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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

November 2016

The Committee for Orphan Medicinal Products held its 183th plenary meeting on 3-4 November 2016.

Orphan medicinal product designation

Positive opinions

The COMP adopted 14 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:

- Avelumab for treatment of gastric cancer, Merck Serono Europe Limited;
- Adeno-associated viral vector serotype 8 encoding engineered rhodopsin DNA-binding repressor and human rhodopsin expression cassettes for treatment of retinitis pigmentosa, Fondazione Telethon;
- Arsenic trioxide for treatment of graft-versus-host disease, Medsenic;
- Cabiralizumab for treatment of tenosynovial giant cell tumour, localised and diffuse type, Albany Regulatory Consulting Ltd;
- Propranolol for treatment of soft tissue sarcoma, The Anticancer Fund.

2. Opinions adopted at the first COMP discussion:

- ^{68}Ga-DOTA-pABzA-DIG-dPhe-Gln-Trp-Ala-Val-Gly-His-NHCH[(CH_2-$CH(CH_3)_2$]$_2$ for diagnosis of gastrointestinal stromal tumours, Advanced Accelerator Applications;
- Adeno-associated viral vector serotype 8 containing the human *CNGA3* gene under the control of a cone arrestin promoter for treatment of achromatopsia caused by mutations in the *CNGA3* gene, Universitätsklinikum Tübingen (UKT);
- Dantrolene sodium for treatment of Wolfram syndrome, Alan Boyd Consultants Ltd;

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- Ibudilast for treatment of amyotrophic lateral sclerosis, MediciNova (Europe) Limited;
- Ivosidenib for treatment of acute myeloid leukaemia, QRC Consultants Ltd;
- Metformin for treatment of progressive myoclonic epilepsy type 2 (Lafora disease), Centro de Investigación Biomédica en Red (CIBER);
- Pegylated recombinant human interleukin-10 for treatment of pancreatic cancer, Larode Ltd;
- Recombinant self-complementary adeno-associated viral vector serotype 9 containing the human *CLN3* gene for treatment of neuronal ceroid lipofuscinosis, Ser-mes Planificación SL;
- Udenafil for treatment of functional single ventricle congenital heart disease, Mapi Ireland Limited.

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.

Negative opinion

The COMP adopted 1 negative opinion recommending the refusal of the orphan medicinal product designation for a product for treatment of poisoning by local anaesthetics. The sponsor was informed about the possibility to appeal.

Further to expiry of the deadline for appeal, the COMP confirmed 1 negative opinion adopted on 13 July 2016 recommending the refusal of the orphan medicinal product designation for the following product:

- 3-(3-methanesulfonyl-phenyl)-1-propyl-piperidine hydrochloride for treatment of narcolepsy, A. Carlsson Research AB.

Lists of questions

The COMP adopted 13 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

6 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.

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

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 3 opinions recommending to the European Commission that the following orphan medicinal product be kept in the EU registry of orphan medicinal product:

- SomaKit-TOC (TOC (gallium (68Ga)-edotreotide, edotreotide)) for diagnosis of gastro-entero-pancreatic neuroendocrine tumours, Advanced Accelerator Applications (EU/3/15/1450). The opinion was adopted by written procedure after the October meeting.
- Venclyxto (venetoclax) for treatment of chronic lymphocytic leukaemia, AbbVie Ltd. (EU/3/12/1080). The opinion was adopted by written procedure after the October meeting.
- Ocaliva (6alpha-ethyl-chenodeoxycholic acid, obeticholic acid) for treatment of primary biliary cirrhosis, Intercept Italia s.r.l. (EU/3/10/753). The opinion was adopted by written procedure after the October meeting.

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 184th meeting of the COMP will be held on 6-8 December 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	292	264	200 (76%)	62 (23%)	2	170	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	**2677**	**2499**	**1807 (72%)**	**669 (27%)**	**23(1%)**	**1766**	**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 October 2016 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
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 invasive aspergillosis	F2G Ltd	8 September 2016	14 October 2016
(6aR,10aR)-3-(1',1'-dimethylheptyl)-delta-8-tetrahydrocannabinol-9-carboxylic acid	Treatment of cystic fibrosis	TMC Pharma Services Ltd	8 September 2016	14 October 2016
Acebutolol hydrochloride	Treatment of Smith-Magenis syndrome	Therapicon Srl	8 September 2016	14 October 2016
Adeno-associated viral vector serotype 5 containing the human *RLBP1* gene	Treatment of retinitis pigmentosa	HORAMA SAS	8 September 2016	14 October 2016
Adeno-associated viral vector serotype 2/2 containing a gene encoding the channelrhodopsin-2 protein	Treatment of retinitis pigmentosa	Alacrita LLP	8 September 2016	14 October 2016
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	Treatment of soft tissue sarcoma	Philogen S.p.A.	8 September 2016	14 October 2016
Autologous mononuclear cells derived from human cord blood	Treatment of periventricular leukomalacia	BrainRepair UG (haftungsbeschränkt)	8 September 2016	14 October 2016
Autologous mononuclear cells derived from human cord blood	Treatment of neonatal encephalopathy	BrainRepair UG (haftungsbeschränkt)	8 September 2016	14 October 2016
Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19	Treatment of diffuse large B-cell lymphoma	Novartis Europharm Limited	8 September 2016	14 October 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Carbamazepine	Treatment of metaphyseal chondrodysplasia, Schmid type	University of Newcastle upon Tyne	8 September 2016	14 October 2016
Chemically modified human recombinant sulfamidase	Treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome)	Swedish Orphan Biovitrum AB (publ)	8 September 2016	14 October 2016
Crenolanib besylate	Treatment of soft tissue sarcoma	Arog Pharmaceuticals Europe Ltd	8 September 2016	14 October 2016
Crenolanib besylate	Treatment of acute myeloid leukaemia	Arog Pharmaceuticals Europe Ltd	8 September 2016	14 October 2016
(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	Treatment of osteomyelitis	Voisin Consulting S.A.R.L.	8 September 2016	14 October 2016
Exendin (9-39)	Treatment of noninsulinoma pancreatogenous hypoglycaemia syndrome	Eiger Biopharmaceuticals Europe Limited	8 September 2016	14 October 2016
Fenretinide	Treatment of peripheral T-cell lymphoma	Clinipace GmbH	8 September 2016	14 October 2016
Haematopoietic stem cells modified with a lentiviral vector containing the *CD18* gene	Treatment of leukocyte adhesion deficiency type I	Centro de Investigación Biomédica en Red (CIBER)	8 September 2016	14 October 2016
Human monoclonal IgG1 antibody against tissue factor pathway inhibitor	Treatment of haemophilia A	Pfizer Limited	8 September 2016	14 October 2016
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-	Treatment of gastro-entero-pancreatic neuroendocrine tumours	Ipsen Pharma	8 September 2016	14 October 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
threonyl-L-cysteinyl-D-tyrosinamide]				
Melatonin	Treatment of Smith-Magenis syndrome	Therapicon Srl	8 September 2016	14 October 2016
Mogamulizumab	Treatment of cutaneous T-cell lymphoma	Kyowa Kirin Limited	8 September 2016	14 October 2016
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	Treatment of myelofibrosis	Imago BioSciences Ltd.	8 September 2016	14 October 2016
P-ethoxy growth factor receptor-bound protein 2 antisense oligonucleotide	Treatment of acute myeloid leukaemia	Clinical Network Services (UK) Ltd	8 September 2016	14 October 2016
Radio-iodinated (^{131}I) anti-CD45 murine monoclonal antibody	Treatment in haematopoietic stem cell transplantation	Wainwright Associates Ltd	8 September 2016	14 October 2016
Recombinant adeno-associated viral vector encoding a human micro-dystrophin gene under the control of a muscle specific promoter	Treatment of Duchenne muscular dystrophy	Pharma Gateway AB	8 September 2016	14 October 2016
Self-complementary adeno-associated viral vector serotype 9 containing the *SGSH* gene	Treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome)	Ser-mes Planificación SL	8 September 2016	14 October 2016
Synthetic 15-amino-acid macrocyclic peptide acylated with a polyethyleneglycol palmitoylated linker	Treatment of paroxysmal nocturnal haemoglobinuria	Ra Europe Limited	8 September 2016	14 October 2016
Tadekinig alfa	Treatment of haemophagocytic lymphohistiocytosis	Coté Orphan Consulting UK Limited	8 September 2016	14 October 2016
Tetrofosmin	Diagnosis of glioma	ProActina	8 September 2016	14 October 2016
Ubiquinol	Treatment of primary coenzyme Q_{10} deficiency syndrome	Centro de Investigación Biomédica en Red (CIBER)	8 September 2016	14 October 2016

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Venetoclax	Treatment of multiple myeloma	Abbvie Ltd.	8 September 2016	14 October 2016
Venetoclax	Treatment of diffuse large B-cell lymphoma	Abbvie Ltd	8 September 2016	14 October 2016
Xenon	Treatment of ischaemia reperfusion injury associated with cardiac arrest	Neuroprotexeon Ltd.	8 September 2016	14 October 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 October 2016 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Caffeine citrate	Prevention of bronchopulmonary dysplasia	Viridian Pharma Ltd	EU/3/14/1261
Glibenclamide	Treatment of neonatal diabetes	Pharma Services	EU/3/15/1589
Velmanase alfa	Treatment of alpha-Mannosidosis	Chiesi Farmaceutici S.p.A.	EU/3/04/260

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	