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EMA/COMP/897858/2022
Human Medicines Division

# Committee for Orphan Medicinal Products (COMP)

## Minutes for the meeting on 8-10 November 2022

Chair: Violeta Stoyanova-Beninska – Vice-Chair: Armando Magrelli

**Health and safety information**

In accordance with the Agency's health and safety policy, delegates were briefed on health, safety and emergency information and procedures prior to the start of the meeting.

**Disclaimers**

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the COMP meeting reports once the procedures are finalised.

Of note, this set of minutes is a working document primarily designed for COMP members and the work the Committee undertakes.

**Note on access to documents**

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

[1] Revision of section 2.1.3.

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# 1. Introduction

## 1.1. Welcome and declarations of interest of members and experts

The Chair opened the meeting by welcoming all participants. Due to the coronavirus (COVID-19) pandemic, and the associated EMA Business Continuity Plan (BCP), the meeting was held in-person with some members connected remotely (hybrid setting).

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

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

Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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

## 1.2. Adoption of agenda

The agenda for 08-10 November 2022 was adopted with no amendments.

## 1.3. Adoption of the minutes

The minutes for 04-06 October 2022 were adopted with no amendments and will be published on the EMA website.

# 2. Applications for orphan medicinal product designation

## 2.1. For opinion

### 2.1.1. serplulimab - EMA/OD/0000099427

Henlius Europe GmbH; Treatment of small cell lung cancer (SCLC)

COMP Rapporteur: Frauke 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:

- Number of people affected

The proposed prevalence appeared to be in line with previous considerations by COMP, however, the sponsor was asked to re-calculate the prevalence estimate based on the most

up-to-date relevant epidemiological studies and registries in Europe, including ECIS. In addition, the sponsor was requested to opt for the use of crude incidence as opposed to age-adjusted and rely on EU-27 data.

For the estimation and presentation of the prevalence estimate the sponsor was advised to refer to the "Points to Consider on the Estimation and Reporting of a Prevalence of a Condition for Orphan Designation".

In the written response, the sponsor presented a revised prevalence calculation following two methods. The first method was based on incidence of SCLC and 3-year and 1-year overall survival (OS) rate using the most conservative estimates. According to ECIS, the 2020 crude incidence of lung cancer in EU-27 was 71.4 in 100,000. In addition, the claim that in the Western world the proportion of patients with SCLC has decreased to 13% of lung cancer was taken into consideration. The estimation of complete prevalence of SCLC in the EU by 2021 was then divided into three parts (2017-2018, 2019-2020 and 2021), yielding an estimate of 1.9 in 10,000. The second method was based on the estimated new cases and deaths extracted from ECIS. In this method, estimation of complete prevalence of SCLC in the EU by 2021 had only one part (2017-2021). The sponsor concluded on a prevalence estimate of 0.9 in 10,000.

The revised calculation resulted in an adjusted prevalence range of 0.9 to 1.9 per 10,000 depending on the methodology and the source of data used. The COMP agreed with the methodology used and considered that the prevalence is 1.2 per 10,000 which is captured within the sponsors' proposal.

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

The intention to treat the condition with the medicinal product containing serplulimab was considered justified based on clinical data from patients affected by the condition which indicate improved survival of the proposed product in combination with chemotherapy.

The condition is chronically debilitating and life threatening due to its rapid progression and the development of widespread metastases, with a poor 5-year overall survival.

The condition was estimated to be affecting approximately 1.2 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing serplulimab will be of significant benefit to those affected by the condition. The sponsor has provided clinical data in treatment-naïve patients with extensive stage small cell lung cancer indicating a higher rate of responses and improved survival when combined with other chemotherapeutic agents authorised for the condition (cisplatin, etoposide). Indirect comparison to additional authorised treatments (atezolizumab and durvalumab) also compare favourably with respect to overall response rate and survival. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for serplulimab, for treatment of small cell lung cancer, was adopted by consensus.

### 2.1.2. - EMA/OD/0000091248

Treatment of haemophilia B

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:

- Number of people affected

The proposed prevalence appeared to be in line with previous considerations by the COMP, however, the sponsor was asked to re-calculate the prevalence estimate based on the most up-to-date relevant epidemiological studies and registers in Europe, including ECIS. In addition, the sponsor was requested to opt for the use of crude incidence as opposed to age-adjusted and rely on EU-27 data.

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

In the written response, and during an oral explanation before the Committee on 8 November 2022, it seemed that the sponsor did not have any additional data to show the potential of the product in the target patient population namely prophylactic therapy. The sponsor did discuss the potential for improved quality of life bridging from data in haemophilia A that they had to support major contribution to patient care. Although the COMP could see the potential both from a clinically relevant advantage and major contribution to patient care, the committee was of the opinion that without a minimal amount of non-clinical in vivo or preliminary clinical data the claim remains completely hypothetical. As such the COMP could not recommend granting the orphan designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 9 November 2022, prior to final opinion.

### 2.1.3. upifitamab rilsodotin - EMA/OD/0000082375

Dlrc Pharma Services Limited; Treatment of ovarian cancer (OC)

COMP Rapporteur: Brigitte Schwarzer-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:

- Significant benefit

The arguments on significant benefit were based on the potential improved efficacy over authorised medicinal products for the proposed orphan condition.

The sponsor was requested to further discuss the arguments provided for significant benefit and to elaborate on any updated results from the ongoing clinical study to justify the assumption of significant benefit over authorised medicinal products for the proposed orphan condition.

In the written response, the sponsor provided updated efficacy data, including additional efficacy measures. The updated efficacy data confirmed the positive trend with increase in ORR, PFS and OS. Benefit was also observed in patients regardless of prior PARP (poly ADP ribose polymerase) inhibitor or prior bevacizumab. The COMP considered that the observed

response rate in heavily pre-treated patients compared favourably to currently authorised products and cancelled the oral hearing as it was no longer needed.

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 medicinal product containing upifitamab rilsodotin was considered justified based on preliminary clinical data showing responses in patients with relapsed disease.

The condition is chronically debilitating due to pain, weight loss, ascites and vaginal bleeding, and life-threatening, with approximately half of the patients surviving less than five years.

The condition was estimated to be affecting approximately 4.9 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor provided sufficient justification for the assumption that the medicinal product containing upifitamab rilsodotin will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrate responses in patients affected by the condition. Indirect comparisons showed that the observed response rate in heavily pre-treated patients compares favourably to the currently authorised products.

The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for upifitamab rilsodotin, for treatment of ovarian cancer, was adopted by consensus.

### 2.1.4. - EMA/OD/0000096261

Treatment of progressive supranuclear palsy (PSP)

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

It was considered that there is no established correlation between the sponsors outcome parameters, as obtained from their in vitro cell culture assays, and clinically relevant functional effects. In order to support medical plausibility, the sponsor was requested to share any functional/efficacy data (non-clinical in vivo model of the disease or clinical data in PSP patients) there may be with their proposed fixed dose combination.

In the written response, and during an oral explanation before the Committee on 8 November 2022, the sponsor presented the new data in a non-clinical in vivo Alzheimer disease model (i.e. Tg2576 model) with the proposed product showing reduced hippocampal amyloid beta 40 and 42 aggregates and a trend towards improved cognitive impairment. However, this additional data in the non-clinical Alzheimer disease model was not considered relevant to support medical plausibility for the applied for condition of PSP. The COMP pointed out that amyloid beta is not known to play a prominent role as disease driver in PSP. Models of tauopathy exist and have been used by the sponsor previously, though only for one of the mono-components.

Overall, the COMP emphasised that functional data is generally preferable to biomarkers, particularly in diseases where biomarkers have not shown to correlate with clinical outcomes, like is the case in PSP.

Considering the above, the COMP did not consider that the data presented by the sponsor is sufficient to support medical plausibility in the applied for condition with the applied for product.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 8 November 2022, prior to final opinion.

### 2.1.5. - EMA/OD/0000098623

Treatment of gastro-entero-pancreatic neuroendocrine tumours (GEP-NET)

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

- Significant benefit

In order to clarify this section, the sponsor was requested to further discuss the arguments provided for significant benefit. In particular, the sponsor was asked to elaborate on:

- the non-clinical data in comparison to standard of care treatments used in GEP-NET. Specifically, on the possible reasons on why a difference was not observed between the vehicle controlled group, and the standard of care treatment groups;
- the clinical data presented in order to bring context to what could be expected in this relapse or refractory patient population, and how this product could be used in the armamentarium of existing products. Any new additional clinical data if available should also be provided.

Furthermore, it would be useful to obtain more information on the ongoing study/planned development.

In the written response, and during an oral explanation before the Committee on 10 November 2022, the sponsor emphasised what was conveyed as part of the initial application. The sponsor argued on the posology of choice, which differs from literature reports, and that showed a lack of effect when compared to the control group. However, the response put forward by the sponsor did not support such decision and did not aid the interpretability of the results.

In addition, the sponsor elaborated on the initially provided preliminary clinical data from the ongoing Phase I/IIa study and added data from one newly reported case study. The sponsor acknowledged the difficulty in drawing conclusions from a small number of patients from an uncontrolled clinical study, however, highlighted the observed outcomes as promising.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 10 November 2022, prior to final opinion.

### 2.1.6. iodine ($^{124}$I) evuzamitide - EMA/OD/0000096686

Regresponse Limited; Diagnosis of ATTR amyloidosis

COMP Rapporteur: Elisabeth Johanne Rook

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

- Significant benefit

The sponsor was invited to elaborate on where in the diagnostic workup of ATTR amyloidosis cardiomyopathy the proposed product would be used, and how it may compare to the standard diagnostic framework as recommended by the European Society of Cardiology (Garcia-Pavia, 2021). This should include a discussion of the positive percent agreement, and negative percent agreement versus the standard methods.

In the written response, the sponsor elaborated on the existing algorithm for the diagnosis of ATTR amyloidosis which varies on a case-by-case basis and can include invasive techniques (e.g., cardiac biopsies or extracardiac biopsies), or non-invasive techniques. In support of such discussion, the sponsor refers to two main publications - Gillmore JD, 2016 and Treglia, 2018. There was also provided a justification on where in the diagnosis armamentarium the proposed product could be envisioned, as an alternative to scintigraphy and concomitant with haematological testing providing an alternative non-invasive diagnostic modality. In support of such claims the sponsor also submitted additional clinical data initially provided from a single case report with a negative scintigraphy, but with a positive fat pad biopsy and a ATTR gene mutation. This patient had positive cardiac uptake of the proposed product but showed no significant cardiac uptake Tc99m pyrophosphate (PYP) scintigraphy. In this patient, an endomyocardial biopsy was performed, which further confirmed a diagnosis of ATTR cardiomyopathy. This result supported by a phase I/II study indicated that the proposed product could bear potential for significant benefit where the standard diagnostic agent fails.

The COMP considered that this level of evidence which includes results from a phase I/II study, could be considered sufficient to fulfil the criterion for significant benefit in the context of an initial orphan designation. The planned oral explanation was therefore cancelled. The Committee agreed that the condition, diagnosis of ATTR amyloidosis, is a distinct medical entity and meets the criteria for orphan designation.

The intention to diagnose the condition with the medicinal product containing iodine ($^{124}$I) evuzamitide was considered justified based on non-clinical data in a valid model of the condition, and preliminary clinical data showing sensitivity and specificity of Positron Emission Tomography imaging with the proposed product in the diagnosis of ATTR amyloidosis.

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

The population of patients eligible for diagnosis of the condition was estimated to be approximately 3.7 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of diagnosis of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing iodine ($^{124}$I) evuzamitide will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing sensitivity and specificity of Positron Emission Tomography imaging with the proposed

product for the diagnosis of patients with ATTR cardiac myopathy, without the need for additional (extra-)cardiac biopsies. This compares favourably to currently available diagnostic methods. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for iodine ($^{124}$I) evuzamitide, for diagnosis of ATTR amyloidosis, was adopted by consensus.

### 2.1.7. - EMA/OD/0000099136

Treatment of perinatal asphyxia

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 20 October 2022, prior to responding to the list of issues.

### 2.1.8. mebendazole - EMA/OD/0000096688

Healx Technology Limited; Treatment of autosomal dominant polycystic kidney disease (ADPKD)

COMP Rapporteur: Enrico Costa

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

Autosomal Dominant Polycystic Kidney Disease (ADPKD) should be justified as a distinct medical entity or a valid subset. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention is drawn to the Orphan regulations and relevant guidelines (especially section A of ENTR/6283/00).

The sponsor was requested to elaborate on:

- the rationale of choosing different routes of administration for mebendazole and controls in the ADPKD models used;
- the dose of tolvaptan used for the study (0.1% w/w) is the final circulating concentration in study subjects or it is the amount of drug in the diet;
- why the once-daily dosing regimen is considered ineffective given that the once-daily 20 mg/kg seems to have similar results than twice a day dosing from the graph.

- Significant benefit

The arguments on significant benefit were based on the potential improved efficacy in the condition as compared to authorized treatment.

The sponsor was requested to further discuss the arguments provided for significant benefit and to explain the reason for using tolvaptan as positive control only in the slowly progressing model when tolvaptan is authorized in a rapidly progressing setting.

In the written response, the sponsor clarified that the choice of different routes of administration (RoA) used for mebendazole (intraperitoneal) and everolimus (oral gavage)

are based on the PK profile of these drugs and on the characteristics of these RoA. In fact, for both RoAs, after the administration the compound is absorbed via mesenteric vessels and then drained into the hepatic vein (Lukas G. et al. in 1971). Since mebendazole administered orally has a low bioavailability, the sponsor developed a new formulation for intraperitoneal injection in order to obtain a better bioavailability and to maintain adequate systemic exposure of the compound. Following these promising bioavailability results, the sponsor decided to administer this new formulation of mebendazole also as oral gavage in the slowly progressing model. On the other hand, tolvapatan was administered in diet in line with its non-clinical development. Furthermore, the sponsor clarified that that the value of 0.1% w/w (weight/weight) tolvaptan was the amount of drug in the diet (consistent with the non-clinical studies of tolvaptan EPAR). In addition, in line with the additional data submitted, the 20 mg/kg once a day is considered ineffective compared to twice a day doses due to a lack of statistical significance of once a day dose in all the endpoint tested (cystic index, cystic grade, kidney weigh/body weight, terminal blood urea). The COMP considered that the clarifications were acceptable.

Regarding the question on the significant benefit, the sponsor acknowledged that a head-to-head comparison between mebendazole and tolvaptan in rapidly progressing ADPKD should have been a logical experiment to perform (as tolvaptan has been licensed for this specific form of the disease). However, the sponsor clarified that administration in medicated food, as in tolvaptan preclinical studies, is not an appropriate or feasible dosing, because the study subjects used for rapidly progressing disease are neonate and thus unable to consume food. Instead, this RoA is feasible in the slowly progressing model because study subjects are older and thus able to eat food. In addition, in response to the LoQ, the sponsor provided new in-vitro comparison data justifying SB over tolvaptan (data not shown). Specifically, tolvaptan showed no dose-dependent effect on cyst growth except for the highest tested dose (100uM) in an unstimulated ((-) ddAVP) patient-derived cells model. This shows that mebendazole is a more-effective anti-cystic agent across heterogeneous conditions of cyst growth and expansion which are likely to be encountered in ADPKD patients in the real world. The COMP concluded that based on the in vivo non-clinical data, mebendazole can have a therapeutic potential in treating both slow and fast progressing disease, not offered by the authorised product tolvaptan which is only indicated for fast progressing disease. Therefore, the justification for the significant benefit was acceptable. The oral explanation was therefore cancelled.

The Committee agreed that the condition, Autosomal Dominant Polycystic Kidney Disease (ADPKD), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing mebendazole was considered justified based on in vivo nonclinical data which showed suppression of kidney cyst growth and kidney size growth.

The condition is chronically debilitating and potentially life-threatening due to renal manifestations such as renal cyst infection, nephrolithiasis, and kidney failure requiring dialysis.

The condition was estimated to be affecting approximately 4.4 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor provided sufficient justification for the assumption that the medicinal product containing mebendazole will be of significant benefit to those affected by

the condition. The sponsor provided in vivo non clinical data that show that mebendazole can have a therapeutic potential in treating both slow and rapidly progressing disease, a solution not offered by the authorised product tolvaptan which is only indicated for rapidly progressing disease. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for mebendazole, for treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD), was adopted by consensus.

## 2.2. For discussion / preparation for an opinion

### 2.2.1. - EMA/OD/0000089519

Treatment of soft tissue sarcoma

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 December 2022 meeting.

*[Post-meeting note: The sponsor withdrew the application for orphan designation on 21 November 2022].*

### 2.2.2. 16-base single stranded RNA targeting miR-23b linked to oleic acid - EMA/OD/0000093338

Arthex Biotech S.L.; Treatment of myotonic disorders

COMP Rapporteur: Darius Matusevicius

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

The intention to treat the condition with the medicinal product containing 16-base single stranded RNA targeting miR-23b linked to oleic acid was considered justified based on non-clinical in vivo data in a valid model showing improvements of muscle strength and reduction in myotonia grade.

The condition is chronically debilitating due to muscle weakness, pain with stiffness which can be associated with falls and serious injury, cognitive and behavioural problems. Certain subtypes of the condition are life-threatening due to cardiac and pulmonary complications.

The condition was estimated to be affecting approximately 3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing 16-base single stranded RNA targeting miR-23b linked to oleic acid will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical in vivo data that suggests that the proposed product may be of benefit in a patient subset of the condition that cannot be treated with the currently authorized product. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for 16-base single stranded RNA targeting miR-23b linked to oleic acid, for treatment of myotonic disorders, was adopted by consensus.

### 2.2.3. - EMA/OD/0000095228

Treatment of carcinoid syndrome

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December 2022 meeting.

### 2.2.4. - EMA/OD/0000096050

Treatment of Duchenne muscular dystrophy

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December 2022 meeting.

*[Post-meeting note: The sponsor withdrew the application for orphan designation on 2 December 2022].*

### 2.2.5. - EMA/OD/0000097397

Treatment of Duchenne muscular dystrophy

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December 2022 meeting.

### 2.2.6. copper ($^{64}$Cu) oxodotreotide - EMA/OD/0000097578

Curium Pet France; Diagnosis of neuroendocrine neoplasms (NEN)

COMP Rapporteur: Bozenna Dembowska-Baginska;

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

The intention to diagnose the condition with the medicinal product containing Copper ($^{64}$Cu) oxodotreotide was considered justified based on clinical data demonstrating sensitivity and specificity of the applied for diagnostic in combination with positron emission tomography/ computed tomography compared to the standard of truth.

The condition is chronically debilitating and life-threatening, in particular due to adverse gastro-intestinal, respiratory and metabolic symptoms and the poor prognosis in patients with localized advanced or metastatic disease.

The population of patients eligible for the diagnosis of the condition was estimated to be approximately 1 in 10,000 persons in the European Union per year, at the time the application was made.

In addition, although satisfactory methods of diagnosis of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing Copper ($^{64}$Cu) oxodotreotide will be of significant benefit to the population eligible to receive this diagnostic agent.

The sponsor has provided preliminary comparative clinical data that demonstrated improved performance on a per-lesion analysis compared to the current standard of care diagnostic agent, which may lead to improvement in patient management.

The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for Copper ($^{64}$Cu) oxodotreotide, for treatment of diagnosis of neuroendocrine neoplasms, was adopted by consensus.

### 2.2.7. utreloxastat - EMA/OD/0000098389

PTC Therapeutics International Limited; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Robert Nistico

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

The intention to treat the condition with the medicinal product containing utreloxastat was considered justified based on non-clinical in vivo data in a model of the condition showing improved grip strength and delayed time to onset of morbidity.

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

The condition was estimated to be affecting approximately 1.1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing utreloxastat will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data that showed an improvement in grip strength and delayed time to onset of morbidity in a non-clinical in vivo model of the condition. The Committee considered that this constitutes a clinically relevant advantage.

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

### 2.2.8. recombinant adeno-associated virus Olig001 containing human aspartoacylase cDNA - EMA/OD/0000099257

Voisin Consulting Life Sciences; Treatment of Canavan disease

COMP Rapporteur: Gloria Maria Palomo Carrasco

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

The intention to treat the condition with the medicinal product containing recombinant adeno-associated virus Olig001 containing human aspartoacylase cDNA was considered justified based on non-clinical data in a valid model of the condition showing improvement in motor function tests as well as preliminary clinical observations in patients indicating improvements in motor function and signs of remyelination using magnetic resonance imaging.

The condition is life-threatening with life expectancy less than 10 years for the infantile variant of the condition and chronically debilitating due to developmental delay, hypotonia

developing into muscle stiffness and spasticity, optic nerve atrophy, seizures, swallowing difficulties and inability to move voluntarily.

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

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

A positive opinion for recombinant adeno-associated virus Olig001 containing human aspartoacylase cDNA, for treatment of Canavan disease, was adopted by consensus.

### 2.2.9. duvelisib - EMA/OD/0000099349

Secura Bio Limited; Treatment of peripheral T-cell lymphoma

COMP Rapporteur: Karri Penttila

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

The intention to treat the condition with the medicinal product containing duvelisib was considered justified based on preliminary clinical data in relapsed/refractory patients who responded to treatment with the proposed product.

The condition is life-threatening and chronically debilitating due to poor response to therapy and high rate of relapses. Clinical presentation and course vary from an indolent clinical behaviour for years in milder subtypes, to fulminant disease in aggressive subtypes.

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

In addition, although satisfactory methods of diagnosis/prevention/treatment of the condition exist in the European Union, the sponsor provided sufficient justification for the assumption that the medicinal product containing duvelisib will be of significant benefit to those affected by the condition/to the population at risk of developing the condition. The sponsor has provided preliminary clinical data that showed tumour responses in a patient population with relapsed/refractory peripheral T-cell lymphoma who is not covered by the only authorised treatment for a specific subtype of the condition. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for duvelisib, for treatment of peripheral T-cell lymphoma, was adopted by consensus.

### 2.2.10. - EMA/OD/0000099774

Prevention of tuberculosis

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 December 2022 meeting.

## 2.2.11. autologous T-cells transduced with a lentiviral vector encoding a chimeric antigen receptor against CD7 - EMA/OD/0000101416

Granzer Regulatory Consulting & Services GmbH; Treatment of acute lymphoblastic leukaemia

COMP Rapporteur: Jana Mazelova

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

The intention to treat the condition with the medicinal product containing autologous T-cells transduced with a lentiviral vector encoding a chimeric antigen receptor against CD7 was considered justified based on preliminary clinical data showing complete responses in heavily pre-treated patients with T-cell acute lymphoblastic leukaemia.

The condition is chronically debilitating and life-threatening depending on the response to treatment, with acute leukemic forms being fatal in a few weeks if left untreated. Symptoms include persistent fever, infections, anaemia, fatigue, breathlessness, bone and joint pain. The invasion of tumour cells in the bloodstream, the bone marrow and/or the lymphatic system result in lack of normal blood cells, bone marrow failure, and organ damage.

The condition was estimated to be affecting approximately 1.6 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing autologous T-cells transduced with a lentiviral vector encoding a chimeric antigen receptor against CD7 will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data showing high rate of responses in relapsed/refractory patients with T-cell acute lymphoblastic leukaemia who had been previously treated with available products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for autologous T-cells transduced with a lentiviral vector encoding a chimeric antigen receptor against CD7, for treatment of acute lymphoblastic leukaemia, was adopted by consensus.

## 2.2.12. briquilimab - EMA/OD/0000102490

Boyd Consultants Limited; Treatment in haematopoietic stem cell transplantation

COMP Rapporteur: Karri Penttila

The Committee agreed that the condition, haematopoietic stem cell transplantation, is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing briquilimab was considered justified based on preliminary clinical data in severe combined immunodeficiency patients who failed first hematopoietic stem cell transplantation engraftment showing good follow-up hematopoietic stem cell transplantation engraftment and in medically infirm or elderly acute myeloid leukaemia / myelodysplastic syndrome patients.

The condition is life-threatening and chronically debilitating due to susceptibility to severe infections and complications such as graft-versus-host disease.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing briquilimab will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that demonstrated successful hematopoietic stem cell transplantation engraftment in severe combined immunodeficiency patients who failed previous hematopoietic stem cell transplantation. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for briquilimab, for treatment in haematopoietic stem cell transplantation, was adopted by consensus.

### 2.2.13. - EMA/OD/0000103269

Treatment of peripheral T-cell lymphoma

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 December 2022 meeting.

### 2.2.14. - EMA/OD/0000103787

Treatment of primary sclerosing cholangitis

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 December 2022 meeting.

### 2.2.15. - EMA/OD/0000104107

Treatment of glioma

The COMP adopted a list of issues that will be sent to the sponsor. The sponsor will be invited to an oral explanation before the Committee at the December 2022 meeting.

### 2.2.16. potassium 2-chloro-3-(1-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-6-oxo-5-phenyl-6,7-dihydrothieno[2,3-b]pyridin-4-olate monohydrate - EMA/OD/0000104148

Poxel; Treatment of adrenoleukodystrophy

COMP Rapporteur: Darius Matusevicius

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

The intention to treat the condition with the medicinal product containing potassium 2-chloro-3-(1-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-6-oxo-5-phenyl-6,7-dihydrothieno[2,3-b]pyridin-4-olate monohydrate was considered justified based on non-clinical data in a model of the condition showing improvements in biochemical and morphological markers, and in motor function as measured by the open field neurologic test scores (total distance and freezing time);

The condition is life-threatening and chronically debilitating taking into consideration the two main phenotypes with which the condition presents. Cerebral adrenoleukodystrophy is associated with behavioural abnormalities, seizures, spastic tetraplegia and cognitive decline and patients usually die within a few years after the onset of symptoms. Adrenomyeloneuropathy is associated with primary adrenocortical insufficiency as well as sexual dysfunction, progressive stiffness and gait disturbance, sphincter dysfunction leading to incontinence, with a fatal outcome within 20 years following the onset of symptoms;

The condition was estimated to be affecting approximately 0.4 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for potassium 2-chloro-3-(1-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-6-oxo-5-phenyl-6,7-dihydrothieno[2,3-b]pyridin-4-olate monohydrate, for treatment of adrenoleukodystrophy, was adopted by consensus.

### 2.2.17. (2S)-4-[2-methoxyethyl-[4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl]amino]-2-(quinazolin-4-ylamino)butanoic acid - EMA/OD/0000105068

Pharma Gateway AB; Treatment of idiopathic pulmonary fibrosis

COMP Rapporteurs: Joao Rocha, Eva Malikova

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

The intention to treat the condition with the medicinal product containing (2S)-4-[2-methoxyethyl-[4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl]amino]-2-(quinazolin-4-ylamino)butanoic acid was considered justified based on non-clinical data in models of the condition showing a reduction in disease biomarkers and fibrosis score. Furthermore, preliminary clinical data demonstrated a reduction in the rate of decline of forced vital capacity compared to control groups.

The condition is chronically debilitating due to progressive dyspnoea and loss of respiratory function, with limited exercise capability and decreased quality of life, and life-threatening due to respiratory failure.

The condition was estimated to be affecting approximately 3 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing (2S)-4-[2-methoxyethyl-[4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl]amino]-2-(quinazolin-4-ylamino)butanoic acid will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data in patients affected by the condition that demonstrate improvement in forced vital capacity and relevant biomarkers when the proposed product was used as add-on therapy to existing standard of care products nintedanib or pirfenidone. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for (2S)-4-[2-methoxyethyl-[4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl]amino]-2-(quinazolin-4-ylamino)butanoic acid, for treatment of idiopathic pulmonary fibrosis, was adopted by consensus.

## 2.2.18. adeno-associated virus serotype rh79 containing the human *OTC* gene, adeno-associated virus serotype rh79 encoding a meganuclease for targeted editing of the human *PCSK9* gene - EMA/OD/0000105169

EMA Regulatory Submissions Expediter Limited; Treatment of ornithine transcarbamylase (OTC) deficiency

COMP Rapporteur: Zsofia Gyulai

The Committee agreed that the condition, ornithine transcarbamylase deficiency, 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 virus serotype rh79 containing the human *OTC* gene, adeno-associated virus serotype rh79 encoding a meganuclease for targeted editing of the human *PCSK9* gene was considered justified based on non-clinical data demonstrating extended survival and reduction in plasma ammonia levels.

The condition is chronically debilitating and life threatening due to the consequences of metabolic decompensation leading to developmental delay, mental disability, and other impairments of the central nervous system.

The condition was estimated to be affecting approximately 0.1 in 10,000 persons in the European Union, at the time the application was made.

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing adeno-associated virus serotype rh79 containing the human OTC gene, adeno-associated virus serotype rh79 encoding a meganuclease for targeted editing of the human *PCSK9* gene will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data in a relevant model of the condition demonstrating restoration of functional ornithine transcarbamylase, and improved survival which cannot be achieved with currently authorized products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for adeno-associated virus serotype rh79 containing the human OTC gene, adeno-associated virus serotype rh79 encoding a meganuclease for targeted editing of the human *PCSK9* gene, for treatment of ornithine transcarbamylase deficiency, was adopted by consensus.

## 2.2.19. - EMA/OD/0000105219

Treatment of diffuse large B-cell lymphoma

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 December 2022 meeting.

## 2.2.20. - EMA/OD/0000106875

Treatment of narcolepsy

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 December 2022 meeting.

*[Post-meeting note: The sponsor withdrew the application for orphan designation on 18 November 2022].*

## 2.3. Revision of the COMP opinions

None

## 2.4. Amendment of existing orphan designations

None

## 2.5. Appeal

None

## 2.6. Nominations

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

COMP rapporteurs were appointed for 24 applications.

## 2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 15 applications for orphan designation.

# 3. Requests for protocol assistance with significant benefit question

## 3.1. Ongoing procedures

### 3.1.1. -

Treatment of primary IgA nephropathy

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

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

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

None

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

### 4.2.1. – etranacogene dezaparvovec - EMEA/H/C/004827, EU/3/18/1999, EMA/OD/0000087180

CLS Behring GmbH; Treatment of haemophilia B

The status of the procedure at CHMP was noted.

### 4.2.2. – omburtamab I-131 - EMEA/H/C/005499, EU/3/17/1839, EMA/OD/0000063579

Y-Mabs Therapeutics A/S; Treatment of neuroblastoma

The status of the procedure at CHMP was noted.

### 4.2.3. Fintepla – fenfluramine hydrochloride - EMEA/H/C/003933/II/0012, EU/3/17/1836, EMA/OD/0000075867

Zogenix ROI Limited; Treatment of Lennox-Gastaut syndrome

CHMP Rapporteur: Thalia Marie Estrup Blicher; CHMP Co-Rapporteur: Johann Lodewijk Hillege

The status of the procedure at CHMP was noted.

## 4.3. Appeal

### 4.3.1. Zynlonta – loncastuximab tesirine - EMEA/H/C/005685, EU/3/21/2481, EMA/OD/0000115078

ADC Therapeutics (NL) B.V.; Treatment of diffuse large B-cell lymphoma

In the grounds for appeal, and during an oral explanation before the Committee on 8 November 2022, the sponsor aimed to address the main issues which led to the negative opinion.

The COMP upheld the negative view and an opinion recommending removing Zynlonta (EU/3/21/2481) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The orphan maintenance assessment report will be publicly available on the EMA website.

## 4.4. On-going procedures

COMP co-ordinators were appointed for 3 applications.

## 4.5. Orphan Maintenance Reports

Documents were tabled for information.

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

## 5.1. After adoption of CHMP opinion

None

## 5.2. Prior to adoption of CHMP opinion

### 5.2.1. Reblozyl – luspatercept - EMEA/H/C/004444/II/0009, EU/3/14/1300, EMA/OD/0000072540

Bristol-Myers Squibb Pharma EEIG; Treatment of beta-thalassaemia intermedia and major

CHMP Rapporteur: Daniela Philadelphy; CHMP Co-Rapporteur: Ewa Balkowiec Iskra

The status of the procedure at CHMP was noted.

## 5.3. Appeal

None

## 5.4. On-going procedures

None

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

None

# 7. Organisational, regulatory and methodological matters

## 7.1. Mandate and organisation of the COMP

### 7.1.1. COMP membership

New membership:

The Chair welcomed Dimitrios Filippou, as the new member for Greece.

End of membership:

The Chair thanked Martin Mozina for their contribution as a member for Slovenia.

### 7.1.2. Vote by proxy

None

### 7.1.3. Strategic Review & Learning meetings

None

### 7.1.4. Protocol Assistance Working Group (PAWG)

The working group on Protocol Assistance met remotely on 8th November 2022.

### 7.1.5. Principal Decisions Database

Document tabled:

The COMP acknowledged the importance of adding further topics to the database.

## 7.2. Coordination with EMA Scientific Committees or CMDh-v

### 7.2.1. Recommendation on eligibility to PRIME – report

Documents were tabled for information

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

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

Documents were tabled for information

## 7.4. Cooperation within the EU regulatory network

### 7.4.1. European Commission

None

## 7.5. Cooperation with International Regulators

### 7.5.1. Food and Drug Administration (FDA)

None

### 7.5.2. Japanese Pharmaceuticals and Medical Devices Agency (PMDA)

None

### 7.5.3. Therapeutic Goods Administration (TGA), Australia

None

### 7.5.4. Health Canada

None

## 7.6. Contacts of the COMP with external parties and interaction with the Interested Parties to the Committee

None

## 7.7. COMP work plan

None

## 7.8. Planning and reporting

### 7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2022

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2022 were circulated.

### 7.8.2. Overview of orphan marketing authorisations/applications

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

# 8. Any other business

## 8.1. Preparation of EMA Regulatory & Scientific Conference on RNA-based medicines

Postponed

## 8.2. Public Consultation on Good Practice Guide and Data Quality Framework

The COMP noted The draft Good Practice Guide for the use of real-world metadata, which provides recommendations to regulators, researchers, data holders, pharmaceutical companies and other interested stakeholders on how to use the catalogue in order to identify suitable real-world data sources for studies including use cases. It also describes the metadata elements that are envisaged to be used in the EU catalogue of real-world data sources that will replace the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) catalogue. COMP was invited to send comments on this guide using this template until 16 November 2022. The completed form should be sent to metadata@ema.europa.eu.

COMP was also reminded about The draft Data Quality Framework document, which provides general considerations that can be applied to a wide range of data sources for the purpose of characterising and assessing data quality for decision making. It also outlines what data quality actions and metrics can be put in place in different regulatory decision-making scenarios and introduces maturity models for the characterisation of data quality for regulatory purposes. The first release of this framework intends to provide an overarching framework to identify, define and further develop data quality assessment procedures and recommendations for current and novel data types. The document has been developed taking into account input from various stakeholder groups that participated in the

EMA/HMA/TEHDAS Data Quality Framework workshop on 7 April 2022. COMP was invited to submit comments on this draft framework using this template until 18 November 2022. The completed form should be sent to dataqualityframework@ema.europa.eu.

The final versions of these documents will be published in early 2023.

A presentation was given and the deadline for comments was set for November 16th. A member of the COMP expressed an interest in making comments.

### 8.3. Upcoming ITF meetings

The COMP noted the upcoming ITF meetings.

## 9. List of participants

including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 08-10 November 2022 meeting.

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Violeta Stoyanova-Beninska | Chair | Netherlands | No interests declared | |
| Armando Magrelli | Vice-Chair | Expert recommended by EMA | No interests declared | |
| Brigitte Schwarzer-Daum | Member | Austria | No restrictions applicable to this meeting | |
| Tim Leest | Member | Belgium | No interests declared | |
| Lyubina Racheva Todorova | Member | Bulgaria | No interests declared | |
| Dinko Vitezic | Member | Croatia | No interests declared | |
| Elli Loizidou | Member | Cyprus | No interests declared | |
| Jana Mazelova | Member | Czechia | No interests declared | |
| Elisabeth Penninga | Member | Denmark | No interests declared | |
| Vallo Tillmann | Member | Estonia | No interests declared | |
| Karri Penttilä | Member | Finland | No interests declared | |
| Cecile Dop | Member | France | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Frauke Naumann-Winter | Member | Germany | No interests declared | |
| Zsofia Gyulai | Member | Hungary | No interests declared | |
| Enrico Costa | Member | Italy | No interests declared | |
| Irena Rogovska | Member | Latvia | No restrictions applicable to this meeting | |
| Michel Hoffmann | Member | Luxembourg | No interests declared | |
| Robert Nistico | Member | Malta | No restrictions applicable to this meeting | |
| Elisabeth Johanne Rook | Member | Netherlands | No interests declared | |
| Maria Elisabeth Kalland | Member | Norway | No interests declared | |
| Bożenna Dembowska-Bagińska | Member | Poland | No restrictions applicable to this meeting | |
| Joao Rocha | Member | Portugal | No restrictions applicable to this meeting | |
| Olimpia Neagu | Member | Romania | No interests declared | |
| Eva Malikova | Member | Slovak Republic | No interests declared | |
| Gloria Maria Palomo Carrasco | Member | Spain | No interests declared | |
| Darius Matusevicius | Member | Sweden | No restrictions applicable to this meeting | |
| Pauline Evers | Member | Patients' Organisation Representative | No interests declared | |
| Julian Isla | Member | Patients' Organisation Representative | No interests declared | |
| Ines Alves | Member | Patients' Organisation Representative | No restrictions applicable to this meeting | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Ingeborg Barisic | Member | Expert recommended by EMA | No restrictions applicable to this meeting | |
| Giuseppe Capovilla | Member | Expert recommended by EMA | No interests declared | |
| Maria Cavaller Bellaubi | Expert - in person* | Patients' Organisation Representative | No restrictions applicable to this meeting | |
| Meeting run with support from relevant EMA staff | | | | |

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

## 10. Explanatory notes

The notes below give a brief explanation of the main sections and headings in the COMP agenda and should be read in conjunction with the agenda or the minutes.

**Abbreviations / Acronyms**

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

EC: European Commission

OD: Orphan Designation

PA: Protocol Assistance

PDCO: Paediatric Committee

PRAC: Pharmacovigilance and Risk Assessment Committee

SA: Scientific Advice

SAWP: Scientific Advice Working Party

**Orphan Designation** *(section 2 Applications for orphan medicinal product designation)*

The orphan designation is the appellation given to certain medicinal products under development that are intended to diagnose, prevent or treat rare conditions when they meet a pre-defined set of criteria foreseen in the legislation. Medicinal products which get the orphan status benefit from several incentives (fee reductions for regulatory procedures (including protocol assistance), national incentives for research and development, 10-year market exclusivity) aiming at stimulating the development and availability of treatments for patients suffering from rare diseases.

Orphan Designations are granted by Decisions of the European Commission based on opinions from the COMP. Orphan designated medicinal products are entered in the Community Register of Orphan Medicinal Products.

**Protocol Assistance** *(section 3 Requests for protocol assistance with significant benefit question)*

The protocol assistance is the help provided by the Agency to the sponsor of an orphan medicinal product, on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of the medicinal product in view of the submission of an application for marketing authorisation.

Sponsor

Any legal or physical person, established in the Community, seeking to obtain or having obtained the designation of a medicinal product as an orphan medicinal product.

**Maintenance of Orphan Designation** *(section 4 Review of orphan designation for orphan medicinal products for marketing authorisation).*

At the time of marketing authorisation, the COMP will check if all criteria for orphan designation are still met. The designated orphan medicinal product should be removed from the Community Register of Orphan Medicinal Products if it is established that the criteria laid down in the legislation are no longer met.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/