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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

September 2017

The Committee for Orphan Medicinal Products held its 192nd plenary meeting on 05-07 September 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:

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

- (S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid for treatment of primary sclerosing cholangitis, Pharma Gateway AB;
- Cannabidiol for treatment of West syndrome, GW Research Ltd;
- Ofranergene obadenovec for treatment of ovarian cancer, Envigo Pharma Consulting Limited;
- Recombinant adeno-associated viral vector serotype 5 encoding *Staphylococcus aureus* Cas9 endonuclease and two guide RNAs complementary to two regions of intron 26 of the *CEP290* gene for treatment of Leber's congenital amaurosis, Pharma Gateway AB;
- Recombinant monoclonal antibody to sialic acid-binding Ig-like lectin 8 for treatment of mastocytosis, Envestia Limited.

2. Opinions adopted at the first COMP discussion:

- 2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-methylbenzylamine for treatment of Charcot-Marie-Tooth disease, Repositioning SAS;

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- 5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate] for treatment of biliary tract cancer, Voisin Consulting S.A.R.L;
- Adenoviral vector of serotype 5 modified to contain a chimeric sequence consisting of a minimal urokinase-type plasminogen activator receptor promoter preceded by three Notch-responsive elements, and coated with oligopeptide end-modified poly (beta-amino) esters for treatment of pancreatic cancer, Sagetis Biotech, S.L.;
- Autologous ex-vivo-expanded peripheral polyclonal lymphocytes enriched in activated natural killer cells for treatment of multiple myeloma, CellProtect Nordic Pharmaceuticals AB;
- Bitopertin for treatment of beta-thalassaemia intermedia and major, Roche Registration Limited;
- Cannabidivarin for treatment of Rett syndrome, GW Research Ltd;
- Entospletinib for treatment of acute myeloid leukaemia, Gilead Sciences International Ltd;
- Glasdegib maleate for treatment of acute myeloid leukaemia, Pfizer Limited;
- Glucopyranosyl lipid A for treatment of follicular lymphoma, Immune Design Ltd;
- Humanised monoclonal antibody targeting B-cell maturation antigen conjugated with maleimidocaproyl monomethyl auristatin F for treatment of multiple myeloma, GlaxoSmithKline Trading Services Limited;
- Pracinostat for treatment of acute myeloid leukaemia, Helsinn Birex Pharmaceuticals Ltd;
- Seladelpar for treatment of primary biliary cholangitis, Larode Ltd;
- Siplizumab for treatment in solid organ transplantation, ITB-MED AB;
- Synthetic cyclic 8 amino acid analogue of human unacylated ghrelin for treatment of Prader-Willi syndrome, Alizé Pharma.

3. 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:

The COMP adopted 1 negative opinion recommending the refusal of the orphan designation for the following product:

- Melatonin for treatment of partial deep dermal and full thickness burns, Therapicon Srl.

2. Opinion(s) following appeal procedures:

None

[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 15 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

7 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.

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)

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

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 6 opinions recommending to the European Commission that the following orphan medicinal products be kept in the Community Register of orphan medicinal products for human use:

- Bavencio (avelumab) for treatment of Merkel cell carcinoma, Merck Serono Europe Limited (EU/3/15/1590). The opinion was adopted by written procedure after the July meeting;
- Lutathera (lutetium 177Lu dotatate) for treatment of gastro-entero-pancreatic neuroendocrine tumours, Advanced Accelerator Applications (EU/3/07/523). The opinion was adopted by written procedure after the July meeting
- Rydapt (midostaurin) for treatment of mastocytosis, Novartis Europharm Ltd (EU/3/10/765). The opinion was adopted by written procedure after the July meeting;
- Rydapt (midostaurin) for treatment of acute myeloid leukaemia, Novartis Europharm Ltd (EU/3/04/214). The opinion was adopted by written procedure after the July meeting;
- Xermelo (telotristat ethyl) for treatment of carcinoid syndrome, Ipsen Pharma (EU/3/09/661). The opinion was adopted by written procedure after the July meeting;
- Soliris (eculizumab) for treatment of myasthenia gravis, Alexion Europe SAS (EU/3/14/1304). Further to a change in the wording of the therapeutic indication, the opinion was re-adopted by written procedure after the CHMP July meeting.

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 the following orphan medicinal product to be removed from the Community Register of orphan medicinal products for human use:

- Verkazia (ciclosporin) for treatment of vernal keratoconjunctivitis, Santen Oy (EU/3/06/360). The opinion was adopted by written procedure after the July 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 193rd meeting of the COMP will be held on 03-05 October 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[4]
2017	169	176	105 (60%)	70 (40%)	1 (1%)	106	9	9
2016	330	304	220 (72%)	82 (27%)	2 (1%)	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] The number of orphan medicinal products authorised includes the products for which the market exclusivity has expired.
[4] The market authorisation of an orphan medicinal product may cover more than one orphan designation.

Year	Applications submitted	Applications discussed in reporting year	Positive COMP opinions	Applications withdrawn	Final negative COMP opinions	EC designations	Orphan medicinal products 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	**2884**	**2715**	**1932 (71%)**	**759 (28%)**	**24 (1%)**	**1911**	**137**	**151**

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
(S)-1-(4-fluorophenyl)-1-(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl)piperazin-yl)pyrimidin-5-yl)ethan-1-amine	Treatment of gastrointestinal stromal tumours	PhaRA bvba;	15 June 2017	17 July 2017
Autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor	Treatment of diffuse large B-cell lymphoma	Celgene Europe Limited	15 June 2017	17 July 2017
Bacillus subtilis oxalate decarboxylase	Treatment of primary hyperoxaluria	Allena Pharmaceuticals Ireland Limited	15 June 2017	17 July 2017
Oxymetazoline hydrochloride	Treatment of spinal cord injury	RDD Pharma Limited	15 June 2017	17 July 2017
Polyphenyl(disodium 3-O-sulfo-beta-D-glucopyranuronate)-(1→3)-beta-D-galactopyranoside	Treatment of anti-MAG neuropathy	SFL Regulatory Affairs Consulting Ltd	15 June 2017	17 July 2017
Recombinant human antibody directed against misfolded human superoxide dismutase 1	Treatment of amyotrophic lateral sclerosis	The Medical & Regulatory Partnership Limited	15 June 2017	17 July 2017
Retinol	Prevention of retinopathy of prematurity	Orphanix GmbH;	15 June 2017	17 July 2017
Sirolimus	Treatment of pachyonychia congenita	Raremoon Consulting Ltd	15 June 2017	17 July 2017
Tirapazamine	Treatment of hepatocellular	PhaRA bvba	15 June 2017	17 July 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
	carcinoma			
Adeno-associated viral vector serotype Anc80 containing the truncated human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter	Treatment of Wilson's disease	Vivet Therapeutics SAS	13 July 2017	23 August 2017
Antisense oligonucleotide targeting exon 13 in the *USH2A* gene	Treatment of retinitis pigmentosa	ProQR Therapeutics IV BV	13 July 2017	23 August 2017
Asunercept	Treatment of myelodysplastic syndromes	Apogenix AG	13 July 2017	23 August 2017
Itraconazole	Treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome)	Mayne Pharma UK Limited	13 July 2017	23 August 2017
N-{2-[(6-{[(2,6-dichloro-3,5-dimethoxyphenyl)carbamoyl](methyl)amino}pyrimidin-4-yl)amino]-5-(4-ethylpiperazin-1-yl)phenyl}prop-2-enamide	Treatment of hepatocellular carcinoma	Eisai Europe Limited	13 July 2017	23 August 2017
Odiparcil	Treatment of mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome)	Inventiva	13 July 2017	23 August 2017
Picropodophyllin	Treatment of glioma	Axelar AB	13 July 2017	23 August 2017
Purified pasteurised and freeze-dried cell-wall fragments from *Mycobacterium tuberculosis* strain RUTI	Treatment of tuberculosis	Archivel Farma S.L.	13 July 2017	23 August 2017
Recombinant adeno-associated viral vector serotype 5 carrying the gene for the human frataxin protein	Treatment of Friedreich's ataxia	Voisin Consulting S.A.R.L.	13 July 2017	23 August 2017
Recombinant fragment of human surfactant	Prevention of bronchopulmonary	Trimunocor Ltd	13 July 2017	23 August 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
protein-D	dysplasia			
Recombinant truncated N-terminal fragment of human lens epithelium-derived growth factor	Treatment of retinitis pigmentosa	Dorian Regulatory Affairs BV	13 July 2017	23 August 2017
Salmonella typhi Ty21a strain transfected with a plasmid vector encoding the human vascular endothelial growth factor receptor 2	Treatment of glioma	Vaximm GmbH	13 July 2017	23 August 2017
Sirolimus	Treatment of tuberous sclerosis	Best Regulatory Consulting Ltd	13 July 2017	23 August 2017
Sodium 2-hydroxylinoleate	Treatment of pancreatic cancer	Ability Pharmaceuticals SL	13 July 2017	23 August 2017
Tacrolimus	Treatment of pulmonary arterial hypertension	Vivus B.V.	13 July 2017	23 August 2017
Teicoplanin	Treatment of cystic fibrosis	Neupharma S.r.l.	13 July 2017	23 August 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
Axicabtagene ciloleucel	a) Treatment of primary mediastinal large B-cell lymphoma b) Treatment of follicular lymphoma c) Treatment of diffuse large B cell lymphoma	Kite Pharma EU B.V.	EU/3/15/1553 EU/3/15/1579 EU/3/14/1393
Lenvatinib	Treatment of hepatocellular carcinoma	Eisai Ltd	EU/3/15/1460
Mexiletine hcl	Treatment of myotonic disorders	LUPIN (EUROPE) LIMITED	EU/3/14/1353
Pacritinib	a) Treatment of post-essential thrombocythaemia myelofibrosis b) Treatment of primary myelofibrosis c) Treatment of post-polycythemia vera myelofibrosis	CTI Life Sciences Ltd - United Kingdom	EU/3/10/767 EU/3/10/768 EU/3/10/769
Tezacaftor / ivacaftor	Treatment of cystic fibrosis	Vertex Pharmaceuticals (Europe) Ltd.	EU/3/17/1828
Volanesorsen	Treatment of familial chylomicronemia syndrome	Akcea Therapeutics UK Ltd	EU/3/14/1249
Voretigene neparvovec	a) Treatment of retinitis pigmentosa b) Treatment of Leber's congenital amaurosis	Spark Therapeutics Ireland Ltd	EU/3/15/1518 EU/3/12/981