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Human Medicines Division

Committee for Orphan Medicinal Products (COMP) meeting report on the review of applications for orphan designation

January 2021

The Committee for Orphan Medicinal Products held its 229th plenary meeting on 19-21 January 2021.

Orphan medicinal product designation

Positive opinions

The COMP adopted 16 positive opinions recommending the following medicines for designation as orphan medicinal products to the European Commission:

1. Opinions adopted at the second COMP discussion, following the sponsor's response to the COMP list of questions:

- (1R,3S,5R)-2-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromo-3-methylpyridin-2-yl)-5-methyl-2-azabicyclo[3.1.0]hexane-3-carboxamide for treatment of paroxysmal nocturnal haemoglobinuria, Alexion Europe S.A.S.;
- (2S)-2-[(2S)-4-cyclohexyl-2-{[(2S)-1-(4-fluorobenzoyl)pyrrolidin-2-yl]formamido}butanamido]-N-(1-{[(1S)-1-{[(1S)-1-({1-[(1-{[2-({1-[(dimethylamino)methyl]cyclobutyl}carbamoyl)ethyl]carbamoyl}-1-methylethyl)carbamoyl]-1-methylethyl}carbamoyl)-3-methylbutyl]carbamoyl}-3-methylbutyl]carbamoyl}-1-methylethyl)-4-methylpentanamide acetate for treatment of leishmaniasis, Biopharma Excellence GmbH;
- 2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride for treatment of sickle cell disease, Vifor France S.A.;
- 2'-O-methyl phosphorothioate RNA oligonucleotide, 5'-m^{5}CUGm^{5}CUGm^{5}CUGm^{5}CUGm^{5}CUGm^{5}CUG-3' for treatment of spinocerebellar ataxia, Vico Therapeutics B.V.;
- Anti-SIGLEC8 IgG1 humanised monoclonal antibody for treatment of eosinophilic gastroenteritis, Turnkey Pharmaconsulting Ireland Limited;

- Autologous CD34+ cells transduced with a lentiviral RNA vector that results in integrated cDNA encoding for functional cystinosin for treatment of cystinosis, Clinical Technology Centre (Ireland) Limited;
- Autologous CD34+ hematopoietic stem and progenitor cells transfected with zinc finger nuclease mRNAs SB-mRENH1 and SB-mRENH2 for treatment of sickle cell disease, Genzyme Europe B.V.;
- Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human claudin 18.2 antigen with CD28 and CD3-zeta intracellular signalling domains for treatment of gastric cancer, ICON Clinical Research Limited;
- Rintatolimod for treatment of pancreatic cancer, Hemispherx Biopharma Europe.

2. Opinions adopted at the first COMP discussion:

- 18-(p-[^{131}I]-iodophenyl)octadecyl phosphocholine for treatment of lymphoplasmacytic lymphoma, Scendea (NL) B.V.;
- 2-[6-(6,7-dimethoxyquinolin-3-yl)pyridin-3-yl]-N-[3-(1,1,1-trifluoro-2-methylpropan-2-yl)-1,2-oxazol-5-yl]acetamide for treatment of medullary thyroid carcinoma, Southwood Research Limited;
- Adeno-associated viral vector serotype 9 expressing codon-optimized human GBA gene for treatment of Gaucher disease, PPD Bulgaria EOOD;
- Adeno-associated virus serotype 5 containing the human *NR2E3* gene for treatment of retinitis pigmentosa, Ocugen Limited;
- Adeno-associated virus serotype 5 containing the human *NR2E3* gene for treatment of Leber's congenital amaurosis, Ocugen Limited;
- Dodecyl creatine ester, dodecyl creatine ester hydrochloride for treatment of creatine deficiency syndromes, Ceres Brain Therapeutics S.A.S.;
- Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-Cys-Asp-Met-Ala-Glu-His-Thr-Glu-Arg-Leu-Lys-Ala-Asn-Asp-Ser-Leu-Lys-Leu-Ser-Gln-Glu-Tyr-Glu-Ser-Ile-NH_2 for treatment of spinal cord injury, Raremoon Consulting Esp S.L..

3. Opinion following appeal procedures:

- Tebentafusp for treatment of uveal melanoma, Pharma Gateway AB.

Public summaries of opinions will be available on the EMA website following adoption of the respective decisions on orphan designation[1] by the European Commission. Please also refer to the Community Register of orphan medicinal products for human use.

Negative opinion

1. Opinion adopted following the sponsor's response to the COMP list of questions:

None

[1] Details of all orphan designations granted to date by the European Commission are entered in the EU Register of Orphan Medicinal Products

2. Opinion following appeal procedures:

None

Lists of questions

The COMP adopted 7 lists of questions on initial applications. These applications will be discussed again at the next COMP meting prior to the adoption of an opinion.

Oral hearings

10 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 9 applications for orphan medicinal product designation were withdrawn by the sponsor before adoption of the COMP opinion.

Detailed information on the orphan designation procedures

The list of medicinal products for which decisions on orphan designation have been granted by the European Commission since the last COMP meeting is provided in Annex 1.

Re-assessment of orphan designation at time of marketing authorisation

(Article 5(12) (b) of Regulation (EC) No 141/2000 of the European Parliament and of the Council)

When a designated orphan medicinal product receives a positive opinion for marketing authorisation from EMA's Committee for Medicinal Products for Human Use (CHMP), the COMP has the responsibility to review whether or not the medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation.

1. Opinions adopted at time of CHMP opinion:

- INREBIC (fedratinib) for treatment of post-essential thrombocythaemia myelofibrosis, Celgene Europe BV (EU/3/10/810).
- INREBIC (fedratinib) for treatment of post-polycythaemia vera myelofibrosis, Celgene Europe BV (EU/3/10/811).
- INREBIC (fedratinib) for treatment of primary myelofibrosis, Celgene Europe BV (EU/3/10/794).
- Lumoxiti (moxetumomab pasudotox) for treatment of hairy cell leukaemia, AstraZeneca AB. (EU/3/08/592). The opinion was adopted by written procedure after the December meeting.

2. Opinion following appeal procedures:

None

Details of the designated orphan medicinal products that have been subject of a new European Union (EU) marketing authorisation application since the last COMP monthly report are provided in Annex 2.

Details on the authorised orphan medicinal products can be found on the EMA website.

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 230th meeting of the COMP will be held on 16-18 February 2021.

Note

This monthly report, together with other information on the work of the European Medicines Agency, can be found on the EMA website: www.ema.europa.eu

Enquiries to: AskEMA (https://www.ema.europa.eu/en/about-us/contact/send-question-european-medicines-agency)

Annex 1

Designations granted by the European Commission following COMP opinion on the fulfilment of the orphan designation criteria since last COMP plenary meeting

Please also refer to the Community Register of orphan medicinal product for human use.

The list includes designation decisions that were revised following the amendment of an existing designated condition (identified by * when applicable)

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
(R)-3-(1-(2,3-dichloro-4-(pyrazin-2-yl)phenyl)-2,2,2-trifluoroethyl)-1-methyl-1-(1-methylpiperidin-4-yl)urea fumarate	Treatment of Prader-Willi syndrome	Helsinn Birex Pharmaceuticals Limited	05 November 2020	09 December 2020
(S)-N-(5-(4-(1-(benzo[d][1,3]dioxol-5-yl)ethyl)piperazin-1-yl)-1,3,4-thiadiazol-2-yl)acetamide, hydrochloride salt	Treatment of progressive supranuclear palsy	Granzer Regulatory Consulting & Services	05 November 2020	09 December 2020
2’-O-(2-methoxyethyl) modified antisense oligonucleotide targeting glycogen synthase 1 pre-mRNA	Treatment of progressive myoclonic epilepsy type 2 (Lafora disease)	Ionis Development (Ireland) Limited	05 November 2020	09 December 2020
2'-O-(2-methoxyethyl) phosphorothioate antisense	Treatment of Duchenne muscular dystrophy	Pharma Gateway AB	05 November 2020	09 December 2020

oligonucleotide targeting CD49d RNA				
4-[(3S)-3-aminopyrrolidin-1-yl]-6-cyano-5-(3,5-difluorophenyl)-n-[(2S)-1,1,1-trifluoropropan-2-yl]pyridine-3-carboxamide	Treatment of congenital hyperinsulinism	Scendea (NL) B.V.	05 November 2020	09 December 2020
Adeno-associated viral vector serotype 9 encoding human *ATP7B*	Treatment of Wilson disease	Ultragenyx Germany GmbH	05 November 2020	09 December 2020
Adeno-associated virus serotype rh74 containing the human sarcoglycan beta gene	Treatment of limb-girdle muscular dystrophy	Sarepta Therapeutics Ireland Limited	05 November 2020	09 December 2020
Allogeneic retinal pigment epithelial cells genetically modified with a non-viral vector to express beta-domain deleted human factor VIII	Treatment of haemophilia A	TMC Pharma (EU) Limited	05 November 2020	09 December 2020
Alpha galactosidase A	Treatment of Fabry disease	Consejo Superior De Investigaciones Cientificas	03 December 2020	06 January 2021
Aspacytarabine	Treatment of acute myeloid leukaemia	Granzer Regulatory Consulting & Services	05 November 2020	09 December 2020
Autologous bone marrow derived CD34+ cells transduced ex vivo with a self-inactivating lentiviral	Treatment of X-linked severe combined immunodeficiency	Real Regulatory Limited	08 October 2020	13 November 2020

vector containing a normal version of the coding region of the *IL2RG* gene				
Autologous CD34+ cells transduced ex vivo with a lentiviral vector containing a modified gamma-globin gene	Treatment of sickle cell disease	Clinical Technology Centre (Ireland) Limited	08 October 2020	13 November 2020
Autologous CD4+ and CD8+ T cells genetically modified with a lentiviral vector encoding a B-cell maturation antigen-specific chimeric antigen receptor	Treatment of multiple myeloma	Celgene Europe B.V.	05 November 2020	09 December 2020
Calcium oxybate, magnesium oxybate, potassium oxybate, sodium oxybate	Treatment of idiopathic hypersomnia	Jazz Pharmaceuticals Ireland Limited	03 December 2020	06 January 2021
Celecoxib, ciprofloxacin	Treatment of amyotrophic lateral sclerosis	Morrison & Foerster	03 December 2020	06 January 2021
Cyclo-L-glycyl-L-2-allylproline	Treatment of Angelman syndrome	Dlrc Pharma Services Limited	03 December 2020	06 January 2021
Cyclo-L-glycyl-L-2-allylproline	Treatment of Phelan-McDermid syndrome	Dlrc Pharma Services Limited	03 December 2020	06 January 2021
Cyclo-L-glycyl-L-2-allylproline	Treatment of Pitt-Hopkins syndrome	Dlrc Pharma Services Limited	03 December 2020	06 January 2021
Dabrafenib mesylate	Treatment of glioma	Novartis Europharm Limited	05 November 2020	09 December 2020

Erlotinib	Treatment of Olmsted syndrome	Institut Des Maladies Genetiques	05 November 2020	09 December 2020
Human interleukin 12 fused with immunoglobulin G4 C-terminal Fc fragment	Treatment of glioma	VH Regulatory Consulting GmbH & Co. KG	05 November 2020	09 December 2020
Human laminin-111, recombinant	Treatment of congenital muscular dystrophy	Maxia Strategies-Europe Limited	03 December 2020	06 January 2021
Humanised IgG1 monoclonal antibody against the extracellular domain of receptor tyrosine kinase-like orphan receptor 1 coupled via a proteolytically cleavable maleimidocaproyl-valine-citrulline-para-aminobenzoate linker to monomethyl auristatin E	Treatment of mantle cell lymphoma	TMC Pharma (EU) Limited	05 November 2020	09 December 2020
Humanised IgG1K monoclonal antibody against interferon beta	Treatment of dermatomyositis	Pfizer Europe MA EEIG	03 December 2020	06 January 2021
Idursulfase	Treatment of mucopolysaccharidosis type II (Hunter's syndrome)	Shire Pharmaceuticals Ireland Limited	03 December 2020	06 January 2021
Perflubron	Treatment of congenital pulmonary hypoplasia	Boyd Consultants Limited	08 October 2020	13 November 2020
Rezafungin acetate	Treatment of invasive candidiasis	Mundipharma Corporation (Ireland) Limited	03 December 2020	06 January 2021

Rilonacept	Treatment of idiopathic pericarditis	Granzer Regulatory Consulting & Services	03 December 2020	06 January 2021
Setanaxib	Treatment of primary biliary cholangitis	GenKyoTex S.A.	03 December 2020	06 January 2021
Sotatercept	Treatment of pulmonary arterial hypertension	IDEA Innovative Drug European Associates (Ireland) Limited	05 November 2020	09 December 2020
Sulindac	Treatment of fragile X syndrome	Aparito Netherlands B.V.	05 November 2020	09 December 2020
Synthetic oligonucleotide selectively targeting UBE3A antisense RNA transcripts	Treatment of Angelman syndrome	Roche Registration GmbH	05 November 2020	09 December 2020
Trametinib dimethyl sulfoxide	Treatment of glioma	Novartis Europharm Limited	05 November 2020	09 December 2020
Tremelimumab	Treatment of hepatocellular carcinoma	AstraZeneca AB	05 November 2020	09 December 2020

Annex 2

Designated orphan medicinal products that have been subject of a new European Union marketing authorisation application under the centralised procedure since the last COMP monthly report

Please also refer to the Community Register of orphan medicinal products for human use.

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Artesunate	Treatment of malaria	B And O Pharm	EU/3/15/1521
Burosumab	Treatment of phosphaturic mesenchymal tumour	Kyowa Kirin Holdings B.V.	EU/3/18/2011
Inebilizumab	Treatment of neuromyelitis optica spectrum disorders	Viela Bio	EU/3/17/1856