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Procedure Management and Committees Support Division

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

September 2016

The Committee for Orphan Medicinal Products held its 181th plenary meeting on 6-8 September 2016.

Orphan medicinal product designation

Positive opinions

The COMP adopted 33 positive opinions recommending the following medicines for designation as orphan medicinal products to the European Commission (EC):

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

- 2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide for treatment of invasive aspergillosis, F2G Ltd;
- (6aR,10aR)-3-(1',1'-dimethylheptyl)-delta-8-tetrahydrocannabinol-9-carboxylic acid for treatment of cystic fibrosis, TMC Pharma Services Ltd;
- A non-covalent trimer of tumour necrosis factor fused to an antibody specific to the extra-domain B of fibronectin in single-chain variable fragment format for treatment of soft tissue sarcoma, Philogen S.p.A.;
- Autologous mononuclear cells derived from human cord blood for treatment of periventricular leukomalacia, BrainRepair UG (haftungsbeschränkt);
- Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 for treatment of diffuse large B-cell lymphoma, Novartis Europharm Limited;
- (E)-(6-((N-methyl-((3-methylbenzofuran-2-yl)methyl)amino)-3-oxoprop-1-en-1-yl)-2-oxo-3,4-dihydro-1,8-naphthyridin-1(2H)-yl)methyl phosphate, bis ethanolamine salt for treatment of osteomyelitis, Voisin Consulting S.A.R.L.;
- Human monoclonal IgG1 antibody against tissue factor pathway inhibitor for treatment of haemophilia A, Pfizer Limited;

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- Lutetium-177(3+), S2,S7-cyclo[N-{4,7,10-tricarboxymethyl-1,4,7,10-tetraaza-cyclododecan-1-yl-acetyl}-4-chloro-L-phenylalanyl-D-cysteinyl-4-[(4S)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteinyl-D-tyrosinamide] for treatment of gastro-entero-pancreatic neuroendocrine tumours, Ipsen Pharma;
- Mogamulizumab for treatment of cutaneous T-cell lymphoma, Kyowa Kirin Limited;
- N-[(2S)-5-{[(1R, 2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt for treatment of myelofibrosis, Imago BioSciences Ltd.;
- Radio-iodinated (^{131}I) anti-CD45 murine monoclonal antibody for treatment in haematopoietic stem cell transplantation, Wainwright Associates Ltd;
- Synthetic 15-amino-acid macrocyclic peptide acylated with a polyethyleneglycol palmitoylated linker for treatment of paroxysmal nocturnal haemoglobinuria, Ra Europe Limited;
- Venetoclax for treatment of multiple myeloma, Abbvie Ltd.;
- Venetoclax for treatment of diffuse large B-cell lymphoma, Abbvie Ltd;
- Xenon for treatment of ischaemia reperfusion injury associated with cardiac arrest, Neuroprotexeon Ltd.

2. Opinions adopted at the first COMP discussion:

- Acebutolol hydrochloride for treatment of Smith-Magenis syndrome, Therapicon Srl;
- Adeno-associated viral vector serotype 5 containing the human *RLBP1* gene for treatment of retinitis pigmentosa, HORAMA SAS;
- Adeno-associated viral vector serotype 2/2 containing a gene encoding the channelrhodopsin-2 protein for treatment of retinitis pigmentosa, Alacrita LLP;
- Autologous mononuclear cells derived from human cord blood for treatment of neonatal encephalopathy, BrainRepair UG (haftungsbeschränkt);
- Carbamazepine for treatment of metaphyseal chondrodysplasia, Schmid type, University of Newcastle upon Tyne;
- Chemically modified human recombinant sulfamidase for treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome), Swedish Orphan Biovitrum AB (publ);
- Crenolanib besylate for treatment of soft tissue sarcoma, Arog Pharmaceuticals Europe Ltd;
- Crenolanib besylate for treatment of acute myeloid leukaemia, Arog Pharmaceuticals Europe Ltd;
- Exendin (9-39) for treatment of noninsulinoma pancreatogenous hypoglycaemia syndrome, Eiger Biopharmaceuticals Europe Limited;
- Fenretinide for treatment of peripheral T-cell lymphoma, Clinipace GmbH;
- Haematopoietic stem cells modified with a lentiviral vector containing the *CD18* gene for treatment of leukocyte adhesion deficiency type I, Centro de Investigación Biomédica en Red (CIBER);
- Melatonin for treatment of Smith-Magenis syndrome, Therapicon Srl;

- P-ethoxy growth factor receptor-bound protein 2 antisense oligonucleotide for treatment of acute myeloid leukaemia, Clinical Network Services (UK) Ltd;
- Recombinant adeno-associated viral vector encoding a human micro-dystrophin gene under the control of a muscle specific promoter for treatment of Duchenne muscular dystrophy, Pharma Gateway AB;
- Self-complementary adeno-associated viral vector serotype 9 containing the *SGSH* gene for treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome), Ser-mes Planificación SL;
- Tadekinig alfa for treatment of haemophagocytic lymphohistiocytosis, Coté Orphan Consulting UK Limited;
- Tetrofosmin for diagnosis of glioma, ProActina;
- Ubiquinol for treatment of primary coenzyme Q_{10} deficiency syndrome, Centro de Investigación Biomédica en Red (CIBER).

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.

Lists of questions

The COMP adopted 20 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 7 applications for orphan medicinal product designation were withdrawn.

Detailed information on the orphan designation procedures

An overview of orphan designation procedures since 2000 is provided in Annex 1.

The list of medicinal products for which decisions on orphan designation have been given by the European Commission since the last COMP meeting is provided in Annex 2.

Applications for marketing authorisation for orphan medicinal products

Details of those designated orphan medicinal products that have been subject of a new European Union (EU) marketing authorisation application through the centralised procedure since the last COMP plenary meeting are provided in Annex 3.

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

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

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

In line with its responsibility to review whether or not a designated orphan medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation:

The COMP adopted 1 opinion recommending to the European Commission that the following orphan medicinal product be kept in the EU registry of orphan medicinal product:

- Onivyde (irinotecan) for treatment of pancreatic cancer, Baxalta Innovations GmbH (EU/3/11/933).

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 182th meeting of the COMP will be held on 4-6 October 2016.

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

Overview for orphan medicinal product designation procedure since 2000

Year	Applications submitted	Applications discussed in reporting year	Positive COMP opinions	Applications withdrawn[2]	Final negative COMP opinions	EC designations	Orphan medicinal products[3] authorised	Orphan designations included in authorised therapeutic indication
2016	220	206	161(78%)	45 (22%)	0	137	8	8
2015	258	272	177 (65%)	94 (35%)	1 (1%)	190	14	21
2014	329	259	196 (76%)	62 (24%)	2 (1%)	187	15	16
2013	201	197	136 (69%)	60 (30%)	1 (1%)	136	7	8
2012	197	192	139 (72%)	52 (27%)	1 (1%)	148	10	12
2011	166	158	111 (70%)	45 (29%)	2 (1%)	107	5	5
2010	174	176	123 (70%)	51 (29%)	2 (1%)	128	4	4
2009	164	136	113 (83%)	23 (17%)	0 (0%)	106	9	9
2008	119	118	86 (73%)	31 (26%)	1 (1%)	73	6	7
2007	125	117	97 (83%)	19 (16%)	1 (1%)	98	13	13
2006	104	103	81 (79%)	20 (19%)	2 (2%)	80	9	11
2005	118	118	88 (75%)	30 (25%)	0 (0%)	88	4	4
2004	108	101	75 (74%)	22 (22%)	4 (4%)	73	6	6
2003	87	96	54 (56%)	37 (40%)	1 (1%)	55	5	5
2002	80	75	43 (57%)	32 (42%)	2 (3%)	49	4	4
2001	83	90	62 (70%)	26 (29%)	1 (1%)	64	3	3
2000	72	32	26 (81%)	3 (10%)	0 (0%)	14	0	0
Total	**2605**	**2441**	**1768 (72%)**	**652 (27%)**	**21 (1%)**	**1733**	**122**	**136**

[2] Revision of the figures for 2015, 2014, 2003, 2002, 2001 and 2000
[3] Number of authorised orphan medicinal products may cover more than one orphan designation

Annex 2

Medicinal products granted a European Union designation as orphan medicinal product by the European Commission since the July 2016 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Melatonin	Treatment of necrotising enterocolitis	Therapicon Srl	19 May 2016	1 August 2016
2-((2-ethyl-6-(4-(2-(3-hydroxyazetidin-1-yl)-2-oxoethyl)-piperazin-1-yl)-8-methylimidazo[1,2-alpha]pyridin-3-yl)-(methyl)amino)-4-(4-fluorophenyl)-thiazole-5-carbonitrile	Treatment of idiopathic pulmonary fibrosis	Galapagos NV	13 July 2016	29 August 2016
2-(1,5-dimethyl-3-phenyl-1H-pyrrol-2-yl)-N-{4-[4-(5-fluoro-pyrimidin-2-yl)piperazin-1-yl]-phenyl}-2-oxo-acetamide	Treatment of scedosporiosis	F2G Ltd	13 July 2016	29 August 2016
6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate	Treatment of mucopolysaccharidosis type I	Coté Orphan Consulting UK Limited	13 July 2016	29 August 2016
Adeno-associated viral vector serotype 9 containing the human mini-dystrophin gene	Treatment of Duchenne muscular dystrophy	Advanced Biotherapeutics Consulting SARL	13 July 2016	29 August 2016
Adenovirus associated viral vector serotype 5 containing the human *RPGR* gene	Treatment of retinitis pigmentosa	Athena Vision Ltd	13 July 2016	29 August 2016
Autologous mesenchymal stromal cells on a decellularised tracheal scaffold from a cadaveric donor	Treatment of tracheal stenosis	Videregen Ltd	13 July 2016	29 August 2016
Cannabidiol	Treatment of graft-versus-host disease	Richardson Associates Regulatory Affairs Ltd	13 July 2016	29 August 2016
Cisplatin	Treatment of malignant mesothelioma	PlumeStars s.r.l.	13 July 2016	29 August 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Fimaporfin	Treatment of cholangiocarcinoma	PCI Biotech AS	13 July 2016	29 August 2016
L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser	Treatment of graft loss in pancreatic islet transplantation	Araim Pharma Europe Ltd	13 July 2016	29 August 2016
Masitinib mesilate	Treatment of amyotrophic lateral sclerosis	AB Science	13 July 2016	29 August 2016
Methotrexate	Treatment of alkaptonuria	aimAKU (Associazione Italiana Malati di Alcaptonuria)	13 July 2016	29 August 2016
Nintedanib	Treatment of systemic sclerosis	Boehringer Ingelheim International GmbH	13 July 2016	29 August 2016
Recombinant protein derived from the saliva of the *Ornithodoros moubata* tick	Treatment of paroxysmal nocturnal haemoglobinuria	Akari Therapeutics Plc	13 July 2016	29 August 2016
Recombinant human acid alpha-glucosidase conjugated with mannose-6-phosphate analogues	Treatment of glycogen storage disease type II (Pompe's disease)	NanoMedSyn	13 July 2016	29 August 2016
Recombinant human interleukin-12	Treatment of acute radiation syndrome	Coté Orphan Consulting UK Limited	13 July 2016	29 August 2016
Recombinant humanised monoclonal antibody against human complement component C5a	Treatment of graft-versus-host disease	Alexion Europe SAS	13 July 2016	29 August 2016
Sodium benzoate	Treatment of ornithine translocase deficiency	Lucane Pharma SA	13 July 2016	29 August 2016
Sodium benzoate	Treatment of lysinuric protein intolerance	Lucane Pharma SA	13 July 2016	29 August 2016
Synthetic double-stranded siRNA oligonucleotide directed against delta-aminolevulinic acid synthase 1 mRNA, covalently linked to a ligand containing three N-acetylgalactosamine residues	Treatment of acute hepatic porphyria	Alnylam UK Limited	13 July 2016	29 August 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Synthetic ribonucleic acid oligonucleotide directed against superoxide dismutase 1 messenger ribonucleic acid	Treatment of amyotrophic lateral sclerosis	Biogen Idec Limited	13 July 2016	29 August 2016
Temozolomide	Treatment of glioma	Double Bond Pharmaceutical AB	13 July 2016	29 August 2016
Valproic acid	Treatment of McArdle's disease	Vall d'Hebron Institute of Research	13 July 2016	29 August 2016
Zoledronic acid	Treatment of glioma	Laboratorio Italiano Biochimico Farmaceutico Lisapharma S.p.A.	13 July 2016	29 August 2016

Annex 3

Designated orphan medicinal products that have been subject of a new European Union marketing authorisation application under the centralised procedure since the June 2016 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Levamisole	Treatment of nephrotic syndrome	ACE Pharmaceuticals BV	EU/3/05/324
Midostaurin	a) Treatment of mastocytosis b) Treatment of acute myeloid leukaemia	Novartis Europharm Ltd	EU/3/10/765 EU/3/04/214