EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 June 2014
EMA/COMP/151064/2014 Rev. 1
Procedure Management and Business Support Division

Committee for Orphan Medicinal Products (COMP)

Minutes of the 8-9 April 2014 meeting

Chair: B. Sepodes – Vice-chair: L. Greene

Note on access to documents

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

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1. Introduction

1.1 Adoption of the agenda, EMA/COMP/15163/2014

The agenda was adopted with no amendments.

1.2 Adoption of the minutes of the COMP meetings held on:

- 4-6 February 2014, EMA/COMP/77369/2014
- 11-12 March 2014, EMA/COMP/74734/2014

The minutes were adopted with no amendments.

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:

P. Evers declared a potential conflict of interest on agenda point 5.2.3 and 5.1.4.

2. Applications for orphan medicinal product designation[1]

2.1. For opinion

2.1.1 (5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]- β-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one for treatment of biliary tree cancer, CellAct Pharma GmbH - EMA/OD/199/13
[Co-ordinators: B. Bloechl-Daum]

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

- Proposed condition

The sponsor is invited to elaborate on the proposed condition as applied for designation vis a vis the ICD classification system or other internationally accepted classifications.

- Number of people affected

As it seems that the sponsor has excluded part of the population affected by intrahepatic disease, the sponsor should indicate on which population the prevalence calculation is based on, and amend the estimate accordingly.

In the written response, and during an oral explanation before the Committee on 8-9 April 2014, the sponsor described that the indication comprises ICD codes C22.1, C23 and C24. The COMP considered that condition should be renamed to “treatment of biliary tract cancer”. With regards to the prevalence, the sponsor revised upwards the prevalence estimate, in order to reflect the whole population including intrahepatic disease. The latter was based on the assumption that approximately 10% of hepatic cancers are due to intrahepatic biliary tract disease.

[1] 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).

Following review of the application by the Committee, it was agreed to rename the indication to “biliary tract cancer”.

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

The intention to treat the condition with the medicinal product containing (5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]-β-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one was considered justified based on preliminary clinical studies showing responses in treated patients affected by the condition.

The condition is life-threatening in particular due to late diagnosis and poor prognosis in case of unresectable disease and chronically debilitating due to liver insufficiency, cholestasis, cholangitis, weight loss and cachexia. The condition was estimated to be affecting approximately 1.7 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing (5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]- β-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one may be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing responses in patients affected by biliary tract cancer that have been refractory to previous treatments. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for (5R,5aR,8aR,9S)-9-[[4,6-O-[(R)-Ethylidene]- β-D-glucopyranosyl]-oxy]-5-(4-({[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]carbonyl}oxy)-3,5-dimethoxyphenyl)-5,8,8a,9-tetrahydroisobenzofuro[5,6-f][1,3]benzodioxol-6(5aH)-one (CAP7.1), for treatment of biliary tract cancer was adopted by consensus.

2.1.2 Product for treatment of inherited retinal disease caused by lecithin: retinol acyltransferase (LRAT) or retinal pigment epithelium protein 65 (RPE65) mutations - EMA/OD/197/13
[Co-ordinators: K. Westermark]

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

- Intention to diagnose, prevent or treat

“Inherited Retinal Disease based on mutations in retinol acyltransferase (*LRAT*) or retinal pigment epithelium protein 65 (*RPE65*)”should be justified as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; your attention is drawn to the Orphan regulations and guidelines to clarify this (especially section A of ENTR/6283/00).

The sponsor is invited to:

Elaborate with regards to the definition of the condition ‘Inherited Retinal Disease based on mutations in retinol acyltransferase (*LRAT*) or retinal pigment epithelium protein 65 (*RPE65*)’ and how this fulfils the requirements for a distinct condition as stated in the Guideline on Format and Content of the applications (ENTR/6283/00).

Explain why treatment with the product should be restricted only to mutations in LRAT and RPE65 considering that it seems to work outside Inherited Retinal Diseases caused by mutations in *LRAT* and *RPE65.*

Refer to any new, generally agreed classification of Inherited Retinal Diseases supporting the condition as applied for designation.

Number of people affected

The sponsor should justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition and further elaborate on the derivation of the conclusion as proposed for the purpose of designation.

In the written response, and during an oral explanation before the Committee on 8 April 2014, the sponsor proposed a new indication "treatment of inherited retinal disease due to an underlying deficiency in endogenous 11-cis-retinal". The sponsor also acknowledged that most patients are diagnosed with Retinitis Pigmentosa (RP), Leber Congenital Amaurosis (LCA) or subsets thereof, based primarily on clinical presentation, mode of inheritance, and age of onset/diagnosis.

The COMP considered that the issues raised remain unaddressed. Neither did the sponsor provide any internationally agreed classification/consensus to support their proposal.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 8 April 2014, prior to final opinion.

2.1.3 ^{177}**Lu-tetraxetan-tetulomab** for treatment of follicular lymphoma, Nordic Nanovector AS - EMA/OD/200/13

[Co-ordinators: F. Naumann-Winter]

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

In order to establish the medical plausibility the sponsor is invited to clarify the relevance of the cell lines used in the generation of the in vitro and in vivo preclinical data to the proposed condition follicular lymphoma.

In addition the sponsor was asked to provide the results of the rituximab group in the preclinical xenograft study and to comment on the survival curve of the control group.

- Significant benefit

In order to support the significant benefit, the sponsor was asked to provide more details on the preliminary clinical data, including the baseline parameters of the five patients with follicular lymphoma, the time since last treatment, the number of betalutin doses given, and the concomitant treatments.

The sponsor was also invited to further discuss the response criteria applied for evaluating treatment success in these patients.

In the written response, and during an oral explanation before the Committee on 8 April 2014, the sponsor further elaborated on the available preliminary clinical data from a dose-finding study with overall seven patients affected by follicular lymphoma who have been treated with the product and of

whom five were evaluated for response. The sponsor explained that patients have received pre-treatment with rituximab and the unlabelled anti-CD37 tetulomab before the administration of the product. The sponsor presented PET images from two patients showing objective responses with regards to reduction of the tumour size at three months. The COMP considered that convincing preliminary evidence of the efficacy of the product in addition to the currently authorized treatments for follicular lymphoma exist. The Committee agreed that the condition, follicular lymphoma is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing ^{177}Lu-tetraxetan-tetulomab was considered justified based on preclinical and on preliminary clinical data showing antitumor activity.

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

The condition was estimated to be affecting less than 3.7 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing ^{177}Lu-tetraxetan-tetulomab may be of significant benefit to those affected by the condition. The sponsor provided preliminary clinical data showing favourable response in relapsed patients when the product was used in combination with rituximab. The Committee considered that this constitutes a clinically relevant advantage for the patients affected by follicular lymphoma.

A positive opinion for ^{177}Lu-tetraxetan-tetulomab, for treatment of follicular lymphoma, was adopted by consensus.

2.1.4 **Lutetium (^{177}Lu) edotreotide** for treatment of gastro-entero-pancreatic neuroendocrine tumours, ITG Isotope Technologies Garching GmbH - EMA/OD/196/13

[Co-ordinators: B. Bloechl-Daum]

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of gastro-entero-pancreatic neuroendocrine tumours, the sponsor should further elaborate on the compassionate use data submitted with particular focus on the length of time of exposure of the 66 GEPNET patients described as well as their disease characteristics (stage, relapsed or refractory) and previous oncological therapy. The sponsor should also identify the patients who received their product in the publications submitted clearly describing the stage of the disease, previous oncological therapy given, comparisons made and outcome.

- Significant benefit

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

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the results from the compassionate use study and the specific publications to justify the

assumption of significant benefit over authorised medicinal products for the proposed orphan indication.

The sponsor should detail the results of any clinical data they have to support the significant benefit assumption in the context of the current therapeutic management of patients.

In the written response, and during an oral explanation before the Committee on 8 April 2014, the sponsor further elaborated on the data generated in their compassionate use programme by clarifying the target patient population. The majority of patients who received the applied product were stage IV and had metastatic disease. They had received previous somatostatin receptor agonists (primarily octreotide) and some also chemotherapy. Outcome data showed favourable responses in progression free survival when patients received more than one dose when compared with what is reported in the literature. The Committee agreed that the condition, gastro-entero-pancreatic neuroendocrine tumours, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing lutetium (^{177}Lu) edotreotide was considered justified based on preliminary clinical data in patients who were affected by the condition.

The condition is chronically debilitating and life-threatening, in particular due to the debilitating symptoms and the poor prognosis in patients with localised advanced or metastatic disease.

The condition was estimated to be affecting approximately 3.5 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing lutetium (^{177}Lu) edotreotide may be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that patients with an advanced stage of the disease had an improved progression free survival time. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for Lutetium (^{177}Lu) edotreotide, for treatment of gastro-entero-pancreatic neuroendocrine tumours, was adopted by consensus.

2.1.5 **Recombinant human alpha 1 chain homotrimer of type VII collagen** for treatment of dystrophic epidermolysis bullosa, Shire Pharmaceuticals (Ireland) Limited - EMA/OD/201/13

[Co-ordinators: F. Naumann-Winter]

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of dystrophic epidermolysis bullosa, the sponsor should elaborate on:

- the transport from blood to the skin basal membrane (and not to organs other than the skin), taking into account the size of the product and the potential to form higher order aggregates;
- the interaction of the proposed product with the different constituents of the dermis
- the possible generation of antibodies against the proposed product.

In the written response, and during an oral explanation before the Committee on 9 April 2014, the sponsor further elaborated on the preclinical part of the application by providing new data from a c7-knock-out model and two further models of the condition, showing improvement in histology endpoints. In these settings, the treatment counters splitting of the dermal-epidermal junction in a dose-dependent manner.

With regards to the kinetics of the proposed product, it appears to home to the basal membrane zone and to be processed to anchoring fibrils, but the underlying mechanism is not understood. The sponsor suggested vasodilation, increased capillary permeability and neo-angiogenesis during the wound healing process to be involved in the homing mechanism.

Moreover, as regards the question on higher order aggregates, the sponsor reported that low levels have been measured by size exclusion chromatography, but both the purification process and the chromatography assay are actively being developed. Therefore any potential product-related variants remain to be further characterized.

Regarding the interaction of the proposed product with the different constituents of the dermis, the sponsor discussed available data in binding ELISA assays with laminin-332 and fibronectin as well as immunofluorescence data with laminin-111.

With respect to antibody generation the sponsor responded that preclinical evidence in the literature suggests that antibody formation occurs but does not interfere with therapeutic efficacy and is not pathogenic. Findings of the sponsor after intradermal injections in a preclinical model of the condition and studies conducted by the sponsor utilizing the IV route demonstrate that anti-C7 antibodies were not detected in the dermal-epidermal junction in the same animal model.

Following review of the application by the Committee, it was agreed to broaden/rename the indication to “treatment of epidermolysis bullosa“.

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

The intention to treat the condition with the medicinal product containing recombinant human alpha 1 chain homotrimer of type VII collagen was considered justified based on preclinical data showing correction of the separation between the epidermis and dermis, and improved survival with the proposed product.

The condition is chronically debilitating and life-threatening due to severe generalised blistering resulting in increased risk of infections with poor quality of life.

the condition was estimated to be affecting not more than 0.8 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for recombinant human alpha 1 chain homotrimer of type VII collagen**,** for treatment of epidermolysis bullosa, was adopted by consensus.

2.2. For discussion / preparation for an opinion

2.2.1 Product for treatment of cystic fibrosis - EMA/OD/002/14
[Co-ordinators: J. Eggenhofer]

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

- Intention to diagnose, prevent or treat

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

  - the results obtained on the expression of the corrected CFTR in vitro, and in particular the choice of the cut-off restoration of function to 10% of WT CFTR, and the clinical relevance of such restoration;
  - the clinical relevance of the results on chloride transport with the level of correction induced by the product;

- Significant benefit

The sponsor is requested to further discuss the data provided for supporting significant benefit and in particular the results of the arm(s) where the proposed product was used in monotherapy in clinical phase.

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.2 4-(4-Methoxy-phenylamino)-6-methylcarbamyl-quinoline-3-carboxylic acid for prevention of scarring in glaucoma filtration surgical procedure, Clanotech AB - EMA/OD/016/14

[Co-ordinators: J. Torrent-Farnell]

Following review of the application by the Committee, it was agreed to rename the indication to "prevention of scarring in post glaucoma filtration surgery".

The Committee agreed that the condition, scarring in glaucoma filtration surgery, is a distinct medical entity and meets the criteria for orphan designation.

The intention to prevent the condition with the medicinal product containing 4-(4-methoxy-phenylamino)-6-methylcarbamyl-quinoline-3-carboxylic acid was considered justified based on non-clinical in vivo data using a validated model.

The condition is chronically debilitating due to visual loss.

The condition was estimated to be affecting approximately 1.9 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for 4-(4-Methoxy-phenylamino)-6-methylcarbamyl-quinoline-3-carboxylic acid, for prevention of scarring post glaucoma filtration surgery, was adopted by consensus.

2.2.3 Adeno-associated viral vector serotype 2 containing the human CHM gene encoding human Rab escort protein 1 for treatment of choroideremia, Alan Boyd Consultants Ltd - EMA/OD/015/14

[Co-ordinators: A. Magrelli]

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

The intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 2 containing the human CHM gene encoding human Rab escort protein 1 was considered justified based on preclinical data showing improved expression and function of Rep1 protein in cell lines derived from patients affected by the condition, as well as published preliminary clinical data in patients affected by condition treated with a different comparable product.

The condition is chronically debilitating due to nyctalopia, loss of visual fields, tunnel vision, and eventually vision loss.

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

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

A positive opinion for Adeno-associated viral vector serotype 2 containing the human CHM gene encoding human Rab escort protein 1, for treatment of choroideraemia was adopted by consensus.

2.2.4 Aganirsen for treatment of ischaemic central retinal vein occlusion, Gene Signal SAS - EMA/OD/008/14
[Co-ordinators: A. Magrelli]

Following review of the application by the Committee, it was agreed to broaden/rename the indication to “treatment of central retinal vein occlusion”.

The Committee agreed that the condition, central retinal vein occlusion, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing aganirsen was considered justified based on data obtained in validated non-clinical in vivo models showing an improvement in inhibiting neovascularisation.

The condition is chronically debilitating due to severe damage to the retina which may lead to blindness.

The condition was estimated to be affecting approximately 2.8 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing aganirsen may be of significant benefit to those affected by the condition. The sponsor has provided preliminary non-clinical in vivo data using validated models of the condition to demonstrate that when the sponsor’s product is given in combination with ranibizumab it significantly reduces neovascularisation. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for Aganirsen, for treatment of central retinal vein occlusion, was adopted by consensus.

2.2.5 Autologous CD34+ cells transduced with a lentiviral vector containing the human SGSH gene for treatment of mucopolysaccharidosis IIIA Cochamo Systems Ltd - EMA/OD/006/14

[Co-ordinators: J. Torrent-Farnell]

Following review of the application by the Committee, it was agreed to broaden/rename the indication to “treatment of mucopolysaccharidosis IIIA (Sanfilippo A syndrome)”.

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

The intention to treat the condition with the medicinal product containing autologous CD34+ cells transduced with a lentiviral vector containing the human *SGSH* gene was considered justified based on in vivo non-clinical data using a validated model which showed that behavioural parameters were improved.

The condition is life-threatening and chronically debilitating due to frequent infections and neurocognitive delay that progresses to profound mental disability and vegetative state. The survival of the patients is limited to 20-30 years.

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

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

A positive opinion for Autologous CD34+ cells transduced with a lentiviral vector containing the human SGSH gene, for treatment of mucopolysaccharidosis IIIA (Sanfilippo A syndrome), was adopted by consensus.

2.2.6 Autologous dendritic cells pulsed with RNA from glioma stem cells for treatment of glioma, Epitarget AS - EMA/OD/001/14

[Co-ordinators: K. Kubáčková]

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

The intention to treat the condition with the medicinal product containing autologous dendritic cells pulsed with RNA from glioma stem cells was considered justified based on early clinical data showing improved survival in patients treated with the proposed product.

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

The condition was estimated to be affecting approximately 2.2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous dendritic cells pulsed with RNA from glioma stem cells may be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate that the product improves survival when given in addition to the currently authorized

methods of treatment when compared to what is reported in the literature. The Committee considered that this constitutes a clinically relevant advantage for patients affected by glioma.

A positive opinion for Autologous dendritic cells pulsed with RNA from glioma stem cells, for treatment of glioma, was adopted by consensus.

2.2.7 Product for treatment of chronic lymphocytic leukaemia/ small lymphocytic lymphoma - EMA/OD/195/13
[Co-ordinators: K. Kubáčková]

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma, the sponsor should:

  - further elaborate on the results obtained in vitro in the treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma, discussing in details the experimental settings, assessments and results.
  - present any further existing data with the specific product as applied for designation, in relevant models or preliminary clinical settings of the condition.
  - elaborate on the relevance of the data presented to draw conclusions for the treatment of the proposed conditions.

- Number of people affected

As it seems that the sponsor has excluded part of the population affected by condition, the sponsor should indicate on which population the prevalence calculation is based on.

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

- Significant benefit

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

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on any available data in relevant models of the condition to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan indication.

It is well known that extrapolation from preclinical or early preclinical studies cannot predict the safety of a product in its clinical setting, thus more relevant data is mandatory to justify safety arguments in most cases.

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.8 Product for treatment of amyotrophic lateral sclerosis - EMA/OD/007/14
[Co-ordinators: V. Stoyanova]

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

- Intention to diagnose, prevent or treat

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

  - the methodology in the SOD1 model studies, including inflammatory and functional endpoints, and how symptom progression was measured;
  - the results obtained in the SOD1 model studies, and the relevance to the proposed use of the product;

The sponsor is also invited to clarify which, among the ones presented in this section, are sponsor's generated data, and indicate the appropriate references for non sponsor's generated data.

- Number of people affected

The sponsor is invited to further elaborate on the methods used to reach the proposed prevalence figure.

- Significant benefit

In order to support the significant benefit the sponsor is requested to further discuss the protocol and the data of the Phase II clinical study performed and published by the company Mitsubishi-Tanabe and presented in this application and in particular:

  - the baseline characteristics of the participants in the study;
  - the choice of endpoints, with clarification on whether any other clinical endpoints have been studied;
  - the way the pre-treatment values for the ALSFRS-R score have been generated, and their values for comparison;
  - the relevance of the changes reported in the ALSFRS-R score at 6 months on top of riluzole in supporting the clinically relevant advantage of adding the proposed product to riluzole;

Furthermore, it would be useful to have clarification about the sponsor' participation in the above study and to obtain more information on the on-going study and planned development programme of the sponsor with the proposed product.

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.9 **Isavuconazonium sulfate** for treatment of mucormycosis, Astellas Pharma Europe B.V. - EMA/OD/010/14
[Co-ordinators: S. Thorsteinsson]

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

The intention to treat the condition with the medicinal product containing isavuconazonium sulfate was considered justified based on preclinical data showing improved survival with the proposed product.

The condition is life-threatening due to possible fungal invasion of the vascular network which results in thrombosis and death of surrounding tissue in different organs.

The condition was estimated to be affecting approximately 0.06 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing isavuconazonium sulfate may be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing favourable response with the proposed product in patients that had not responded to treatment with some of the currently authorized medicinal products for the condition. The Committee considered that this constitutes a clinically relevant advantage for patients affected by mucormycosis.

A positive opinion for Isavuconazonium sulfate, for treatment of mucormycosis, was adopted by consensus.

2.2.10 Product for treatment of invasive aspergillosis - EMA/OD/009/14
[Co-ordinators: A. Moraiti]

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

- Significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit and in particular:

  - the relevance of the efficacy results of the study showing non-inferiority versus voriconazole, taking into account the high rate of discontinuation for insufficient therapeutic response in the treated group;
  - the claimed significant benefit on the grounds of an improved safety profile, and in particular:

- The different dosing regimens used in the phase III study as compared to the phase II study, and the implications for safety.
- The occurrence of fewer adverse events with the product in only three organ classes and the relevance of this to clinical safety.

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.11 Product for treatment of Stargardt's disease - EMA/OD/005/14
[Co-ordinators: J. Torrent-Farnell]

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of Stargardt’s disease, the sponsor should further:

- elaborate on the specific particulars of the vectors proposed for designation, specifying the promoter of the product as applied for designation
- elaborate on the relevance of the data submitted for the specific product as applied for designation, since it appears that several different products are used for the justification of the intention to treat
- specify which data pertain to the specific mixture proposed for designation, with relevance to the above questions

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.12 Product for treatment of Usher syndrome - EMA/OD/004/14
[Co-ordinators: A. Magrelli]

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

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of Usher syndrome, the sponsor should further:

- elaborate on the specific particulars of the vectors proposed for designation, specifying the promoter of the product as applied for designation
- elaborate on the relevance of the data submitted for the specific product as applied for designation, since it appears that several different products are used for the justification of the intention to treat
- specify which data pertain to the specific mixture proposed for designation, with relevance to the above questions

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.13 Paclitaxel-succinate- Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe for treatment of glioma, CLL Pharma - EMA/OD/003/14
[Co-ordinators: B. Bloechl-Daum]

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

The intention to treat the condition with the medicinal product containing paclitaxel-succinate-Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe was considered justified based on preclinical studies showing improved survival.

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.

The condition was estimated to be affecting approximately 2.2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing paclitaxel-succinate-Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe may be of significant benefit to those affected by the condition. The sponsor has provided data in preclinical models of the condition that compare favourably to results obtained with an authorised product in published studies. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for Paclitaxel-succinate- Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe, for treatment of glioma, was adopted by consensus.

2.2.14 Plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent for treatment of cystic fibrosis, Imperial Innovations Limited - EMA/OD/013/14
[Co-ordinators: V. Saano]

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

The intention to treat the condition with the medicinal product containing plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent was considered justified based on preclinical and preliminary clinical data showing correction of the CFTR-mediated chloride secretion in treated patients.

The condition is life-threatening and chronically debilitating due to the recurrent and resistant respiratory infections with development of bronchiectasis and terminal respiratory failure.

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

In addition, although satisfactory methods of treatment of the condition have been authorised in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent may be of significant benefit to those affected by the condition. The product offers the potential to treat the genetic defect at the base of cystic fibrosis. This is supported by preliminary clinical data provided by the sponsor showing correction of the CFTR-mediated chloride secretion. The Committee considered that this constitutes a clinically relevant advantage for the patients affected by cystic fibrosis.

A positive opinion for Plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent, for treatment of cystic fibrosis, was adopted by consensus.

2.2.15 Product for treatment of non-infectious uveitis - EMA/OD/014/14
[Co-ordinators: K. Westermark]

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of non-infectious uveitis, the sponsor should further elaborate on the validity of the use

of preclinical and clinical data obtained with a different product to the one proposed for designation, to support the medical plausibility of their product.

- Number of people affected

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

- Significant benefit

The sponsor is requested to further discuss the arguments provided for significant benefit and to elaborate on the advantages of their product compared with other authorised treatments. In particular, the sponsor is asked to elaborate on the assumption of significant benefit over dexamethasone which is authorised in Europe for non-infectious uveitis.

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.2.16 Product for treatment of Glucose Transporter Type-1 Deficiency Syndrome - EMA/OD/011/14
[Co-ordinators: A. Corrêa Nunes]

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

- Intention to diagnose, prevent or treat

To establish correctly if there exists a scientific rationale for the development of the proposed product for treatment of glucose transporter type-1 deficiency syndrome, and with reference to the updated guideline ENTR/6283/00 Rev 04, the sponsor is invited to submit their own data with the specific product as applied for designation in either a specific model of the condition or in patients affected by the condition as applied for designation.

The sponsor should also discuss the relevance of the preclinical models used for the treatment of glucose transporter type-1 deficiency syndrome.

The COMP adopted a list of issues for a written response and during an oral explanation before the Committee at the May meeting.

2.3. Evaluation on-going

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

2.4. Validation on-going

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

3. Requests for protocol assistance

3.1 Product for treatment of follicular lymphoma.

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 7 applications submitted and 31 upcoming applications.

4.2 Update on orphan applications for Marketing Authorisation

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

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 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. (EU/3/12/1043) [Co-ordinators: B. Bloechl-Daum]

The COMP noted that CHMP opinion on MA adopted at 17-20 March 2014 meeting.

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

Currently Approved Diagnostics

1. Additional information should be provided to support the use of Folcepri in the context of the currently used diagnostics for ovarian cancer. A discussion on the currently endorsed diagnostic techniques which are available and used within the context of the condition should be further elaborated.

Justification of Significant Benefit

2. Additional argumentation should be provided to justify the potential significant benefit of Folcepri over the currently used diagnostics for ovarian cancer. The clinically relevant advantage should be supported with data with the product used within the context of the condition.

In its written response, and during an oral explanation before the Committee on 8 April 2014, the sponsor re-presented the data they had used in their submission to the CHMP to support the diagnostic properties of their product. Current diagnostic techniques in Europe use the classical “gold standard” tumour biomarker, CA125 in the diagnosis of epithelial ovarian cancer as it is enhanced in 90% of patients (Sarojini S. et al Journal of Oncology, Vol 2012, Article ID 709049). Early detection of ovarian cancer includes transvaginal ultrasonography, biomarker analysis or a combination of both. The sponsor’s product is used as a secondary diagnostic to identify a subset of folate receptor positive

ovarian cancer patients after they have been identified by the more classical early detection methods. It was noted that 80-90% of ovarian cancers over-express this marker.

The COMP also discussed the condition identified at the time of designation i.e. “folate-receptor positive ovarian cancer”. As there has been further evolution in the discussions around biomarkers and their use in the identification of distinct medical entities, the COMP considered that in this case the original indication as identified comes under ovarian cancer, which is a distinct medical entity.

The COMP concluded that: The proposed therapeutic indication falls entirely within the scope of the orphan indication of the designated Orphan Medicinal Product. The COMP considered that the product is to be used for diagnosing positive folate receptor status in ovarian cancer patients and that ovarian cancer is a recognised distinct medical entity.

The prevalence of ovarian cancer (hereinafter referred to as “the condition”) was estimated to be 4.3 in 10,000 at the time of the review of the designation criteria.

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.

Although several methods are considered satisfactory for the diagnosis of ovarian cancer, the assumption that Folcepri could be of potential significant benefit still holds as there is currently no authorised product for diagnosing positive folate receptor status in ovarian cancer patients in the European Union. The sponsor has produced data to show that folcepri can be used in patients who have been diagnosed with ovarian cancer with the aim to further identify those ovarian cancer patients who are folate receptor positive. This supports the principle that this diagnostic offers a clinically relevant advantage regarding the selection of the specific patient population who can benefit from anti-folate receptor therapy as defined in the granted therapeutic indication.

An opinion not recommending the removal of 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) (EU/3/12/1043) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The draft public summary of the COMP opinion was adopted for publication on the EMA website.

5.1.2 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. (EU/3/12/1044) [Co-ordinators: B. Bloechl-Daum]

The COMP noted that CHMP opinion on MA adopted at 17-20 March 2014 meeting.

As agreed during the previous 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

Additional argumentation should be provided to justify the potential significant benefit of folic acid used in combination with Folcepri over folic acid used as a diagnostic for ovarian cancer. This should be supported with data with the product within the context of the condition. The sponsor should also explain how this form of folic acid shows significant benefit over other forms of folic acid authorised for this purpose in this condition.

In its written response, and during an oral explanation before the Committee on 8 April 2014, the sponsor further elaborated on the raised issue. The sponsor clarified that folic acid iv is given before using Folcepri, the radio-nucleotide folate receptor marker, used as a diagnostic in folate receptor positive ovarian cancer. Folic acid i.v. used in this manner enhances the quality of the SPECT produced by the Folcepri. The sponsor has conducted a multi-center study comparing the SPECT scan of chest, abdomen and pelvis (qualitative analysis) and whole-body planar images (quantitative analysis) in normal volunteers to evaluate the utility of FA pre-injection to reduce the background activity of Folcepri. Data submitted showed an enhanced image when folic acid was used before administration of the 99mTc radio-labelled Folcepri.

The COMP noted that several countries had iv authorised formulations of folic acid. However, the authorised indications did not cover the field of diagnostics as in the current application but were associated with treatment of vitamin deficiencies for example. The COMP noted that provided that it was clear that the product was to be used before the use of Folcepri in the diagnosis of folate receptor positive ovarian cancer that the basis for significant benefit could be supported within the context of the classical diagnostics used in the identification of ovarian cancer.

The COMP also discussed the condition identified at the time of designation i.e. “folate-receptor positive ovarian cancer”. As there has been further evolution in the discussions around biomarkers and their use in the identification of distinct medical entities the COMP considered that in this case the original condition identified comes under ovarian cancer that is a distinct medical entity. The COMP concluded that:

The proposed therapeutic indication falls entirely within the scope of the orphan indication of the designated Orphan Medicinal Product. The COMP considered that the product is to be used for diagnosing positive folate-receptor status in ovarian cancer patients and that ovarian cancer is a recognized distinct medical entity.

The prevalence of ovarian cancer (hereinafter referred to as “the condition”) was estimated to be 4.3 in 10,000 at the time of the review of the designation criteria.

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.

Although several methods are considered satisfactory for the diagnosis of ovarian cancer, the assumption that Neocepri could be of potential significant benefit still holds as there is currently no authorised product for diagnosing positive folate receptor status in ovarian cancer patients in the European Union. The sponsor has submitted data to support that the administration of the product before the use of the radionucleotide diagnostic Folcepri enhances the quality of the SPECT image produced in patients who have folate receptor positive ovarian cancer. These findings support the clinically relevant advantage of using Neocepri before Folcepri in the selection of the specific patient population who can benefit from anti-folate receptor therapy.

An opinion not recommending the removal of (EU/) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The draft public summary of the COMP opinion was adopted for publication on the EMA website.

5.1.3 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. (EU/3/12/959) [Co-ordinators: B. Bloechl-Daum]

The COMP noted that CHMP opinion on MA adopted at 17-20 March 2014 meeting.

The COMP concluded that:

The proposed therapeutic indication falls entirely within the scope of the orphan indication of the designated Orphan Medicinal Product.

The prevalence of ovarian cancer (hereinafter referred to as “the condition”) was estimated to be 4.3 in 10,000 at the time of the review of the designation criteria.

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

Although satisfactory methods of treatment of the condition have been authorised in the European Union, the assumption that vynfinit may be of potential significant benefit still holds. The sponsor has presented clinical data to support the use of the product in combination with pegylated liposomal doxorubicin in folate receptor positive ovarian cancer patients who were platinum resistant or refractory where an increase in progression free survival was reported. Therefore the assumption of a clinically relevant advantage in ovarian cancer still holds.

An opinion not recommending the removal of 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) (EU/3/12/959) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The draft public summary of the COMP opinion was adopted for publication on the EMA website.

5.1.4 Sylvant (Chimeric-anti-interleukin-6 monoclonal antibody) for treatment of Castleman's disease; Janssen-Cilag International N.V. (EU/3/07/508) [Co-ordinators: J. Torrent-Farnell]

The COMP noted that CHMP opinion on MA adopted at 17-20 March 2014 meeting.

The COMP concluded that:

The proposed therapeutic indication falls entirely within the scope of the orphan indication of the designated Orphan Medicinal Product.

The prevalence of Castleman's disease (hereinafter referred to as “the condition”) was estimated to remain below 5 in 10,000 at the time of the review of the designation criteria, and was estimated to be less than 1 in 10,000 people at the time of the review.

The condition is chronically debilitating and life threatening due to the development of secondary neoplasias, infections and poor prognosis of multicentric forms resulting in increased mortality.

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

An opinion not recommending the removal of Sylvant (Chimeric-anti-interleukin-6 monoclonal antibody) (EU/3/07/508) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The draft public summary of the COMP opinion was adopted for publication on the EMA website.

5.1.5 Masican N-(methyl-diazacyclohexyl-methylbenzamide)-azaphenyl-aminothiopyrrole for treatment of malignant gastrointestinal stromal tumours; AB Science (EU/3/04/251)

The COMP noted the CHMP re-examination negative opinion adopted at the March 2014 meeting.

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

5.2.1 Obinutuzumab for treatment of chronic lymphocytic leukaemia; Roche Registration Limited (EU/3/12/1054)

5.2.2 Sorafenib tosylate Bayer HealthCare AG for:

a) treatment of follicular thyroid cancer (EU/3/13/1199)

b) treatment of papillary thyroid cancer (EU/3/13/1200)

5.2.3 Pasireotide for treatment of Cushing's disease; Novartis Europharm Limited (EU/3/09/671)

5.2.4 Tobramycin (inhalation use) for treatment of *Pseudomonas Aeruginosa* lung infection in cystic fibrosis; PARI Pharma GmbH (EU/3/09/613)

5.3. On-going procedures

5.3.1 Autologous tumour-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin for treatment of follicular lymphoma; Biovest Europe Ltd (EU/3/06/394)

5.3.2 (1R,2R)-octanoic acid[2-(2',3'-dihydro-benzo[1,4] dioxin-6'-yl)-2-hydroxy-1-pyrrolidin-1-ylmethyl-ethyl]-amide-L-tartaric acid salt for treatment of Gaucher disease; Genzyme Europe BV (EU/3/07/514)

5.3.3 Mifepristone for treatment of hypercortisolism (Cushing's syndrome) of endogenous origin; FGK Representative Service GmbH (EU/3/11/925)

5.3.4 Ramucirumab for treatment of gastric cancer; Eli Lilly Nederland B.V. (EU/3/12/1004)

5.3.5 Human heterologous liver cells (for infusion); Cytonet GmbH&Co KG

a) treatment of carbamoyl-phosphate synthase-1 deficiency (EU/3/10/821)

b) treatment of ornithine-transcarbamylase deficiency (EU/3/07/470)

c) treatment of citrullinaemia type 1 (EU/3/10/818)

d) treatment of hyperargininaemia (EU/3/10/819)

e) treatment of argininosuccinic aciduria (EU/3/10/820)

5.3.6 Ex vivo expanded autologous human corneal epithelium containing stem cells for treatment of corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns; Chiesi Farmaceutici S.p.A. (EU/3/08/579)

5.3.7 1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H- pyrazolo [3,4-d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one for treatment of mantle cell lymphoma; Janssen-Cilag International N.V. (EU/3/13/1115)

5.3.8 Tolvaptan for treatment of autosomal dominant polycystic kidney disease; Otsuka Pharmaceutical Europe Ltd (EU/3/13/1175)

5.3.9 Ketoconazole for treatment of Cushing's syndrome; Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare (EU/3/12/1031)

5.3.10 Ketoconazole for treatment of Cushing's syndrome; Laboratoire HRA (EU/3/12/965)

5.3.11 Levofloxacin hemihydrate for treatment of cystic fibrosis; Aptalis Pharma SAS (EU/3/08/566)

5.3.12 Masitinib mesilate for treatment of pancreatic cancer; AB Science (EU/3/09/684)

5.3.13 Dexamethasone (40 mg tablet) for treatment of multiple myeloma; Laboratoires CTRS (Cell Therapies Research & Services) (EU/3/10/745)

5.3.14 Olaparib for treatment of ovarian cancer; AstraZeneca AB (EU/3/07/501)

5.3.15 [Nle4, D-Phe7]-alfa-melanocyte stimulating hormone for treatment of erythropoietic protoporphyria; Clinuvel (UK) Limited (EU/3/08/541)

5.3.16 L-Asparaginase for treatment of acute lymphoblastic leukaemia; medac Gesellschaft fuer klinische Spezialpraeparate mbH (EU/3/04/258)

5.3.17 (3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid) for treatment of Duchenne muscular dystrophy; PTC Therapeutics Ltd (EU/3/05/278)

5.3.18 Chimeric monoclonal antibody against GD2 for treatment of neuroblastoma; United Therapeutics Europe Ltd (EU/3/11/879)

6. Procedural aspects

7. Any other business

7.1 Committees Secretariat Service introduction

7.2 4th presentation on the EMA move to 30 Churchill Place

Following the presentation given in the previous meeting, the COMP was briefed further on the conference rooms' equipment in the new building.

7.3 Adaptive licencing project

Date of next COMP meeting: 13-14 May 2014

List of participants

Chair:

Bruno Sepodes

Vice-Chair:

Lesley Greene	Volunteer patient representative for Eurordis

COMP Members:

André Lhoir	België/Belgique/Belgien
Irena Bradinova	Бълга̀рия
Frauke Naumann-Winter	Deutschland
Vallo Tillmann	Eesti
Geraldine O'Dea	Éire/Ireland
Nikolaos Sypsas	Ελλάδα
Josep Torrent Farnell	España
Annie Lorence	France
Adriana Andrić	Hrvatska
Sigurdur B. Thorsteinsson	Iceland
Armando Magrelli	Italia
Dainis Krievins	Latvija
Aušra Matulevičienė	Lietuva
Judit Eggenhofer	Magyarország
Albert Vincenti	Malta
Violeta Stoyanova-Beninska	Nederland
Lars Gramstad	Norway
Bożenna Dembowska-Bagińska	Polska
Ana Corrêa-Nunes	Portugal
Martin Možina	Slovenija
Zuzana Batová	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
Aikaterini Moraiti	EMA representative

Observers:

Maria Mavris	Eurordis