EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 February 2013
EMA/COMP/722237/2012 Rev. 1[1]
Human Medicines Development and Evaluation

Committee for Orphan Medicinal Products (COMP)

Minutes of the 5 - 6 December 2012 meeting

Note on access to documents

Documents under points 1.1 and 2 to 7 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).

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[1] Point 2.2.2 - prevalence number corrected

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1. Introduction

The Committee welcomed Dr Dorthe Meyer, the new COMP member representing Denmark and Dr Frauke Naumann-Winter, the observer who will replace Dr Rembert Elbers, representing Germany as of 1 February 2013.

The COMP noted a resignation of Dr Milica Molitorisova (Slovak Republic) dated 30 November 2012.

1.1 Adoption of the agenda, EMA/COMP/718183/2012 Rev. 3.

The agenda was adopted with no amendments.

1.2 Adoption of the minutes of the previous meeting dated 6 - 7 November 2012 EMA/COMP/648772/2012.

The minutes were adopted with minor corrections to points 2.1.11 and 2.2.1.

1.3 Conflicts of Interest

The COMP secretariat identified the potential conflict of interest as follows:

Potential conflict of interest:			
Member	**Agenda point**	**COI**	**Consequences**
B. Dembowska-Baginska	2.2.1	On-going investigator for a potentially competitor product (Bevacizumab, Roche) for the proposed indication.	Cannot act as a coordinator, or vote. Replaced by B. Bloech-Daum.
	5.2.2	On-going investigator for a potentially competitor product (Bevacizumab, Roche) for the proposed indication.	Cannot act as a coordinator, or vote. Replacement not required (MA application withdrawn).

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

The COMP secretariat was informed as follows:

- Eurordis receives funding from the sponsors who have submitted dossier to be considered for orphan designation at the current meeting (2.2.1, 2.2.9, 2.2.13-14 and 2.2.18). Nevertheless, no direct conflicts of interest have been identified for L. Greene and B. Byskov Holm, who are the volunteer patient representatives for EURORDIS.

- EGAN received a grant from the sponsor of a product under the review of the orphan medicinal product designation at the time of type II variation (5.1.1). Nevertheless, no direct conflicts of interest have been identified for P. Evers, who represents EGAN in the COMP.

2. Applications for orphan medicinal product designation[2]

2.1. For opinion

2.1.1 Eflornithine in combination with Sulindac for treatment of Familial Adenomatous Polyposis, Cancer Prevention Pharma Limited - EMA/OD/130/12
[Co-ordinators: D. O'Connor / S. Tsigkos]

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

- Medical plausibility

To establish correctly if there exists a scientific rationale for the development of eflornithine in combination with sulindac for treatment of familial adenomatous polyposis, the sponsor was invited to further elaborate on:

- the availability of a specific product using a combination of eflornithine and sulindac, as proposed for designation,

- any proof of concept study in a relevant preclinical model or clinical setting with the specific product as proposed for designation, since orphan designation refers to a specific condition and one specific product,

- the relevance of the clinical studies presented with regards to any existing specific product for designation.

- Development of Medicinal Product

The sponsor was asked to clarify if the product applied for will be developed, and provide detailed information and update the Committee on the current stage of development of the product.

In the written response, and during an oral explanation before the Committee on 5 December 2012, the sponsor discussed that there is an on-going development plan to co-formulate the two products, and stressed that that two tablets of the co-formulated product will equal the drug doses used in the proof of concept clinical trial discussed in the medical plausibility section of the application.

The Committee considered that this would suffice for justifying the medical plausibility since there are clinical results versus placebo with the proposed combination showing that treated patients improve as per (a) the recurrence of one or more adenomas (b) number of advanced adenomas (c) number of patients with final adenomas.

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

The intention to treat the proposed condition was considered justified on the grounds of preclinical experimental models and clinical studies that show decreased number of polyps in the treated subjects compared to control. Familial adenomatous polyposis (hereinafter referred to as "the condition") was estimated to be affecting about 0.2 in 10,000 people in the European Union, at the time the application was made. The condition is chronically debilitating and life threatening due to the high risk of developing colorectal cancer as well as extra colonic manifestations which include polyps of the gastric

[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).

fundus and duodenum, desmoids and several extra colonic malignancies such as gastric and duodenal carcinoma, follicular or papillary thyroid cancer, and CNS tumours. There are no satisfactory methods that have been authorised in the European Union for the treatment of the proposed condition.

A positive opinion for eflornithine in combination with sulindac, for treatment of familial adenomatous polyposis, was adopted by consensus.

2.1.2 For treatment of paracetamol toxicity - EMA/OD/132/12
(active time: day 88)
[Co-ordinators: M. Možina / S. Mariz]

The Committee noted that the sponsor withdrew the application prior to responding to the COMP list of questions.

2.1.3 Recombinant Modified Human Growth Hormone for treatment of growth hormone deficiency, Richardson Associates Regulatory Affairs Ltd - EMA/OD/133/12
[Co-ordinators: V. Tillmann / S. Tsigkos]

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

- Prevalence

The sponsor was asked to justify the sources of the prevalence data and describe the methodology used for the prevalence calculation and in particular to discuss the duration of the condition as used in the prevalence calculation. The duration of treatment and the duration of the disease are different concepts and it is not justified why they might be used interchangeably for the prevalence calculation.

- Significant Benefit

The sponsor was invited to comment on the therapeutic impact of the pharmacokinetic profile of the weekly administration in particular with regards to the absence of daily peaks in plasma levels and to compare this with the pharmacokinetics profile of the daily administration with the authorised counterparts.

In the written response, and during an oral explanation before the Committee on 5 December 2012, the sponsor acknowledged the use of treatment duration as an estimate for the duration of the condition for the purpose of the prevalence calculation. This approach was justified on the grounds that in this case the duration of the treatment corresponds with the condition being clinically recognised. During the subsequent discussion, it was pointed out to the sponsor that this position would have to be considered in the context of guideline ENTR/6283/00 Rev 03 that specifically states that "different stages of severity or stages of a disease would generally not be considered as distinct condition" and that "the fact that a subset of patients exists in whim the medicinal product is expected to show favourable benefit risk (as defined in the proposed therapeutic indication) would generally not be sufficient to define a distinct condition".

However, the Committee considered that even if the prevalence values for the paediatric patients were to be projected for further durations of treatment (up to 18 years) the prevalence criterion would still be met.

A discussion on the pharmacokinetic properties of the product, was held and the sponsor discussed the kinetic profile of daily hGH in relation to the physiological pulsatile excretion of the hormone. The sponsor presented additional clinical and preclinical data comparing PK between daily administration of hGH and weekly administration. The Committee accepted that a weekly administration scheme may be possible and that this would be more convenient, potentially better complied with and it might constitute a major contribution to patient care.

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

The intention to treat the proposed condition appears justified on the grounds of preliminary clinical data with patients affected by the condition showing normalisation of IGF-1 levels. The condition was estimated to be affecting approximately 4 in 10,000 people in the European Union, at the time the application was made. The sponsor has provided satisfactory argumentation to establish that the condition is chronically debilitating and life-threatening due to the psychosocial impact, the cardiovascular risk, and risk of decreased bone mass and fractures. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that recombinant modified human growth hormone may be of significant benefit to those affected by the condition. This appears justified on the grounds of improved pharmacokinetic properties that may allow for a less frequent administration compared to currently authorised products. This would constitute a major contribution to patient care, and is supported by preliminary clinical data that show a once-weekly administration potential.

A positive opinion for recombinant modified human growth hormone, for treatment of growth hormone deficiency, was adopted by consensus.

2.1.3 For treatment of complex regional pain syndrome- EMA/OD/125/12

[Co-ordinators: L. Gramstad / L. Fregonese]

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

- Medical plausibility

To establish correctly if there exists a scientific rationale for the development of the proposed product for the treatment of CRPS, the sponsor was invited to further elaborate on:

- the extent and relevance of bone reabsorption and other osteoclastic mechanisms in CRPS;

- the methodology, the scientific validity and relevance of the two cited references on the product in CRPS, as the only study on 24 CRPS patients has been published as an abstract (Zaspel et al), and never as a full article;

- the characteristics of the patients that responded to treatment with the product in the abstract from Zaspel et al, and in particular on whether the responders had local or generalized osteoporosis;

- the extrapolation of data from conditions other than CRPS in relation to the proposed action of the product in reducing pain;

- the possible extrapolation to the product of data from other products tested in CRPS.

In addition the sponsor was invited to comment on the expected low bioavailability using the oral route of administration, and how this would influence the expected action of the product on pain and on bone reabsorption in CRPS.

- Prevalence

In order to correctly establish the prevalence of CRPS in the EU the sponsor was invited to elaborate on:

- the extrapolation of the data from the US survey to the EU population, taking into account the possible differences in the definition of the condition between the US and the EU, and across time;

- the impact on the prevalence of the cases characterised by long-term course of the disease, i.e. more than one year. The sponsor was invited to add these cases to the overall prevalence of the disease, taking into account the average duration in these cases.

- Development of Medicinal Product

It appears unclear to what extent the product is developed into a medicinal product for oral administration. As yet the pharmaceutical formulation is briefly described in prospected terms. The sponsor was invited to provide a description of the medicinal product as developed at this stage.

In the written response, and during an oral explanation before the Committee on 5 December 2012, the sponsor cited bibliographic references and elaborated on the role of osteoporosis in the condition as applied for. The plausibility to treat the condition with the proposed product was discussed. Even though the COMP acknowledged the presence of osteoporosis in CRPS, it was considered that the relevance of osteoporosis as a target for treatment of the condition had not been satisfactorily justified. It was considered that the bibliographic data as presented to support the use of the product in the proposed condition lacked essential details that made it not conclusive for the purposes of orphan designation evaluable. The Committee concluded that complex regional pain syndrome was estimated to be affecting not more than 3 in 10,000 people in the European Union, at the time the application was made. The prevalence estimate was based on relevant international literature. The condition is chronically debilitating in those cases which do not undergo spontaneous resolution. In those cases, the chronically debilitating nature of the disease is due to symptoms such as pain, oedema, motor, sensorial, and vasomotor disturbances in the affected region. Continuous disabling pain has been described as the hallmark of the disease; it is disproportionate to the inciting event and lasts beyond the healing period. As the disease progresses, the pain often spreads beyond the affected limb. Autonomic symptoms and motor dysfunction can develop, including dystonia, tremor, myoclonus and muscle weakness. However, the intention to treat the condition with the above-mentioned product has been considered by the Committee not to be sufficiently justified by the sponsor. The sponsor did not provide a satisfactory discussion of the pharmacological action of the product in the proposed condition. In addition, the Committee was of the opinion that the sponsor did not provide sufficient data to support the potential clinical use of the product in complex regional pain syndrome. The data presented by the sponsor, based on a single non-sponsor generated abstract (Zaspel at al, 2007, never published as a full article) were not considered sufficient to justify the intention to treat the condition. Similarly, the bibliographic case report (De Castro et al, 2011) presented by the sponsor was considered to lack sufficient details for evaluation. Further, the sponsor did not sufficiently justify the extrapolation of data from clinical trials of other products of the same pharmacological class in complex regional pain syndrome, to the proposed product.

The Committee has therefore considered that the sponsor has not established that the product is intended for the treatment of the proposed condition as required for orphan designation under Article 3(1)(a) of Regulation (EC) 141/2000.

The sponsor has demonstrated, as required under Article 3(1)(b), Regulation (EC) No 141/2000 of 16 December 1999, that there exists no satisfactory method of treatment of the condition in question that has been authorised in the European Union. Therefore a demonstration of significant benefit has not been required.

A negative opinion for the proposed product, for treatment of complex regional pain syndrome, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1 1,2:5,6-Dianhydrogalactitol for treatment of glioma, IDIS Ltd - EMA/OD/148/12
[Co-ordinators: B. Bloechl-Daum / S. Mariz]

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 product was considered justified on the grounds of preclinical and clinical data in the condition. It was shown that product effectively killed glioma derived cells in the in vitro setting and clinical preliminary data showed its effectiveness in inducing partial response or stable disease in patients. Glioma was estimated to be affecting approximately 2.2 in 10,000 people in the European Union, at the time the application was made; the Rarecare registry and European epidemiological publications found in the public domain were used to calculate the prevalence. The sponsor has provided satisfactory argumentation to establish that the condition is chronically debilitating, in particular due to compression and invasion 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 1,2:5,6-Dianhydrogalactitol may be of significant benefit to those affected by the condition. This appears justified on the grounds of the clinically relevant advantage of improved efficacy. This is based on clinical data in patients who have treatment resistant forms of glioma where partial response was seen.

A positive opinion for 1,2:5,6-Dianhydrogalactitol, for treatment of glioma, was adopted by consensus.

2.2.2 Adeno-associated viral vector serotype 9 containing the human *N-acetylglucosaminidase alpha* gene for treatment of mucopolysaccharidosis type IIIB (Sanfilippo B syndrome), Laboratorios del Dr. Esteve, S.A. - EMA/OD/150/12
[Co-ordinators: A. Matulevičienė / S. Tsigkos]

The Committee agreed that the condition, of mucopolysaccharidosis type IIIB (Sanfilippo B syndrome), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the product was considered justified on the grounds of preclinical data from a model of the condition. In this model, treatment with an adeno-associated viral vector serotype 9 containing the murine N-acetylglucosaminidase alpha gene showed restoration of the enzyme activity and improvement in the condition-related pathology. The condition was estimated to

be affecting approximately 0.009 in 10,000 people in the European Union, at the time the application was made. The condition is chronically debilitating due to cognitive and behavioural deficits and life-threatening with most patients dying by the third decade of life. There is, at present, no satisfactory treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for adeno-associated viral vector serotype 9 containing the human *N-acetylglucosaminidase alpha* gene, for treatment of of mucopolysaccharidosis type IIIB (Sanfilippo B syndrome), was adopted by consensus.

2.2.3 Allogeneic motor neuron progenitor cells derived from human embryonic stem cells

for treatment of 5q spinal muscular atrophy, California Stem Cell (UK) Ltd - EMA/OD/140/12
[Co-ordinators: J. Torrent-Farnell / L. Fregonese]

Following review of the application by the Committee, it was agreed to broaden/rename the indication

The Committee agreed that the condition, 5q spinal muscular atrophy, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the proposed product was supported by preclinical studies in relevant models, where engraftment of the motor neurons was shown, followed by improvement of morphologic and functional endpoints. In particular the studies showed reduction of muscle atrophy, preservation of muscular junctions, amelioration of abnormal polyphasic potentials, weight gain, increased number of neurones, and improvement of arterial oxygen saturation, breathing and heart rate. There was a small but significant effect on survival in one of the pre-clinical studies. 5q spinal muscular atrophy was estimated to be affecting less than 0.4 in 10,000 people in the European Union, at the time the application was made. The sponsor based the prevalence calculation on valid literature sources. The condition is chronically debilitating and life-threatening, due to progressive muscle weakness caused by the degeneration of the lower motor neurons. This results in wasting, weakness, failure to thrive, pulmonary and orthopaedic complications. The prognosis varies depending on the type of 5qSMA, with type I being the most severe. In most cases, children affected by Type I 5qSMA do not live past two years of age. Death usually occurs due to respiratory complications with terminal respiratory failure. 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 allogeneic motor neuron progenitor cells derived from human embryonic stem cells, for treatment of 5q spinal muscular atrophy, was adopted by consensus.

2.2.4 Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β^{A-T87Q}-globin gene

for treatment of beta-thalassemia major and intermedia, bluebird bio France - EMA/OD/146/12
[Co-ordinators: R. Elbers / L. Fregonese]

Following review of the application by the Committee, it was agreed to rename the indication to "treatment of beta-thalassemia intermedia and major".

The Committee agreed that the condition, beta-thalassemia intermedia and major, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition was supported by preclinical results in a model of beta-thalassemia intermedia where treatment with the product improved haemoglobin concentration, haematocrit level,

red blood cell counts and reticulocyte percentage. Beta-thalassemia intermedia and major was estimated to be affecting approximately 1 in 10,000 people in the European Union, at the time the application was made. The sponsor performed an extensive literature search and calculated the prevalence using a valid methodology. The condition is life-threatening and chronically debilitating due to the severe anaemia, the need for blood transfusions, and the complications related to these. Beta-thalassemia major causes a hypochromic, microcytic anaemia developing in in the first year of life. Without transfusions, approximately 85% of patients die by five years of age. Bone marrow expansion due to severe ineffective erythropoiesis results in characteristic deformities of the skull and face, and painful periarticular syndrome with microfractures and osteomalacia. Progressive hepatic, cardiac and endocrine disturbances develop, due to the accumulation of iron from transfusion and its deposition in the tissues. Without chelation therapy, iron overload results in death in the second or third decade, usually from cardiac failure. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human *beta$^{A\text{-}T87Q}$-globin* gene may be of significant benefit to those affected by the condition. This appeared justified by the mechanism of action of the product as a gene therapy product, offering the potential of being curative, differently from the currently authorized products which only target the manifestations of the disease, namely iron overload. The significant benefit is supported by preclinical data showing improvement of haemoglobin concentration, haematocrit level, red blood cell counts and reticulocyte percentage. In addition the benefit is supported by one clinical case where transfusion independence and stable haemoglobin levels where obtained 5 years post treatment with the proposed product.

A positive opinion for autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human *beta$^{A\text{-}T87Q}$-globin* gene, for treatment of beta-thalassemia intermedia and major, was adopted by consensus.

2.2.5 Chimeric monoclonal antibody against claudin 6 for treatment of ovarian cancer, GANYMED Pharmaceuticals AG - EMA/OD/147/12

[Co-ordinators: B. Bloechl-Daum / S. Mariz]

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

The intention to treat the condition with the product was considered justified on the grounds of preclinical data from a murine model of the condition. In this model, treatment with the sponsor's product showed reduction in tumour size and increased survival. Ovarian cancer was estimated to be affecting approximately 3 in 10,000 people in the European Union, at the time the application was made; the prevalence calculation is based primarily on Globocan and the EUROCARE-4 as well as some publications relating to the epidemiology of the condition in Europe. The sponsor has provided satisfactory argumentation to establish that the condition is chronically debilitating, in particular due to abdominal pain or discomfort, an abdominal mass, bloating, back pain, urinary urgency, constipation, tiredness and a range of other non-specific symptoms, as well as more specific symptoms such as pelvic pain, abnormal vaginal bleeding or involuntary weight loss. There can be a build-up of fluid (ascites) in the abdominal cavity. The life threatening nature of the condition is associated with the fact that most patients with ovarian cancer have widespread disease at presentation. This may be partly explained by the relatively early spread of high grade papillary serous cancers to the rest of the peritoneal cavity. Five year survival in Europe has been estimated to be 40%. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that chimeric monoclonal antibody against claudin 6 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 non-clinical data using an ovarian cancer xenograft model in mice which established the effect on the inhibition of tumour growth of the product.

A positive opinion for chimeric monoclonal antibody against claudin 6, for treatment of ovarian cancer, was adopted by consensus.

2.2.6 Choline tetrathiomolybdate for treatment of Wilson's disease, Medical Need Europe AB - EMA/OD/142/12
[Co-ordinators: K. Westermark / S. Mariz]

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

The intention to treat the condition with the product was considered justified on the grounds that the effects seen with ammonium tetrathiomolybdate could be applicable to choline tetrathiomolybdate. The use of ammonium tetrathiomolybdate is well established in man. Wilson's disease was estimated to be affecting approximately 0.6 in 10,000 people in the European Union, at the time the application was made; several European publications and the Eurowilson Registry were used to establish the prevalence of the condition in Europe. The condition is a recessively inherited disorder of copper metabolism. It is chronically debilitating and can be life-threatening due to the toxic effects of copper, first accumulating in the liver and later on in the brain. The liver disease can present with symptoms ranging from mildly elevated transaminases to acute liver failure or liver cirrhosis. Around 5% of all patients are diagnosed only when they develop fulminant acute liver failure, sometimes fatal. Haemolytic anaemia can be the first sign of the disease. Around 50% of patients with Wilson's disease have neurological or neuropsychiatric symptoms. Psychiatric problems due to Wilson's disease may include behavioral changes and depression. The neurological symptoms include tremor, dystonia and seizures. If left untreated the neurological symptoms progress to extremely incapacitating and sometimes fatal states. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that choline tetrathiomolybdate may be of significant benefit to those affected by the condition. In particular, this applies to patients presenting with neurological symptoms who sometimes deteriorate during the initiation of treatment with authorised copper chelators. The objective of tetrathiomolybdate therapy is to initially stabilise the patient and prevent deterioration. Tetrahiomolybdate has demonstrated an ability to decrease copper levels very rapidly, within a few weeks and potently through highly specific copper chelation.

A positive opinion for choline tetrathiomolybdate, for treatment of Wilson's disease, was adopted by consensus.

2.2.7 For treatment of high altitude pulmonary oedema - EMA/OD/144/12
[Co-ordinators: M. Možina / L. Fregonese]

The Committee considered that the condition requires clarification by the sponsor. The sponsor is invited to justify high altitude pulmonary oedema (HAPE) as a distinct condition, in particular in relation to a potential overlap with acute lung injury, for which the sponsor already holds and orphan designation, taking into account the pathophysiology of the two conditions and the mechanism of action of the product in the two conditions.

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

2.2.8 Encapsulated human retinal pigment epithelial cell lines transfected with plasmid vector expressing human ciliary neurotrophic factor for treatment of retinitis pigmentosa, Enpharma Ltd - EMA/OD/159/11

[Co-ordinators: V. Saano / S. Tsigkos]

For the purpose of orphan designation, the COMP considered that the active ingredient should be renamed as "encapsulated human retinal pigment epithelial cell line transfected with plasmid vector expressing human ciliary neurotrophic factor".

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

The intention to treat the condition with the proposed active ingredient was considered justified on the basis of preclinical and clinical studies showing improved number of photoreceptor cells in the retinas. Retinitis pigmentosa was estimated to be affecting approximately 3 in 10,000 people in the European Union, at the time the application was made based on literature studies. The condition is chronically debilitating based on the development of night blindness and tunnel vision that may progress to total blindness. There is, at present, no satisfactory treatment that has been authorised in the European Union for patients affected by the condition.

A positive opinion for encapsulated human retinal pigment epithelial cell line transfected with plasmid vector expressing human ciliary neurotrophic factor, for treatment of retinitis pigmentosa, was adopted by consensus.

2.2.9 Modified recombinant human C-type natriuretic peptide for treatment of achondroplasia, BioMarin Europe Ltd. - EMA/OD/149/12

[Co-ordinators: V. Tillmann / L. Fregonese]

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

Achondroplasia was estimated to be affecting approximately 0.42 in 10,000 people in the European Union, at the time the application was made. The prevalence has been calculated based on literature data. The intention to treat the condition with the proposed product was supported by pre-clinical studies showing chondrocyte proliferation and differentiation leading to widening of the growth plates and skeletal growth. The condition is chronically debilitating and may result in shortened life expectancy. In addition to the disproportionate short stature that causes considerable functional limitation, several medical complications associated with the condition cause considerable morbidity. These complications include cervicomedullary compression, spinal stenosis, restrictive and obstructive lung disease, hearing loss, and tibial bowing. Individuals homozygous for the genetic mutation which causes achondroplasia die within a few weeks to months after birth. The life expectancy of heterozygous individuals has been shown to be decreased by 15 years compared with the general population. The main cause of reduced life expectancy in adult patients is increased cardiovascular disease. 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 modified recombinant human C-type natriuretic peptide, for treatment of achondroplasia, was adopted by consensus.

2.2.10 For treatment of moderate and severe traumatic brain injury - EMA/OD/141/12
[Co-ordinators: D. Krievins / L. Fregonese]

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

- Medical plausibility

The sponsor is invited to elaborate on the justifications for excluding the use of the product in mild forms of traumatic brain injury, taking into account: the mechanism of action of the proposed product, its potential efficacy in the mild forms, and the pharmacological and clinical arguments for restricting the therapeutic use to moderate and severe traumatic brain injury.

If it is medically plausible to include the mild form, the incidence calculation and the significant benefit discussion would have to be updated to the broadened condition.

- Prevalence

The sponsor should provide a final acceptable value of the incidence of the condition. The sponsor states that, based on the consulted literature sources, the incidence ranges from 0.95 to 6.6 per 10,000 population. The sponsor did not explain the scientific reasons for discarding in the final calculations the studies where incidence was above 5 in 10,000.

In addition the sponsor is invited to clarify whether the currently presented incidence data include also pre-hospital incidence.

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

2.2.11 For treatment of beta-thalassemia intermedia and major - EMA/OD/138/12
[Co-ordinators: R. Elbers / S. Mariz]

The Committee considered that the medical plausibility requires clarification by the sponsor. To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of beta-thalassemia intermedia and major, the sponsor is invited to further elaborate on:

- the relevance of the results of the single preclinical study used to support the medical plausibility of the product for the treatment of beta-thalassemia intermedia and major. It is not clear how the results seen on erythrocytes are applicable considering the underlying causes of the condition.

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

2.2.12 For treatment of myelodysplastic syndromes - EMA/OD/139/12
[Co-ordinators: R. Elbers / S. Tsigkos]

The Committee considered that the justification of significant benefit requires clarification by the sponsor. The justification of significant benefit is based on a novel mechanism of action, which may allow the product to treat the anaemia as a prominent symptom of the proposed condition. It is

postulated by the sponsor that the mechanism of action is independent from that of epoietins, as it involves the maturation phase of RBC development.

The sponsor however does not translate this new mechanism into a clinically relevant advantage or a major contribution to patient care. The sponsor is requested to further elaborate on the justification of significant benefit by discussing any available data and providing any comparative discussion vis a vis the standard of care for the proposed condition as applied for designation, including epoietins.

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

2.2.13 For treatment of haemophilia A - EMA/OD/152/12
[Co-ordinators: L. Gramstad / S. Tsigkos]

The Committee considered that the justification of significant benefit requires clarification by the sponsor. The arguments on significant benefit are based on the potential for improved efficacy and a less frequent dosing scheme in haemophilia patients requiring treatment with bypassing agents. The sponsor is basing this assumption on improved catalytic activity and pharmacological potency.

The sponsor is requested to elaborate on these claims by any available data in relevant preclinical or preliminary clinical settings, and to provide a comparative discussion based on data vis a vis other bypassing agents, in order to justify a clinically relevant advantage or major contribution to patient care.

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

2.2.14 For treatment of haemophilia B - EMA/OD/151/12
[Co-ordinators: L. Gramstad / S. Tsigkos]

The Committee considered that the justification of significant benefit requires clarification by the sponsor. The arguments on significant benefit are based on the potential for improved efficacy and a less frequent dosing scheme in haemophilia patients requiring treatment with bypassing agents. The sponsor is basing this assumption on improved catalytic activity and pharmacological potency.

The sponsor is requested to elaborate on these claims by any available data in relevant preclinical or preliminary clinical settings, and to provide a comparative discussion based on data vis a vis other bypassing agents, in order to justify a clinically relevant advantage or major contribution to patient care.

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

2.2.15 Recombinant human monoclonal antibody of the IgG1 kappa class against prostate stem cell antigen for treatment of pancreatic cancer, Astellas Pharma Europe B.V. - EMA/OD/145/12
[Co-ordinators: B. Bloechl-Daum / S. Mariz]

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

The intention to treat the condition with the product was considered justified on the grounds that the effects seen with recombinant human monoclonal antibody of the IgG1 kappa class against prostate stem cell antigen was seen in preclinical and clinical data. The product has shown promise in reducing tumour size in non-clinical models and improved survival in patients. Pancreatic cancer was estimated to be affecting approximately 1.4 in 10,000 people in the European Union, at the time the application was made. Several databases and registries have been used by the sponsor to establish the prevalence of pancreatic cancer. The sponsor has established that the condition is chronically debilitating and life threatening due to a poor prognosis, partly because the cancer usually causes no symptoms early on, leading to locally advanced or metastatic disease at time of diagnosis. It can be associated with pain in the upper abdomen, loss of appetite and/or nausea and vomiting and weight loss. Jaundice occurs when a cancer of the head of the pancreas (75% of cases) obstructs the common bile duct. The jaundice may be associated with itching as the salt from excess bile can cause skin irritation. It may occasionally cause the appearance of diabetes where insulin production is hampered. Fatigue, weakness and depression are also often noted. Survival at one year in patients diagnosed with pancreatic cancer has been estimated to be 20%. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that recombinant human monoclonal antibody of the IgG1 kappa class against prostate stem cell antigen may be of significant benefit to those affected by the condition. The sponsor has some preliminary clinical data from a phase II study which suggest some improvement in survival in patients with adenocarcinoma when it is used in combination with gemcitabine.

A positive opinion for recombinant human monoclonal antibody of the IgG1 kappa class against prostate stem cell antigen, for treatment of pancreatic cancer, was adopted by consensus.

2.2.16 Terguride for treatment of systemic sclerosis, Serodapharm UG (haftungsbeschränkt) - EMA/OD/153/12
[Co-ordinators: J. Torrent-Farnell/ I. Bradinova / S. Mariz]

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

The intention to treat the condition with the product was considered justified on the grounds on preliminary clinical data. In this model, treatment with terguride showed promise of effectiveness in the condition. Systemic sclerosis was estimated to be affecting approximately 1.6 in 10,000 people in the European Union, at the time the application was made; the sponsor has used the results of a literature search to establish the prevalence. The condition is chronically debilitating due to the deposition of collagen in the skin and, less commonly, in the kidneys, heart, lungs and stomach. This deposition presents in two forms: diffuse scleroderma which affects the skin as well as the heart, lungs, gastrointestinal tract and kidneys and localized scleroderma which affects the skin of the face, neck, elbows and knees and late in the disease causes isolated pulmonary hypertension. Common complications seen with the diffuse form are pulmonary hypertension, reflux esophagitis and dysphagia, as well as the appearance of sclerodermal renal crisis. Symptoms of scleroderma renal crisis are malignant hypertension, hyperreninemia, azotemia and microangiopathic haemolytic anaemia. Renal involvement is associated with poor prognosis and is frequently associated with mortality. It is also life-threatening due to a 5-year survival which has been reported to lie between 34% and 73%. Frequent causes of mortality are pulmonary arterial hypertension and sclerodermal renal crisis. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that terguride, may be of significant benefit to those affected by the condition. The current approved therapy in Europe is bosentan which targets

pulmonary hypertension a consequence of diffuse scleroderma and not the underlying cause. Terguride offers the possibility of targeting an alternative aspect of the condition which is driven by a systemic autoimmune process. The sponsor has provided preliminary clinical data supporting the effectiveness of terguride on the fibrotic process in patients with systemic sclerosis. This would offer significant benefit since the therapy offers the possibility of reducing the fibrosis process which is directly associated with the condition not targeted by the current approved therapy.

A positive opinion for terguride, for treatment of systemic sclerosis, was adopted by consensus.

2.2.17 For treatment of inoperable chronic thromboembolic pulmonary hypertension - EMA/OD/154/12
[Co-ordinators: V. Saano / S. Tsigkos]

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

- Proposed indication and medical plausibility

The sponsor is proposing a subset of chronic thromboembolic pulmonary hypertension (CTEPH), focusing on inoperable patients. The sponsor's attention is drawn to the updated guideline ENTR 6283/00, which provisions against using stages of severity or degrees to define a valid condition for designation. Unless the sponsor would be in a position to justify that there would be no pharmacodynamic effects in the excluded patients the proposed indication as applied for cannot be accepted. The sponsor should hence revise the proposed indication.

- Significant benefit

In light of an amended indication, the sponsor should position the product in the current management of these patients. The sponsor is also requested to provide a comparative discussion versus authorised counterparts for the broader indication of pulmonary hypertension, including products containing the same active substance authorised in several Member States authorised for pulmonary arterial hypertension.

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

2.2.18 Lenalidomide for treatment of follicular lymphoma, Celgene Europe Limited - EMA/OD/158/12
[Co-ordinators: K. Kubáčková / L. Fregonese]

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

Follicular lymphoma was estimated to be affecting approximately 2.2 in 10,000 people in the European Union, at the time the application was made. The prevalence was estimated based on relevant international literature and cancer registries. The intention to treat the condition with the proposed product was supported by preclinical studies showing reduction of tumour size when the product was used in monotherapy or in combination with rituximab, and clinical studies showing favourable response in refractory and relapsing follicular lymphoma. The condition is life-threatening and chronically debilitating due to frequent relapses and increasing resistance to treatment. Organ obstruction, organ dysfunction and pain may occur depending on the location of the tumour. Although satisfactory methods of treatment of the condition have been authorised in the European Union, sufficient justification has been provided that lenalidomide may be of significant benefit to those

affected by the condition. This appears justified by the clinical data presented by the sponsor, showing favourable response rates in relapsing and refractory follicular lymphoma, particularly when the product is used in combination with rituximab. This represents a preliminary evidence of potential improved clinical efficacy when the product is used in combination with currently authorised products.

A positive opinion for lenalidomide, for treatment of follicular lymphoma, was adopted by consensus.

2.3. Evaluation on-going

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

2.4. Validation on-going

The Committee was informed that validation was on-going for twenty five applications for orphan designation.

3. Requests for protocol assistance

3.1 For treatment of cystic fibrosis [Co-ordinator: B. Blöchl-Daum]

The Committee was briefed on the significant benefit issues. The protocol assistance letter was adopted.

3.2 For treatment of pancreatic cancer [Co-ordinator: R. Elbers]

The Committee was briefed on the significant benefit issues. The protocol assistance letter was adopted.

4. Overview of applications

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

COMP co-ordinators were appointed for two applications submitted and seventeen upcoming applications. One expert was appointed for an on-going application.

4.2 Update on orphan applications for Marketing Authorisation

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

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 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]
Type II variation – extention of indication:

The CHMP positive opinion was adopted in November 2012 for the treatment of chronic iron overload requiring chelation therapy when deferoxamine therapy is contraindicated or inadequate in patients with non-transfusion-dependent thalassaemia syndromes aged 10 years and older The COMP had extensive discussions regarding how the proposed extension to the therapeutic indication fitted within the broader orphan condition. Consultation with the CHMP Rapporteur was sought regarding clarification of the group of patients the indication was being extended to.

5.1.2 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: D. O'Connor / L. Fregonese]

The Committee noted the CHMP negative opinion adopted in November 2012.

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

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

5.2.2 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); Merck Sharp & Dohme Limited [Co-ordinators: TBC / L. Fregonese]

- treatment of soft tissue sarcoma (OD/050/05, EU/3/05/312)
- treatment of primary malignant bone tumours (OD/055/05, EU/3/05/321)

The Committee noted the withdrawal of the MA application by the sponsor in November 2012.

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

5.3. On-going procedures

5.3.1 Bedaquiline ((1R,2S) 6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-(1-naphthyl)-beta-phenyl-3-quinolineethano) for treatment of tuberculosis; Janssen-Cilag International N.V. (OD/024/05 , EU/3/05/314) [Co-ordinators: N. Sypsas / L. Fregonese].

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) [Co-ordinators: A. Magrelli / S. Tsigkos].

5.3.3 Cometriq [Cyclopropane-1,1-dicarboxylic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide (4-fluoro-phenyl)-amide, (L)-malate salt] for treatment of medullary thyroid carcinoma; TMC Pharma Services Ltd (OD/088/08, EU/3/08/610) [Co-ordinators: B. Bloechl-Daum / TBC].

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

5.3.5 Defitelio (Defibrotide); Gentium S.p.A. [Co-ordinators: J. Torrent-Farnell / S. Mariz]

- prevention of hepatic veno-occlusive disease (OD/025/04, EU/3/04/211)
- treatment of hepatic veno-occlusive disease (OD/026/04, EU/3/04/212).

5.3.6 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].

5.3.7 Folcepri (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, Endocyte Europe, B.V. (OD/055/12, EU/3/12/1043, [Co-ordinators: B. Bloechl-Daum / TBC].

5.3.8 Iclusig (benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]-); ARIAD Pharma Ltd [Co-ordinators: K. Kubackova / L. Fregonese]

- treatment of chronic myeloid leukaemia (OD/121/09, EU/3/09/716);
- treatment of acute lymphoblastic leukaemia (OD/122/09, EU/3/09/715).

5.3.9 Kinaction (Masitinib mesilate) for treatment of pancreatic cancer; AB Science (OD/063/09, EU/3/09/684) [Co-ordinators: B. Bloech-Daum / S. Tsigkos].

5.3.10 Masican N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole for treatment of malignant gastrointestinal stromal tumours; AB Science (OD/061/04, EU/3/04/251) [Co-ordinators: D. O'Connor / S. Mariz].

5.3.11 Neocepri (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; Endocyte Europe, B.V. (OD/056/12, EU/3/12/1044) [Co-ordinators: B. Bloechl-Daum / TBC].

5.3.12 Opsumit (Macitentan) for treatment of pulmonary arterial hypertension; Actelion Registration Ltd. (OD/023/11, EU/3/11/909) [Co-ordinators: V. Saano / TBC].

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

5.3.14 Pheburane (Sodium phenylbutyrate) for treatment of carbamoyl-phosphate synthase-1 deficiency; Lucane Pharma SA (OD/098/11, EU/3/12/951) [Co-ordinators: J. Torrent-Farnell / L. Fregonese].

5.3.15 Pomalidomide Celgene (Pomalidomide) for treatment of multiple myeloma, Celgene Europe Ltd. (OD/053/09, EU/3/09/672) [Co-ordinators: R. Elbers/ S. Mariz].

5.3.16 Raxone (previously 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].

5.3.17 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 / S. Tsigkos], tpe II variation.

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

5.3.19 Translarna (3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid) for treatment of Duchenne muscular dystrophy; PTC Therapeutics Ltd (OD/106/04, EU/3/05/278, EMA/H/C/002720) [Co-ordinators: P. Evers / TBC].

5.3.20 Vynfinit (Vincaleukoblastin-23-oic acid, O4-deacetyl-2-[(2-mercaptoethoxy)carbonyl]hydrazide, disulfide with N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-L-gamma-glutamyl-L-alpha-aspartyl-L-arginyl-L-alpha-aspartyl-L-alpha-aspartyl-L-cysteine) for treatment of ovarian cancer; Endocyte Europe, B.V. (OD/094/11, EU/3/12/959) [Co-ordinators: B. Bloechl-Daum / TBC].

5.3.21 Winfuran (-)-17(cyclopropylmethyl)-1,14 ß-dihydroxy-4,5 alpha-epoxy-6ß-[N-methyl-trans-3-(3-furyl) acrylamido] morphinan hydrochloride for treatment of uremic pruritus; Toray International U.K. Limited (OD/020/02, EU/3/02/115) [Co-ordinators: S. Thorsteinsson / S. Mariz].

5.3.22 Vantobra Tobramycin (inhalation use) for treatment of *Pseudomonas Aeruginosa* lung infection in cystic fibrosis; PARI Pharma GmbH (OD/094/08, EU/3/09/613) [Co-ordinators: J. Eggenhofer, V. Stoyanova / TBC].

6. Procedural aspects

6.1 Appointment of the COMP representatives to the EMA Scientific Advice Working Party (SAWP) to be held at the January 2013 meeting

http://www.ema.europa.eu/ema/index.jsp?curl=pages/contacts/CHMP/people_listing_000022.jsp&mid=WC0b01ac0580028d94

The potential candidates were reminded to send their motivation letters and CVs to the COMP secretariat by 20 December 2012.

6.2 European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP)

The Draft PCWP Work Plan for 2013, EMA/571572/2012 was presented to the Committee and adopted.

6.3 European Medicines Agency Human Scientific Committees' Working Party with Healthcare Professionals' Organisations (HCPWP)

The Draft HCPWP Work Plan 2013, EMA/526726/2012 was tabled for information.

7. Any other business

7.1 COMP Informal meeting held on 22-23 November 2012 in Rome

The topic as postponed.

7.2 COMP Informal meeting to be held on 28 February - 1 March 2013 in Dublin

The Committee was informed about the forthcoming meeting.

7.3 Managing Meeting Documents (MMD)

The follow-up training on the system was given to the COMP members.

7.4 COMP Work Programme 2013-2015

The proposal document EMA/COMP/600966/2012 was tabled and will be discussed at the January 2013 meeting.

Date of next COMP meeting: 8 - 9 January 2013

List of participants

Chair:

Bruno Sepodes

Vice-Chair:

Lesley Greene	Volunteer patient representative for Eurordis

COMP Members:

André Lhoir	België/Belgique/Belgien
Irena Bradinova	България
Dorthe Meyer	Danmark
Rembert Elbers	Deutschland
Vallo Tillmann	Eesti
Geraldine O'Dea	Éire/Ireland
Nikolaos Sypsas	Ελλάδα
Annie Lorence	France
Sigurdur B. Thorsteinsson	Iceland
Armando Magrelli	Italia
Dainis Krievins	Latvija
Aušra Matulevičienė	Lietuva
Henri Metz	Luxembourg
Judit Eggenhofer	Magyarország (present on the 1st day only)
Albert Vincenti	Malta
Violeta Stoyanova-Beninska	Nederland
Lars Gramstad	Norway
Brigitte Blöchl-Daum	Österreich
Bożenna Dembowska-Bagińska	Polska
Ana Corrêa-Nunes	Portugal
Flavia Saleh	Romãnia
Martin Možina	Slovenija
Vacant	Slovensko
Veijo Saano	Suomi/Finland
Kerstin Westermark	Sverige
Daniel O'Connor	United Kingdom
Birthe Byskov Holm	Volunteer patient representative for Eurordis
Pauline Evers	Patient representative representing the European Genetic Alliances Network
János Borvendég	CHMP Representative (present on the 1st day only)
Aikaterini Moraiti	CHMP Representative
Vacant	EMA Representative

Observers:

Vesna Osrecki	Croatia
Frauke Naumann-Winter	Germany
Maria Mavris	Eurordis

EMA:

Jordi Llinares Garcia	Head of Orphan Medicines
Laura Fregonese	Scientific Administrator
Segundo Mariz	Scientific Administrator
Stylianos Tsigkos	Scientific Administrator
Carla Paganin	EMA Expert
Agnieszka Wilk-Kachlicka	Assistant
Frederique Dubois	Assistant
Nathalie Bere	Medical Information (for 6.2)
Hanne Thisen	IT (for 7.3)

Apologies

Members:

Kateřina Kubáčková	Česká Republika
Josep Torrent Farnell	España
Ioannis Kkolos	Κύπρος

European Commission:

Mirjam Söderholm	DG Health and Consumers

Observers:

Ivana Martinovic	Croatia
Antonio Blazquez	Agencia Española de Medicamentos y Productos Sanitarios