24 May 2018
EMA/COMP/171165/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Orphan Medicinal Products (COMP)

Minutes for the meeting on 17-19 April 2018

Chair: Bruno Sepodes – Vice-Chair: Lesley Greene

17 April 2018, 09:00-19:30, room 2F

18 April 2018, 08:30-19:30, room 2F

19 April 2018, 08:30-13:00, 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).

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1. Intro duction

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. 23 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 17-19 April 2018 was adopted with no amendments.

1.3. Adoption of the minutes

The minutes for 13-15 March 2018 were adopted with no amendments and will be published on the EMA website.

2. Applications for orphan medicinal product designation

2.1. For opinion

2.1.1. - EMA/OD/259/17

Treatment of acute myeloid leukaemia

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

- Significant benefit

The arguments on significant benefit are based mainly on safety arguments and on non-clinical studies. It is well known that extrapolation from non-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 is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from conducted studies engaging in a data driven discussion

in order to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan indication.

In the written response, and during an oral explanation before the Committee on 18 April 2018, the sponsor provided new *in vitro* data on cardiotoxicity, further elaborated on an indirect comparison of the efficacy of the proposed product and other chemotherapeutics in the relapsed/ refractory acute myeloid leukaemia setting. With regard to the *in vitro* data, the COMP was of the opinion that extrapolation from non-clinical studies cannot fully predict the safety of a product in its clinical setting, thus other relevant data is required to justify safety arguments. With regard to the indirect comparison in the relapsed/ refractory AML setting the COMP considered that the methodology employed for calculating the treatment effect of the comparators was flawed as no discussion on the comparability of populations, interventions, comparators, endpoints, trial methodologies was attempted. In conclusion, the Committee was of the opinion that the applicant failed to establish the significant benefit of the proposed product over the authorised counterparts.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 18 April 2018, prior to final opinion.

2.1.2. H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-Actinium - EMA/OD/252/17

Dr. Regenold GmbH; Treatment of glioma

COMP coordinator: Dinko Vitezic

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of glioma, the sponsor should further elaborate on the clinical data that was presented with similar radiolabelled substance P products (different chelator, or different radionuclide) and how this data can be extrapolated to the proposed product H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-actinium. In addition, sponsor is asked to provide a literature discussion on the influence of a change in chelator or radionuclide on the efficacy of radiolabelled substance P.

- Significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the clinical studies in the refractory glioblastoma multiforme patient population generated with similar radiolabelled substance P products (different chelator, or different radionuclide) and how this data can be extrapolated to the proposed product H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-actinium. In addition, sponsor is asked to provide a literature discussion on the influence of a change in chelator or radionuclide on the efficacy of radiolabelled substance P.

In the written response, the sponsor clarified that some of the preliminary clinical data were generated with a medicinal product that contained the same vector peptide and the chelator DOTA. The data generated with the radiopharmaceutical containing DOTA and radionuclide 213Bi showed that treated patients survived for longer when indirectly compared to clinical data generated with the currently authorised products. The COMP accepted this level of

evidence to support medical plausibility and significant benefit for the purpose of orphan designation. The oral explanation was cancelled.

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

The intention to treat the condition with the medicinal product containing H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-actinium was considered justified based on preliminary clinical data showing that treatment with the product improved overall survival.

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

The condition was estimated to be affecting approximately 2.6 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-actinium will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data demonstrating that treatment with the product improved overall survival. Indirect comparisons showed that the preliminary overall survival results compared favourably with data from authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-actinium, for treatment of glioma, was adopted by consensus.

2.1.3. Autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor - EMA/OD/260/17

Celgene Europe Limited; Treatment of follicular lymphoma

COMP coordinator: 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:

- Significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from any non-clinical or clinical data in follicular lymphoma to justify either clinically relevant data or a major contribution to patient care.

In the absence of more data in follicular lymphoma the significant benefit cannot be established.

In the written response, and during an oral explanation before the Committee on 17 April 2018, the sponsor proposed a potential clinically relevant advantage, specifically in the subpopulation third line 3B disease. Some longer follow-up data for the two patients with R/R FL3B was added to the application in the supplementary responses, as well as some additional *in vitro* data. With respect to the clinical data, it was noted that subjects remain

in complete remission after at least 269 days and 547, respectively. The applicant is pointing out that these two patients are fifth line, and therefore have practically exhausted available options. An indirect comparison versus pixantrone was also provided in R/R DLBCL and FL3B , with the sponsor arguing that has more than double remission rates in the comparison performed (CR 20% vs 56% for the proposed product). The COMP considered the long-duration of responses seen in follicular lymphoma type 3B patients, who had relapsed or were refractory to multiple previous lines of existing treatments, would be considered as a clinically relevant advantage.

A separate argument put forward is with regards to a major contribution to patient care, where the sponsor juxtaposes up to 18 infusions of pixantrone within approximately 6 months versus 1 infusion required by . The major contribution to patient care argument was not supported by clinical outcomes, such adherence or quality of life improvements, and therefore was not considered acceptable.

The Committee agreed that the condition, follicular 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 preliminary clinical observations in relapsed/refractory patients who responded to treatment with the proposed product.

The condition is life-threatening and chronically debilitating due to lymphadenopathy, splenomegaly, bone marrow dysfunction and the potential of transformation to aggressive lymphoma.

The condition was estimated to be affecting approximately 3.8 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing 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 preliminary clinical observations in relapsed/refractory patients who had durable responses. 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 follicular lymphoma, was adopted by consensus.

2.1.4. - EMA/OD/196/17

Treatment of biliary tract cancer

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 3 April 2018, prior to responding to the list of issues.

2.1.5. - EMA/OD/250/17

Treatment of invasive aspergillosis

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for the treatment of invasive aspergillosis, the sponsor is invited to discuss the rationale of extrapolating the results of studies in preventive setting to a therapeutic use.

The discussion should be supported by data and should take into account the clinical differences between preventive and therapeutic setting, and the plasma and tissue levels needed for the active substance to be efficacious in invasive aspergillosis.

- Significant benefit

In order to justify the significant benefit, the sponsor is invited to provide any available data in comparison with the products authorised for the treatment of invasive aspergillosis, including the active substance in the currently available formulations.

In the written response, and during an oral explanation before the Committee on 18 April 2018, the sponsor further discussed possible extrapolations of efficacy mainly based on pharmacokinetic data in comparison with the current oral formulation of the product but the Committee considered that more data would be needed.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 19 April 2018, prior to final opinion.

2.1.6. Itraconazole - EMA/OD/251/17

Galephar M/F; Prevention of invasive aspergillosis

COMP coordinator: Nikolaos Sypsas

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

In order to justify the significant benefit, the sponsor is invited to provide any available data in comparison with the products authorized for the treatment of invasive aspergillosis, including itraconazole in the currently available formulations.

In the written response, and during an oral explanation before the Committee on 18 April 2018, the sponsor further discussed the potential significant benefit of itraconazole (ITZ) for prevention of invasive aspergillosis.

Regarding comparison with oral ITZ, the sponsor presented pharmacokinetic data from clinical studies showing that ITZ levels in alveolar macrophages and epithelial lining fluid obtained with the proposed formulation for inhalation (ITZ-DPI) are higher than those obtained with oral ITZ, which would ensure comparable efficacy. On the other hand, ITZ-DPI administration resulted in lower plasma levels of ITZ than the oral formulation, offering the potential of a better safety profile. The sponsor also presented some preliminary data from a phase I study showing good tolerability of the proposed formulation for inhalation, with lack of bronchospasm, dyspnoea, cough, or throat irritation.

The sponsor then further discussed the non-clinical data in immuno-compromised BALB/c mice with pulmonary infection of aspergillus fumigatus where inhaled ITZ and oral voriconazole (VCZ) were used as prevention. In this study the higher of the two tested therapeutic doses of ITZ was more efficacious than voriconazole in clearing aspergillus infection and in increasing survival of infected mice.

The COMP considered that the assumption of significant benefit at this stage can be justified based on better preliminary efficacy than voriconazole in non-clinical studies and based on potential better safety than the currently authorised products for the prevention of invasive aspergillosis that are administered intravenously or orally.

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

The intention to prevent the condition with the medicinal product containing itraconazole was considered justified based on non-clinical studies showing clearance of aspergillus fumigatus infection and improved survival in valid models of the condition.

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

The population of patients eligible for prevention of the condition was estimated to be less than 2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of prevention of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing itraconazole will be of significant benefit to the population at risk of developing the condition. The sponsor has provided non-clinical data in valid models of the condition, showing higher clearance of aspergillus fumigatus infection and better survival than some of the current standard of care. In addition the inhalation route of the proposed product, resulting in low systemic concentration, may offer the potential of better safety than the currently authorised products. The Committee considered that this constitutes a clinically relevant advantage for the patients affected by the condition.

A positive opinion for itraconazole, for prevention of invasive aspergillosis, was adopted by consensus.

2.1.7. - EMA/OD/223/17

Treatment of multiple myeloma

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

- Intention to diagnose, prevent or treat

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

- the relevance of the nonclinical model used for the treatment of multiple myeloma, and the interpretation of the results obtained in the experiments,

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

• Number of people affected

The sponsor is basing their prevalence calculation on a partial prevalence of 5years obtained from Globocan and European Union Cancer Database. The sponsor is instead requested to recalculate the point prevalence.

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

• Significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit over authorised medicinal products for the proposed orphan indication.

In the written response, and during an oral explanation before the Committee on 18 April 2018, the sponsor provided a revised prevalence calculation of 4.4 in 10,000 which reflected a more current estimate for the condition. The COMP accepted the revised calculation.

Concerning the medical plausibility and the significant benefit the sponsor did not supply any additional data although they clarified that they had conducted some clinical work in other haematological malignancies in the clinical setting but not in multiple myeloma. The COMP therefore considered that there continued to be inadequate data to support the medical plausibility and significant benefit assessment at the time of an initial orphan designation. The COMP therefore continued to be of the opinion that it could not recommend granting of the orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 19 April 2018, prior to final opinion.

2.1.8. - EMA/OD/256/17

Treatment of glioma

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

• Significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit over authorised medicinal products for the proposed orphan indication.

In the written response, and during an oral explanation before the Committee on 17 April 2018, the sponsor further elaborated on the issue of significant benefit. It was argued that there are no medicinal products authorised in refractory patients, however the COMP was of the opinion that efficacy in refractory patients would need to be demonstrated in order to conclude on significant benefit. The sponsor could not present additional efficacy data and the COMP considered that there was insufficient evidence to support significant benefit for the purpose of orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 18 April 2018, prior to final opinion.

2.1.9. Equine immunoglobulin F(ab')2 fragments targeting Shiga toxin - EMA/OD/248/17

Chemo Research S.L.; Prevention of haemolytic uraemic syndrome

COMP coordinator: Armando Magrelli

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

- Condition

While the proposal to develop the product specifically in "STEC-HUS" is understood, the sponsor is invited to broaden the proposed condition to "HUS". This is considered on the basis of common features shared between primary and secondary cases of HUS, and the fact that "distinct" medical entities are generally considered valid for designation in the EU regulatory framework.

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of Shiga-Toxin Producing *Escherichia Coli* Haemolytic Uremic Syndrome, a secondary form of HUS, the sponsor should further elaborate on:

- The presence of HUS manifestations in the studied infection model,
- The relevance of survival improvements seen in the STEC infection model for the treatment (not prevention) indication as applied for designation.
- The interest of developing the product in STEC infection rather than STEC-HUS.

- Prevalence

The sponsor is invited to submit a prevalence calculation covering all primary and secondary cases of HUS.

In the written response, and during an oral explanation before the Committee on 18 April 2018, the sponsor clarified that the product was to be administered in patients with (bloody) diarrhoea, after a positive identification of shiga toxin in the stools. This would be before the onset of any complication of HUS. The COMP accepted that "prevention of HUS" would be the appropriate condition for orphan designation.

During the oral explanation the sponsor also clarified that the non-clinical model manifested renal injury, which is a salient feature of HUS. In that model, survival was significantly improved upon administration of the product. Therefore the medical plausibility for the prevention of HUS was considered acceptable by the COMP.

With regards to the prevalence criterion, the COMP considered that based on the mechanism of action of the product, the population eligible for prevention would refer to the annual number of infections by Shiga-toxin producing pathogens. It was considered that this would be primarily Shiga-toxin producing *Echerichia coli*, and exceptionally *Shigella Dysenteriae*. The European Centre for Disease Prevention and Control notification rate for STEC-infections of the years 2014 (0.14 per 10,000) and 2015 (0.15 per 10,000) was considered to be the basis of estimating this population. An approximately 0.2 per 10,000 was concluded to also account for rare non-E.Coli HUS.

Finally, for the new proposed indication, no specifically authorised products were identified in the EU, and as such no significant benefit justification was considered necessary at the time of designation.

A strong recommendation of protocol assistance was also voiced during the meeting to help with quality, non-clinical, and clinical development.

Following review of the application by the Committee, it was agreed to rename the indication to prevention of haemolytic uraemic syndrome.

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

The intention to prevent the condition with the medicinal product containing equine immunoglobulin $F(ab')_2$ fragments targeting Shiga toxin was considered justified based on improved survival seen in an *in vivo* infection model by Shiga-toxin producing *Escherichia coli*.

The condition is life-threatening and chronically debilitating in particular due to microangiopathic haemolytic anaemia, thrombocytopenia, and acute kidney injury, as well as neurological, intestinal or cardiac complications.

The population of patients eligible for prevention of the condition was estimated to be approximately 0.2 in 10,000 persons in the European Union, at the time the application was made. This was considered on the basis of European Centre for Disease Prevention and Control notification rates for Shiga-toxin producing *Escherichia coli* infection.

The sponsor has also established that there exists no satisfactory method of prevention in the European Union for the population at risk of developing the condition.

A positive opinion for equine immunoglobulin $F(ab')_2$ fragments targeting Shiga toxin, for prevention of haemolytic uraemic syndrome, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1. - EMA/OD/003/18

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 May meeting.

2.2.2. 1-(3-{4-[3,4-difluoro-2-trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4- c]pyridin-6-yl)ethan-1-one - EMA/OD/018/18

IQVIA RDS Ireland Limited; Treatment of Stargardt's disease

COMP coordinator: Dinah Duarte

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

The intention to treat the condition with the medicinal product containing 1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one was considered justified based on non-clinical data which

showed a reduction in bisretinoid levels and an improvement in photoreceptor neuroprotection.

The condition is chronically debilitating, in particular due to loss of visual acuity and central vision loss, which may progress to complete blindness.

The condition was estimated to be affecting approximately 1.3 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for 1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one, for treatment of Stargardt's disease, was adopted by consensus.

2.2.3. - EMA/OD/020/18

Treatment of Duchenne muscular dystrophy

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

2.2.4. Three human monoclonal antibodies against the Ebola virus glycoprotein - EMA/OD/008/18

Regeneron Ireland U.C.; Treatment of Ebola virus disease

COMP coordinator: Dinah Duarte;

Following review of the application by the Committee, it was agreed to rename the active substance to three human monoclonal antibodies against the Ebola virus glycoprotein.

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

The intention to treat the condition with the medicinal product containing three human monoclonal antibodies against the Ebola virus surface glycoprotein was considered justified based on non-clinical data in valid models of the condition showing improved survival with the proposed product.

The condition is life-threatening due to severe, fluid-depleting diarrhoea leading to hypotension and shock, with diffuse haemorrhage in the severe forms of the disease.

The condition was estimated to be affecting less than 0.001 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 three human monoclonal antibodies against the Ebola virus glycoprotein, for treatment of Ebola virus disease, was adopted by consensus.

2.2.5. Adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII - EMA/OD/010/18

Baxalta Innovations GmbH; Treatment of haemophilia A

COMP coordinator: Karri Penttila

The Committee agreed that the condition, haemophilia A, 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 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII was considered justified based on reduced bleeding in a non-clinical *in vivo* model of the proposed condition.

The condition is chronically debilitating due to recurrent bleeding in joints, gastrointestinal tract or in surgery, which may be also be life-threatening.

The condition was estimated to be affecting approximately 0.7 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data in valid *in vivo* models of the condition that demonstrate sustained restoration of plasma factor VIII activity levels and reduction of blood loss after a single administration, which may result in reduction of the need for on-demand and prophylactic replacement therapy. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII, for treatment of haemophilia A, was adopted by consensus.

2.2.6. Adeno-associated viral vector serotype 9 containing the human *CLN1* gene - EMA/OD/013/18

Abeona Therapeutics Europe SL; Treatment of neuronal ceroid lipofuscinosis

COMP coordinator: Giuseppe Capovilla

Following review of the application by the Committee, it was agreed to rename the active substance to adeno-associated viral vector serotype 9 containing the human *CLN1* gene.

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 adeno-associated viral vector serotype 9 containing the human *CLN1* gene was considered justified based on non-clinical *in vivo* data in a model of the condition where improved survival and motor function was noted.

The condition is life-threatening and chronically debilitating due to visual loss and epileptic seizures that rapidly became pharmacoresistant which are accompanied by psychomotor regression.

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.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing adeno-associated viral vector serotype 9 containing the human *CLN1* gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that demonstrate an improvement in survival and motor function in neuronal ceroidal lipofuscinosis Type 1 where no treatment exists. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated viral vector serotype 9 containing the human *CLN1* gene, for treatment of neuronal ceroid lipofuscinosis, was adopted by consensus.

2.2.7. Ambroxol hydrochloride - EMA/OD/236/17

Spedding Research Solutions SAS; Treatment of amyotrophic lateral sclerosis

COMP coordinator: Violeta Stoyanova

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 ambroxol hydrochloride was considered justified based on non-clinical *in vivo* data in a model of the condition which showed improvement in muscle function and survival.

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

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing ambroxol hydrochloride will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that demonstrate an improvement in muscle function and survival. The Committee considered that this constitutes a clinically relevant advantage.

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

2.2.8. Bardoxolone methyl - EMA/OD/011/18

Dr Stefan Blesse; Treatment of Alport syndrome

COMP coordinator: Brigitte Bloechl-Daum

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

The intention to treat the condition with the medicinal product containing bardoxolone methyl was considered justified based on improvements in estimated Glomerular Filtration Rate, observed in treated patients.

The condition is chronically debilitating and life-threatening in particular due to progressive renal failure and sensorineural hearing loss.

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

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

A positive opinion for bardoxolone methyl, for treatment of Alport syndrome, was adopted by consensus.

2.2.9. - EMA/OD/014/18

Treatment of epidermolysis bullosa

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

2.2.10. - EMA/OD/007/18

Treatment of haematopoietic stem cell transplantation

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

2.2.11. Daratumumab - EMA/OD/207/17

Janssen-Cilag International N.V.; Treatment of AL amyloidosis

COMP coordinator: Kerstin Westermark

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

The intention to treat the condition with the medicinal product containing daratumumab was considered justified based on preliminary clinical observations supporting reduction of free plasma light chains in treated patients affected by the condition.

The condition is chronically debilitating and life-threatening due to the accumulation of fibril deposits which disrupts normal tissue structure and function, notably in the heart, kidneys, liver, peripheral nervous system, gastrointestinal tract, and soft tissues.

The condition was estimated to be affecting approximately 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 daratumumab, for treatment of AL amyloidosis, was adopted by consensus.

2.2.12. - EMA/OD/006/18

Treatment of neurodegeneration with brain iron accumulation

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

2.2.13. - EMA/OD/001/18

Treatment of transthyretin-mediated amyloidosis

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

2.2.14. - EMA/OD/009/18

Treatment of growth hormone 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 May meeting.

2.2.15. - EMA/OD/015/18

Treatment of malignant cerebral 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 May meeting.

2.2.16. Glucagon analogue linked to a human immunoglobulin Fc fragment - EMA/OD/257/17

Hanmi Europe Limited; Treatment of congenital hyperinsulinism

COMP coordinator: Vallo Tillmann

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

The intention to treat the condition with the medicinal product containing glucagon analogue linked to a human immunoglobulin Fc fragment was considered justified based on non-clinical *in vivo* data where blood glucose levels were normalised.

The condition is life-threatening due to severe hypoglycaemia and chronically debilitating due to symptoms of hypoglycaemia such as pallor, sweat, tachycardia and neurological effects of chronic hypoglycaemia.

The condition was estimated to be affecting approximately 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 glucagon analogue linked to a human immunoglobulin Fc fragment, for treatment of congenital hyperinsulinism, was adopted by consensus.

2.2.17. - EMA/OD/012/18

Treatment of cystinuria

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

2.2.18. - EMA/OD/002/18

Treatment of transthyretin-mediated amyloidosis

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

2.2.19. Modified mRNA encoding human methylmalonyl-coenzyme A mutase encapsulated into lipid nanoparticles - EMA/OD/017/18

Pharma Gateway AB; Treatment of methylmalonic acidaemia

COMP coordinator: Fernando Méndez Hermida

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

Having examined the application, the COMP considered that the sponsor has established the following:

The intention to treat the condition with the medicinal product containing modified mRNA encoding human methylmalonyl-coenzyme A mutase encapsulated into lipid nanoparticles was considered justified based on *in vivo* models of the condition, showing reduction of plasma methylmalonic concentration and improvement in survival.

The condition is chronically debilitating and life-threatening due to neurological, gastroenterological and haematological complications.

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 modified mRNA encoding human methylmalonyl-coenzyme A mutase encapsulated into lipid nanoparticles will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data in *in vivo* models of the condition, supporting reduction of plasma methylmalonic concentrations and improvement in survival. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for modified mRNA encoding human methylmalonyl-coenzyme A mutase encapsulated into lipid nanoparticles, for treatment of methylmalonic acidaemia, was adopted by consensus.

2.2.20. - EMA/OD/005/18

Treatment of progressive supranuclear palsy

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

2.2.21. Synthetic double-stranded siRNA oligonucleotide targeted against transthyretin mRNA, with six phosphorothioate linkages in the backbone, and nine 2'-fluoro and thirty-five 2'-O-methyl nucleoside residues in the sequence, which is covalently linked via a phosphodiester group to a ligand containing three N-acetylgalactosamine residues - EMA/OD/019/18

Alnylam UK Limited; Treatment of transthyretin-mediated amyloidosis

COMP coordinator: Melinda Sobor

Following review of the application by the Committee, it was agreed to rename the indication to treatment of transthyretin-mediated amyloidosis and to rename the active substance to synthetic double-stranded siRNA oligonucleotide targeted against transthyretin mRNA, with six phosphorothioate linkages in the backbone, and nine 2'-fluoro and thirty-five 2'-O-methyl nucleoside residues in the sequence, which is covalently linked via a phosphodiester group to a ligand containing three N-acetylgalactosamine residues

The Committee agreed that the condition, transthyretin-mediated amyloidosis, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing synthetic double-stranded siRNA oligonucleotide targeted against transthyretin mRNA, with six phosphorothioate linkages in the backbone, and nine 2'-fluoro and thirty-five 2'-O-methyl nucleoside residues in the sequence, which is covalently linked via a phosphodiester group to a ligand containing three N-acetylgalactosamine residues was considered justified based on non-clinical *in vivo* data showing a reduction in levels of circulating transthyretin after administration of the proposed product.

The condition is life-threatening and chronically debilitating due to the development of polyneuropathy and cardiomyopathy.

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

A positive opinion for synthetic double-stranded siRNA oligonucleotide targeted against transthyretin mRNA, with six phosphorothioate linkages in the backbone, and nine 2'-fluoro and thirty-five 2'-O-methyl nucleoside residues in the sequence, which is covalently linked via a phosphodiester group to a ligand containing three N-acetylgalactosamine residues, for treatment of transthyretin-mediated amyloidosis, was adopted by consensus.

2.3. Revision of the COMP opinions

None

2.4. Amendment of existing orphan designations

2.4.1. Interferon beta – EMA/OD/080/07

Faron Pharmaceuticals Limited; Treatment of acute lung injury

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 at the May meeting.

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 thirty five upcoming applications.

2.7. Evaluation on-going

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

3. Requests for protocol assistance with significant benefit question

3.1. Ongoing procedures

3.1.1. -

Treatment of amyotrophic lateral sclerosis

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 sickle cell disease

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 soft tissue sarcoma

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

3.1.4. -

Treatment of acute myeloid leukaemia

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

3.1.5. -

Treatment of pemphigus

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

3.1.6. -

Treatment of small cell lung cancer

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

3.1.7. -

Treatment of tuberous sclerosis

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

3.1.8. -

Treatment of acute sensorineural hearing loss (acute acoustic trauma, sudden deafness and surgery induced acoustic trauma)

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

3.1.9. -

Treatment of Cushing's syndrome

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

3.1.10. -

Treatment of acute myeloid leukaemia

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

3.2. Finalised letters

3.2.1. -

Treatment of acute hepatic porphyria

The finalised letter was circulated for information.

3.2.2. -

Treatment of eosinophilic oesophagitis

The finalised letter was circulated for information.

3.2.3. -

Treatment of gastrointestinal stromal tumours

The finalised letter was circulated for information.

3.2.4. -

Treatment of pulmonary arterial hypertension

The finalised letter was circulated for information.

3.2.5. -

Treatment of partial deep dermal and full thickness burns

The finalised letter was circulated for information.

3.3. New requests

3.3.1. -

Treatment of Fabry disease

The new request was noted.

3.3.2. -

Treatment of acute myeloid leukaemia

The new request was noted.

3.3.3. -

Prevention of oral mucositis in head and neck cancer patients undergoing radiation therapy

The new request was noted.

3.3.4. -

Treatment of congenital hyperinsulinism

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. Tegsedi - inotersen – EMEA/H/C/004782, EMA/OD/098/13, EU/3/14/1250

IONIS USA Ltd; Treatment of ATTR amyloidosis

The status of the procedure at CHMP was noted.

4.2.2. –daunorubicin/ cytarabine - EMEA/H/C/004282, EMA/OD/070/11, EU/3/11/942

Jazz Pharmaceuticals Ireland Limited; Treatment of adults with high-risk acute myeloid leukaemia (AML)

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

4.2.3. - vestronidase alfa – EMA/OD/127/11, EU/3/12/973, EMEA/H/C/004438

Ultragenyx Germany GmbH; Treatment of mucopolysaccharidosis type VII (Sly syndrome)

The status of the procedure at CHMP was noted.

4.2.4. Exondys – eteplirsen – EMEA/OD/049/08, EU/3/08/586, EMEA/H/C/004355

AVI Biopharma International Ltd; Treatment of Duchenne muscular dystrophy

The status of the procedure at CHMP was noted.

4.2.5. - caplacizumab - EMEA/OD/109/08, EU/3/09/629, EMEA/H/C/004426

Ablynx NV; Treatment of thrombotic thrombocytopenic purpura

The status of the procedure at CHMP was noted.

4.2.6. - autologous t cells transduced with lentiviral vector containing a chimeric antigen receptor directed against cd19 – EMEA/H/C/004090

Novartis Europharm Limited;

Treatment of diffuse large B-cell lymphoma, EMA/OD/087/16, EU/3/16/1745

Treatment of B-lymphoblastic leukaemia/lymphoma, EMA/OD/187/13, EU/3/14/1266

The status of the procedure at CHMP was noted.

4.3. Revision of the COMP opinions

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

Santen Oy; Treatment of vernal keratoconjunctivitis

Based on a request from the European Commission for COMP to re-discuss its assessment, the COMP discussed the grounds for the opinion issued in January.

4.4. Appeal

None

4.5. On-going procedures

COMP co-ordinators were appointed for four applications.

4.6. Orphan Maintenance Reports

Documents were circulated in MMD.

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. Kalydeco - Ivacaftor – Type II variation – EMEA/H/C/002494/II/0069, EMEA/OD/010/08, EU/3/08/556

Vertex Pharmaceuticals (Europe) Ltd.; Treatment of cystic fibrosis

CHMP rapporteur: Concepcion Prieto Yerro

The status of the procedure at CHMP was noted.

5.2.2. Venclyxto – Venetoclax – Type II variation – EMEA/H/C/004106/II/0008, EMA/OD/124/12, EU/3/12/1080

AbbVie Limited; Treatment of chronic lymphocytic leukaemia

CHMP rapporteur: Filip Josephson

The status of the procedure at CHMP was noted.

5.2.3. Adcetris - Brentuximab vedotin – Type II variation – EMEA/H/C/002455/II/0055, EMEA/OD/073/08, EU/3/08/596

Takeda Pharma A/S;

Treatment of Hodgkin lymphoma

CHMP rapporteur: Paula Boudewina van Hennik

The status of the procedure at CHMP was noted.

5.2.4. Mozobil - Plerixafor – Type II variation – EMEA/H/C/001030/II/0034, EMEA/OD/045/04, EU/3/04/227

Genzyme Europe BV; Treatment to mobilize progenitor cells prior to stem cell transplantation

CHMP rapporteur: Paula Boudewina van Hennik

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 one application.

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

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the COMP

7.1.1. COMP Strategic Review & Learning meeting, 26-28 March 2018, Amsterdam, The Netherlands

Action: For information

7.1.2. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met on 17 April 2018

7.1.3. Condition Working Group

The working group on Condition met on 19 April 2018

7.1.4. Prevalence Working Group

The working group on Prevalence met on 18 April 2018

7.1.5. Committee for Orphan Medicinal Products Rules of Procedure

COMP Rules of Procedure Rev. 4 were adopted.

7.2. Coordination with EMA Scientific Committees or CMDh-v

7.2.1. Recommendations on eligibility to PRIME – report from CHMP

Documents were circulated in MMD.

Document tabled:
PRIME eligibility requests - list of adopted outcomes March 2018

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

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

None

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

None

7.4. Cooperation within the EU regulatory network

7.4.1. European Commission

None

7.5. Cooperation with International Regulators

7.5.1. Food and Drug Administration (FDA)

None

7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

7.5.3. 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

None

7.8. Planning and reporting

7.8.1. List of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2018

An updated list of all applications submitted/expected and the COMP coordinatorship distribution of valid applications submitted in 2018 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. Update on the EMA relocation

Action: For information

8.2. Preparedness of the system and capacity increase

The discussion was postponed.

8.3. EMA Business Pipeline activity and Horizon scanning

Document was circulated in MMD.

Document tabled:
Q1/2018 Update of the Business Pipeline report for the human scientific committees

8.4. Judgment of the General Court in Shire v EMA, T-80/16

Document was circulated.

Link to judgment: *Shire v EMA*, T-80/16, EU:T:2018:165

List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 17-19 April 2018 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	
Tim Leest	Member	Belgium	No interests declared	
Lyubina Racheva Todorova	Member	Bulgaria	No interests declared	
Dinko Vitezic	Member	Croatia	No restrictions applicable to this meeting	
Elisabeth Penninga	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	Member	Ireland	No interests declared	
Irena Rogovska	Member	Latvia	No interests declared	
Aušra Matulevičienė	Member	Lithuania	No interests declared	
Michel Hoffmann	Member	Luxembourg	No interests declared	
Robert Nistico	Member	Malta	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Violeta Stoyanova-Beninska	Member	Netherlands	No interests declared	
Ingrid Wang	Member	Norway	No interests declared	
Bożenna Dembowska-Bagińska	Member	Poland		
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	
Darius Matusevicius	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	
Mario Ricciardi	Member	Patients' Organisation Representative	No interests declared	
Kerstin Westermark	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Ingeborg Barisic	Member	Expert recommended by EMA	No restrictions applicable to this meeting	
Giuseppe Capovilla	Member	Expert recommended by EMA	No interests declared	
Virginie Hivert	Expert - in person*		No restrictions applicable to this meeting	
Elisabeth Johanne Rook	Expert - via telephone*		No interests declared	
A representative from the European Commission attended the meeting				

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Meeting run with support from relevant EMA staff				

*Experts were only evaluated against the product(s) they have been invited to talk about.

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/