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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

December 2016

The Committee for Orphan Medicinal Products held its 184th plenary meeting on 6-8 December 2016.

Orphan medicinal product designation

Positive opinions

The COMP adopted 20 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:

- [5,10,15,20-tetrakis(4-carboxyphenyl)-21H,23H-porphine]manganese(III) chloride for treatment of Cockayne syndrome, Institut Pasteur;
- 5-aminolevulinic acid for treatment of glioma, Centre Hospitalier Universitaire de Lille;
- Hydroxychloroquine for treatment of antiphospholipid syndrome, Centre Hospitalier Universitaire d' Angers;
- Leuprorelin acetate for treatment of congenital hypogonadotropic hypogonadism, Stichting Centre for Human Drug Research (CHDR);
- Pioglitazone hydrochloride for treatment of sudden sensorineural hearing loss, Regiomedica GmbH.

2. Opinions adopted at the first COMP discussion:

- (6aR, 10aR)-3-(1',1'-dimethylheptyl)-delta-8-tetrahydro-cannabinol-9-carboxylic acid for treatment of systemic sclerosis, TMC Pharma Services Ltd;
- 3-pentylbenzeneacetic acid sodium salt for treatment of Alström syndrome, ProMetic Pharma SMT Limited;
- Antroquinonol for treatment of pancreatic cancer, Biological Consulting Europe Ltd;

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- Autologous dendritic cells incubated ex vivo with zebularine and factor VIII for treatment of haemophilia A, Idogen AB;
- Doxorubicin hydrochloride in a lipid-based pegylated nanoparticle modified with a 31-aminoacid peptide targeting nucleolin for treatment of malignant mesothelioma, TREAT U, S.A.;
- Fluticasone propionate for treatment of eosinophilic oesophagitis, Adare Pharmaceuticals srl;
- Genetically modified adeno-associated viral vector serotype 9 expressing shRNA as well as a codon-optimised shRNA-insensitive wildtype PABPN1 for treatment of oculopharyngeal muscular dystrophy, Clinipace GmbH;
- Human donor haematopoietic stem and progenitor cells that have been treated ex vivo with the protein transduction domain of the HIV-1 transactivation protein fused to MYC transcription factor for treatment in haematopoietic stem cell transplantation, Coté Orphan Consulting UK Limited;
- Human hepatoma cell line HepaRG in bioartificial liver for treatment of acute liver failure, Hep-Art Medical Devices BV;
- Humanised IgG1 monoclonal antibody against the receptor-binding site of human placental growth factor for treatment of medulloblastoma, Oncurious NV;
- Pentosan polysulfate sodium for treatment of interstitial cystitis, Kyoto Tech Limited;
- Pr-D-Cys-Met-Pip-Arg-Leu-Arg-Sar-Cys-Lys-Arg-Pro-Tyr-Tle-Leu-OH for treatment of perinatal asphyxia, VECT-HORUS;
- Recombinant adeno-associated viral vector serotype 9 containing the human N-alpha-acetylglucosaminidase gene for treatment of mucopolysaccharidosis type IIIB (Sanfilippo B syndrome), Ser-mes Planificación SL;
- Recombinant IgG degrading enzyme of *Streptococcus pyogenes* for prevention of graft rejection following solid organ transplantation, Hansa Medical AB;
- Trans-resveratrol for treatment of spinocerebellar ataxia, Luis Pereira de Almeida.

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 17 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

9 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 8 applications for orphan medicinal product designation were withdrawn.

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

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:

- Cystadrops (mercaptamine) for treatment of cystinosis, Orphan Europe S.A.R.L. (EU/3/08/578).

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 185th meeting of the COMP will be held on 17-19 January 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[2]	Final negative COMP opinions	EC designations	Orphan medicinal products[3] authorised	Orphan designations included in authorised therapeutic indication
2016	328	296	220 (74%)	74 (25%)	2	209	12	12
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	**2713**	**2531**	**1827 (72%)**	**681 (27%)**	**23(1%)**	**1805**	**126**	**140**

[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 November 2016 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde	Treatment of sickle cell disease	SynteractHCR Deutschland GmbH	6 October 2016	18 November 2016
5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochloride	Treatment of adrenoleukodystrophy	Minoryx Therapeutics S.L.	6 October 2016	18 November 2016
Adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene	Treatment of glycogen storage disease type Ia	Pharma Gateway AB	6 October 2016	18 November 2016
Adeno-associated viral vector serotype 8 containing the human *UGT1A1* gene	Treatment of Crigler-Najjar syndrome	Audentes Therapeutics UK Limited	6 October 2016	18 November 2016
Alpha-tocopherol	Treatment of facioscapulohumeral muscular dystrophy	Université de Montpellier	6 October 2016	18 November 2016
Allogeneic cytomegalovirus-specific cytotoxic T lymphocytes	Treatment of cytomegalovirus infection in patients with impaired cell-mediated immunity	Wainwright Associates Ltd	6 October 2016	18 November 2016
Allogeneic peripheral blood mononuclear cells incubated ex-vivo with 16, 16-dimethyl prostaglandin E2 and dexamethasone	Treatment in haematopoietic stem cell transplantation	Fate Therapeutics Ltd	6 October 2016	18 November 2016
Ascorbic acid	Treatment of facioscapulohumeral muscular dystrophy	Université de Montpellier	6 October 2016	18 November 2016
Brincidofovir	Treatment of smallpox	Chimerix UK Ltd	6 October 2016	18 November 2016
Budesonide	Treatment of primary IgA nephropathy	Pharmalink AB	6 October 2016	18 November 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Human monoclonal antibody against activin A	Treatment of fibrodysplasia ossificans progressiva	Regeneron Ireland	6 October 2016	18 November 2016
Ibrutinib	Treatment of graft-versus-host disease	Janssen-Cilag International N.V.	6 October 2016	18 November 2016
Live-attenuated non-replicative *Pseudomonas aeruginosa* strain expressing large T antigen of Merkel cell polyomavirus	Treatment of Merkel cell carcinoma	APCure SAS	6 October 2016	18 November 2016
L-selenomethionine	Treatment of facioscapulohumeral muscular dystrophy	Université de Montpellier	6 October 2016	18 November 2016
N-(5-(6-chloro-2,2-difluorobenzo[d][1,3]dioxol-5-yl)pyrazin-2-yl)-2-fluoro-6-methylbenzamide	Treatment of acute pancreatitis	EMAS Pharma Limited	6 October 2016	18 November 2016
Particles comprised of methacrylic acid based co-polymer, cross-linked with a bi-functional cross-linker, purified to bind L-phenylalanine and L-phenylalanine containing peptides	Treatment of hyperphenylalaninaemia	MipSalus ApS – Denmark	6 October 2016	18 November 2016
R-azasetron besylate	Treatment of sudden sensorineural hearing loss	Sensorion	6 October 2016	18 November 2016
Recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein	Treatment of aromatic L-amino acid decarboxylase deficiency	Voisin Consulting S.A.R.L.	6 October 2016	18 November 2016
Sodium benzoate	Treatment of argininosuccinic aciduria	Lucane Pharma SA	6 October 2016	18 November 2016
Sodium benzoate	Treatment of N-acetylglutamate synthase deficiency	Lucane Pharma SA	6 October 2016	18 November 2016
Synthetic human hepcidin	Treatment of sickle cell disease	EMAS Pharma Limited	6 October 2016	18 November 2016
Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Gly-Gly-Asp-Leu-Leu-Pro-Arg-Gly-Ser	Treatment of Huntington's disease	Dr Ulrich Granzer	6 October 2016	18 November 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Vaccine consisting of 5 survivin peptides with different human leukocyte antigen restrictions	Treatment of ovarian cancer	Dr Ulrich Granzer	6 October 2016	18 November 2016
Valproic acid	Treatment of diffuse large B-cell lymphoma	Valcuria AB	6 October 2016	18 November 2016
Zinc gluconate	Treatment of facioscapulohumeral muscular dystrophy	Université de Montpellier	6 October 2016	18 November 2016
^{68}Ga-DOTA-pABzA-DIG-dPhe-Gln-Trp-Ala-Val-Gly-His-NHCH[(CH_2-$CH(CH_3)_2$]$_2$	Diagnosis of gastrointestinal stromal tumours	Advanced Accelerator Applications	4 November 2016	12 December 2016
Adeno-associated viral vector serotype 8 encoding engineered rhodopsin DNA-binding repressor and human rhodopsin expression cassettes	Treatment of retinitis pigmentosa	Fondazione Telethon	4 November 2016	12 December 2016
Adeno-associated viral vector serotype 8 containing the human *CNGA3* gene under the control of acone arrestin promoter	Treatment of achromatopsia caused by mutations in the *CNGA3* gene	Universitätsklinikum Tübingen (UKT)	4 November 2016	12 December 2016
Arsenic trioxide	Treatment of graft-versus-host disease	Medsenic	4 November 2016	12 December 2016
Avelumab	Treatment of gastric cancer	Merck Serono Europe Limited	4 November 2016	12 December 2016
Cabiralizumab	Treatment of tenosynovial giant cell tumour, localised and diffuse type	Albany Regulatory Consulting Ltd	4 November 2016	12 December 2016
Dantrolene sodium	Treatment of Wolfram syndrome	Alan Boyd Consultants Ltd	4 November 2016	12 December 2016
Ibudilast	Treatment of amyotrophic lateral sclerosis	MediciNova (Europe) Limited	4 November 2016	12 December 2016
Ivosidenib	Treatment of acute myeloid leukaemia	QRC Consultants Ltd	4 November 2016	12 December 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Metformin	Treatment of progressive myoclonic epilepsy type 2 (Lafora disease)	Centro de Investigación Biomédica en Red (CIBER)	4 November 2016	12 December 2016
Pegylated recombinant human interleukin-10	Treatment of pancreatic cancer	Larode Ltd	4 November 2016	12 December 2016
Propranolol	Treatment of soft tissue sarcoma	The Anticancer Fund	4 November 2016	12 December 2016
Recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN3* gene	Treatment of neuronal ceroid lipofuscinosis	Ser-mes Planificación SL	4 November 2016	12 December 2016
Udenafil	Treatment of functional single ventricle congenital heart disease	Mapi Ireland Limited	4 November 2016	12 December 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 November 2016 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Avelumab	Treatment of Merkel cell carcinoma	Merck Serono Europe Limited	EU/3/15/1590
Cenegermin	Treatment of neurotrophic keratitis	Dompe farmaceutici s.p.a.	EU/3/15/1586
Niraparib	Treatment of ovarian cancer	Tesaro UK Limited	EU/3/10/760
Nusinersen	Treatment of 5q spinal muscular atrophy	Biogen Idec Ltd	EU/3/12/976
Plitidepsi	Treatment of Multiple Myeloma	Pharma Mar, S.A.	EU/3/04/245
Rucaparib	Treatment of ovarian cancer	Clovis Oncology UK Ltd	EU/3/12/1049

Annex 4

COMP opinions on amendment of existing orphan drug designations since October 2016 COMP monthly report

Active substance	Initial orphan indication	Amended orphan indication	Sponsor/applicant	EU designation number
Recombinant human acid sphingomyelinase	Treatment of Niemann-Pick disease, type B	Treatment of Niemann-Pick disease	Genzyme Europe BV	EU/3/01/056