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Human Medicines Division

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

September 2020

The Committee for Orphan Medicinal Products held its 225th plenary meeting on 08-10 September 2020.

Orphan medicinal product designation

Positive opinions

The COMP adopted 22 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:

- (4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)) for treatment of primary IgA nephropathy, Novartis Europharm Limited;
- (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 for treatment of sickle cell disease, Clinipace GmbH;
- 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 for treatment of polycythaemia vera, Scendea (NL) B.V.;
- 2-(2-(^{18}F)fluoropyridin-4-yl)-9H-pyrrolo[2,3-b:4,5-c']dipyridine for diagnosis of corticobasal degeneration, Life Molecular Imaging GmbH;
- Autologous CD34+ cells transduced with a lentiviral vector encoding galactosidase alpha for treatment of Fabry disease, Clinical Technology Centre (Ireland) Limited;

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- 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 acute lymphoblastic leukaemia, Kite Pharma EU B.V.;
- Decitabine, tetrahydrouridine for treatment of sickle cell disease, Novo Nordisk A/S;
- Retifanlimab for treatment of anal cancer, Incyte Biosciences Distribution B.V.;
- Retigabine for treatment of KCNQ2 developmental and epileptic encephalopathy, FGK Representative Service GmbH;
- Teclistamab for treatment of multiple myeloma, Janssen-Cilag International N.V.

2. Opinions adopted at the first COMP discussion:

- Adeno-associated viral vector serotype 9 encoding a codon-optimised human aspartylglucosaminidase transgene for treatment of aspartylglucosaminuria, Real Regulatory Limited;
- Adeno-associated virus serotype 5 containing the human *RDH12* gene for treatment of *RDH12* mutation associated retinal dystrophy, MeiraGTx B.V.;
- Adeno-associated virus serotype hu68 containing the human *GLB1* gene for treatment of GM1 gangliosidosis, Pharma Gateway AB;
- Highly branched poly(beta-amino ester) complexed with a nanoplasmid containing the human *COL7A1* gene for treatment of epidermolysis bullosa, Amryt Genetics Limited;
- Leniolisib for treatment of activated phosphoinositide 3-kinase delta syndrome, Pharming Group N.V.;
- Miglustat for treatment of neuronal ceroid lipofuscinosis, Theranexus S.A.S.;
- Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with cystathionine γ-lyase [Pyridoxal 5'-phosphate cofactor] (synthetic engineered human), tetramer for treatment of homocystinuria, Aeglea Biotherapeutics UK Limited;
- 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) for treatment of hypoparathyroidism, Ascendis Pharma Bone Diseases A/S;
- Ribitol for treatment of limb-girdle muscular dystrophy, Premier Research Group S.L.;
- Sparsentan for treatment of primary IgA nephropathy, Retrophin Europe Limited;
- Tipifarnib for treatment of peripheral T-cell lymphoma, TMC Pharma (EU) Limited;
- Trehalose for treatment of neuronal ceroid lipofuscinosis, Theranexus S.A.S..

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.

Negative opinion

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

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

2. Opinion following appeal procedures:

None

Lists of questions

The COMP adopted 9 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

10 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 5 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:

- Adakveo (crizanlizumab) for treatment of sickle cell disease, Novartis Europharm Limited (EU/3/12/1034);
- Arikayce liposomal (amikacin) for treatment of nontuberculous mycobacterial lung disease, Insmed Netherlands B.V. (EU/3/14/1259);

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

- Ayvakit (avapritinib) for treatment of gastrointestinal stromal tumours, Blueprint Medicines (Netherlands) B.V. (EU/3/17/1889). The opinion was adopted by written procedure after the July meeting.
- Blenrep (belantamab mafodotin) for the treatment of multiple myeloma, GlaxoSmithKline (Ireland) Limited (EU/3/17/1925). The opinion was adopted by written procedure after the July meeting.
- Kalydeco (ivacaftor) - Type II variation, for the treatment of cystic fibrosis, Vertex Pharmaceuticals (Ireland) Limited (EU/3/08/556). The opinion was adopted by written procedure after the July 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 226th meeting of the COMP will be held on 06-08 October 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

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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
2-(2-(18F)fluoropyridin-4-yl)-9H-pyrrolo[2,3-b:4,5-c']dipyridine	Diagnosis of progressive supranuclear palsy	Life Molecular Imaging GmbH	16 July 2020	21 August 2020
3-(((1S,2S,3R)-2,3-difluoro-1-hydroxy-7-(methylsulfonyl)-2,3-dihydro-1H-inden-4-yl)oxy)-5-fluorobenzonitrile	Treatment of von Hippel-Lindau disease	Merck Sharp & Dohme B.V.	16 July 2020	21 August 2020
6-[(3S,4S)-4-methyl-1-(pyrimidin-2-ylmethyl)pyrrolidin-3-yl]-3-tetrahydropyran-4-yl-7H-imidazo[1,5-a]pyrazin-8-one	Treatment of sickle cell disease	TMC Pharma (EU) Limited	16 July 2020	21 August 2020
Adeno-associated viral vector expressing acid alpha-glucosidase gene	Treatment of glycogen storage disease type II (Pompe's disease)	Audentes Therapeutics Netherlands B.V.	18 June 2020	27 July 2020
Adeno-associated viral vector serotype 3B encoding shortened human ATP7B	Treatment of Wilson's disease	Vivet Therapeutics S.A.S.	16 July 2020	21 August 2020

Adeno-associated virus serotype 2/8 vector containing the human *PDE6A* gene	Treatment of retinitis pigmentosa	Institute For Ophthalmic Research	16 July 2020	21 August 2020
Allogeneic hepatoblastoma cells encapsulated in alginate, ex vivo expanded	Treatment of acute liver failure	ESPL Regulatory Consulting Limited	16 July 2020	21 August 2020
Allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured	Treatment in haematopoietic stem cell transplantation	Smart Immune	16 July 2020	21 August 2020
Allogeneic umbilical cord tissue-derived mesenchymal stromal cells ex vivo expanded	Prevention of bronchopulmonary dysplasia	MDTB Cells GmbH	16 July 2020	21 August 2020
Anti-CD123 IgG1 humanised monoclonal antibody conjugated to N1-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)-N6-((S)-1-(((S)-1-((3-((((S)-8-methoxy-6-oxo-11,12,12a,13-tetrahydro-6H-benzo[5,6][1,4]diazepino[1,2-a]indol-9-yl)oxy)methyl)-5-((((S)-8-methoxy-6-oxo-12a,13-dihydro-6Hbenzo[5,6][1,4]diazepino[1,2-a]indol-9-yl)oxy)methyl)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopropan-2-yl)adipamide	Treatment of blastic plasmacytoid dendritic cell neoplasm	ImmunoGen BioPharma (Ireland) Limited	20 May 2020	26 June 2020

Autologous CD34+ cells transduced with a lentiviral vector encoding glucosylceramidase beta	Treatment of Gaucher disease	Clinical Technology Centre (Ireland) Limited	16 July 2020	21 August 2020
Autologous T cells transduced with lentiviral vector containing a tandem chimeric antigen receptor directed against CD20 and CD19	Treatment of diffuse large B-cell lymphoma	Miltenyi Biomedicine GmbH	16 July 2020	21 August 2020
Bis-(3-deoxy-3-(4-(3-fluorophenyl)-1H-1,2,3-triazol-1-yl)-beta-D-galactopyranosyl) sulfane	Treatment of idiopathic pulmonary fibrosis	Galecto Biotech AB	16 July 2020	21 August 2020
C-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker	Treatment of achondroplasia	Ascendis Pharma Growth Disorders A/S	18 June 2020	27 July 2020
Dextran sulfate low molecular weight	Treatment of amyotrophic lateral sclerosis	TikoMed AB	16 July 2020	21 August 2020
Fasudil hydrochloride	Treatment of non-traumatic subarachnoid haemorrhage	Aneuryst (Ireland) Limited	18 June 2020	27 July 2020
Hemopexin, human	Treatment of sickle cell disease	CSL Behring GmbH	18 June 2020	27 July 2020
Human frataxin fused to TAT cell-penetrating peptide	Treatment of Friedreich's ataxia	YES Pharmaceutical Development Services GmbH	16 July 2020	21 August 2020

Humanised IgG1 monoclonal antibody against human eotaxin-2	Treatment of primary sclerosing cholangitis	Granzer Regulatory Consulting & Services	16 July 2020	21 August 2020
Imetelstat sodium	Treatment of myelodysplastic syndromes	Parexel International GmbH	18 June 2020	27 July 2020
Infigratinib	Treatment of cholangiocarcinoma	YES Pharmaceutical Development Services GmbH	16 July 2020	21 August 2020
Maralixibat chloride	Treatment of biliary atresia	Granzer Regulatory Consulting & Services	18 June 2020	27 July 2020
Pegylated adrenomedullin	Treatment of acute respiratory distress syndrome	Bayer AG	18 June 2020	27 July 2020
Pentosan polysulfate sodium	Treatment of mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome)	Paradigm Biopharmaceuticals (Ireland) Limited	16 July 2020	21 August 2020
Protein-based delivery vector carrying a DNA payload encoding an RNA-guided nuclease that targets *stx* genes of Shiga toxin-producing *Escherichia coli*	Prevention of haemolytic uraemic syndrome	Eligo Bioscience	16 July 2020	21 August 2020
Retinol palmitate	Prevention of bronchopulmonary dysplasia	Provepharm S.A.S.	18 June 2020	27 July 2020
Sodium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-	Treatment of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency	Scendea (NL) B.V.	16 July 2020	21 August 2020

prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate				
Sodium (4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop1ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate	Treatment of mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes	Scendea (NL) B.V.	16 July 2020	21 August 2020
Tinostamustine	Treatment of T-cell prolymphocytic leukaemia	Mundipharma Corporation (Ireland) Limited	18 June 2020	27 July 2020
Triheptanoin	Treatment of carnitine-acylcarnitine translocase deficiency	Ultragenyx Germany GmbH	18 June 2020	27 July 2020
Venglustat	Treatment of GM2 gangliosidosis	Genzyme Europe B.V.	16 July 2020	21 August 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
Glucarpidase	Adjunctive treatment in patients at risk of methotrexate toxicity	Protherics Medicines Development Europe B.V.	EU/3/02/128
Risdiplam	Treatment of Spinal Muscular Atrophy	Roche Registration GmbH	EU/3/19/2145
Vosoritide	Treatment of Achondroplasia	BioMarin International Limited	EU/3/12/1094