27 February 2017
EMA/COMP/863805/2016 Corr.1
Inspections, Human Medicines Pharmacovigilance and Committees Division

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

January 2017

The Committee for Orphan Medicinal Products held its 185th plenary meeting on 17-19 January 2017.

Orphan medicinal product designation

Positive opinions

The COMP adopted 19 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:

- 5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine for treatment of diffuse large B-cell lymphoma, Voisin Consulting S.A.R.L.;
- 26 base synthetic single-stranded fully phosphorothioated 2'-O-methyl-RNA and DNA mixmer oligonucleotide-based compound for treatment of Dravet syndrome, Eirgen Pharma Limited;
- Alpha-tocopherol and ascorbic acid for treatment of fragile X syndrome, Advanced Medical Projects;
- 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 for treatment of primary ciliary dyskinesia, Polyphor UK Ltd;
- Fenfluramine hydrochloride for treatment of Lennox-Gastaut syndrome, Zogenix International Limited;
- N-(4-(1-cyanocyclopentyl)phenyl)-2-(4-pyridinylmethyl)amino-3-pyridinecarboxamide methanesulfonate for treatment of gastric cancer, Sirius Regulatory Consulting Limited;
- Recombinant human club cell 10 KDa protein for treatment of bronchiolitis obliterans syndrome, EUDRAC Limited.

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2. Opinions adopted at the first COMP discussion:

- 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 for treatment of cystic fibrosis, Vertex Pharmaceuticals (Europe) Limited;
- 505 amino acid protein, corresponding to amino acids 2-506 of the wild-type human histidyl-tRNA synthetase for treatment of limb-girdle muscular dystrophy, Voisin Consulting S.A.R.L.;
- Autologous T-cells transduced with lentiviral vector encoding an anti-SLAMF7 CD28/CD3-zeta chimeric antigen receptor for treatment of plasma cell myeloma, Dr. Michael Hudecek;
- Ex-vivo-expanded autologous keratinocytes transduced with retroviral vector containing the *COL7A1* gene for treatment of epidermolysis bullosa, Ser-mes Planificación SL;
- Humanised IgG4 monoclonal antibody to the human toll-like receptor type 2 for treatment of pancreatic cancer, Opsona Therapeutics Ltd;
- Humanised IgG4 monoclonal antibody to the human toll-like receptor type 2 for treatment of myelodysplastic syndromes, Opsona Therapeutics Ltd;
- Iodine (^{131}I) murine IgG1 monoclonal antibody against CD276 for treatment of neuroblastoma, Y-mAbs Therapeutics A/S;
- Propranolol hydrochloride for treatment of von Hippel-Lindau disease, Consejo Superior de Investigaciones Cientificas (CSIC);
- Soluble recombinant human fibroblast growth factor receptor 3 for treatment of achondroplasia, TherAchon SAS;
- Tauroursodeoxycholic acid for treatment of amyotrophic lateral sclerosis, Bruschettini s.r.l.;
- Thalidomide for treatment of hereditary haemorrhagic telangiectasia, PlumeStars s.r.l.;
- Vemurafenib for treatment of Erdheim-Chester disease, Groupe d'étude des histiocytoses.

The COMP also recommended the amendment to 1 existing orphan designation:

- Synthetic double-stranded siRNA oligonucleotide directed against transthyretin mRNA for treatment of transthyretin-mediated amyloidosis, Alnylam UK Limited - United Kingdom (initially for treatment of familial amyloid polyneuropathy).

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 for human use.

Negative opinion

The COMP did not adopt any negative opinions recommending the refusal of orphan medicinal product designations to the European Commission (EC).

[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 18 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 10 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.

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 2 opinions 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

- Ledaga (chlormethine) for treatment of cutaneous T-cell lymphoma, Actelion Registration Ltd. (EU/3/12/963).

2. Opinion(s) following appeal procedures

- Chenodeoxycholic acid sigma-tau (chenodeoxycholic acid) for treatment of inborn errors of primary bile acid synthesis, Sigma-tau Arzneimittel GmbH (EU/3/14/1406).

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

[2] Correction of the text referring to Annex 3 to be in line with the title of Annex 3

Upcoming meetings

- The 186th meeting of the COMP will be held on 14-16 February 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

Year	Applications submitted	Applications discussed in reporting year	Positive COMP opinions	Applications withdrawn[3]	Final negative COMP opinions	EC designations	Orphan medicinal products[4] authorised	Orphan designations included in authorised therapeutic indication
2017	5	25	19	6	0	20	1	1
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
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	**2720**	**2564**	**1846 (72%)**	**695 (27%)**	**23(1%)**	**1825**	**129**	**143**

[3] Revision of the figures for 2015, 2014, 2003, 2002, 2001 and 2000
[4] 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 December 2016 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
3-pentylbenzeneacetic acid sodium salt	Treatment of Alström syndrome	ProMetic Pharma SMT Limited	08 December 2016	12 January 2017
[5,10,15,20-tetrakis(4-carboxyphenyl)-21H,23H-porphine]manganese(III) chloride	Treatment of Cockayne syndrome	Institut Pasteur	08 December 2016	12 January 2017
5-aminolevulinic acid	Treatment of glioma	Centre Hospitalier Universitaire de Lille	08 December 2016	12 January 2017
(6aR, 10aR)-3-(1',1'-dimethylheptyl)-delta-8-tetrahydro-cannabinol-9-carboxylic acid	Treatment of systemic sclerosis	TMC Pharma Services Ltd	08 December 2016	12 January 2017
Antroquinonol	Treatment of pancreatic cancer	Biological Consulting Europe Ltd	08 December 2016	12 January 2017
Autologous dendritic cells incubated ex vivo with zebularine and factor VIII	Treatment of haemophilia A	Idogen AB	08 December 2016	12 January 2017
Doxorubicin hydrochloride in a lipid-based pegylated nanoparticle modified with a 31-aminoacid peptide targeting nucleolin	Treatment of malignant mesothelioma	TREAT U, S.A.	08 December 2016	12 January 2017
Fluticasone propionate	Treatment of eosinophilic oesophagitis	Adare Pharmaceuticals srl	08 December 2016	12 January 2017
Genetically modified adeno-associated viral vector serotype 9 expressing shRNA as well as a codon-optimised shRNA-insensitive wildtype PABPN1	Treatment of oculopharyngeal muscular dystrophy	Clinipace GmbH	08 December 2016	12 January 2017
Human donor haematopoietic stem and progenitor cells that have been treated ex vivo with the protein transduction domain of the	Treatment in haematopoietic stem cell transplantation	Coté Orphan Consulting UK Limited	08 December 2016	12 January 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
HIV-1 transac tivation protein fused to MYC transcription factor				
Human hepatoma cell line HepaRG in bioartificial liver	Treatment of acute liver failure	Hep-Art Medical Devices BV	08 December 2016	12 January 2017
Humanised IgG1 monoclonal antibody against the receptor-binding site of human placental growth factor	Treatment of medulloblastoma	Oncurious NV	08 December 2016	12 January 2017
Hydroxychloroquine	Treatment of antiphospholipid syndrome	Centre Hospitalier Universitaire d' Angers	08 December 2016	12 January 2017
Leuprorelin acetate	Treatment of congenital hypogonadotropic hypogonadism	Stichting Centre for Human Drug Research (CHDR)	08 December 2016	12 January 2017
Pentosan polysulfate sodium	Treatment of interstitial cystitis	Kyoto Tech Limited	08 December 2016	12 January 2017
Pioglitazone hydrochloride	Treatment of sudden sensorineural hearing loss	Regiomedica GmbH	08 December 2016	12 January 2017
Pr-D-Cys-Met-Pip-Arg-Leu-Arg-Sar-Cys-Lys-Arg-Pro-Tyr-Tle-Leu-OH	Treatment of perinatal asphyxia	VECT-HORUS	08 December 2016	12 January 2017
Recombinant adeno-associated viral vector serotype 9 containing the human N-alpha-acetylglucosaminidase gene	Treatment of mucopolysaccharidosis type IIIB (Sanfilippo B syndrome)	Ser-mes Planificación SL	08 December 2016	12 January 2017
Recombinant IgG degrading enzyme of *Streptococcus pyogenes*	Prevention of graft rejection following solid organ transplantation	Hansa Medical AB	08 December 2016	12 January 2017
Trans-resveratrol	Treatment of spinocerebellar ataxia	Luis Pereira de Almeida	08 December 2016	12 January 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 December 2016 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Burosumab	Treatment of X-linked hypophosphataemia	Kyowa Kirin Limited	EU/3/14/1351
Eteplirsen	Treatment of Duchenne muscular dystrophy	AVI Biopharma International Ltd	EU/3/08/586
Gemtuzumab ozogamicin	Treatment of acute myeloid leukaemia (AML)	Pfizer Limited	EU/3/00/005
Ngr-htnf	Treatment of malignant mesothelioma	MolMed SpA	EU/3/08/549
Plitidepsin	Treatment of multiple myeloma	Pharma Mar SA	EU/3/04/245