20 January 2021
EMA/COMP/687971/2020
Human Medicines Division

# Committee for Orphan Medicinal Products (COMP)

## Minutes for the meeting on 01-03 December 2020

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

01 December 2020, 08:30-18:30, remote virtual meeting

02 December 2020, 08:30-20:30, remote virtual meeting

03 December 2020, 08:30-18:10, remote virtual 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.

Further information with relevant explanatory notes can be found at the end of this document.

**Note on access to documents**

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

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**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
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# 1. Introduction

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

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

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

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

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

## 1.2. Adoption of agenda

The agenda for 1-3 December 2020 was adopted with no amendments.

## 1.3. Adoption of the minutes

The minutes for 3-5 November 2020 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. setanaxib - EMA/OD/0000040564

GenKyoTex S.A.; Treatment of primary biliary cholangitis

COMP Rapporteur: Geraldine O'Dea

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

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".

The sponsor was asked to justify the inclusion/choice of the sources selected for the estimation of the prevalence of the condition and should give an estimate of the prevalence in the EU, not just stating that it is below 5 in 10,000.

In the written response, the sponsor included a new reference publication by Lv et al., entitled "regional variation and temporal trend of PBC epidemiology: a systematic review and meta-analysis" (J Gastroenterol Hepatol. 2020 Nov 3 PMID: 3314195). Among 38 included studies reporting PBC incidence, 26 were from Europe and the sponsor concluded on a prevalence of 2 in 10,000.

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

The intention to treat the condition with the medicinal product containing setanaxib was considered justified based on clinical data supporting reduction in liver stiffness and improvement in biomarkers of liver function as well as quality of life including fatigue and pruritus, in affected patients treated with the product.

The condition is chronically debilitating due to pruritus, fatigue, hyperlipidaemia, hypothyroidism, deficiency of fat-soluble vitamins and osteopenia and life-threatening due to progressive hepatic dysfunction, with development of portal hypertension and hepatic failure, and the increased risk of developing hepatocellular cancer.

The condition was estimated to be affecting approximately 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 setanaxib will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that setanaxib can be used on top of, and in patients who did not respond to one of the two currently authorised treatments, as well as reduction in liver stiffness and fatigue which has not been shown with the approved products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for setanaxib, for treatment of primary biliary cholangitis, was adopted by consensus.

### 2.1.2. - EMA/OD/0000041707

Treatment of glioma

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

- Significant benefit

The sponsor was requested to further discuss the available clinical observations in recurrent glioma, in order to document responses or improvement in survival that can be attributed to the product. Any updated information from the clinical study was expected in that regard.

There was a comparative discussion versus the available treatment options to justify a clinically relevant advantage or major contribution to patient care requested from the applicant.

In the written response, and during an oral explanation before the Committee on 1 December 2020, the sponsor elaborated on the available clinical observations. An improved survival effect was argued in particular for patients that had not been previously treated with bevacizumab, on the basis of an indirect comparison to bibliography. Moreover, the imaging of two treated patients was discussed and an argument for improved safety was also put forward.

The Committee considered that the assumption of improved efficacy was not conclusive, as the comparability of the juxtaposed populations was not justified and on the basis of the paucity of the available observations. With regards to the safety argument, this was considered unknown given the early stage of development.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 2 December 2020, prior to final opinion.

### 2.1.3. - EMA/OD/0000037877

Treatment of focal segmental glomerulosclerosis

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

The sponsor provided some arguments and data to describe the mechanism of action of the product. However, conclusive results to support these arguments were not presented. This is of importance in the context of the arguments used to support the significant benefit of the product.

- Number of people affected

The sponsor provided a range of values of the prevalence which is not extensively discussed. It is also significantly lower than the previously accepted values by the COMP in other applications.

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".

The sponsor was asked to 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, the sponsor should perform a sensitivity analysis of the reported calculations.

- Significant benefit

The arguments on significant benefit were based on the new mechanism of action and the potential improved efficacy in the condition. The mechanism of action was however not very well understood or explained.

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

The sponsor was asked to detail the results of any data in the proposed condition to support the significant benefit assumption in the context of the current therapeutic management of patients.

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

In the written response, and during an oral explanation before the Committee on 1 December 2020, the sponsor elaborated on the assumed mechanism of action of the product, with two theories outlined. The COMP noted an absence of data in non-clinical or clinical settings that would allow for a favourable juxtaposition versus the existing treatments.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 1 December 2020, prior to final opinion.

### 2.1.4. human laminin-111, recombinant - EMA/OD/0000041257

Maxia Strategies-Europe Limited; Treatment of LAMA2 congenital muscular dystrophy

COMP Rapporteur: Elisabeth Penninga

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

LAMA2 congenital muscular dystrophy also known as merosin deficient congenital muscular dystrophy type 1A (MDC1A), should be justified as a distinct medical entity or a valid subset. The proposed condition is nosologically included in a larger group of conditions grouped under the term of Congenital Muscular Dystrophies (CMDs). These are clinically and genetically heterogenous neuromuscular disorders with onset at birth or infancy in which the muscle histology is compatible with a dystrophic myopathy. The COMP considered that CMDs could be the appropriate condition for designation. Note that this is for the purposes of orphan medicinal product designation; the sponsor's attention was drawn to the Orphan regulations and relevant guidelines (especially section A of ENTR/6283/00).

- Number of people affected

The COMP noted that the proposed condition is nosologically included in a larger group of conditions grouped under the term of Congenital Muscular Dystrophies (CMDs). The COMP considered that the sponsor should provide a revised prevalence estimate for the term of Congenital Muscular Dystrophies. The sponsor was asked to re-calculate the prevalence estimate based on relevant epidemiological studies and registers across the EEA for the proposed orphan condition.

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 accepted the COMP's proposal to amend the condition to congenital muscular dystrophy. The prevalence estimate was as a result revised to 0.2 in 10,000, based on peer-reviewed literature and multiple publications for 5 countries (Denmark, Italy, Norway, Sweden, United Kingdom). Following review of the application by the Committee, it was agreed to rename the indication to treatment of congenital muscular dystrophy.

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

The intention to treat the condition with the medicinal product containing human laminin-111, recombinant was considered justified based on data using non clinical in vivo data in a model of the condition showing a prevention of progression of muscle pathology, improvement in muscle regeneration and in muscle strength, and increased life expectancy.

The condition is life-threatening and/or chronically debilitating due to muscle weakness which can lead to loss of ambulation and progressive respiratory weakness and insufficiency. Other organs may be involved and approximately 30% patients present with seizures. Life expectancy is in the majority of patients decreased.

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

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 human laminin-111, recombinant, for treatment of congenital muscular dystrophy, was adopted by consensus.

### 2.1.5. - EMA/OD/0000034920

Treatment of mitochondrial epilepsy

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

Mitochondrial epilepsy is not currently recognised in the international epilepsy classification.

Mitochondrial epilepsy, the condition proposed by the sponsor, 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).

In the written response, and during an oral explanation before the Committee on 1 December 2020, the sponsor maintained that mitochondrial epilepsy is condition suitable for orphan designation. They claimed that, "mitochondrial epilepsy" is a distinct clinical entity including all epileptic disorders due to mtDNA or nuclear mutations of mitochondrial proteins without being restricted to the most commonly described mitochondrial disorders and that it differs from mitochondrial disorders, which is associated with a clinical heterogeneity of symptom.

The sponsor did acknowledge that mitochondrial epilepsy is not currently classified in the following international systems: the International Classification of Diseases (ICD), 10th

version (ICD-10), the Medical Dictionary for Regulatory Activities (MedDRA) or the International League Against Epilepsy (ILAE) classification. However, the sponsor also referred to ICD-11 which includes a specific group named "8A60.A – Epilepsy due to genetic syndromes with widespread or progressive effects" as well as the Orphanet classification, and "Mitochondrial disease with epilepsy" ORPHA:225700.

For the purpose of orphan designation, the COMP considered that mitochondrial epilepsy would not be an acceptable condition because it was spanning several distinct entities that would include epileptic seizures as a manifestation. It was considered that the term used in Orphanet is "mitochondrial disease with epilepsy" and refers to "a group of diseases". It was also noted that in the ILAE classification, 5 specific etiological groups are recognised. In each of these 5 groups several different and distinct clinical medical entities exist (for example Lennox-Gastaut Syndrome, West Syndrome, MELAS (mitochondrial encephalopathy, lactic acidosis and stroke), etc.)

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 2 December 2020, prior to final opinion.

### 2.1.6. - EMA/OD/0000042085

Treatment of primary intracerebral hemorrhage

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

Primary intracerebral hemorrhage (pICH) was asked to 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). In particular, the sponsor was invited to justify the exclusion of other ICH cases, including traumatic and other secondary cases, or broaden the definition of the condition accordingly.

- Number of people affected

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 light of the need to reconsider the proposed indication, the sponsor was invited to elaborate on:

a) the choice of prevalence versus annual incidence rates for the purpose of reporting the number of affected individuals,

b) the reference to older studies as more current publications e.g. Wafa et al., Stroke. 2020;51:2418–2427, suggest higher prevalence rates than what was proposed by the sponsor,

c) the number of patients affected by the broader ICH definition.

In the written response, and during an oral explanation before the Committee on 1 December 2020, the sponsor discussed the raised issues. With regards to exclusion of traumatic and non-traumatic secondary cases, the sponsor referred to an FDA procedure, and noted that it did not have an interest to develop in other forms of ICH. Moreover, several publications were discussed that list the causes of ICH as either primary or

secondary. The definition of the applied designation was reiterated and this was put in context of other designations such "non-traumatic subarachnoid hemorrhage".

The COMP remained sceptical with regards to the exclusion of certain aetiologies, and made reference to one of its previous considerations and in particular procedure EMA/OD/0000036026 of June 2020. It was also noted that drawing of parallels with extra-european frameworks was out of context for the case in the EU.

With regards to the questions raised on prevalence the sponsor did not amend the proposed estimate and assumed 3.19 /10,000 with a range of 2.7to 0.2 per 10,000. The COMP noted that there is an absence of justification regarding the need to consider yearly incidence versus other available epidemiological indices. Estimates for broader populations than pICH, as per the COMP's request, were also not provided.

In view of the above, the committee considered that the responses did not address the raised points.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 1 December 2020, prior to final opinion.

### 2.1.7. - EMA/OD/0000042012

Treatment of follicular lymphoma (FL)

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 sponsor presented data and a calculation of prevalence and a sensitivity analysis to support the notion that follicular lymphoma meets the prevalence criterion. However, many of the more conservative assumptions lead to the overall calculation being over 5 in 10,000 persons in the EU.

The sponsor was requested to further elaborate on the assumptions made to calculate the complete prevalence and to discuss the validity of the references used to determine:

a) proportion of FL within NHL (non-Hodgkin's lymphoma) as registered in ECIS (European Cancer Information System),

b) duration of the condition in terms of overall survival,

c) decline of incidence in view of the ageing population as reported in Howlader et al., (2019).

A sensitivity analysis of all assumptions used (such as the proportion of FL within NHL, and the duration of the condition) was also expected to be included in the sponsor's responses.

In the written response, and during an oral explanation before the Committee on 2 December 2020, the sponsor elaborated on the prevalence calculation of follicular lymphoma and the sensitivity analysis. The proposed conclusion is approximately 4.77 in 10,000 people. The COMP questioned the assumption made to arrive at this conclusion. The assumption that the incidence of FL is declining in the EU was based on the data from the American database SEER. The data from the EU does not support the decline in FL incidence. The assumption that FL affects only 13% of NHL cases was also not considered robust, due to several citations suggesting much higher proportions. Last but not least, the

COMP agreed that the total duration of the condition is probably less than 20 years (being somewhere between 15-20 years). However, based on the incidence from ECIS database and assuming reasonably conservative FL proportion and duration, there was no certainty that the condition would fall under 5 in 10,000 persons in the EU.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 3 December 2020, prior to final opinion.

### 2.1.8. - EMA/OD/0000020657

Treatment of renal transplant interstitial fibrosis and tubular atrophy

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 indication

Renal transplant interstitial fibrosis and tubular atrophy (IFTA) was asked to 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 invited to elaborate on the differences between IFTA in renal allografts compared to renal IFTA in other diseases, such as hypertension, diabetes, or autoimmune diseases.

- Intention to diagnose, prevent or treat

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of renal transplant interstitial fibrosis and tubular atrophy the sponsor was requested to further elaborate on:

a) the relevance of the nonclinical models used for the treatment of renal transplant interstitial fibrosis and tubular atrophy, and the interpretation of the results obtained in the experiments,

b) the methodology used in the non-clinical studies as well as the results from these studies and their relevance for the development of the product in the condition.

- Significant Benefit

In light of the need to reconsider the proposed condition, the sponsor was invited to elaborate on the existing authorised products and provide a comparative discussion to justify a clinically relevant advantage or a major contribution to patient care.

In the written response, and during an oral explanation before the Committee on 2 December 2020, the sponsor proposed to revise the proposed condition to "Chronic Allograft Nephropathy" with reference to medDRA and CHMP documents. As regards to the relevance of the models used, the sponsor noted that their use was by way of elucidating the causative role of the target protein in fibrotic remodelling. It was argued that these models would be relevant for the proposed indication, because the purpose of the intervention is to inhibit the evolution of fibrosis, in the remaining and yet unaffected tubulointerstitium. Cross-species limitations were also discussed in order to justify the absence of data in more relevant graft-bearing models.

The Committee considered that while the proposed condition has been amended to also include a functional aspect, chronic allograft nephropathy could still be regarded as a consequence of other conditions and therefore the concerns raised regarding the validity of the condition for orphan designation had not been addressed. The Committee was also concerned about the absence of data in the specific transplantation settings as proposed for designation.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 2 December 2020, prior to final opinion.

### 2.1.9. - EMA/OD/0000037806

Treatment of soft tissue sarcoma (STS)

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

Significant benefit was argued based on an alternative mechanism of action and a potential for improved efficacy and safety. The sponsor was requested to further discuss the arguments and to elaborate on the results from the non-clinical studies to justify the assumption of significant benefit over all authorised medicinal products for the proposed orphan condition. The sponsor was asked also asked to provide any additional data if available with the product in non-clinical or clinical settings of soft tissue sarcoma.

In the written response, and during an oral explanation before the Committee on 2 December 2020, the sponsor addressed the raised issues. Indirect comparisons were discussed, focusing on second line treatments. The mechanism of action of the product was discussed in more detail and the rhabdomyosarcoma model used was reported to be resistant to doxorubicin, cisplatin and the combination of the two.

Trabectedin, eribulin and pazopanib were considered to be relevant by the sponsor for a comparative discussion. Of these three agents, the effects versus pazopanib had already been included as a control in a nonclinical rhabdomyosarcoma model, while eribulin, was only authorised for liposarcoma. With regards to trabectedin, the sponsor referred to its pivotal trial, noting that the effect on progression-free survival (PFS) was notably better in myxoid liposarcoma but was not different from dacarbazine in other subtypes of soft tissue sarcoma.

In evaluation of the submitted justifications, the committee considered that as long as the authorized indication of a medicinal product covers rhabdomyosarcoma as was the case for trabectedin, data versus that product would be expected to justify a favourable comparison. Moreover, in was considered that the rhabdomyosarcoma model studied by the sponsor used cisplatin and doxorubicin resistant cells, but this would not allow for the contextualisation of the proposed treatment taking into consideration that cisplatin is not part of the standard of care. Overall, the committee would expect more data in STS settings that would allow for a significant benefit justification versus the authorised product.

In communicating to the sponsor the outcome of the discussion, the sponsor formally withdrew the application for orphan designation, on 2 December 2020, prior to final opinion.

## 2.1.10. - EMA/OD/0000040482

Treatment of pancreatic cancer

As agreed during the previous meeting, a list of issues was sent to the sponsor for response. The sponsor formally withdrew the application for orphan designation, on 17 November 2020, prior to responding to the list of issues.

## 2.1.11. rilonacept - EMA/OD/0000042079

Granzer Regulatory Consulting & Services; Treatment of pericarditis

COMP Rapporteur: Eva Malikova

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 proposed condition was asked to be justified as a distinct medical entity or a valid subset for the purpose of orphan medicinal product designation, with reference to guideline on the format and content of applications ENTR/6283/00 Rev 05.

In particular, the sponsor was requested to clarify whether pericarditis can be regarded as a manifestation or sequela of other underlying diseases

- Prevalence

For the estimation and reporting of prevalence the sponsor was referred to the "Points to Consider on the Estimation and Reporting of a Prevalence of a Condition for Orphan Designation" (436/01).

The sponsor was also invited to re-calculate the prevalence by additional methodologies, such as multiplication of annual incidence rates by mean disease duration. All underlying causes of pericarditis should be taken into account for the proposed estimate.

- Significant benefit

The sponsor was asked to further elaborate on the issue of significant benefit, taking into consideration any effect of the existing products in the recurrence of pericarditis. A comparative discussion is expected based on the sponsor's data in the proposed indication, to justify a clinically relevant advantage and/or major contribution to patient care.

In the written response, and during an oral explanation before the Committee on 2 December 2020, the sponsor further elaborated on the raised issues as follows:

With regards to the validity of the condition, the sponsor discussed that most cases are idiopathic, and remained open to reword the indication to "idiopathic pericarditis". This was considered acceptable by the COMP, as it excludes the cases of pericarditis in patients that are affected by other underlying conditions.

As for the number of affected individuals, the sponsor the incidence of pericarditis to be 2.74/10,000 (Imazio 2008) times mean duration of 0.82, yielding 2.25 per 10,000. It was also noted that idiopathic cases would be up to 80% of the above calculation (Imazio 2010). The COMP considered instead that the initial calculation of the sponsor should be taken into consideration (see relevant section above) and in light of uncertainty about the

assumptions, a conservative conclusion of approximately 2.5/10,000 may be considered for the new amended indication, by considering a worst case scenario where most cases would be idiopathic.

As for the issue of significant benefit, the sponsor embarked in an indirect comparison of the phase 3 results as presented above versus colchicine. In an Italian study (Imazio 2011), colchicine was studied for recurrent pericarditis and at 18 months, the recurrence rate was 24% in the colchicine group vs 55% in the placebo arm. In an additional study (Imazio 2014), colchicine was studied in population of multiple recurrences in addition to conventional anti-inflammatory treatment; the proportion of subjects who had further episodes during the study duration was 21.6% in the colchicine group and 42.5% in the placebo group. The COMP considered that the reported clinical efficacy of the proposed product would compare favourably to the above studies and support an assumption of improved efficacy compared to colchicine at the stage of designation.

A protocol assistance was recommended to further address the issue of significant benefit in a potential future procedure of maintenance of orphan designation criteria.

Following review of the application by the Committee, it was agreed to rename the indication to treatment of idiopathic pericarditis.

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

The intention to treat the condition with the medicinal product containing rilonacept was considered justified based on clinical observations supporting a decrease in the risk of recurrence in treated patients;

The condition is life-threatening and chronically debilitating due to chest-pain, pericardial effusion, and the risk of developing cardiac tamponade and constrictive pericarditis, leading to heart failure.

The condition was estimated to be affecting approximately 2.5 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 exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing rilonacept will be of significant benefit to those affected by the condition. The sponsor has provided clinical observations showing a decrease in recurrence rate which compares favourably to the currently authorised products. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for rilonacept, for treatment of idiopathic pericarditis, was adopted by consensus.

### 2.1.12. calcium oxybate, magnesium oxybate, potassium oxybate, sodium oxybate - EMA/OD/0000039384

Jazz Pharmaceuticals Ireland Limited; Treatment of idiopathic hypersomnia (IH)

COMP Rapporteur: Michel Hoffmann

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

The sponsor bridged data with the proposed product from another, related condition. The data in patients with the condition originated from one centre and constitute a case series with the use of a related product. The results in IH patients were generated using subjective outcome measures. It was therefore, difficult to justify the dual extrapolation proposed by the sponsor, based on the level of details submitted in the application.

To establish correctly whether there exists a scientific rationale for the development of the proposed product for treatment of idiopathic hypersomnia the sponsor was asked to further elaborate on:

a) the clinical results obtained in the retrospective study of sodium oxybate in patients with idiopathic hypersomnia,

b) the relevance of the data with the use of sodium oxybate for the treatment of idiopathic hypersomnia, and the interpretation of the results obtained,

c) the methodology used in the clinical studies with the use of the proposed product as well as the results from these studies and their relevance for the development of the product in the condition.

- Prevalence

The sponsor provided a prevalence calculation and proposed a wide range of values to support the estimate.

The sponsor was invited to re-calculate the prevalence and to justify the methodology and the inclusion of sources used for the estimate.

In the written response, the sponsor provided additional data to support the assumption of medical plausibility of the product in the proposed orphan condition. The sponsor presented the top line results from Study JZP080-301 in adult patients with idiopathic hypersomnia (IH). The primary endpoint of the Epworth Sleepiness Scale (ESS) and the key secondary endpoints of Patient Global Impression of Change (PGIc) and Idiopathic Hypersomnia Severity Scale (IHSS) were measured during the randomized withdrawal portion of the trial, which included 115 patients. Those who were administered JZP-258 showed clinically meaningful maintenance of efficacy for ESS, PGIc and IHSS, and there were highly statistically significant worsening in patients administered placebo compared with JZP-258 for ESS (p-value <0.0001), PGIc (p-value <0.0001) and IHSS (p-value <0.0001). The COMP considered these results supportive of medical plausibility and the issue was considered resolved.

In addition, the sponsor provided a further analysis of the literature found with respect to the prevalence of the condition. Based on these sources a conservative conclusion was proposed, that the prevalence of IH is approximately 3 in 10,000 persons in the EU. In view of the acceptability of the written responses the COMP cancelled the oral hearing.

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

The intention to treat the condition with the medicinal product containing calcium oxybate, magnesium oxybate, potassium oxybate, sodium oxybate was considered justified based on preliminary clinical data showing improvements in excessive daily sleepiness score.

The condition is chronically debilitating due to episodes of excessive daytime sleepiness;

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

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

A positive opinion for calcium oxybate, magnesium oxybate, potassium oxybate, sodium oxybate, for treatment of idiopathic hypersomnia, was adopted by consensus.

## 2.2. For discussion / preparation for an opinion

### 2.2.1. - EMA/OD/0000030100

Treatment of uterine serous carcinoma

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

### 2.2.2. rezafungin acetate - EMA/OD/0000033964

Mundipharma Corporation (Ireland) Limited; Treatment of invasive candidiasis

COMP Rapporteur: Olimpia Neagu

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

The intention to treat the condition with the medicinal product containing rezafungin acetate was considered justified based on early clinical data showing clinically meaningful treatment success rate in patients who received the proposed product.

The condition is life-threatening with 30-day mortality rates in intensive care units reported to be over 50%.

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 rezafungin acetate will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that suggest that in one of tested doses a higher proportion of patients treated with the proposed product achieved treatment success as compared to patients treated with caspofungin. The advantage over azoles and amphotericin B could be also assumed due to inferior safety and efficacy profiles of these products compared to echinocandins. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for rezafungin acetate, for treatment of invasive candidiasis, was adopted by consensus.

### 2.2.3. - EMA/OD/0000038364

Treatment of spinocerebellar ataxia

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

### 2.2.4. cyclo-L-glycyl-L-2-allylproline - EMA/OD/0000041637

Dlrc Pharma Services Limited; Treatment of Angelman syndrome

COMP Rapporteur: Dinah Duarte

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

The intention to treat the condition with the medicinal product containing cyclo-L-glycyl-L-2-allylproline was considered justified based on non-clinical data in a valid model of the condition showing improvements in behavioural deficits.

The condition is chronically debilitating due to developmental delay, motor and cognitive impairment, hyperactivity and epileptic seizures that are often treatment resistant.

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.

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 cyclo-L-glycyl-L-2-allylproline, for treatment of Angelman syndrome, was adopted by consensus.

### 2.2.5. - EMA/OD/0000042048

Treatment of acute respiratory distress 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 January meeting.

*[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 05 January 2021.]*

### 2.2.6. idursulfase - EMA/OD/0000042795

Shire Pharmaceuticals Ireland Limited; Treatment of mucopolysaccharidosis, type II (Hunter syndrome)

COMP Rapporteur: Gloria Maria Palomo Carrasco

The Committee agreed that the condition, of mucopolysaccharidosis type II (Hunter's syndrome), is a distinct medical entity and meets the criteria for orphan designation.

The intention to treat the condition with the medicinal product containing idursulfase was considered justified based on preliminary clinical data showing a reduction in GAG levels in CSF and a potential stabilisation of cognitive function in a small number of children under the age of 6.

The condition is chronically debilitating due to neurological decline, cardiovascular and pulmonary complications and life-threatening as indicated by the survival of the patients that can be limited to 10-15 years.

The condition was estimated to be affecting approximately 0.04 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 idursulfase will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that indicate a potential stabilisation in cognitive function in children under the age of 6 years where there are currently no treatments for cognitive decline. The Committee considered that this constitutes a clinically relevant advantage or major contribution to patient care.

A positive opinion for idursulfase, for treatment of mucopolysaccharidosis type II (Hunter's syndrome), was adopted by consensus.

### 2.2.7. - EMA/OD/0000042924

Treatment of eosinophilic gastritis

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

### 2.2.8. humanised IgG1K monoclonal antibody against interferon beta - EMA/OD/0000043059

Pfizer Europe MA EEIG; Treatment of dermatomyositis

COMP Rapporteur: Olimpia Neagu

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

The intention to treat the condition with the medicinal product containing humanised IgG1K monoclonal antibody against interferon beta was considered justified based on preliminary clinical observations showing reduction in the Cutaneous Dermatomyositis Disease Area and Severity Index in treated patients.

The condition is life-threatening and chronically debilitating due to skin lesions, cardiac impairment, and progressively debilitating muscle weakness and increased risk of malignancy.

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing humanised IgG1K monoclonal antibody against interferon beta will be of significant benefit to those affected by the condition. The sponsor has provided clinical data that demonstrate that the product improves cutaneous manifestations in a population that has not responded to at least one previous systemic treatment. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for humanised IgG1K monoclonal antibody against interferon beta, for treatment of dermatomyositis, was adopted by consensus.

### 2.2.9. - EMA/OD/0000043071

Treatment of paroxysmal nocturnal haemoglobinuria

The COMP adopted a list of issues that will be sent to the sponsor. The Committee will discuss the submitted answers to the list of issues at the January meeting.

### 2.2.10. - EMA/OD/0000043102

Treatment of haemophilia A

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

### 2.2.11. - EMA/OD/0000043114

Treatment of sickle cell disease

The COMP adopted a list of issues that will be sent to the sponsor. The Committee will discuss the submitted answers to the list of issues at the January meeting.

### 2.2.12. - EMA/OD/0000043121

Treatment of haemophilia B

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

### 2.2.13. cyclo-L-glycyl-L-2-allylproline - EMA/OD/0000043209

Dlrc Pharma Services Limited; Treatment of Pitt-Hopkins syndrome

COMP Rapporteur: Ausra Matuleviciene

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

The intention to treat the condition with the medicinal product containing cyclo-L-glycyl-L-2-allylproline was considered justified based on non-clinical data demonstrating improvements in several behavioural abnormalities and in muscle strength.

The condition is chronically debilitating due to severe intellectual disability, hyperventilation, apnoea, seizures, gastrointestinal symptoms and self-injurious behaviour.

The condition was estimated to be affecting approximately 0.3 in 10,000 persons in the European Union, at the time the application was made.

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

A positive opinion for cyclo-L-glycyl-L-2-allylproline, for treatment of Pitt-Hopkins syndrome, was adopted by consensus.

## 2.2.14. - EMA/OD/0000043217

Treatment of pancreatic cancer

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

## 2.2.15. cyclo-L-glycyl-L-2-allylproline - EMA/OD/0000043391

Dlrc Pharma Services Limited; Treatment of Phelan-McDermid syndrome

COMP Rapporteur: Giuseppe Capovilla

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

The intention to treat the condition with the medicinal product containing cyclo-L-glycyl-L-2-allylproline was considered justified based on non-clinical data in a valid model of the condition showing improvements in several behavioural abnormalities.

The condition is chronically debilitating due to developmental delay, intellectual disability, severe language impairments with majority of patients being nonverbal, seizures and gastrointestinal symptoms.

The condition was estimated to be affecting approximately 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 in the European Union for patients affected by the condition.

A positive opinion for cyclo-L-glycyl-L-2-allylproline, for treatment of Phelan-McDermid syndrome, was adopted by consensus.

## 2.2.16. - EMA/OD/0000043404

Treatment of leishmaniasis

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

## 2.2.17. - EMA/OD/0000043454

Treatment of acute myeloid leukaemia

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

*[Post-meeting note: The sponsor formally withdrew the application for orphan designation, on 17 December 2020.]*

## 2.2.18. - EMA/OD/0000043459

Treatment of hepatocellular carcinoma

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

## 2.2.19. - EMA/OD/0000043498

Treatment of eosinophilic enteritis

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

## 2.2.20. - EMA/OD/0000043607

Prevention of retinopathy of prematurity

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

## 2.2.21. celecoxib, ciprofloxacin - EMA/OD/0000043612

Morrison & Foerster; Treatment of amyotrophic lateral sclerosis

COMP Rapporteur: Robert Nistico

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

The intention to treat the condition with the medicinal product containing celecoxib, ciprofloxacin was considered justified based on non-clinical data showing improvements in motor function as well as preliminary clinical data suggesting slowing of the disease progression as measured by forced vital capacity and ALS functional rating scale compared to a simulation control arm.

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

The condition was estimated to be affecting 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 celecoxib, ciprofloxacin will be of significant benefit to those affected by the condition. The sponsor has provided preliminary clinical data that suggest that patients who were on stable riluzole background therapy may achieve slowing down of the disease progression as compared to an external control arm. The Committee considered that this would constitute a clinically relevant advantage.

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

## 2.2.22. - EMA/OD/0000043730

Treatment of primary aldosteronism

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

## 2.2.23. - EMA/OD/0000043828

Treatment of gastric cancer

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

## 2.2.24. - EMA/OD/0000043829

Treatment of sickle cell disease

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

## 2.2.25. - EMA/OD/0000043857

Treatment of cystinosis

The COMP adopted a list of issues that will be sent to the sponsor. The Committee will discuss the submitted answers to the list of issues at the January meeting.

## 2.2.26. alpha galactosidase A - EMA/OD/0000043899

Consejo Superior De Investigaciones Cientificas; Treatment of Fabry disease

COMP Rapporteur: Ingeborg Barisic

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

The intention to treat the condition with the medicinal product containing alpha galactosidase A was considered justified based on non-clinical data in a model of the condition showing decrease of globotriaosylceramide levels in various tissues after administration of the product.

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

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

In addition, although satisfactory methods of treatment of the condition exist in the European Union, the sponsor has provided sufficient justification for the assumption that the medicinal product containing alpha galactosidase A will be of significant benefit to those affected by the condition. The sponsor has provided non-clinical data in a knockout model of the condition, showing improved globotriaosylceramide levels in several tissues compared to the effects of agalsidase alpha. The Committee considered that this constitutes a clinically relevant advantage.

A positive opinion for alpha galactosidase A, for treatment of Fabry disease, was adopted by consensus.

## 2.3. Revision of the COMP opinions

None

## 2.4. Amendment of existing orphan designations

None

## 2.5. Appeal

### 2.5.1. tebentafusp - EMA/OD/0000047566

Pharma Gateway AB; Treatment of uveal melanoma

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

*[Post-meeting note: the final list of experts was adopted via written procedure on 11 January 2021.]*

## 2.6. Nominations

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

COMP coordinators were appointed for 13 applications.

## 2.7. Evaluation on-going

The Committee noted that evaluation was on-going for 14 applications for orphan designation.

# 3. Requests for protocol assistance with significant benefit question

## 3.1. Ongoing procedures

### 3.1.1. -

Treatment of ATTR amyloidosis-cardiomyopathy

The discussion was postponed.

### 3.1.2. -

Treatment of cutaneous T-cell lymphoma

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

### 3.1.3. -

Treatment of thalassaemia

The Committee was briefed on the significant benefit issues.

*[Post-meeting note: The COMP adopted the proposed answers on the significant benefit issues by written procedure following its December meeting.]*

### 3.1.4. -

Treatment of glioblastoma

The Committee was briefed on the significant benefit issues.

*[Post-meeting note: The COMP adopted the proposed answers on the significant benefit issues by written procedure following its December meeting.]*

### 3.1.5. -

Treatment of ornithine transcarbamylase deficiency

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

## 3.2. Finalised letters

### 3.2.1. -

Treatment of desmoid tumours

The finalised letter was circulated for information.

### 3.2.2. -

Treatment of marginal zone lymphoma

The finalised letter was circulated for information.

### 3.2.3. -

Treatment of diffused large B-cell lymphoma

The finalised letter was circulated for information.

## 3.3. New requests

### 3.3.1. -

Treatment of sickle cell disease

The new request was noted.

### 3.3.2. -

Treatment of paediatric patients with severe combined immunodeficiency (SCID) receiving allogeneic haematopoietic stem cell transplantation

The new request was noted.

### 3.3.3. -

Treatment of multiple myeloma

The new request was noted.

### 3.3.4. -

Treatment of ATTR amyloidosis-polyneuropathy

The new request was noted.

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

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

None

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

### 4.2.1. Nexpovio - selinexor - EMEA/H/C/005127, EMA/OD/087/14, EU/3/14/1355, EMA/OD/0000043722

Karyopharm Europe GmbH; Treatment of plasma cell myeloma

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

### 4.2.2. Sibnayal – potassium - EMEA/H/C/005407, EMA/OD/016/17, EU/3/17/1888, EMA/OD/0000032257

Advicenne Pharma S.A.; Treatment of distal renal tubular acidosis

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

### 4.2.3. INREBIC – fedratinib

Celgene Europe BV

COMP Rapporteurs: Karri Penttila; Dinko Vitezic

a) Treatment of primary myelofibrosis, EMEA/H/C/005026/0000, EMA/OD/069/10, EU/3/10/794, EMA/OD/0000029092

An opinion recommending not to remove INREBIC, fedratinib, EU/3/10/794 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.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its December meeting.]*

b) Treatment of post-essential thrombocythaemia myelofibrosis EMEA/H/C/005026/0000, EMA/OD/084/10, EU/3/10/810, EMA/OD/0000029093

An opinion recommending not to remove INREBIC, fedratinib, EU/3/10/810 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.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its December meeting.]*

c) Treatment of post-polycythaemia vera myelofibrosis EMEA/H/C/005026/0000, EMA/OD/092/10, EU/3/10/811, EMA/OD/0000029095

An opinion recommending not to remove INREBIC, fedratinib, EU/3/10/811 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.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its December meeting.]*

### 4.2.4. Pemazyre – pemigatinib - EMEA/H/C/005266, EMA/OD/038/18, EU/3/18/2066, EMA/OD/0000039241

Incyte Biosciences Distribution B.V.; Treatment of biliary tract cancer

The status of the procedure at CHMP was noted.

### 4.2.5. Lumoxiti – moxetumomab pasudotox- EMEA/H/C/005322, EMA/OD/066/08, EU/3/08/592, EMA/OD/0000013333

AstraZeneca AB; Treatment of hairy cell leukaemia

COMP Rapporteurs: Karri Penttila; Maria Elisabeth Kalland; CHMP Rapporteur: Filip Josephson; CHMP Co-Rapporteur: Bjorg Bolstad;

An opinion recommending not to remove Lumoxiti, moxetumomab pasudotox, EU/3/08/592 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.

*[Post-meeting note: The COMP adopted the opinion by written procedure following its December meeting.]*

### 4.2.6. – duvelisib

Verastem Europe GmbH

a) Treatment of Follicular lymphoma, EMEA/H/C/005381/0000, EMA/OD/047/13, EU/3/13/1157, EMA/OD/0000024085

b) Treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma EMEA/H/C/005381/0000, EMA/OD/196/12, EU/3/13/1125, EMA/OD/0000026423

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

### 4.2.7. – idecabtagene vicleucel - EMEA/H/C/004662/0000, EU/3/17/1863, EMA/OD/0000035635

**Accelerated assessment**

Celgene Europe BV; Treatment of multiple myeloma

The status of the procedure at CHMP was noted.

### 4.2.8. – risdiplam - EMEA/H/C/005145/0000, EMA/OD/0000001899, EU/3/19/2145, EMA/OD/0000039037

**Accelerated assessment**

Roche Registration GmbH; Treatment of spinal muscular atrophy

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

## 4.3. Appeal

None

## 4.4. On-going procedures

COMP co-ordinators were appointed for 4 applications.

## 4.5. Orphan Maintenance Reports

Documents were tabled for information.

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

## 5.1. After adoption of CHMP opinion

### 5.1.1. Blincyto – blinatumomab - EMEA/H/C/003731/II/0030, EMA/OD/029/09, EU/3/09/650, EMA/OD/00000016144

Amgen Europe B.V.; Treatment of acute lymphoblastic leukaemia

COMP Rapporteurs: Karri Penttilä; Bozenna Dembowska-Baginska; CHMP Rapporteur: Alexandre Moreau; CHMP Co-Rapporteur: Daniela Melchiorri

A list of issues was adopted on 9 October 2020.

The Committee discussed the submitted answers.

The Committee confirmed that all issues previously identified in this application had been addressed.

An opinion recommending not to remove Blincyto, blinatumomab (EU/3/09/650) 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.

## 5.2. Prior to adoption of CHMP opinion

### 5.2.1. Blincyto – blinatumomab - EMEA/H/C/003731/II/0038, EMA/OD/029/09, EU/3/09/650, EMA/OD/0000048837

Amgen Europe B.V.; Treatment of acute lymphoblastic leukaemia

CHMP Rapporteur: Alexandre Moreau

The COMP agreed that a formal review of the maintenance of the orphan designation for the applied indication is not needed.

## 5.3. Appeal

None

## 5.4. On-going procedures

COMP co-ordinators were appointed for 3 applications.

# 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. Strategic Review & Learning meetings

None

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

The working group on Protocol Assistance met remotely on 27 November 2020.

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

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

Documents were tabled for information.

### 7.2.2. COMP-CAT Working Group

The COMP-CAT Working Group meeting took place on 30 November 2020 by teleconference.

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

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

None

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

None

## 7.4. Cooperation within the EU regulatory network

### 7.4.1. European Commission

None

## 7.5. Cooperation with International Regulators

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

None

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

None

### 7.5.3. 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

The discussion was postponed.

## 7.8. Planning and reporting

### 7.8.1. List of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2020

An updated list of all applications submitted/expected and the COMP rapporteurship distribution of valid applications submitted in 2020 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. Big Data Training Signpost

The discussion was postponed.

## 8.2. ENCePP in the time of COVID

The discussion was postponed.

## 8.3.

## 8.4. EMA Business Pipeline activity and Horizon scanning

The document was tabled for information.

## 8.5. Revision of the EU legislation on medicines for children and rare diseases

EU rules to incentivise the development of medicines for children and for people with rare diseases have been in place for nearly 20 years. The revision addresses shortcomings identified in a recent evaluation, aiming to ensure that:

a) products addressing the specific needs of children and patients with rare diseases are developed,

b) these groups have timely access to medicines,

c) there are efficient assessment & authorisation procedures.

The COMP was reminded the feedback period 25 November 2020 - 06 January 2021.

# 9. List of participants

List of participants including any restrictions with respect to involvement of members / experts following evaluation of declared interests for the 1-3 December 2020 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 | Member (Vice-Chair) | Italy | No interests declared | |
| Brigitte Schwarzer-Daum | Member | Austria | No interests declared | |
| Tim Leest | Member | Belgium | No interests declared | |
| Lyubina Racheva Todorova | Member | Bulgaria | No interests declared | |
| Dinko Vitezic | Member | Croatia | No interests declared | |
| Vasileios Loutas | Member | Cyprus | No interests declared | |
| Lenka Gaidadzi | Member | Czech Republic | 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 | |
| Frauke Naumann-Winter | Member | Germany | No interests declared | |
| Zsofia Gyulai | Member | Hungary | No interests declared | |
| Geraldine O'Dea | Member | Ireland | No interests declared | |
| Irena Rogovska | Member | Latvia | No interests declared | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Aušra Matulevičienė | Member | Lithuania | No interests declared | |
| Michel Hoffmann | Member | Luxembourg | No interests declared | |
| Robert Nistico | Member | Malta | No interests declared | |
| 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 | |
| Dinah Duarte | Member | Portugal | No interests declared | |
| Eva Malikova | Member | Slovak Republic | No interests declared | |
| Martin Mozina | Member | Slovenia | 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 | |
| Angelo Loris Brunetta | Member | Patients' Organisation Representative | No interests declared | |
| Ingeborg Barisic | Member | Expert recommended by EMA | No restrictions applicable to this meeting | |
| Giuseppe Capovilla | Member | Expert recommended by EMA | No interests declared | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Virginie Hivert | Expert* | Patients' Organisation Representative | No restrictions applicable to this meeting | |
| A representative from the European Commission attended the meeting | | | | |
| Meeting run with support from relevant EMA staff | | | | |

* Experts were only 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/