superoxide dismutase 1, for treatment of amyotrophic lateral sclerosis, was adopted by consensus.

2.1.3. Sirolimus - EMA/OD/025/17

Raremoon Consulting Ltd; Treatment of pachyonychia congenita

COMP coordinator: 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:

- Intention to diagnose, prevent or treat

The currently submitted preliminary clinical data are not considered sufficient to justify medical plausibility. The sponsor should present additional data to support medical plausibility with the proposed topical formulation or alternatively the sponsor is invited to resubmit when such data becomes available.

In the written response, the sponsor presented currently unpublished data from 2 pachyonychia congenita patients who were refractory to their previous treatments and were treated with a topical formulation of sirolimus. The outcome suggests improvement of painful plantar keratoderma in both patients. The COMP considered that the additional preliminary clinical data, which is supported by published evidence on systemic sirolimus treatment in pachyonychia congenita, were sufficient to establish medical plausibility for the purpose of orphan designation. The Committee accepted these arguments and the oral hearing was cancelled.

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

The intention to treat the condition with the medicinal product containing sirolimus was considered justified based on preliminary clinical data showing that the proposed product was able to improve plantar keratoderma of patients affected by the condition.

The condition is chronically debilitating due to impaired ambulation associated with plantar keratoderma, blistering and pain.

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

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

A positive opinion for sirolimus, for treatment of pachyonychia congenita, was adopted by consensus.

2.1.4. - EMA/OD/263/16

Treatment of neonatal abstinence syndrome

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 26 May 2017, prior to responding to the list of issues.

2.1.5. - EMA/OD/295/16

Treatment of invasive candidiasis

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 19 May 2017, prior to responding to the list of issues.

2.1.6. - EMA/OD/032/17

Treatment of myotonic disorders

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

- Significant benefit

The sponsor should further elaborate on the argument of lack of supply which can lead to harm to patients, as the COMP has noted that there are supplies of the products containing the same active substance in EU member states.

In the written response, and during an oral explanation before the Committee on 14 June 2017, the sponsor presented data from those countries where products with the same active substance were available and indicated that there is import from production sites outside the EU. The COMP acknowledged that there may be a lack of supply in the EU, but how this impacts patient outcome was not clear as the sponsor had not adequately discussed this in their reply to the question.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 15 June 2017, prior to final opinion.

2.1.7. - EMA/OD/023/17

Treatment of sudden sensorineural hearing loss

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 is invited to further elaborate on the relevance of the preclinical settings used for the purpose of justifying the intention to treat the proposed condition.

- Prevalence

The sponsor is invited to justify the epidemiological index used for the prevalence calculation in the context of the duration of the proposed condition.

The sponsor is also invited to elaborate on the population covered by the estimation exercise and account for all patients affected by the proposed condition as applied for designation.

The sponsor is requested to provide a sensitivity analysis of all assumptions used and update the estimate for the time the application is made.

- Significant benefit

No data are presented supporting a clinically relevant advantage or major contribution to patient care. A discussion based on data juxtaposing the product with the authorised counterparts is expected.

In the written response, and during an oral explanation before the Committee on 14 June 2017, the sponsor further discussed the preclinical data and the validity of the preclinical model. The COMP acknowledged that the presented evidence was supportive for the purpose of medical plausibility, in the absence of clinical studies.

Regarding prevalence, the sponsor presented a revised estimate. The COMP considered that the prevalence criterion can be considered justified.

Regarding significant benefit, the sponsor' arguments were focused on the proposed different mode of action. The COMP considered that an alternative mechanism of action *per se* would not suffice for the justification of significant benefit, notwithstanding that the mechanism may actually be overlapping with the mechanism of action of the already authorised products. It was concluded that no data were provided to allow for a comparison *versus* the authorised counterparts and as such the significant benefit criterion could not be considered met.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 14 June 2017, prior to final opinion.

2.1.8. - EMA/OD/024/17

Treatment of mastocytosis

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 is requested to establish with data if there is a scientific rationale for the development of the proposed product for treatment of mastocytosis.

- Number of people affected

The sponsor should revise its prevalence calculation taking into consideration prevalence data on all types of mastocytosis. The sponsor should justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition. The sponsor should describe and justify the methodology used for the prevalence calculation.

- Significant benefit

The current level of evidence presented is not considered sufficient to establish significant benefit *versus* authorised products. The sponsor is invited to present a data-driven comparative discussion on significant benefit over all authorised treatments in the condition.

In the written response, and during an oral explanation before the Committee on 14 June 2017, the sponsor further elaborated on the preliminary clinical data and the rationale to develop the product for the treatment of mastocytosis. The COMP considered that at the current stage of development there was not sufficient evidence to support medical plausibility for the purpose of orphan designation.

Regarding prevalence, the sponsor provided an updated estimate of 3.1 per 10,000 that took into consideration all forms of mastocytosis. This figure was accepted by the COMP.

Regarding significant benefit, the sponsor discussed the presented preliminary clinical data. The COMP disagreed that the data was sufficient to address significant benefit *versus* authorised treatments and satisfactory methods.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 14 June 2017, prior to final opinion.

2.1.9. - EMA/OD/033/17

Treatment of ischemic optic neuropathy

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

For the purposes of orphan medicinal product designation, ischaemic optic neuropathy should be justified as a distinct medical entity or a valid subset. The condition has multiple aetiologies and has been reported in some sources as being a stage of optic atrophy. The sponsor's attention is drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

- Number of people affected

The sponsor has provided a prevalence estimate of the anterior form of the condition but not the other forms of the condition. The sponsor should also note the difficulty in diagnosing the condition and how this can affect the prevalence calculation. For the calculation and presentation of the prevalence estimate it is advised to refer to the "Points to Consider on the Calculation and Reporting of a Prevalence of a Condition for Orphan Designation".

In the written response, and during an oral explanation before the Committee on 14 June 2017, the sponsor presented a justification of the condition as a separate medical entity by describing the presentation and differences in the underlying aetiologies to other vascular complications associated ischemic optic accidents. The multiple aetiologies which are not strictly linked to thrombotic accidents lead to the controversial nature of the condition. The COMP also referred to published scientific literature, where ischemic optic neuropathy is described as degree of degradation of the optic nerve, which will lead to the broader condition of optic atrophy. It was also discussed that ophthalmologists often see the consequences of ischemic optic neuropathy after the event has occurred and that diagnosis at the time when the condition presents is not often possible. This would affect the number of cases which can be accurately reported and therefore the final prevalence calculation. The COMP acknowledged the discussion however concluded that the condition could be described as a stage or degree of a much broader condition which is optic nerve atrophy.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 14 June 2017, prior to final opinion.

2.1.10. - EMA/OD/029/17

Treatment of neuroblastoma

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 30 May 2017, prior to responding to the list of issues.

2.2. For discussion / preparation for an opinion

2.2.1. (S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine - EMA/OD/037/17

PhaRA bvba; Treatment of gastrointestinal stromal tumours

COMP coordinator: Katerina Kopečková

The Committee agreed that the condition, gastrointestinal stromal tumours, 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-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine was considered justified based on preliminary clinical data demonstrating that patients affected by the condition respond to treatment.

The condition is chronically debilitating and life-threatening, in particular due to the high rate of relapse and development of metastatic disease resulting in a poor survival.

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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing (S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrated clinical responses in patients, who have relapsed or were refractory after treatment with best standard of care including authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for (S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine, for treatment of gastrointestinal stromal tumours, was adopted by consensus.

2.2.2. - EMA/OD/057/17

Treatment of glioma

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

2.2.3. - EMA/OD/054/17

Treatment of spinal cord injury

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

2.2.4. - EMA/OD/050/17

Treatment of myelodysplastic syndromes

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

2.2.5. Autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor - EMA/OD/045/17

Celgene Europe Limited; Treatment of diffuse large B-cell lymphoma

COMP coordinator: Fernando Méndez Hermida

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

The intention to treat the condition with the medicinal product containing autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor was considered justified based on clinical data showing that complete responses may be achieved in patients with disease relapsed and refractory to the second line treatment.

The condition is chronically debilitating due to involvement of single or multiple nodal or extra nodal sites, including the gastrointestinal tract and bone marrow and life-threatening with 5-year survival rates reported as low as 26% for the high risk patients.

The condition was estimated to be affecting approximately 4.3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that patients who are relapsed and refractory to the second line treatment achieved either partial or complete responses. The overall response rate compared favourably at 3 months of treatment to that of the currently authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor, for treatment of diffuse large B-cell lymphoma, was adopted by consensus.

2.2.6. *Bacillus subtilis* Oxalate decarboxylase - EMA/OD/058/17

Allena Pharmaceuticals Ireland Limited; Treatment of primary hyperoxaluria

COMP coordinator: Kerstin Westermark

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

The intention to treat the condition with the medicinal product containing *Bacillus subtilis* oxalate decarboxylase was considered justified based on non-clinical data demonstrating a reduction in oxalate levels, reduced nephrocalcinosis and improved survival.

The condition is life-threatening and chronically debilitating due to recurrent nephrolithiasis and progressive nephrocalcinosis leading to renal insufficiency. The majority of the patients develop end stage renal disease during the 3rd to 5th decade of life.

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 that has been authorised in the European Union for patients affected by the condition.

A positive opinion for *Bacillus subtilis* oxalate decarboxylase, for treatment of primary hyperoxaluria, was adopted by consensus.

2.2.7. - EMA/OD/053/17

Treatment of primary mitochondrial myopathy

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

2.2.8. - EMA/OD/044/17

Treatment of lung allograft dysfunction associated with lung transplantation

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

2.2.9. - EMA/OD/036/17

Treatment of sickle cell disease

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

2.2.10. - EMA/OD/056/17

Treatment of basal cell carcinoma Nevus syndrome (Gorlin syndrome)

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

2.2.11. - EMA/OD/003/17

Treatment of N-acetylglutamate synthase deficiency

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

2.2.12. - EMA/OD/327/16

Treatment in cardiopulmonary by-pass

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

2.2.13. - EMA/OD/052/17

Treatment of hepatocellular carcinoma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to respond in writing before the Committee July meeting.

2.2.14. - EMA/OD/043/17

Treatment of mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome)

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

2.2.15. Polyphenyl(disodium 3-O-sulfo-beta-D-glucopyranuronate)-(1→3)-beta-D-galactopyranoside - EMA/OD/048/17

SFL Regulatory Affairs Consulting Ltd; Treatment of anti-MAG neuropathy

COMP coordinator: Melinda Sobor

The Committee agreed that the condition, anti-MAG neuropathy, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing poly phenyl(disodium 3-O-sulfo-beta-D-glucopyranuronate)-(1→3)-beta-D-galactopyranoside was considered justified based on preclinical studies supporting the reduction of anti-MAG antibody activity in a model of the condition.

The condition is chronically debilitating due to progressive ataxia or sensorimotor deficits.

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

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

A positive opinion for polyphenyl(disodium 3-O-sulfo-beta-D-glucopyranuronate)-(1→3)-beta-D-galactopyranoside, for treatment of anti-MAG neuropathy, was adopted by consensus.

2.2.16. - EMA/OD/049/17

Prevention of bronchopulmonary dysplasia

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

2.2.17. Retinol - EMA/OD/051/17

orphanix GmbH; Prevention of Retinopathy of Prematurity

COMP coordinator: Armando Magrelli/Olimpia Neagu

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

The intention to prevent the condition with the medicinal product containing retinol was considered justified based on published clinical studies demonstrating significantly reduced

risk of development of retinopathy in patients at risk who received an intramuscular injection of retinol.

The condition is chronically debilitating due to severe eyesight impairment in some patients and a risk of blindness.

The population of patients eligible for prevention of the condition was estimated to be approximately 1.4 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 prevention that has been authorised in the European Union for the population at risk of developing the condition.

A positive opinion for retinol, for treatment of retinopathy of prematurity, was adopted by consensus.

2.2.18. Tirapazamine - EMA/OD/038/17

PhaRA bvba; Treatment of hepatocellular carcinoma

COMP coordinator: Bożenna Dembowska-Bagińska

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

The intention to treat the condition with the medicinal product containing tirapazamine was considered justified based on preliminary clinical data showing prolonged duration of the complete response induced.

The condition is life-threatening and chronically debilitating due to increased mortality and liver dysfunction. Median survival without therapy can be greater than 36 months for stage 0 and A, 16 months for stage B, 4-8 months for stage C and less than 4 months for stage D.

The condition was estimated to be affecting approximately 1.5 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 have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing tirapazamine will be of significant benefit to those affected by the condition. The sponsor has provided preclinical and clinical data that would support an improved response to currently used treatments in this condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for tirapazamine, for treatment of hepatocellular carcinoma, was adopted by consensus.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

None

2.5. Appeal

None

2.6. Nominations

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

COMP coordinators were appointed for 37 applications submitted.

2.7. Evaluation on-going

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

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of myasthenia gravis

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

3.1.2. -

Treatment of mercury toxicity

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

3.1.3. -

Treatment of acute hepatic porphyria

The Committee was briefed on the significant benefit issues in preparation of the July meeting.

3.1.4. -

Treatment of Prader-Willi syndrome

The Committee was briefed on the significant benefit issues in preparation of the July meeting.

3.1.5. -

Treatment of plasminogen deficiency

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

3.1.6. -

Treatment of graft-versus-host disease

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

3.2. Finalised letters

3.2.1. -

Treatment of haemophilia A

The finalised letter was circulated for information.

3.2.2. -

Prevention of graft-versus-host disease

The finalised letter was circulated for information.

3.2.3. -

Treatment of soft tissue sarcoma

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment in solid organ transplantation

The new request was noted.

3.3.2. -

Treatment of haemophilia A

The new request was noted.

3.3.3. -

Treatment of metaphyseal chondrodysplasia, Schmid-type

The new request was noted.

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

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

None

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

4.2.1. - ciclosporin – EMEA/OD/106/05, EU/3/06/360, EMEA/H/C/004411

Santen Oy; Treatment of vernal keratoconjunctivitis

The COMP discussed the responses presented by the sponsor in writing and during the oral hearing. The status of the procedure at CHMP was noted.

4.2.2. - alpha-1-antitrypsin – EMEA/OD/054/04, EU/3/04/244, EMEA/H/C/003934

Kamada BioPharma Limited; Treatment of emphysema secondary to congenital alpha-1-antitrypsin deficiency

The status of the procedure at CHMP was noted.

4.2.3. - midostaurin – EMEA/H/C/004095

Novartis Europharm Ltd;

a) Treatment of mastocytosis, EMA/OD/016/10, EU/3/10/765

b) Treatment of acute myeloid leukaemia, EMEA/OD/028/04, EU/3/04/214

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

4.2.4. - telotristat ethyl – EMEA/OD/047/09, EU/3/09/661, EMEA/H/C/003937

Ipsen Pharma; Treatment of carcinoid syndrome

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to respond in writing before the Committee July meeting.

4.2.5. - lutetium 177Lu dotatate – EMEA/OD/093/07, EU/3/07/523, EMEA/H/C/004123

Advanced Accelerator Applications; Treatment of gastro-entero-pancreatic neuroendocrine tumours

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to respond in writing before the Committee July meeting.

4.2.6. Adcetris - Brentuximab vedotin – Type II variation - EMA/OD/100/11, EU/3/11/939, EMEA/H/C/002455/II/0048

Takeda Pharma A/S - Denmark; Treatment of cutaneous T-cell lymphoma

CHMP rapporteur: Paula Boudewina van Hennik; CHMP co-rapporteur: Jan Mueller-Berghaus

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.

4.2.7. Soliris - eculizumab – Type II variation - EMEA/OD/062/14, EU/3/14/1304, EMEA/H/C/000791/II/0090

Alexion Europe SAS - France; Treatment of myasthenia gravis

CHMP rapporteur: Jorge Camarero Jiménez

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to respond in writing before the Committee July meeting.

4.3. Appeal

None

4.4. On-going procedures

COMP co-ordinators were appointed for 37 applications.

4.5. Public Summary of Opinions

The draft public summaries of the COMP opinions adopted last month were endorsed for publication on the EMA website.

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

5.1. After adoption of CHMP opinion

None

5.2. Prior to adoption of CHMP opinion

5.2.1. Blincyto (blinatumomab) - Type II variation – EMEA/OD/029/09, EU/3/09/650, EMEA/H/C/003731/II/0011

Amgen Europe BV - The Netherlands; Treatment of acute lymphoblastic leukaemia

CHMP rapporteur: Alexandre Moreau; CHMP co-rapporteur: Daniela Melchiorri

The status of the procedure at CHMP was noted.

5.2.2. Lynparza - Olaparib – EMEA/OD/063/07, EU/3/07/501, EMEA/H/C/003726/X/0016/G

AstraZeneca AB - Sweden; Treatment of ovarian cancer

CHMP rapporteur: Alexandre Moreau; CHMP co-rapporteur: Bart Van der Schueren;

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

5.3. Appeal

None

5.4. On-going procedures

Documents were circulated in MMD.

Document(s) tabled:
Review of orphan designation for OMP for MA extension - On-going procedures

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

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the COMP

7.1.1. Strategic Review & Learning meetings

The Committee was informed that the next Strategic Review & Learning meeting will be host by Portugal and held in Lisbon on 19-21 September 2017.

7.1.2. Protocol Assistance Working Group

The working group on Protocol Assistance met on 13 June 2017.

7.1.3. Preclinical Models Working Group

The working group on Preclinical Models met on 15 June 2017.

7.1.4. Conditions Steering Group

The Conditions Steering Group met on 14 June 2017.

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. PDCO/COMP Working Group

Cancelled

7.2.2. Recommendations on eligibility to PRIME – report from CHMP

Documents were circulated in MMD.

Document(s) tabled:
PRIME eligibility requests - list of adopted outcomes May 2017

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

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

PCWP/HCPWP joint meeting – 27/28 June 2017

Documents were circulated in MMD.

Document(s) tabled:
Draft Agenda of the PCWP/HCPWP joint meeting – 27/28 June (EMA/213892/2017)

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

Presentation on EC studies on pharmaceutical incentives

The economic study on pharmaceutical incentives conducted by the Commission was presented. This included: objectives, timelines and methodology.

Notes: To be presented by EC representative

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

The draft Agenda of EMA/FDA teleconference on Orphan Medicines May 16, 2017 is available in MMD for information.

Document(s) tabled:
Draft Agenda of EMA/FDA teleconference on Orphan Medicines May 16, 2017

Notes: Monthly teleconference

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. The 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

7.7.1. COMP Work Plan 2017

Documents were circulated in MMD.

Document(s) tabled:
COMP Work Plan 2017

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2017

An updated list of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2017 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. Presentation "Bridging the regulator and the payer world, how far are we?"

A presentation on payer organisation in EU and payer and regulator collaboration was held.

8.2. EMA Business Pipeline activity and Horizon scanning

Documents were circulated in MMD.

Document tabled:
Upcoming Q2/2017 Update of the Business Pipeline report for the human scientific committees

List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 13-15 June 2017 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bruno Sepodes	Chair	Expert recommended by EMA	No interests declared	
Brigitte Blöchl-Daum	Member	Austria	No interests declared	
Lyubina Racheva Todorova	Member	Bulgaria	No interests declared	
Dinko Vitezic	Member	Croatia	No restrictions applicable to this meeting	
Katerina Kopeckova	Member	Czech Republic	No restrictions applicable to this meeting	
Jens Ersbøll	Member	Denmark	No interests declared	
Vallo Tillmann	Member	Estonia	No interests declared	
Karri Penttilä	Member	Finland	No interests declared	
Annie Lorence	Member	France	No interests declared	
Nikolaos Sypsas	Member	Greece	No restrictions applicable to this meeting	
Melinda Sobor	Member	Hungary	No interests declared	
Sigurdur B. Thorsteinsson	Member	Iceland	No interests declared	
Geraldine O'Dea *via TC*	Member	Ireland	No interests declared	
Armando Magrelli	Member	Italy	No interests declared	
Irena Rogovska	Member	Latvia	No interests declared	
Aušra Matulevičienė	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Robert Nistico	Member	Malta	No interests declared	
Violeta Stoyanova-Beninska	Member	Netherlands	No interests declared	
Ingrid Wang	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	
Fernando Mendez Hermida	Member	Spain	No interests declared	
Dan Henrohn	Member	Sweden	No restrictions applicable to this meeting	
Daniel O'Connor	Member	United Kingdom	No interests declared	
Pauline Evers	Member	Patients' Organisation Representative	No interests declared	
Lesley Greene	Member (Vice-Chair)	Patients' Organisation Representative	No interests declared	
Kerstin Westermark	Member	Expert recommended by EMA	No participation in final deliberations and voting on:	5.2.2.[1]
Virginie Hivert	Expert - in person*	Patients' Organisation Representative	No restrictions applicable to this meeting	
Simon Pinnell	Expert - via telephone*	Patients' Organisation Representative	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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

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/

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/