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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

March 2017

The Committee for Orphan Medicinal Products held its 187th plenary meeting on 14-15 March 2017.

Orphan medicinal product designation

Positive opinion(s)

The COMP adopted 10 positive opinion(s) recommending the following medicines for designation as orphan medicinal products to the European Commission:

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

- N-[(1R)-1-phenylethyl]-6-{1H-pyrazolo[3,4-d]pyrimidin-4-yl}quinazolin-2-amine for treatment of fragile X syndrome, Sentinel Oncology Limited;
- (S)-8-{2-amino-6-[1-(5-chloro-biphenyl-2-yl)-(R)-2,2,2-trifluoro-ethoxy]-pyrimidin-4-yl}-2,8-diaza-spiro[4.5]decane-3-carboxylic acid ethyl ester for treatment of pulmonary arterial hypertension, Biological Consulting Europe Ltd;
- Rituximab for treatment in solid organ transplantation, Hôpital Foch;
- Human normal immunoglobulin for treatment in solid organ transplantation, Hôpital Foch;
- Autologous adult bone marrow-derived non-expanded CD133+ haematopoietic stem cells for treatment of Asherman's syndrome, Igenomix, S.L.;
- Estetrol for treatment of neonatal encephalopathy, Mithra Pharmaceuticals S.A.;
- Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains for treatment of multiple myeloma, Bluebird bio France.

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2. Opinions adopted at the first COMP discussion:

- Emeramide for prevention of mercury toxicity, NBMI Science Limited;
- Modified messenger ribonucleic acid encoding human ornithine transcarbamylase enzyme encapsulated into lipid nanoparticles for treatment of ornithine transcarbamylase deficiency, PhaseRx Ireland, Ltd;
- Thymidine and deoxycytidine for treatment of mitochondrial DNA depletion syndrome, myopathic form, Vall d'Hebron Institute of Research.

5. Opinion(s) 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(s)

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

None

2. Opinion(s) following appeal procedures

Following the appeal to the COMP opinion adopted on 09 November 2016, the COMP adopted their final opinion recommending the refusal of the orphan designation for the following product:

- 20% intravenous fat emulsion consisting of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, and water for injection for treatment of poisoning by local anaesthetics, Alan Boyd Consultants Ltd.

Lists of questions

The COMP adopted 4 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

11 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 by the sponsor before adoption of the COMP opinion.

Detailed information on the orphan designation procedures

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

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

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 2.

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)

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:

1. Opinion(s) adopted at time of CHMP opinion

- Natpar (parathyroid hormone) for treatment of hypoparathyroidism, NPS Pharma UK Ltd (EU/3/13/1210). The opinion was adopted by written procedure after the February meeting.

2. Opinion(s) 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 3.

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 188th meeting of the COMP will be held on 10-12 April 2017.

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

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

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
2017	33	76	43 (57%)	32 (42%)	1	39	2	2
2016	330	304	220 (72%)	82 (27%)	2	209	14	14
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

[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

Year	Applications submitted	Applications discussed in reporting year	Positive COMP opinions	Applications withdrawn[4]	Final negative COMP opinions	EC designations	Orphan medicinal products[5] authorised	Orphan designations included in authorised therapeutic indication
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	**2748**	**2615**	**1870 (72%)**	**721(27%)**	**28(1%)**	**1844**	**130**	**144**

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

Annex 2

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
1-(2,2-difluoro-2H-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropane-1-carboxamide and ivacaftor	Treatment of cystic fibrosis	Vertex Pharmaceuticals (Europe) Limited	19 January 2017	27 February 2017
505 amino acid protein, corresponding to amino acids 2-506 of the wild-type human histidyl-tRNA synthetase	Treatment of limb-girdle muscular dystrophy	Voisin Consulting S.A.R.L.	19 January 2017	27 February 2017
5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine	Treatment of diffuse large B-cell lymphoma	Voisin Consulting S.A.R.L.	19 January 2017	27 February 2017
26 base synthetic single-stranded fully phosphorothioated 2'-O-methyl-RNA and DNA mixmer oligonucleotide-based compound	Treatment of Dravet syndrome	Eirgen Pharma Limited	19 January 2017	27 February 2017
Alpha-tocopherol and ascorbic acid	Treatment of fragile X syndrome	Advanced Medical Projects	19 January 2017	27 February 2017
Autologous T-cells transduced with lentiviral vector encoding an anti-SLAMF7 CD28/CD3-zeta chimeric antigen receptor	Treatment of plasma cell myeloma	Dr. Michael Hudecek	19 January 2017	27 February 2017
Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl]acetate salt	Treatment of primary ciliary dyskinesia	Polyphor UK Ltd	19 January 2017	27 February 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Ex-vivo-expanded autologous keratinocytes transduced with retroviral vector containing the *COL7A1* gene	Treatment of epidermolysis bullosa	Ser-mes Planificación SL	19 January 2017	27 February 2017
Fenfluramine hydrochloride	Treatment of Lennox-Gastaut syndrome	Zogenix International Limited	19 January 2017	27 February 2017
Humanised IgG4 monoclonal antibody to the human toll-like receptor type 2	Treatment of pancreatic cancer	Opsona Therapeutics Ltd	19 January 2017	27 February 2017
Humanised IgG4 monoclonal antibody to the human toll-like receptor type 2	Treatment of myelodysplastic syndromes	Opsona Therapeutics Ltd	19 January 2017	27 February 2017
Iodine (^{131}I) murine IgG1 monoclonal antibody against CD276	Treatment of neuroblastoma	Y-mAbs Therapeutics A/S	19 January 2017	27 February 2017
N-(4-(1-cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamide methanesulfonate	Treatment of gastric cancer	Sirius Regulatory Consulting Limited	19 January 2017	27 February 2017
Propranolol hydrochloride	Treatment of von Hippel-Lindau disease	Consejo Superior de Investigaciones Cientificas (CSIC)	19 January 2017	27 February 2017
Recombinant human club cell 10 KDa protein	Treatment of bronchiolitis obliterans syndrome	EUDRAC Limited	19 January 2017	27 February 2017
Soluble recombinant human fibroblast growth factor receptor 3	Treatment of achondroplasia	TherAchon SAS	19 January 2017	27 February 2017
Synthetic double-stranded siRNA oligonucleotide directed against transthyretin mRNA *	Treatment of transthyretin-mediated amyloidosis	Alnylam UK Limited - United Kingdom	19 January 2017	27 February 2017
Tauroursodeoxycholic acid	Treatment of amyotrophic lateral sclerosis	Bruschettini s.r.l.	19 January 2017	27 February 2017
Thalidomide	Treatment of hereditary haemorrhagic telangiectasia	PlumeStars s.r.l.	19 January 2017	27 February 2017
Vemurafenib	Treatment of Erdheim-Chester disease	Groupe d'étude des histiocytoses	19 January 2017	27 February 2017

Annex 3

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
Ropeginterferon alfa-2b	Treatment of polycythaemia vera	AOP Orphan Pharmaceuticals AG	EU/3/11/932
Caplacizumab	Treatment of thrombotic thrombocytopenic purpura	Ablynx NV	EU/3/09/629
Sodium benzoate	a) Treatment of ornithine transcarbamylase deficiency	Lucane Pharma	EU/3/16/1705
	b) Treatment of lysinuric protein intolerance		EU/3/16/1729
	c) Treatment of ornithine translocase deficiency		EU/3/16/1730
	d) Treatment of carbamoyl-phosphate synthase-1 deficiency		EU/3/16/1706
	e) Treatment of citrullinaemia type 1		EU/3/16/1707
	f) Treatment of hyperargininaemia		EU/3/16/1708
	g) Treatment of argininosuccinic aciduria		EU/3/16/1787
	h) Treatment of N-acetylglutamate synthase deficiency		EU/3/16/1788
	e) Treatment of non-ketotic hyperglycinaemia		EU/3/02/111