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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

July 2016

The Committee for Orphan Medicinal Products held its 180th plenary meeting on 11-13 July 2016.

Orphan medicinal product designation

Positive opinions

The COMP adopted 24 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:

- Autologous mesenchymal stromal cells on a decellularised tracheal scaffold from a cadaveric donor for treatment of tracheal stenosis, Videregen Ltd;
- Masitinib mesilate for treatment of amyotrophic lateral sclerosis, AB Science;
- Recombinant protein derived from the saliva of the *Ornithodoros moubata* tick for treatment of paroxysmal nocturnal haemoglobinuria, Akari Therapeutics Plc;
- Sodium benzoate for treatment of ornithine translocase deficiency, Lucane Pharma SA;
- Sodium benzoate for treatment of lysinuric protein intolerance, Lucane Pharma SA;
- Valproic acid for treatment of McArdle's disease, Vall d'Hebron Institute of Research;
- Zoledronic acid for treatment of glioma, Laboratorio Italiano Biochimico Farmaceutico Lisapharma S.p.A.

2. Opinions adopted at the first COMP discussion:

- 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 for treatment of idiopathic pulmonary fibrosis, Galapagos NV;

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- 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 scedosporiosis, F2G Ltd;
- 6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate for treatment of mucopolysaccharidosis type I, Coté Orphan Consulting UK Limited;
- Adeno-associated viral vector serotype 9 containing the human mini-dystrophin gene for treatment of Duchenne muscular dystrophy, Advanced Biotherapeutics Consulting SARL;
- Adenovirus associated viral vector serotype 5 containing the human *RPGR* gene for treatment of retinitis pigmentosa, Athena Vision Ltd;
- Cannabidiol for treatment of graft-versus-host disease, Richardson Associates Regulatory Affairs Ltd;
- Cisplatin for treatment of malignant mesothelioma, PlumeStars s.r.l.;
- Fimaporfin for treatment of cholangiocarcinoma, PCI Biotech AS;
- L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser for treatment of graft loss in pancreatic islet transplantation, Araim Pharma Europe Ltd;
- Methotrexate for treatment of alkaptonuria, aimAKU (Associazione Italiana Malati di Alcaptonuria);
- Nintedanib for treatment of systemic sclerosis, Boehringer Ingelheim International GmbH;
- Recombinant human acid alpha-glucosidase conjugated with mannose-6-phosphate analogues for treatment of glycogen storage disease type II (Pompe's disease), NanoMedSyn;
- Recombinant human interleukin-12 for treatment of acute radiation syndrome, Coté Orphan Consulting UK Limited;
- Recombinant humanised monoclonal antibody against human complement component C5a for treatment of graft-versus-host disease, Alexion Europe SAS;
- Synthetic double-stranded siRNA oligonucleotide directed against delta-aminolevulinic acid synthase 1 mRNA, covalently linked to a ligand containing three N-acetylgalactosamine residues for treatment of acute hepatic porphyria, Alnylam UK Limited;
- Synthetic ribonucleic acid oligonucleotide directed against superoxide dismutase 1 messenger ribonucleic acid for treatment of amyotrophic lateral sclerosis, Biogen Idec Limited;
- Temozolomide for treatment of glioma, Double Bond Pharmaceutical AB.

Negative opinion

The COMP adopted 2 negative opinions recommending the refusal of the orphan designation for a product for treatment of fibromyalgia and for a product for the treatment of narcolepsy. The sponsors were informed about the possibility to appeal.

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.

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

Lists of questions

The COMP adopted 22 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

8 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 6 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.

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:

- Zalmoxis (allogeneic T cells genetically modified to express suicide gene) for adjunctive treatment in haematopoietic cell transplantation, MolMed S.p.A. (EU/3/03/168). The opinion was adopted by written procedure after the June meeting.

Appeal opinion

Following the appeal to the COMP opinion of 18 February 2016, the COMP adopted their final opinion recommending to the European Commission that the following orphan medicinal products be kept in the EU registry of orphan medicinal product:

- Revlimid (lenalidomide) for treatment of mantle cell lymphoma, Celgene Europe Limited (EU/3/11/924). The opinion was adopted by written procedure after the June meeting.

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 181th meeting of the COMP will be held on 6-8 September 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	173	163	128(79%)	35 (21%)	0	112	7	7
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	**2558**	**2398**	**1735 (72%)**	**642 (27%)**	**21 (1%)**	**1708**	**121**	**135**

[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 June 2016 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
2'-O-(2-methoxyethyl) phosphorothioate antisense oligonucleotide targeting the growth hormone receptor	Treatment of acromegaly	Coté Orphan Consulting UK Limited	19 May 2016	2 June 2016
3-(5-amino-2-methyl-4-oxoquinazolin-3(4H)-yl)piperidine-2,6-dione hydrochloride	Treatment of diffuse large B-cell lymphoma	Celgene Europe Limited	19 May 2016	2 June 2016
Allogeneic donor-derived ex-vivo expanded T lymphocytes transduced with a retroviral vector containing inducible caspase 9 and truncated CD19	Treatment in haematopoietic stem cell transplantation	QRC Consultants Ltd	19 May 2016	2 June 2016
Citric acid monohydrate	Treatment of acute liver failure	CATS Consultants GmbH	19 May 2016	2 June 2016
Cyclocreatine	Treatment of creatine deficiency syndromes	Pharma Gateway AB	19 May 2016	2 June 2016
Diclofenamide	Treatment of periodic paralysis	Sun Pharmaceutical Industries Europe B.V.	19 May 2016	2 June 2016
Donor T lymphocytes depleted ex vivo of host alloreactive T cells using photodynamic treatment	Treatment in haematopoietic stem cell transplantation	Kiadis Pharma Netherlands B.V.	19 May 2016	2 June 2016
Eflornithine	Treatment of glioma	Orbus Therapeutics Limited	19 May 2016	2 June 2016
Humanised anti-IL-6 receptor monoclonal antibody	Treatment of neuromyelitis optica spectrum disorders	Chugai Pharma Europe Ltd	19 May 2016	2 June 2016
Humanised monoclonal antibody targeting interleukin-15	Treatment of eosinophilic oesophagitis	Dr Alain Vicari	19 May 2016	2 June 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Melatonin	Treatment of neonatal sepsis	Therapicon Srl	19 May 2016	2 June 2016
Modified mRNA encoding the UGT1A1 protein	Treatment of Crigler-Najjar syndrome	Alexion Europe SAS	19 May 2016	2 June 2016
Molgramostim	Treatment of acute respiratory distress syndrome	Serendex Pharmaceuticals A/S	19 May 2016	2 June 2016
Pyridoxine and L-pyroglutamic acid	Treatment of fragile X syndrome	FGK Representative Service Ltd.	19 May 2016	2 June 2016
Recombinant humanised monoclonal IgG2 lambda antibody against human sclerostin	Treatment of osteogenesis imperfecta	Mereo Biopharma Group Limited	19 May 2016	2 June 2016
Recombinant protein derived from the saliva of the *Ornithodoros moubata* tick	Treatment of Guillain-Barré syndrome	Akari Therapeutics Plc	19 May 2016	2 June 2016
Setmelanotide	Treatment of Prader-Willi syndrome	TMC Pharma Services Ltd	19 May 2016	2 June 2016
Teriparatide	Treatment of hypoparathyroidism	Alacrita LLP	19 May 2016	2 June 2016
16-base single-stranded peptide nucleic acid oligonucleotide linked to a 7 amino acid peptide	Treatment of soft tissue sarcoma	Biogenera SpA	16 June 2016	18 July 2016
2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxymethyl]-quinoline succinic acid	Treatment of Huntington's disease	Pfizer Limited	16 June 2016	18 July 2016
3-[4-(1H-imidazol-1-ylmethyl)phenyl]-5-(2-methylpropyl)thiophene-2-[(N-butyloxylcarbamate)-sulphonamide] sodium salt	Treatment of idiopathic pulmonary fibrosis	Vicore Pharma AB	16 June 2016	18 July 2016
Adeno-associated viral vector serotype 2.7m8 containing the *ChrimsonR-tdTomato* gene	Treatment of retinitis pigmentosa	GenSight Biologics	16 June 2016	18 July 2016
Autologous CD4+ and CD8+ T cells transduced with lentiviral vector containing an affinity-enhanced T-cell receptor targeting the New York esophageal antigen-1	Treatment of soft tissue sarcoma	Adaptimmune Limited	16 June 2016	18 July 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Autologous Epstein-Barr virus specific T cells derived from peripheral blood mononuclear cells, expanded ex vivo	Treatment of extranodal NK/T-cell lymphoma	Cell Medica Ltd.	16 June 2016	18 July 2016
Autologous Epstein-Barr virus specific T cells derived from peripheral blood mononuclear cells, expanded ex vivo	Treatment of post-transplant lymphoproliferative disorder	Cell Medica Ltd.	16 June 2016	18 July 2016
Brincidofovir	Treatment of adenovirus infection in immunocompromised patients	Chimerix UK Ltd	16 June 2016	18 July 2016
Dimethyl fumarate	Treatment of bullous pemphigoid	Immungenetics AG	16 June 2016	18 July 2016
Mifamurtide	Treatment of echinococcosis	Delta Proteomics SAS	16 June 2016	18 July 2016
Mifamurtide	Treatment of hepatocellular carcinoma	Delta Proteomics SAS	16 June 2016	18 July 2016
Poly(oxy-1,2-ethanediyl), alpha-(carboxymethyl)-omega-methoxy-, amide with arginase 1 [cobalt cofactor] (synthetic human) (1:10), trimer	Treatment of hyperargininaemia	ERA Consulting GmbH	16 June 2016	18 July 2016
Recombinant human monoclonal antibody to insulin receptor	Treatment of congenital hyperinsulinism	XOMA UK Limited	16 June 2016	18 July 2016
Setmelanotide	Treatment of pro-opiomelanocortin deficiency	TMC Pharma Services Ltd	16 June 2016	18 July 2016
Sirolimus	Treatment of sporadic lymphangioleiomyomatosis	Best Regulatory Consulting Ltd	16 June 2016	18 July 2016
Sodium benzoate	Treatment of carbamoyl-phosphate synthetase-1 deficiency	Lucane Pharma SA	16 June 2016	18 July 2016
Sodium benzoate	Treatment of citrullinaemia type 1	Lucane Pharma SA	16 June 2016	18 July 2016
Sodium benzoate	Treatment of hyperargininaemia	Lucane Pharma SA	16 June 2016	18 July 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Sodium benzoate	Treatment of ornithine transcarbamylase deficiency	Lucane Pharma SA	16 June 2016	18 July 2016
Sodium hypochlorite	Treatment of partial deep dermal and full thickness burns	Hypo-Stream Ltd	16 June 2016	18 July 2016
Triheptanoin	Treatment of McArdle's disease	Vall d'Hebron Institute of Research	16 June 2016	18 July 2016
Volanesorsen sodium	Treatment of familial partial lipodystrophy	Ionis USA Ltd	16 June 2016	18 July 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
Obeticholic acid	Treatment of primary biliary cirrhosis	Intercept Italia s.r.l	EU/3/10/753