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Human Medicines Division

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

November 2020

The Committee for Orphan Medicinal Products held its 227th plenary meeting on 03-05 November 2020.

Orphan medicinal product designation

Positive opinions

The COMP adopted 20 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:

- Autologous CD4+ and CD8+ T cells genetically modified with a lentiviral vector encoding a B-cell maturation antigen-specific chimeric antigen receptor for treatment of multiple myeloma, Celgene Europe B.V.;
- Human interleukin 12 fused with immunoglobulin G4 C-terminal Fc fragment for treatment of glioma, VH Regulatory Consulting GmbH & Co. KG;
- Sotatercept for treatment of pulmonary arterial hypertension, IDEA Innovative Drug European Associates (Ireland) Limited;
- Tremelimumab for treatment of hepatocellular carcinoma, AstraZeneca AB.

2. Opinions adopted at the first COMP discussion:

- (R)-3-(1-(2,3-dichloro-4-(pyrazin-2-yl)phenyl)-2,2,2-trifluoroethyl)-1-methyl-1-(1-methylpiperidin-4-yl)urea fumarate for treatment of Prader-Willi syndrome, Helsinn Birex Pharmaceuticals Limited;

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- (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 for treatment of progressive supranuclear palsy, Granzer Regulatory Consulting & Services;
- 2'-O-(2-methoxyethyl) modified antisense oligonucleotide targeting glycogen synthase 1 pre-mRNA for treatment of progressive myoclonic epilepsy type 2 (Lafora disease), Ionis Development (Ireland) Limited;
- 2'-O-(2-methoxyethyl) phosphorothioate antisense oligonucleotide targeting CD49d RNA for treatment of Duchenne muscular dystrophy, Pharma Gateway AB;
- 4-[(3S)-3-aminopyrrolidin-1-yl]-6-cyano-5-(3,5-difluorophenyl)-N-[(2S)-1,1,1-trifluoropropan-2-yl]pyridine-3-carboxamide for treatment of congenital hyperinsulinism, Scendea (NL) B.V..
- Adeno-associated viral vector serotype 9 encoding human *ATP7B* for treatment of Wilson disease, Ultragenyx Germany GmbH;
- Adeno-associated virus serotype rh74 containing the human sarcoglycan beta gene for treatment of limb-girdle muscular dystrophy, Sarepta Therapeutics Ireland Limited;
- Allogeneic retinal pigment epithelial cells genetically modified with a non-viral vector to express beta-domain deleted human factor VIII for treatment of haemophilia A, TMC Pharma (EU) Limited;
- Aspacytarabine for treatment of acute myeloid leukaemia, Granzer Regulatory Consulting & Services;
- Dabrafenib mesylate for treatment of glioma, Novartis Europharm Limited;
- Erlotinib for treatment of Olmsted syndrome, Institut Des Maladies Genetiques;
- 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 for treatment of mantle cell lymphoma, TMC Pharma (EU) Limited;
- Perflubron for treatment of respiratory distress syndrome, Boyd Consultants Limited;
- Sulindac for treatment of fragile X syndrome, Aparito Netherlands B.V.;
- Synthetic oligonucleotide selectively targeting UBE3A antisense RNA transcripts for treatment of Angelman syndrome, Roche Registration GmbH;
- Trametinib dimethyl sulfoxide for treatment of glioma, Novartis Europharm Limited.

3. Opinion following appeal procedures:

None

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.

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

Negative opinion

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

None

2. Opinion following appeal procedures:

None

Lists of questions

The COMP adopted 12 lists of questions on initial applications. These applications will be discussed again at the next COMP meeting prior to the adoption of an opinion.

Oral hearings

3 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 3 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:

- Fintepla (fenfluramine hydrochloride) for treatment of Dravet syndrome, Zogenix ROI Limited (EU/3/13/1219). The opinion was adopted by written procedure after the October meeting.
- Libmeldy (autologous CD34+ cell enriched population that contains hematopoietic stem and progenitor cells transduced ex vivo using a lentiviral vector encoding the human arylsulfatase A gene) for treatment of metachromatic leukodystrophy, Orchard Therapeutics (Netherlands) B.V. (EU/3/07/446). The opinion was adopted by written procedure after the October meeting.
- Oxlumo (lumasiran) for treatment of primary hyperoxaluria type 1, Alnylam Netherlands B.V. (EU/3/16/1637). The opinion was adopted by written procedure after the October meeting.
- Tecartus (autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor

and cultured) for treatment of mantle cell lymphoma, Kite Pharma EU B.V. (EU/3/19/2220). The opinion was adopted by written procedure after the October 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 228th meeting of the COMP will be held on 1-3 December 2020.

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
(4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1h-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1))	Treatment of primary IgA nephropathy	Novartis Europharm Limited	10 September 2020	19 October 2020
(S)-1-(5-((2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-7-yl)sulfonyl)-3,4,5,6-tetrahydropyrrolo[3,4-c]pyrrol-2(1h)-yl)-3-hydroxy-2-phenylpropan-1-one	Treatment of sickle cell disease	Clinipace GmbH	10 September 2020	19 October 2020
1-(3-methylbutanoyl)-l-aspartyl-l-threonyl-l-histidyl-l-phenylalanyl-l-prolyl-(l-cystinyl-l-isoleucyl-[(n6-(s)-4-carboxy-4-palmitamidobutanoyl)-l-lysinyl]-l-phenylalanyl-l-glutamyl-l-prolyl-l-arginyl-l-serinyl-l-lysinyl-l-glycinyl-l-cystinyl)-l-lysinamide, disulfide, acetate	Treatment of polycythaemia vera	Scendea (NL) B.V.	10 September 2020	19 October 2020
2-(2-(^{18}F)fluoropyridin-4-yl)-9H-pyrrolo[2,3-b:4,5-c']dipyridine	Diagnosis of corticobasal degeneration	Life Molecular Imaging GmbH	10 September 2020	19 October 2020
Adeno-associated viral vector serotype 9 encoding a codon-optimised human aspartylglucosaminidase transgene	Treatment of aspartylglucosaminuria	Real Regulatory Limited	10 September 2020	19 October 2020

Adeno-associated virus serotype 5 containing the human *RDH12* gene	Treatment of *RDH12* mutation associated retinal dystrophy	MeiraGTx B.V.	10 September 2020	19 October 2020
Adeno-associated virus serotype hu68 containing the human *GLB1* gene	Treatment of GM1 gangliosidosis	Pharma Gateway AB	10 September 2020	19 October 2020
Decitabine, tetrahydrouridine	Treatment of sickle cell disease	Novo Nordisk A/S	10 September 2020	19 October 2020
Leniolisib	Treatment of activated phosphoinositide 3-kinase delta syndrome	Pharming Group N.V.	10 September 2020	19 October 2020
Miglustat	Treatment of neuronal ceroid lipofuscinosis	Theranexus S.A.S.	10 September 2020	19 October 2020
Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [Pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer	Treatment of homocystinuria	Aeglea Biotherapeutics UK Limited	10 September 2020	19 October 2020
Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1)	Treatment of hypoparathyroidism	Ascendis Pharma Bone Diseases A/S	10 September 2020	19 October 2020
Retigabine	Treatment of KCNQ2 developmental and epileptic encephalopathy	FGK Representative Service GmbH	10 September 2020	19 October 2020

Ribitol	Treatment of limb-girdle muscular dystrophy	Premier Research Group S.L.	10 September 2020	19 October 2020
Trehalose	Treatment of neuronal ceroid lipofuscinosis	Theranexus S.A.S.	10 September 2020	19 October 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	Amivas Ireland Ltd	EU/3/20/2251
Avacopan	Treatment of microscopic polyangiitis	Vifor Fresenius Medical Care Renal Pharma France	EU/3/14/1372
Avalglucosidase alfa	For long-term enzyme replacement therapy for the treatment of patients with Pompe disease	Genzyme Europe BV	EU/3/14/1251
Lenadogene nolparvovec	Treatment of Leber's hereditary optic neuropathy	GenSight Biologics S.A.	EU/3/11/860
Lonapegsomatropin	Treatment of growth hormone deficiency	Ascendis Pharma Endocrinology Division A/S,	EU/3/19/2213
Pegcetacoplan	Paroxysmal nocturnal haemoglobinuria	Apellis Ireland Limited	EU/3/17/1873
Ripretinib	Treatment of patients with advanced gastrointestinal stromal tumour	Deciphera Pharmaceuticals (Netherlands) B.V	EU/3/17/1936