1 October 2012
EMA/COMP/404711/2012 Rev.1 [1]
Human Medicines Development and Evaluation

Committee for Orphan Medicinal Products (COMP)

Minutes of the 10 - 11 July 2012 meeting held in Uppsala, Sweden

Note on access to documents

Documents marked with an asterisk (*) in these minutes cannot be released at present as they are currently in draft format or are classified as confidential. They will become public when adopted in their final form or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

1. Introduction

1.1 Adoption of the draft agenda EMA/COMP/404710/2012 Rev. 3

The agenda was adopted with no amendments.

1.2 Adoption of the draft minutes of the COMP meeting held on 12 - 13 June 2012 EMA/COMP/404710/2012

The minutes were adopted with minor corrections to point 3.2.

1.3 Conflicts of Interest

The Chair asked the Committee members to declare their potential conflict of interest.

The COMP secretariat was informed as follows:

-The sponsor/s for agenda points 2.1.8, 2.2.8, 2.2.14, 2.2.16[1] and 2.2.17[1] provide/s funding to EURORDIS. Nevertheless, no direct conflicts of interest have been identified for L. Greene and B. Byskov Holm, the volunteer patient representatives for EURORDIS.

-The sponsor/s for agenda points 2.1.8, 2.2.8 and 2.2.14 provide/s funding to EGAN, the organisation represented by P. Evers. Nevertheless, no direct conflicts of interest have been identified.

No further conflicts of interest were declared.

[1] Number corrected

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

2. Applications for orphan medicinal product designation

2.1 For opinion

2.1.1 Cytomegalovirus (CMV) DNA vaccine with plasmids expressing phosphoprotein 65 (pp65) and glycoprotein B (gB) genes

for prevention of CMV viremia and/or disease in patients with impaired cell-mediated immunity due to transplantation, Astellas Pharma Europe B.V. - EMA/OD/003/12

L. Fregonese (EMA Co-ordinator) and V. Stoyanova (COMP Co-ordinator) updated the Committee on the application.

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

- Orphan Indication

Previously the Committee designated “Prevention of cytomegalovirus disease in patients with impaired cell-mediated immunity deemed at risk”. The Committee is of the opinion that prevention of disease includes treating viremia and therefore “Prevention of CMV disease” is the suggested orphan indication for this application, in line with what has been previously designated by the Committee.

The sponsor was invited to justify the reasons for excluding patients with impaired cell-mediated immunity from causes other than transplantation (including e.g. HIV patients with very low CD4+ counts, some cancer patients). Previously the definition of “patients with cell-mediated immunity deemed at risk” has been accepted by the COMP as the target population for prevention of CMV disease and any exclusion of patient groups from this population should be based on a clear scientific rationale rather than on the potential therapeutic indication.

- Medical Plausibility

The sponsor was invited to briefly discuss the results of the phase I study.

- Prevalence

The sponsor was invited to re-calculate the prevalence taking into account the broadening of the patient population target of the orphan condition as suggested by the COMP.

In its written response, and during an oral explanation before the Committee on 10 July 2012, the sponsor stated that the relative importance of each antigen (referring to gB and pp65) may vary depending upon the risk group in each of the haematological stem cell transplantation (HSCT) and solid organ transplantation (SOT) populations. The sponsor also submitted updated prevalence calculations taking into consideration the remarks of the Committee.

The relative extent and clinical significance of the humoral and cell-mediated responses was discussed, with particular regard to the humoral response.

The time-lag of the antibody response was also discussed, with its clinical relevance and impact on the future development of the product and the possible position of the product in the prevention of CMV disease in the clinical setting.

In conclusion the COMP was of the opinion that the plausibility of the product is sufficiently justified, taking into account the evidence of stimulation of immune response presented and discussed by the sponsor. In addition, the medical plausibility is supported by the preliminary clinical efficacy data of the phase II study, showing a reduction of viremia in the treated patients and in related endpoints such as time to initial viremia, number of CMV episodes and duration of viremia.

For the purpose of orphan designation, the COMP considered that the active ingredient should be renamed as “covalently linked DNA plasmids coding for cytomegalovirus *phosphoprotein 65* and *glycoprotein B* genes”.

The Committee agreed that the condition, cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk, is a distinct medical entity and meets the criteria for orphan designation.

The target population for “prevention of cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk” was estimated to be less than 3 in 10,000 persons in the European Union, at the time the application was made. The sponsor has based the calculations on valid literature data and comprehensive databases, with an adequate geographic coverage of the EU.

The condition is life-threatening due to complications such as pneumonia, hepatitis, inflammation of the gastrointestinal tract and acute graft rejection in transplanted patients. It is the leading viral cause of morbidity and mortality in patients with human stem cell or solid organ transplantation, with direct damage resulting from viral invasion of different organs, and indirect effects on the immune system that increase the risk of other infections and promote acute graft rejection. The condition can be chronically debilitating in case of the development of long-term sequelae in the affected organs and in case of reduced graft survival.

Although satisfactory methods of prevention of the condition have been authorised in the European Union, sufficient justification has been provided that covalently linked DNA plasmids coding for cytomegalovirus phosphoprotein 65 and glycoprotein B genes may be of significant benefit to those at risk of developing the condition. This appears justified in particular with regards to a potential clinically relevant advantage based on the new mechanism of action, as the product is a first-in-class product designed for the prevention of cytomegalovirus disease through the stimulation of both humoral and cell-mediated immunity. This represents a potential significant benefit compared to the currently authorized preventive methods for the condition, which have a direct antiviral activity. The proposed product, either used alone or in combination with antiviral medicinal products, is expected to reduce the risk of cytomegalovirus disease and to reduce the need of antiviral treatment which carries several side-effects. The preliminary clinical results presented by the sponsor are encouraging toward the clinical efficacy of the product, in particular a phase II study, where reduction of viremia was noted in cytomegalovirus seropositive subjects undergoing haematopietic cells transplantation from matched related donors.

A positive opinion for covalently linked DNA plasmids coding for cytomegalovirus phosphoprotein 65 and glycoprotein B genes, for prevention of cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.1.2 **Humanised monoclonal antibody targeting P-selectin** for treatment of sickle cell disease, Quintiles Ireland Ltd - EMA/OD/026/12

S. Tsigkos (EMA Co-ordinator) and L. Gramstad (COMP Co-ordinator) updated the Committee on the application. The Committee was informed that there are currently 3 designations for this condition.

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

- Medical plausibility

P-selectin is recognized to be a key adhesion molecule in the initial inflammatory response common to several conditions. According to the sponsor, targeting P-selectin could represent an approach for the treatment of sickle cell disease. Nevertheless the preclinical data presented need to be further elaborated with regards to the non-specific mechanism of action (interfering with the inflammatory response claimed to be associated to this condition) and the absence of any relevant animal model specific for the proposed indication as applied for.

To establish if a scientific rationale exists for the development of humanised monoclonal antibody targeting P-selectin for treatment of sickle cell disease, the sponsor was invited to further elaborate on:

- the relevance of the preclinical model used with the parent antibody for the treatment of sickle cell disease;

- the absence of any proof of concept study either with the parent antibody or the specific product subject of this application in any clinically relevant preclinical model or preliminary clinical settings.

- Justification of significant benefit

The arguments on significant benefit are based on the new mechanism of action. The sponsor was invited to elaborate on the clinically relevant advantage or major contribution to patient care that the proposed product may hold for the patients affected by the proposed condition, and to position the proposed treatment vis a vis the authorised product for this indication.

In its written response, and during an oral explanation before the Committee on 10 July 2012, the sponsor satisfactorily elaborated on the preclinical model. The sponsor also defended the validity of the model as highly relevant and referred to literature data with surrogate antibodies targeting P selectin.

The sponsor also presented further data with the parent antibody. With regards to the significant benefit, the sponsor elaborated that given the different mechanism of action the product may be used in addition to currently authorised treatments, and stressed that the only one approved drug for SCD vasoocculusive pain crisis, hydroxycarbamide, works by increasing levels of foetal haemoglobin.

For the purpose of orphan designation, the COMP considered that the active ingredient should be renamed as “humanised monoclonal antibody against P-selectin”.

The Committee agreed that the condition, sickle cell disease, is a distinct medical entity and meets the criteria for orphan designation. Sickle cell disease was estimated to be affecting approximately 1.3 in 10,000 persons in the European Union, at the time the application was made based on published literature studies. The condition is chronically debilitating and life-threatening, in particular due to anaemia, vaso-occlusive ischemic incidences, and bacterial infections resulting in reduced survival. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that humanised monoclonal antibody against P-selectin may be of significant benefit to those affected by the condition. This is based on a novel mechanism of action that may result in reduction of vasooclusive crises and related complications. This is supported by preclinical data in valid models of the proposed condition as applied for.

A positive opinion for humanised monoclonal antibody against P-selectin, for treatment of sickle cell disease, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.1.3 **Recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein** for treatment of CD3-positive peripheral T-cell Lymphoma (PTCL) (leukemic, nodal, extranodal), AOP Orphan Pharmaceuticals AG - EMA/OD/047/12

L. Fregonese (EMA Co-ordinator) and D. O'Connor (COMP Co-ordinator) updated the Committee on the application.

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

- Orphan indication

The COMP recommends broadening the orphan indication to “treatment of peripheral T-cell Lymphoma (PTCL) (leukaemic, nodal, extranodal)”, as from previous designations of the same condition.

- Medical plausibility

The sponsor was invited to better describe the preclinical studies presented to support the medical plausibility. This includes:

- clarifying whether the proof-of-concept published preclinical studies presented by the sponsor in this section were performed with the product under consideration for this application. If this is not the case, the sponsor is invited to discuss how the products from these studies relate to the proposed product and how the results can be extrapolated to the proposed product.

- discuss the relevance of the preclinical model to the treatment of patients with peripheral T-cell lymphoma.

The sponsor was also invited to further discuss the preliminary clinical data, with particular regard to outcome in the patient with peripheral T-cell lymphoma.

- Significant benefit

The sponsor was invited to further discuss the grounds for significant benefit, taking into account the possible advantages of the proposed product as compared to what is at present used for the treatment of the condition.

In its written response, and during an oral explanation before the Committee on 10 July 2012, the sponsor clarified the issues raised and provided satisfactory arguments in response to the list of questions.

For the purpose of orphan designation, the COMP considered that the indication should be renamed as “treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated)”.

The Committee agreed that the condition, peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated), is a distinct medical entity and meets the criteria for orphan designation. Peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated) was estimated to be

affecting less than 1 in 10, 000 persons in the EU, at the time the application was made. The sponsor has based the calculations on valid literature data and comprehensive databases including Globocan and the Rarecare project, with an adequate geographic coverage of the EU.

The condition is chronically debilitating and life-threatening due to poor response to therapy and high rate of relapses shortly after first response to therapy. Five year overall survival is reported at average 25% to 40%, depending on sub-type, with most relapses occurring within 12 months. Clinical presentation and course vary from an indolent clinical behaviour for years in milder subtypes, to fulminant disease in aggressive sub-types.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein may be of significant benefit to those affected by the condition. This appears justified in particular with regards to a potential clinically relevant advantage based on the alternative mechanism of action, which specifically targets the CD3 receptor on T lymphocytes resulting in penetration of the diphtheria toxin into the cells. The sponsor has presented preclinical results supporting the antitumoral effects of the product, including one animal study in which administration of the product resulted in almost complete depletion of T-lymphocytes.

A positive opinion recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein, for treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated), was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.1.4 (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro- 1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid for treatment of Alagille syndrome, Albireo AB - EMA/OD/023/12

A. Corrêa Nunes (COMP Co-ordinator) updated the Committee on the application.

As agreed during the June meeting, a list of issues was sent to the sponsor for response. The sponsor was invited to re-calculate the prevalence based on relevant epidemiological studies and registers for the proposed orphan condition, and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations. The life-expectancy should be included in the calculation.

In its written response the sponsor recalculated the prevalence as per the COMP recommendations.

The Committee agreed that the condition, Alagille syndrome, is a distinct medical entity and meets the criteria for orphan designation. Alagille syndrome was estimated to be affecting not more than 0.3 in 10,000 persons in the European Union, at the time the application was made; this is based on a literature search conducted by the sponsor. The condition is chronically debilitating due to hepatic and cardiac dysfunction. Pruritus is a common symptom associated with cholestasis. Portal hypertension develops in up to 1/3 of patients. In 75% of patients life expectancy is around 20 years and death is associated with liver failure, cardiac problems and blood vessel abnormalities. There is, at present, no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro- 1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid, for treatment of Alagille syndrome, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation.

2.1.5 (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro- 1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid (A4250) for treatment of primary biliary cirrhosis, Albireo AB - EMA/OD/024/12

A. Corrêa Nunes (COMP Co-ordinator) updated the Committee on the application. The Committee was informed that there is currently 1 designation for this condition.

As agreed during the June meeting, a list of issues was sent to the sponsor for response. The sponsor was invited to re-calculate the prevalence based on recent published European relevant epidemiological studies and registers for the proposed orphan condition, and given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

In its written response the sponsor recalculated the prevalence as per the COMP recommendations.

The Committee agreed that the condition, primary biliary cirrhosis, is a distinct medical entity and meets the criteria for orphan designation. Primary biliary cirrhosis was estimated to be affecting not more than 1.5 in 10,000 persons in the European Union, at the time the application was made; the sponsor has based this on a literature search.

The condition is chronically debilitating due to pruritus which may be a very distressing symptom, usually occurring at night. Other common findings include hyperlipidemia, hypothyroidism, deficiency of fat-soluble vitamins and osteopenia. If the disease progresses, symptoms and signs of liver failure will develop including portal hypertension, ascites and hepatic encephalopathy. The condition is life – threatening due to a risk for liver failure including portal hypertension and due to risk of developing hepatocellular cancer. The estimated 10-year survival in patients can be as low as 57%.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro- 1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid may be of significant benefit to those affected by the condition due to a clinically relevant advantage associated with an alternative mode of action and the potential to be used in combination with cholestyramine. This has been supported by two non-clinical in vivo studies.

A positive opinion for (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl- 2,3,4,5-tetrahydro- 1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid (A4250), for treatment of primary biliary cirrhosis, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.1.6 **Humanized Monoclonal Antibody Against EGFR** for treatment of glioma, Abbott Laboratories - EMA/OD/049/12

S. Tsigkos (EMA Co-ordinator) and R. Elbers (COMP Co-ordinator) updated the Committee on the application. The Committee was informed that there are currently 26 designations for this condition.

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

- Justification of significant benefit

The arguments on significant benefit are based on a new mechanism of action and the potential improved efficacy in the condition based on a model showing add-on effects to temozolomide and radiotherapy. However, in the past ten years several phase 2 and phase 3 clinical trials have been performed in glioma patients with substances blocking the EGFR like tyrosine kinase inhibitors or EGFR specific monoclonal antibodies. Some of these studies had been performed on top of temozolomide and/or radiotherapy. All these studies had disappointing outcomes regarding relevant clinical endpoints like progression free survival (PFS) or overall survival (OS). The sponsor was invited to discuss the relevance of these published results for the expected benefit of this new antibody against EGFR. Furthermore, the sponsor was invited to discuss the potential influence of K-ras status on the activity of this new antibody against EGFR in glioma treatment.

In its written response the sponsor agreed with the Committee that previous trials have failed as noted, but argued that a different development outcome may be anticipated based on the target epitope. For the designation step, this justification was considered acceptable as it was supported by proof of concept data in relevant preclinical models.

The Committee agreed that the condition, glioma, is a distinct medical entity and meets the criteria for orphan designation. Glioma was estimated to be affecting approximately 1 in 10,000 persons in the European Union, at the time the application was made, based on the Globocan database.

The sponsor has provided satisfactory argumentation to establish that the condition is chronically debilitating, in particular due to compression of the surrounding brain structures leading to neurological deficits, and life-threatening with poor overall survival. Survival for glioblastoma multiforme patients is less than 5% at 5 years post diagnosis.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that humanised monoclonal antibody against epidermal growth factor receptor may be of significant benefit to those affected by the condition. This appears justified on the grounds of the clinically relevant advantage. This is based on preclinical data in a model that show improved inhibition of tumour growth when the product is used in combination with temozolomide and radiotherapy, compared to temozolomide and radiotherapy alone.

A positive opinion for humanised monoclonal antibody against epidermal growth factor receptor, for treatment of glioma, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

2.1.7 **N-Butyldeoxygalactonojirimycin** for treatment of Fabry disease, Actelion Registration Limited - EMA/OD/042/12

S. Tsigkos (EMA Co-ordinator) and A. Corrêa Nunes (COMP Co-ordinator) updated the Committee on the application. The Committee was informed that there are currently 3 designations for this condition.

As agreed during the June meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to elaborate on the prevalence. The sponsor is using birth prevalence reported in different studies in order to provide an estimation of the prevalence of the proposed condition. Given that the survival in patients with Fabry disease is less than the general population, it can be understood that this strategy leads to an overestimation of the prevalence. The sponsor was requested to provide an updated prevalence taking into consideration the duration of the condition as applied for.

In its written response the sponsor provided a literature-based calculation using a "simplified survival correction factor " applied to birth prevalence of 3/10,000 and arrived to a conclusion of up to 2.3 per 10,000 people in the EU.

The Committee agreed that the condition, Fabry disease, is a distinct medical entity and meets the criteria for orphan designation. Fabry disease was estimated to be affecting less than 2.3 in 10,000 persons in the European Union at the time the application was made, based on published literature studies.

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

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that N-Butyldeoxygalactonojirimycin may be of significant benefit to those affected by the condition. This is due to a clinically relevant advantage based on an alternative mechanism of action, which may offer an alternative to patients not responding or not eligible for treatment with currently authorised products for the condition. This alternative mechanism is supported by preclinical data.

A positive opinion for N-Butyldeoxygalactonojirimycin, for treatment of Fabry disease, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.1.8 **Recombinant human monoclonal antibody against activin receptor type IIB** for treatment of sporadic inclusion body myositis, Novartis Europharm Limited - EMA/OD/046/12

V. Saano (COMP Co-ordinator) updated the Committee on the application.

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

- Medical condition

Sporadic inclusion body myositis should be changed to inclusion body myositis or justified as a distinct medical entity (this is for the purposes of Orphan Medicinal Product designation and not a request for a definition of the proposed therapeutic indications).

- Prevalence

The sponsor was invited to re-calculate the prevalence calculation based on relevant epidemiological studies and registries for inclusion body myositis.

In its written response the sponsor asserted that because of the different aetiology (spontaneous vs hereditary with distinct mutations), pathophysiology (inflammation vs no inflammation), mean age of onset (>50 years vs 20-30 years) and disease presentation (quadriceps being the most commonly affected muscle group vs quadriceps spared) “sporadic inclusion body myositis” and “hereditary inclusion body myopathy” are different conditions. The sponsor also asserted that the original prevalence remains valid because “Inclusion Body Myositis” is sometimes used in place of “sporadic inclusion body myositis”.

The Committee concluded that “Inclusion Body Myositis” was a distinct medical entity. “Sporadic inclusion body myositis” should be considered as a subgroup of this medical entity. Hence the prevalence for sporadic inclusion body myositis should be added to the prevalence of hereditary inclusion body myopathy for the purpose of establishing the prevalence of the condition. In Europe the figure provided for this sum would be approximately 0.05 in 10,000 persons.

For the purpose of orphan designation, the COMP considered that the proposed indication should be amended to “treatment of inclusion body myositis”.

The Committee agreed that the condition, inclusion body myositis, is a distinct medical entity and meets the criteria for orphan designation”. Inclusion body myositis was estimated to be affecting approximately 0.05 in 10,000 persons in the European Union, at the time the application was made based on literature studies.

The condition is life-threatening due to the development of progressive weakness and atrophy of the distal and proximal muscles.

There is, at present, no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for recombinant human monoclonal antibody against activin receptor type IIB, for treatment of inclusion body myositis, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the Agency prior to submission of the application for marketing authorisation, particularly with regard to the clinical development of the product and that data that will be required for the submission of the marketing authorisation.

2.2 For discussion / preparation for an opinion[2]

2.2.1 For treatment of spinal cord injury - EMA/OD/088/12

S. Tsigkos (EMA Co-ordinator) and H. Metz (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 3 designations for this condition.

The Committee considered that the following issues require clarification by the sponsor:

- Proposed condition

2 The procedures under assessment discussed by the COMP are considered confidential. COMP meeting reports and subsequent minutes will contain additional details on these procedures once these are finalised. Access to documents in relation to these procedures is possible after marketing authorisation is granted according to the Agency policy on access to documents (EMA/127362/2006).

The sponsor is invited to amend the proposed indication to “treatment of traumatic spinal cord injury”.

- Prevalence

The sponsor is invited to recalculate the prevalence of traumatic spinal cord injury taking into account the duration of the condition.

The COMP adopted a list of issues that will be sent to the sponsor for a written response.

2.2.2 For treatment of acute lung injury - EMA/OD/062/12

L. Fregonese (EMA Co-ordinator) and M. Možina (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 6 designations for this condition.

The Committee considered that the following issues require clarification by the sponsor:

- Medical plausibility

To establish correctly if there exists a scientific rationale for the development of the product for the treatment of acute lung injury, the sponsor is invited to clarify whether the studies presented for supporting the medical plausibility are sponsor-generated or are literature studies.

In the latter case, the sponsor is invited to discuss how the sponsor’s product relates to the products used in the published studies. In addition the sponsor is invited to discuss the relevance of the preclinical studies.

In relation to the aforementioned studies, the sponsor is invited to further discuss the possible mechanism of action of the product in the observed responses in acute lung injury (ALI).

The sponsor presented several studies related to fibrosis in animal models. The sponsor is invited to clarify the relevance of the anti-fibrotic activity to the proposed condition.

- Summary of the development of the product

The sponsor is invited to further describe the development of the product in the proposed condition, including some more extended discussion on the planned clinical studies (e.g. planned protocol and feasibility).

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 its September meeting.

2.2.3 For treatment of cystic fibrosis - EMA/OD/052/12

L. Fregonese (EMA Co-ordinator) and J. Eggenhofer (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 25 designations for this condition.

The Committee considered that the following issues require clarification by the sponsor:

- Medical plausibility

To establish correctly if there exists a scientific rationale for the development of the proposed product for cystic fibrosis, the sponsor is invited to further elaborate on the relevance of the preliminary clinical data with the product as proposed in single dose studies in non-cystic fibrosis (CF) bronchiectasis patients for the treatment of cystic fibrosis.

The sponsor is invited to provide:

a) any available clinical data in patients with CF with the product as proposed for designation,

b) any data which could justify the sustained presence of the product over 24 hours in the lungs after using it once daily

c) to elaborate on the therapeutic advantage of the product in a sustained release formulation in continuous therapy

d) to discuss microbial resistance in the proposed setting.

- Justification of significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit by commenting on specific data obtained with the proposed product subject of this application. The sponsor should also discuss the clinical advantages compared to other inhalation products in the treatment of CF.

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 its September meeting.

2.2.4 **Elotuzumab** for treatment of multiple myeloma, Bristol-Myers Squibb Pharma EEIG - EMA/OD/061/12

L. Fregonese (EMA Co-ordinator) and R. Elbers (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 19 designations for this condition.

The Committee agreed that the condition, multiple myeloma, is a distinct medical entity and meets the criteria for orphan designation. Multiple myeloma was estimated to be affecting approximately 1.6 in 10,000 persons in the European Union, at the time the application was made. The sponsor has based the calculations on valid literature data and comprehensive databases, with an adequate geographic coverage of the EU.

The condition is life-threatening and chronically debilitating due to the accumulation of monoclonal myeolomatous cells in the bone marrow, causing disruption of the normal bone marrow function with pancytopenia and osteolysis. Opportunistic infections, hypercalcemia, and kidney failure are common clinical consequences of the disease. The median survival is 5 years.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that Elotuzumab may be of significant benefit to those affected by the condition. This appears justified in particular with regards to a potential clinically relevant advantage due to the new mechanism of action of the product, which targets a cell surface glycoprotein with homology to the CD2 family highly expressed in multiple myeloma cells. The assumption of potential clinically relevant advantage is supported by preclinical and preliminary clinical data showing increased antitumoral effect when the product is used in combination with some of the currently authorised treatments for the disease.

A positive opinion for Elotuzumab, for treatment of multiple myeloma, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.2.5 N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine (EC20) for diagnosis of folate receptor positive ovarian cancer, Endocyte Europe B.V. - EMA/OD/056/12

L. Fregonese (EMA Co-ordinator) and B. Dembowska-Bagińska (COMP Co-ordinator) summarised the application.

The Committee has considered the application for the designation of folic acid to be used with N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine for the diagnosis of folate receptor positive ovarian cancer.

The COMP expressed a favourable trend on the designation of the product as proposed, in the indication “diagnosis of positive folate receptor status in ovarian cancer”, as it improves N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine image quality in the assessment of folate receptor status of cancer lesions.

The COMP noted that there is complete overlap of the proposed orphan indication with the indication of the designation already obtained by the sponsor on 9 February 2012 for N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine and folic acid for diagnosis of positive folate receptor status in ovarian cancer (EU/3/12/958), which causes regulatory concerns.

The COMP adopted a list of issues that will be sent to the sponsor for a written response.

Post-meeting note:

Following receipt of the COMP list of questions the sponsor decided to withdraw the designation EU/3/12/958 on 16 July 2012. The Committee initiated a written procedure for adoption of the opinion.

The COMP draft summary report(*) EMA/COMP/399658/2012 with grounds for the positive opinion was circulated for adoption via written procedure on 17 July.

The Committee agreed that the condition, ovarian cancer, is a distinct medical entity and meets the criteria for orphan designation. For the purpose of orphan designation and to reflect the intended use of the product, the COMP considered that the orphan indication should be renamed as “diagnosis of positive folate receptor status in ovarian cancer”.

There exists scientific rationale for the development of folic acid to be used with N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine for the diagnosis of positive folate receptor status in ovarian cancer. Folic acid is intended to be used as pre-injection before the administration of N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine. The plausibility of the use of folic acid as pre-injection is based on the need of inducing a certain level of saturation of the folate receptors in non-tumour tissue to reduce the uptake of N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine by non-tumour tissue.

The population of patients eligible for diagnosis of positive folate receptor status in ovarian cancer was estimated to be not more than 1.3 in 10,000 persons per year in the European Union, at the time the application was made.

The sponsor has established that the condition is chronically debilitating and life threatening due to the spread of the cancer to extra-abdominal region that causes malignant pleural effusion and haematogenous metastases to the liver, spleen, or lung.

Currently several methods are considered satisfactory for the diagnosis of ovarian cancer, including physical examination, transvaginal ultrasound or abdominal/pelvic computer tomography (CT). Such diagnostic methods represent the current standard for diagnosis of ovarian cancer. Nevertheless, there is, at present, no satisfactory method of diagnosis that has been authorised in the European Union for positive folate receptor status in ovarian cancer.

A positive opinion for folic acid to be used with N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine, for diagnosis of positive folate receptor status in ovarian cancer, was adopted by consensus on 23 July 2012.

2.2.6 **Ketoconazole** for treatment of Cushing's syndrome, Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare - EMA/OD/084/12

L. Fregonese (EMA Co-ordinator) and V. Tillmann (COMP Co-ordinator) summarised the application. The Committee was informed that there is currently 1 designation for this condition.

The Committee agreed that the condition, Cushing's syndrome, is a distinct medical entity and meets the criteria for orphan designation. Cushing's syndrome was estimated to be affecting approximately 0.9 in 10,000 persons in the European Union, at the time the application was made. The sponsor has based the calculations on valid literature data.

The condition is life-threatening and chronically debilitating due to the consequences of hypercortisolism, including cardiovascular disease, diabetes, clotting disorders, muscular weakness and osteoporosis, and psychiatric conditions.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that ketoconazole may be of significant benefit to those affected by the condition. This appears justified in particular with regards to a potential clinically relevant advantage based on an alternative mechanism of action which allows: the use of the product for bridging to surgery or as an alternative when surgery is not possible; the use of the product in combination; and the use in sub-populations within the condition where other currently authorized medicinal products are not indicated. This is supported by preclinical literature and by clinical retrospective and prospective studies showing the efficacy of the product alone and in combination, including a recent study where administration of ketoconazole resulted in lowering cortisol levels in patients not responding to other treatments.

A positive opinion for Ketoconazole, for treatment of Cushing's syndrome, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the Agency prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.2.7 For treatment of sarcoidosis - EMA/OD/044/12

S. Tsigkos (EMA Co-ordinator), B. Sepodes (COMP Co-ordinator) and J. Eggenhofer (COMP Co-ordinator) summarised the application. The Committee was informed that there is currently 1 designation for this condition.

The Committee considered that the following issues require clarification by the sponsor:

- Medical plausibility

The data provided by the sponsor relates solely to the neuropathy component described to be associated to sarcoidosis. This is not sufficient to support the indication “treatment of sarcoidosis”. To establish correctly if there exists a scientific rationale for the development of the product for the treatment of sarcoidosis, the sponsor is invited to further elaborate on:

- the specificity of neuropathic pain as a clinical feature of sarcoidosis;

- the existence of data concerning preclinical models of sarcoidosis or other preclinical models that are related to direct manifestations of sarcoidosis (e.g. granuloma formation) besides neuropathic pain;

- the relevance of the preclinical models of surgically induced neuropathic pain in regards to the neuropathic pain developed in sarcoidosis patients;

- the preliminary clinical data pertaining to sarcoidosis patients with regards to any further endpoints available which are relevant for the specific condition subject of this application.

- Prevalence

The sponsor should justify the sources of the prevalence data and describe the methodology used for the prevalence calculation, and invited to re-calculate the prevalence based on relevant epidemiological studies and registries for the proposed orphan condition. Given the substantial uncertainty about many of the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

- Satisfactory methods

The sponsor is requested to clearly discuss the authorised medicines for the treatment of sarcoidosis in the EU.

- Justification of significant benefit

The arguments on significant benefit are based on a clinically relevant advantage based on potentially improved efficacy in the condition.

Taking also into account the previous sections, the sponsor is invited to elaborate and discuss the arguments provided on the significant benefit of the product vis a vis the approved medicines for sarcoidosis and also for the management of neuropathy associated with sarcoidosis.

The sponsor is also requested to elaborate on the available preliminary clinical data in patients with sarcoidosis, in particular with regards to the previous treatments received

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 its September meeting.

2.2.8 For treatment of Fragile X Syndrome - EMA/OD/059/12

S. Tsigkos (EMA Co-ordinator) and J. Torrent-Farnell (COMP Co-ordinator) summarised the application.

The Committee considered that the prevalence requires clarification by the sponsor.

The COMP adopted a list of issues that will be sent to the sponsor for a written response. The sponsor is invited to re-calculate the prevalence based on relevant epidemiological studies and registries for the proposed orphan condition, and given the substantial uncertainty about the assumptions regarding the prevalence, the sponsor should perform a sensitivity analysis of the reported calculations.

2.2.9 N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine (EC20); Folic Acid (FA) for diagnosis of folate receptor positive ovarian cancer, Endocyte Europe B.V. - EMA/OD/055/12

L. Fregonese (EMA Co-ordinator) and B. Dembowska-Bagińska (COMP Co-ordinator) summarised the application.

The Committee has considered the application for the designation of N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine to be used with folic acid for the diagnosis of folate receptor positive ovarian cancer.

The COMP expressed a favourable trend on the designation of the product as proposed, in the indication “diagnosis of positive folate receptor status in ovarian cancer”.

The COMP noted that there is complete overlap of the proposed orphan indication with the indication of the designation already obtained by the sponsor on 9 February 2012 for N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine and folic acid for diagnosis of positive folate receptor status in ovarian cancer (EU/3/12/958).

The COMP adopted a list of issues that will be sent to the sponsor for a written response.

Post-meeting note:

Following receipt of the COMP list of questions the sponsor decided to withdraw the designation status EU/3/12/958 on 16 July 2012. The Committee initiated a written procedure for adoption of the opinion.

The COMP draft summary report(*) EMA/COMP/399309/2012 with grounds for the positive opinion was circulated for adoption via written procedure on 17 July.

The Committee agreed that the condition, ovarian cancer, is a distinct medical entity and meets the criteria for orphan designation. For the purpose of orphan designation and to reflect the intended use of the product, the COMP considered that the orphan indication should be renamed as “diagnosis of positive folate receptor status in ovarian cancer”.

There exists scientific rationale for the development of N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine to be used with folic acid for the diagnosis of positive folate receptor status in ovarian cancer. N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine is intended to be used after pre injection with folic acid. The plausibility of the use of folic acid as pre-injection before the administration of N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine is based on the need of inducing a certain level of saturation of the folate receptors in non-tumour tissue to reduce the uptake of N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine by non-tumour tissue.

The population of patients eligible for diagnosis of positive folate receptor status in ovarian cancer was estimated to be not more than 1.3 in 10,000 persons per year in the European Union, at the time the application was made.

The sponsor has established that the condition is chronically debilitating and life threatening due to the spread of the cancer to extra-abdominal region that causes malignant pleural effusion and haematogenous metastases to the liver, spleen, or lung.

Currently several methods are considered satisfactory for the diagnosis of ovarian cancer, including physical examination, transvaginal ultrasound or abdominal/pelvic computer tomography (CT). Such diagnostic methods represent the current standard for diagnosis of ovarian cancer. Nevertheless, there is, at present, no satisfactory method of diagnosis that has been authorised in the European Union for positive folate receptor status in ovarian cancer.

A positive opinion for N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine to be used with folic acid, for diagnosis of positive folate receptor status in ovarian cancer, was adopted by consensus on 23 July 2012.

2.2.10 For treatment of opioid overdose- EMA/OD/067/12

L. Fregonese (EMA Co-ordinator) and L. Gramstad (COMP Co-ordinator) summarised the application.

The Committee considered that the following issues require clarification by the sponsor:

- Medical plausibility

It appears unclear to what extent the product is developed into a medicinal product for intranasal administration. As yet the pharmaceutical formulation as well as the nasal spray device is briefly described in prospected terms. The sponsor is invited to provide a description of the medicinal product as developed at this stage. The sponsor should also explain how data in the literature can be extrapolated to their coming product, since the strength of the planned formulation is much higher than reported in the published references.

- Prevalence

The sponsor is invited to clarify how “opioid overdose” in the sought condition is defined as reported in the provided statistical data. The data used from EMCDDA seems to include overdoses primarily linked to illicit opioids. Since occurrences of opioid overdose have become an increasing concern in opioid pain therapies, the sponsor should present available data and discuss to what extent opioid overdoses in this population will influence the overall prevalence estimate.

The sponsor is also invited to clarify the reasons for not taking the number of episodes into account in the calculation of the incidence of opioid overdose, since the same subject can have more than one episode in one year.

- Justification of significant benefit

The sponsor claims significant benefit based on the development of a formulation for intranasal use. However, as already said such formulation has not yet been completely developed. The sponsor should better clarify the impact of the intranasal formulation on the treatment of opioid overdose, providing e.g. quantification of the cases when other administration routes (i.v., i.m, or s.c.) are not possible and taking into account the characteristics of the proposed product.

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 its September meeting.

2.2.11 Recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein for treatment of cutaneous T-cell lymphoma, AOP Orphan Pharmaceuticals AG - EMA/OD/066/12

R. Demlová (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 8 designations for this condition.

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

Cutaneous T-cell lymphoma was estimated to be affecting less than 1 in 10,000 persons in the European Union, at the time the application was made. The sponsor has used several publications and databases (Globocan and Eurocare) to establish the prevalence of the condition.

The condition is chronically debilitating due to the development of generalized erythroderma, often with a leukaemic phase (Sezary syndrome), and with lymphadenopathy. Visceral spreading of the tumour may lead to death from the disease. Ulceration of tumours, with secondary bacterial infections is also a common cause of morbidity and death. The overall five-year survival rates vary between 24% and 68% according to the subtype of cutaneous T-cell lymphoma.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that Recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein may be of significant benefit to those affected by the condition. This appears justified in particular with regards to a potential clinically relevant advantage based on the alternative mechanism of action, which specifically targets the CD3 receptor on T lymphocytes resulting in penetration of the diphtheria toxin into the cells. Once in the cells, diphtheria toxin causes cessation of protein synthesis and cell death. The sponsor has provided preliminary clinical data with cutaneous T-cell lymphomas that had failed or were refractory to approved therapeutic agents. Favorable overall survival was shown, including complete remission partial remission.

A positive opinion for recombinant anti-CD3-bi-single-chain-Fv-diphtheria toxin fusion protein, for treatment of cutaneous T-cell lymphoma, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.2.12 For treatment of ovarian cancer - EMA/OD/085/12

B. Bloechl-Daum (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 18 designations for this condition.

The Committee considered that the following issues require clarification by the sponsor:

- Medical plausibility

In the application, the sponsor provides non-clinical data in tumour models, including ovarian cancer, to support the effect of the product.

These data show that of the tumours tested, ovarian cancer is the one showing one of the most modest responses to the product with regards to LC50. The sponsor should elaborate on this finding also in relation to the clinical data, which indicates that only partial and stable disease have been reported in ovarian cancer.

- Justification of significant benefit

Patients with ovarian, primary peritoneal, or fallopian tube cancer have been included in trials with the medicinal product. Partial responses and stable disease have been observed. Stable disease, according to RECIST criteria, can include progression of the tumour mass up to 20%. Some of the treatment cycles have been discontinued but the application does not discuss this and the implications for the significant benefit justification.

The sponsor is requested to provide updated results and to elaborate on the justification for significant benefit, including a critical discussion of the background treatments of the patients showing response and the effect versus homologous recombination status

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 its September meeting.

2.2.13 For treatment of pancreatic cancer - EMA/OD/068/12

S. Tsigkos (EMA Co-ordinator) and B. Bloechl-Daum (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 24 designations for this condition.

The Committee considered that the following issues require clarification by the sponsor:

- Medical plausibility

To establish that a scientific rationale exists for the proposed condition as applied for, the sponsor is requested to provide the results and discuss in detail the phase I clinical study discussed in the medical plausibility section.

- Significant Benefit

The sponsor is requested to further elaborate on the justification of significant benefit based on the detailed results and further particulars of the above mentioned phase I clinical study.

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 its September meeting.

2.2.14 Trans-4-[4-[5-[[6-(trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl] cyclohexane acetic acid, sodium salt for treatment of familial chylomicronaemia, Novartis Europharm Limited - EMA/OD/071/12

H. Bosch-Traberg (COMP Co-ordinator) summarised the application. The Committee was informed that there is currently 1 designation for this condition.

The Committee agreed that the condition, familial chylomicronaemia syndrome (type I hyperlipoproteinaemia), is a distinct medical entity and meets the criteria for orphan designation.

Familial chylomicronaemia syndrome (type I hyperlipoproteinaemia) was estimated to be affecting approximately 0.1 in 10,000 persons in the European Union, at the time the application was made. The prevalence calculation is based on four publications on the condition in Europe.

The condition is chronically debilitating and life threatening due to the development of recurrent episodes of pancreatitis. This can lead to pancreatic failure resulting in malabsorption and diabetes mellitus.

There is, at present, no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for trans-4-[4-[5-[[6-(trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl] cyclohexane acetic acid sodium salt, for treatment of familial chylomicronaemia syndrome (type I hyperlipoproteinaemia), was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

2.2.15 For treatment of patients with Coenzyme Q10 primary deficiency syndrome - EMA/OD/057/12

L. Fregonese (EMA Co-ordinator), R. Elbers (COMP Co-ordinator) and L. Greene (COMP Co-ordinator) summarised the application.

The Committee considered that the following issues require clarification by the sponsor:

- Proposed condition

The sponsor should justify the exclusion of secondary deficiencies from the orphan indication and if appropriate revise the proposed indication to “treatment of Coenzyme Q10 deficiency” and recalculate prevalence accordingly.

- Medical plausibility

To establish correctly if there exists a scientific rationale for the development of the product for treatment of patients with Coenzyme Q10 deficiency syndrome, the sponsor is invited to further elaborate on the relevance of the literature studies supporting the medical plausibility. In particular the sponsor is invited to provide a critical review of such studies, including information on the studies’ populations, the design, the end-points, the products (dietary supplement versus medicinal product) and the validity of the results.

The sponsor is asked to provide pharmacodynamic data from models of Coenzyme Q10 deficiency syndrome (e.g. models with genetic defects in Q10 synthesis and low inner mitochondrial membrane Q10 content) or from patients suffering from the condition to support the rationale of the treatment.

- Justification of significant benefit

To provide evidence in support of the assumption that the product (with the claimed aspects of bioavailability and resorption kinetics) will be of significant benefit to patients with Coenzyme Q10 deficiency, the sponsor is invited to provide data regarding an improvement in the function of mitochondrial activity (see above) in Q10 deficiency in comparison with the proposed product.

- Development of Medicinal Product

The sponsor should provide detailed information and update the Committee on the current stage of development of the product, and describe future development plans.

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 its September meeting.

2.2.16 Vatreptacog alfa (activated) for treatment of haemophilia A, Novo Nordisk A/S - EMA/OD/069/12

L. Gramstad (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 6 designations for this condition.

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

Haemophilia A was estimated to be affecting approximately 0.73 in 10,000 persons in the European Union, at the time the application was made; the sponsor has referred to the World Federation of Hemophilia (WFH) 2010 Global Survey of Hemophilia (published in December 2011).

The condition is chronically debilitating due to recurrent bleeding episodes – most commonly in a weight bearing-joint – which frequently lead to chronic arthropathy, muscular atrophy and deformities. Patients with haemophilia who are not treated have a much shorter life expectancy and experience severe morbidities including multiple episodes of joint, muscle and deep tissue bleeding which can be life- and/or limb-threatening. The average life expectancy of untreated patients with haemophilia is 17 – 20 years. With current available treatments the life expectancy is reported to be 65 – 72 years.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that vatreptacog alfa (activated) may be of significant benefit to those affected by the condition. This is based on a clinically relevant advantage and major contribution to patient care, based on improved control of bleeding episodes, reduction of administration time and potential improvement of compliance. This is supported by data obtained in preclinical studies and preliminary results from clinical studies where vatreptacog alfa (activated) has been shown to result in increased intrinsic activity as compared to other FVIIa analogues. Vatreptacog alfa (activated) was compared to rFVIIa in a dose-escalating double-blind randomised phase II study in patients with haemophilia A and B complicated by high-responding inhibitors to FVIII or FIX. In the upper dose-range, the new compound controlled 98% of bleeds within 9 hours compared to 90% for rFVIIa.

A positive opinion for vatreptacog alfa (activated), for treatment of haemophilia A, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly the data that will be required for the demonstration of significant benefit.

2.2.17 Vatreptacog alfa (activated) for treatment of haemophilia B, Novo Nordisk A/S - EMA/OD/070/12

L. Gramstad (COMP Co-ordinator) summarised the application. The Committee was informed that there are currently 6 designations for this condition.

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

Haemophilia B was estimated to be affecting not more than 0.14 in 10,000 persons in the European Union, at the time the application was made; the prevalence calculation has been based on the World Federation of Hemophilia (WFH) Global Survey of Hemophilia published in 2010.

The condition is chronically debilitating due to a deficiency or dysfunction of FIX, which leads to a severe impairment of activation of coagulation factor X. Consequently the haemostatic plug, if formed, in these patients, is fragile and easily dissolved by normal fibrinolytic activity, leading to impaired haemostasis. The clinical symptoms of haemophilia are spontaneously occurring bleeds or prolonged bleeding episodes. Life expectancy is related to the severity of the hemophilia. The mortality rate is 4 to 6 times greater in individuals with a severe condition than those with a mild condition. HIV-negative individuals with mild hemophilia have a normal life expectancy.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that vatreptacog alfa (activated) may be of significant benefit to those affected by the condition. This is based on a clinically relevant advantage and major contribution to patient care, based on improved control of bleeding episodes, reduction of administration time and potential improvement of compliance. This is supported by data obtained in preclinical studies and preliminary results from clinical studies where vatreptacog alfa (activated) has been shown to result in increased intrinsic activity as compared to several FVIIa analogues. Vatreptacog alfa (activated) was compared to rFVIIa in a dose-escalating double-blind randomised phase II study in patients with haemophilia A and B complicated with high-responding inhibitors to FVIII and FIX. In the upper dose-range, the new compound controlled 98% of bleeds within 9 hours compared to 90% for rFVIIa.

A positive opinion for vatreptacog alfa (activated), for treatment of haemophilia B, was adopted by consensus. The draft summary report(*) was updated in line with the discussion.

The COMP recommends that protocol assistance is sought from the EMA prior to submission of the application for marketing authorisation, particularly with regard to the data that will be required for the demonstration of significant benefit.

2.3 Appeal procedures

2.3.1 Tariquidar for treatment of P-gp positive breast cancer, Avaant Holdings Ltd - EMA/OD/146/11
[Co-ordinators: D. O'Connor / S. Mariz]

The appeal withdrawal letter, dated 25 June 2012 was circulated for information.

2.4 Evaluation ongoing

The Committee noted that evaluation was ongoing for eleven applications for orphan designation.

2.5 Validation ongoing

The Committee was informed that validation was ongoing for twenty eight applications for orphan designation.

3. Requests for protocol assistance (see note on access to documents at the beginning of minutes)

3.1 For treatment of traumatic spinal cord injury. [Coordinator: B. Bloech-Daum]

B. Bloech-Daum updated the COMP on the significant benefit issues. The protocol assistance letter EMA/COMP/SAWP/381661/2012(*) was adopted by the Committee.

3.2 For treatment of chronic non-infectious uveitis [Coordinator: B. Bloech-Daum]

B. Bloech-Daum updated the COMP on the significant benefit issues. The protocol assistance letter EMA/COMP/SAWP/381662/2012(*) was adopted by the Committee.

4. Overview of applications

4.1 Update on applications for orphan medicinal product designation submitted/expected

COMP co-ordinators were appointed for 1 application submitted and 15 upcoming applications. No Experts were appointed for upcoming/ongoing applications.

The statistics on the COMP members' co-ordinatorship distribution for applications submitted and validated in 2012 were circulated for information.

4.2 Update on orphan applications for Marketing Authorisation

An updated overview of orphan applications for Marketing Authorisation will be circulated for information in the September meeting post-mailing.

5. Review of orphan designation for orphan medicinal products for Marketing Authorisation

5.1 Orphan designated products for which CHMP opinions have been adopted

5.1.1 Inlyta (Axitinib) for treatment of renal cell carcinoma; Pfizer Limited – UK (OD/119/10, EU/3/10/844)

S. Tsigkos (Co-ordinator) and B. Bloechl-Daum (COMP Co-ordinator) summarised the argumentation provided by the sponsor. The comments from the COMP expert, G. Gatta were presented to the Committee.

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

- Prevalence

Maintenance of orphan drug designation based on prevalence can only be successful if the sponsor can establish that the condition affects not more than five in 10,000 persons in the EU. In its position on the maintenance of criteria, the sponsor has provided two different conclusions based on a) 5-year prevalence derived from Globocan incidence when combined with earlier (2003) published survival

data, and b) 3-year prevalence data derived directly from the Globocan database. In addition, some assumptions by the sponsor including survival rates, annual incidence increases and the RCC/kidney cancer ratio are referenced on published literature of about a decade old.

The sponsor was therefore requested to provide an updated calculation based on current literature, and in particular 5-year prevalence data directly from GLOBOCAN, projected for the year the application is made. The sponsor is requested to clearly discuss recent changes in the survival of RCC patients and incidence of the condition over time.

- Significant benefit

The applicant discusses inter alia one pivotal trial in patients with advanced RCC after failure of treatment with one prior systemic therapy.

The sponsor was invited to further elaborate on available endpoints including overall survival, and to further justify the clinically relevant advantage or major contribution to patient care of the proposed product to currently used treatments.

In its written response, and during an oral explanation before the Committee on 10 July 2012, the sponsor argued that a) 5-year projected prevalence for 2013 (based on Globocan and the assumption that up to 95% of kidney cancer is RCC) ranges from 4.34 to 4.85 cases per 10,000 people and b) with regards to significant benefit Axitinib phase 3 study demonstrated clinically-meaningful and statistically-significant decrease in risk of disease progression or death compared to control and that improved efficacy was also demonstrated in subgroups of patients with prior treatment.

With regards to the prevalence calculations, the committee pointed out that as per the published results of the RARECARE project, the complete prevalence for RCC was 6,718 per 10,000 people. Thus, the Committee was not convinced that the prevalence of the condition remained below the threshold provisioned in the orphan regulation.

In addition, the Committee considered that for the purpose of justification of significant benefit, a clear improvement in overall survival versus the discussed counterpart would be required, in contrast to the sponsors' position which focused on progression free survival as an endpoint. It was stressed that this was a review of criteria of orphan designation and not an evaluation for marketing authorisation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally requested a withdrawal of the orphan designation, on 11 July 2012, prior to final opinion.

5.1.2 Elelyso (previously Uplyso) (Taliglucerase Alfa), EMA/H/C/002250 for treatment of Gaucher disease; Pfizer Limited – UK; (OD/125/09, EU/3/10/726); [Co-ordinators: V. Stoyanova, P. Evers / S. Mariz]
The Committee was informed about the CHMP refusal of the marketing authorisation adopted in June 2012.

5.1.3 NovoThirteen (Recombinant human factor XIII (composed of two A subunits)) for treatment of hereditary factor XIII deficiency; Novo Nordisk A/S (OD/052/03, EU/3/03/179)

L. Fregonese (EMA Co-ordinator) and L. Gramstad (COMP Co-ordinator) summarised the argumentation provided by the sponsor.

As agreed during the June meeting, a list of issues was sent to the sponsor for response. The sponsor was asked to elaborate on the justification of significant benefit. Additional argumentation should be provided to justify the potential significant benefit of NovoThirteen over the authorised treatments for the treatment of hereditary factor XIII deficiency.

The assumption of significant benefit made at the moment of orphan designation needs to be confirmed by data at the moment of marketing authorization. According to the Communication from the Commission on Regulation (EC) No 141/2000 of the European Parliament and the Council on Orphan Medicinal Products, "if the argument of significant benefit is based on an increase in supply/availability of the method, the sponsor must provide details of the supply/availability problem and explain why this results in the unmet need of patients. All claims should be substantiated by qualitative and quantitative references. If the supply of existing methods is sufficient to meet patients' needs in the orphan indication an increase in supply will not be viewed as significant benefit".

On this basis the sponsor was invited to justify whether lack of availability of the current treatment methods is an issue resulting in unmet need for the patients affected by the condition in the EU.

In its written response, and during an oral explanation before the Committee on 10 July 2012, the sponsor argued that fibrogammin P is currently authorised in only 5 countries in the EU, while Novothirteen would be approved across the EU. The sponsor also discussed that the product would be a recombinant protein expressed in in yeast, identical to endogenous FXIII A2, highly purified without animal or human derived raw materials and no risk of virus or TSE transmission.

The Committee considered that in order to endorse claims of improved availability, documentation or other proof would have to be available to justify that patients in need of factor XIII could not have access to the medicinal product. Such justifications were not provided by the sponsors. In addition, the claims for improved viral safety as a significant benefit were not considered to be satisfactorily justified.

In communicating to the sponsor the outcome of the discussion, the sponsor formally requested a withdrawal of the orphan designation, on 11 July 2012, prior to final opinion.

5.1.4 Revestive ([gly2]-recombinant human glucagon-like peptide) for treatment of short bowel syndrome; NYCOMED DANMARK APS (OD/045/01, EU/3/01/077)

S. Tsigkos (EMA Co-ordinator) and H. Bosch-Traberg (COMP Co-ordinator) summarised the argumentation provided by the sponsor.

The Committee agreed that the proposed therapeutic indication "treatment of adult patients with short bowel syndrome. Patients should be stable following a period of intestinal adaptation after surgery" falls entirely within the scope of the designated orphan condition which is worded at broader terms as: "treatment of short bowel syndrome".

The prevalence of short bowel syndrome was estimated to remain below 5 in 10,000 at the time of the review of the designation criteria; based on existing registry data the prevalence of the condition was estimated to be less than 0.44 in 10,000 people in the EU.

The condition is life-threatening and chronically debilitating due to severe nutritional deficiency, which is characterised by inability to maintain protein-energy, fluid, electrolyte, or micronutrient balances when on a conventionally accepted, normal diet and may necessitate dependence on parenteral infusions. Use of parenteral nutrition may lead to infections and sepsis, central venous thrombosis and

embolism. In addition, parenteral constituents and chronic dehydration may contribute to parental nutrition associated liver and renal disease and eventually even organ failure.

There is, at present, no satisfactory treatment that has been authorised in the European Union for patients affected by the condition.

The Committee has recommended that Revestive, [gly2]-recombinant human glucagon-like peptide, Teduglutide, EU/3/01/077 for the treatment of short bowel syndrome is not removed from the Community Register of Orphan Medicinal Products.

An opinion not recommending the removal from the EC Register of Orphan Medicinal Products was adopted by consensus. The Draft Report review of OMP designation EMA/COMP/429306/2012(*) was updated in line with the discussion.

5.2 Orphan designated products for discussion prior to adoption of CHMP opinion

5.2.1 Glybera (adeno-associated viral vector expressing lipoprotein lipase) for treatment of lipoprotein lipase deficiency; Amsterdam Molecular Therapeutics BV., (OD/079/03, EU/3/04/194) [Co-ordinators: A. Voordouw / S. Mariz]

5.2.2 Dacogen (Decitabine) for treatment of acute myeloid leukaemia; Janssen-Cilag International NV (OD/004/06, EU/3/06/370)

S. Tsigkos (EMA Co-ordinator) and R. Elbers (COMP Co-ordinator) summarised the argumentation provided by the sponsor.

During the meeting the COMP expressed a positive trend for the review of criteria for designation. The committee decided to wait for the CHMP opinion before initiating a written procedure for adoption.

Post-meeting note:

Following the CHMP positive opinion adopted at their 16-19 July 2012 meeting, the COMP draft report on review of OMP designation EMA/COMP/442447/2012(*) with grounds for the positive opinion was circulated for adoption and adopted via written procedure on 2 August 2012.

The COMP agreed that the proposed therapeutic indication “treatment of adult patients age 65 years and above with newly diagnosed de novo or secondary acute myeloid leukaemia (AML), according to the World Health Organisation (WHO) classification, who are not candidates for standard induction chemotherapy” falls entirely within the scope of the orphan indication of the designated orphan medicinal product, “treatment of acute myeloid leukaemia”.

Acute myeloid leukaemia was estimated to be affecting less than 2 in 10,000 people in the EU based on databases and literature. Thus, the prevalence of the condition remained below 5 in 10,000 at the time of the review of the designation criteria.

The condition is life-threatening and chronically debilitating due to the consequences of the bone marrow dysfunction, such as intracranial or gastro-intestinal haemorrhagic episodes, disseminated intravascular coagulation, and the risk of severe infections. The condition progresses rapidly and is fatal within days to a few months if left untreated. The 5-year survival rate with the currently available treatments is about 40% for patients aged below 65 years and 5% for patients aged 65 years or older.

Although satisfactory methods of treatment of the condition have been authorised in the European Union, the assumption that Dacogen may be of potential significant benefit to the subset of the orphan condition as defined in the proposed therapeutic indication still holds. This is based on the clinically relevant advantage of improved efficacy, as demonstrated in a randomized, open-label, multicenter Phase III study of the proposed product versus patient's choice of treatment with physician's advice of either supportive care or low-dose cytarabine in older patients affected by the condition. The results of this study showed an improvement in median survival of 2.7 months in favour of the Dacogen treated patients.

An opinion not recommending the removal from the EC Register of Orphan Medicinal Products was adopted by consensus. The Committee has recommended that Dacogen, (Decitabine, EU/3/06/370) for treatment of acute myeloid leukaemia is not removed from the Community Register of Orphan Medicinal Products.

5.2.3 Istodax (previously Romidepsin) ((E)-(1S,4S,10S,21R)-7-[(Z)-ethylidene]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23- tetraazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone) for treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated); Celgene Europe Limited (OD/056/05, EU/3/05/328) [Co-ordinators: B. Sepodes/ L. Fregonese]

5.2.4 NexoBrid (Purified bromelain) for treatment of partial deep dermal and full thickness burns; Teva Pharma GmbH (OD/012/02, EU/3/02/107)

5.2.5 Adcetris (Monoclonal antibody against human CD30 covalently linked to the cytotoxin monomethylauristatin E) for treatment of anaplastic large cell lymphoma (OD/072/08, EU/3/08/595) and for treatment of Hodgkin lymphoma (OD/073/08, EU/3/08/596); Takeda Global Research and Development Centre (Europe) Ltd

It has been agreed that prior to adopting of an opinion on Adcetris (brentuximab vedotin) for the treatment of Hodgkin lymphoma (HL) and systemic anaplastic large cell lymphoma (sALCL) the COMP would like to receive further information from the sponsor.

The Committee considered that the justification of significant benefit requires clarification by the sponsor. The list of question will be circulated and adopted via written procedure and the sponsor will be invited to an oral explanation before the Committee at its September meeting.

Post-meeting note:

The lists of questions were adopted via written procedure on 1 August.

5.3 Ongoing procedures

5.3.1 Bosulif (Bosutinib) for treatment of chronic myeloid leukaemia; Pfizer Limited (OD/160/09, EU/3/10/762) [Co-ordinators: R. Elbers / S. Tsigkos]

5.3.2 Cholic Acid FGK for treatment of inborn errors of primary bile acid synthesis responsive to treatment with cholic acid; FGK Representative Service GmbH (OD/080/09, EU/3/09/683, EMA/H/C/002081) [Co-ordinators: B. Sepodes / TBC]

5.3.3 Cysteamine bitartrate [Cysteamine bitartrate (gastroresistant)] for treatment of cystinosis; Raptor Pharmaceuticals Europe B.V. (OD/034/10, EU/3/10/778, EMA/H/C/002465) [Co-ordinators: V. Saano / S. Mariz]

5.3.4 Defitelio (Defibrotide) for prevention of hepatic veno-occlusive disease (OD/025/04, EU/3/04/211) and for treatment of hepatic veno-occlusive disease (OD/026/04, EU/3/04/212); Gentium S.p.A. [Co-ordinators: J. Torrent-Farnell / S. Mariz]

5.3.5 Delamanid ((R)-2-Methyl-6-nitro-2-{4-[4-(4-trifluoromethoxyphenoxy)piperidin-1-yl]phenoxymethyl}-2,3-dihydroimidazo[2,1-b]oxazole) for treatment of tuberculosis (OD/094/07, EU/3/07/524); Otsuka Novel Products GmbH [Co-ordinators: V. Stoyanova/ L. Fregonese]

5.3.6 Exjade (4-(3,5-bis(hydroxy-phenyl)-1,2,4) triazol-1-yl) benzoic acid) for treatment of chronic iron overload requiring chelation therapy; Novartis Europharm Limited (OD/061/01, EU/3/02/092) [Co-odinators: M. Mozina/ S. Mariz]

5.3.7 Jenzyl ((1R, 2R, 4S)-4-{(2R)-2-[(3S,6R,7E,9R,10R,12R,14S,15E,17E,19E,21S,23S,26R, 27R,34aS)-9,27-dihydroxy-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-1,5,11,28,29-pentaoxo-1,4,5,6,9,10,11,12,13,14,21,22,23,24,25,26,27,28,29,31,32,33,34,34a-tetra-cosahydro-3H-23,27-epoxypyrido[2,1-c][1,4]oxazacyclohentriacontin-3-yl]propyl}-2-methoxy-cyclohexyldimethyl-phosphinate) for treatment of soft tissue sarcoma (OD/050/05, EU/3/05/312) and for treatment of primary malignant bone tumours (OD/055/05, EU/3/05/321); Merck Sharp & Dohme Limited [Co-ordinators: B. Dembowska-Baginska/ L. Fregonese]

5.3.8 Loulla (Mercaptopurine) for treatment of acute lymphatic leukaemia, Only For Children Pharmaceuticals (OD/065/07, EU/3/07/496, EMA/H/C/002501) [Co-ordinators: D. O'Connor / S. Tsigkos]

5.3.9 PAS-GR (Para-aminosalicylic acid) for treatment of tuberculosis; Lucane Pharma SA (OD/072/10, EU/3/10/826, EMA/H/C/002709) [Co-ordinators: V. Stoyanova / S. Mariz]

5.3.10 Pheburane (Sodium phenylbutyrate) for treatment of carbamoyl-phosphate synthase-1 deficiency; Lucane Pharma SA (OD/098/11, EU/3/12/951, EMA/H/C/002500) [Co-ordinators: B. Sepodes / TBC]

5.3.11 Pomalidomide Celgene (Pomalidomide) for treatment of multiple myeloma, Celgene Europe Ltd. (OD/053/09, EU/3/09/672, EMA/H/C/002682) (Co-ordinators: TBC / S. Mariz]

5.3.12 Revlimid (3-(4'aminoisoindoline-1'-one)-1-piperidine-2,6-dione) for treatment of myelodysplastic syndromes; Celgene Europe Limited – UK (OD/083/03, EU/3/04/192) [Co-ordinators: L. Gramstad/ TBC]

5.3.13 SAN Idebenone (Idebenone) for treatment of Leber's hereditary optic neuropathy; Santhera Pharmaceuticals (Deutschland) GmbH (OD/076/06, EU/3/07/434) [Co-ordinators: J. Torrent-Farnell / S. Mariz]

5.3.14 Scenesse ([Nle4, D-Phe7]-alfa-melanocyte stimulating hormone, Afamelanotide) for treatment of erythropoietic protoporphyria; Clinuvel (UK) Limited (OD/108/07, EU/3/08/541, EMA/H/C/002548) [Co-ordinators: L. Gramstad/ S. Mariz]

6. Procedural aspects

6.1 Reminder about the Chair and Vice-Chair election to be held during the 4-5 September 2012 COMP meeting

The members were reminded that the nominations and candidates' résumés in support of their candidature should be forwarded to the COMP secretariat by 30 August 2012.

7. Any other business

7.1 Informal COMP meeting

The adoption on the draft minutes of COMP/CAT/PCDO meeting held on 24 May 2012 in Copenhagen was postponed to the September meeting.

Date of next COMP meeting: on 4 - 5 September 2012

Annex A

List of participants on 10 - 11 July 2012

Chair:
Kerstin Westermark

Vice-Chair:

Birthe Byskov Holm	Volunteer patient representative for Eurordis

COMP Members:

André Lhoir	België/Belgique/Belgien
Irena Bradinova	България
Regina Demlová	Česká Republika
Heidrun Bosch-Traberg	Danmark
Rembert Elbers	Deutschland
Vallo Tillmann	Eesti
Geraldine O'Dea	Éire/Ireland
Vacant	Ελλάδα
Josep Torrent Farnell	España
Annie Lorence	France
Sigurdur B. Thorsteinsson	Iceland
Armando Magrelli	Italia
Dainis Krievins	Latvija
Henri Metz	Luxembourg
Judit Eggenhofer	Magyarország
Violeta Stoyanova	Nederland
Lars Gramstad	Norway
Brigitte Blöchl-Daum	Österreich
Bożenna Dembowska-Bagińska	Polska
Ana Corrêa-Nunes	Portugal
Martin Možina	Slovenija
Veijo Saano	Suomi/Finland
Björn Beermann	Sverige
Daniel O'Connor	United Kingdom
Pauline Evers	Representig European Genetic Alliances Network (present on 1st day only)
Lesley Greene	Volunteer patient representative for Eurordis
János Borvendég	CHMP Representative
Katerina Moraiti	CHMP Representative
Bruno Sepodes	EMA Representative

Observers:

Ivana Martinovic	Croatia
Maria Mavris	Eurordis

European Commission:

Mirjam Soderholm	DG Health and Consumers

EMA Secretariat:

Jordi Llinares Garcia	Head of Orphan Medicines Section
Laura Fregonese	Scientific Administrator

Stylianos Tsigkos	Scientific Administrator
Agnieszka Wilk-Kachlicka	Assistant
Monica Gomar Mengod	Assistant

Apologies from members:

Ioannis Kkolos	Κύπρος
Aušra Matulevičienė	Lietuva
Albert Vincenti	Malta
Flavia Saleh	România
Milica Molitorisová	Slovensko