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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

30-31 October 2017

The Committee for Orphan Medicinal Products held its 194th plenary meeting on 30-31 October 2017.

Orphan medicinal product designation

Positive opinions

The COMP adopted 9 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:

- 2-isopropyl-3H-naphtho[1,2-d]imidazole-4,5-dione for treatment of mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes, NeuroVive Pharmaceutical AB;
- 4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl for treatment of familial cerebral cavernous malformation, Premier Research Group Limited;
- Pegunigalsidase alfa for treatment of Fabry disease, Protalix B.V.

2. Opinions adopted at the first COMP discussion:

- (2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidine-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridine-2-yl)-4-fluoropyrrolidine-2-carboxamide for treatment of paroxysmal nocturnal haemoglobinuria, FGK Representative Service GmbH;
- Acetylleucine for treatment of GM2 gangliosidosis, IntraBio Ltd;
- Adenovirus-associated viral vector serotype 8 containing the human *AIPL1* gene for treatment of Leber's congenital amaurosis, MeiraGTx UK II Limited;
- Agammaglobulinaemia tyrosine kinase for treatment of pemphigus, Clinical Network Services (UK) Ltd;

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- Modified messenger ribonucleic acid encoding human argininosuccinate lyase enzyme encapsulated into lipid nanoparticles for treatment of argininosuccinic aciduria, PhaseRx Ireland, Ltd;
- Venetoclax for treatment of mantle cell lymphoma, Abbvie Ltd.

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:

None

2. Opinion(s) following appeal procedures:

None

Lists of questions

The COMP adopted 14 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

3 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 3 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 adopted at time of CHMP opinion:

None

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

2. Opinion(s) following appeal procedures:

Following the appeal to the COMP opinion of 28 July 2017, the COMP adopted their final opinion recommending to the European Commission that the following orphan medicinal product 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 30-31 October 2017 meeting.

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 195th meeting of the COMP will be held on 5-7 December 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	222	210	127 (60%)	82 (39%)	1 (1%)	138	13	14
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	**2937**	**2749**	**1954 (71%)**	**771 (28%)**	**24 (1%)**	**1943**	**141**	**156**

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'R,6'R)-3-(benzylamine)-6-hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione	Treatment of systemic sclerosis	Quintiles Ireland Limited	5 October 2017	8 November 2017
(R)-troloxamide quinone	Treatment of amyotrophic lateral sclerosis	Edison Orphan Pharma BV	5 October 2017	8 November 2017
(S)-3-((S)-2-(2-((2,6-difluorophenyl)amino)-2-oxoacetamido)propanamido)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid	Treatment of primary sclerosing cholangitis	Pharma Gateway AB	7 September 2017	16 October 2017
1,4-diamino-2,3-dicyano-1,4-bis[2-aminophenylthio]butadiene	Treatment of non-traumatic subarachnoid haemorrhage	Edvince AB	5 October 2017	8 November 2017
1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea	Treatment of gastrointestinal stromal tumours	Worldwide Clinical Trials Limited	5 October 2017	8 November 2017
2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-methylbenzylamine	Treatment of Charcot-Marie-Tooth disease	Repositioning SAS	7 September 2017	16 October 2017
4-amino-1-[(1S,4R,5S)-2-fluoro-4,5-dihydroxy-3-(hydroxymethyl)cyclopent-2-en-1-	Treatment of pancreatic cancer	Quintiles Ireland Limited	5 October 2017	8 November 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
yl]pyrimidin-2-one				
5-amino-1-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazol-4-yl 1H-indol-2-yl ketone mono[(S)-2-hydroxysuccinate]	Treatment of biliary tract cancer	Voisin Consulting S.A.R.L	7 September 2017	16 October 2017
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	Treatment of pancreatic cancer	Sagetis Biotech, S.L.	7 September 2017	16 October 2017
Antisense oligonucleotide targeting exon 73 in the *COL7A1* gene	Treatment of epidermolysis bullosa	ProQR Therapeutics VII BV	5 October 2017	8 November 2017
Autologous ex-vivo-expanded peripheral polyclonal lymphocytes enriched in activated natural killer cells	Treatment of multiple myeloma	CellProtect Nordic Pharmaceuticals AB	7 September 2017	16 October 2017
Bitopertin	Treatment of beta-thalassaemia intermedia and major	Roche Registration Limited	7 September 2017	16 October 2017
C1-esterase-inhibitor human	Treatment in solid organ transplantation	CSL Behring GmbH	5 October 2017	8 November 2017
Cannabidiol	Treatment of West syndrome	GW Research Ltd	7 September 2017	16 October 2017
Cannabidivarin	Treatment of Rett syndrome	GW Research Ltd	7 September 2017	16 October 2017
Concizumab	Treatment of haemophilia B	Novo Nordisk A/S	5 October 2017	8 November 2017
Diazoxide choline	Treatment of Prader-Willi syndrome	Capnia (UK) Ltd	5 October 2017	8 November 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Entospletinib	Treatment of acute myeloid leukaemia	Gilead Sciences International Ltd	7 September 2017	16 October 2017
Glasdegib maleate	Treatment of acute myeloid leukaemia	Pfizer Limited	7 September 2017	16 October 2017
Glucopyranosyl lipid A	Treatment of follicular lymphoma,	Immune Design Ltd	7 September 2017	16 October 2017
Humanised monoclonal antibody targeting B-cell maturation antigen conjugated with maleimidocaproyl monomethyl auristatin F	Treatment of multiple myeloma	GlaxoSmithKline Trading Services Limited	7 September 2017	16 October 2017
N-(2-aminophenyl)-4-(1-[(1,3-dimethyl-1H-pyrazol-4-yl)methyl]piperidin)benzamide	Treatment of peripheral T-cell lymphoma	Celleron Therapeutics Limited	5 October 2017	8 November 2017
Ofranergene obadenovec	Treatment of ovarian cancer	Envigo Pharma Consulting Limited	7 September 2017	16 October 2017
Pracinostat	Treatment of acute myeloid leukaemia	Helsinn Birex Pharmaceuticals Ltd	7 September 2017	16 October 2017
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	Treatment of Leber's congenital amaurosis	Pharma Gateway AB	7 September 2017	16 October 2017
Recombinant adeno-associated viral vector serotype 9 containing human iduronate-2-sulfatase gene	Treatment of mucopolysaccharidosis type II (Hunter's syndrome)	REGENXBIO EU Limited	5 October 2017	8 November 2017
Recombinant monoclonal antibody to sialic acid-binding Ig-like lectin 8	Treatment of mastocytosis	Envestia Limited	7 September 2017	16 October 2017
Seladelpar	Treatment of primary biliary cholangitis	Larode Ltd	7 September 2017	16 October 2017

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Siplizumab	Treatment in solid organ transplantation	ITB-MED AB	7 September 2017	16 October 2017
Synthetic cyclic 8 amino acid analogue of human unacylated ghrelin	Treatment of Prader-Willi syndrome	Alizé Pharma	7 September 2017	16 October 2017
Tamoxifen citrate	Treatment of Duchenne muscular dystrophy	Duchenne UK	5 October 2017	8 November 2017
Tiratricol	Treatment of Allan-Herndon-Dudley syndrome,	Medical Need Europe AB	5 October 2017	8 November 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
Entolimod	Treatment of acute radiation syndrome	TMC Pharma Services Ltd	EU/3/15/1607
Mogamulizumab	Treatment of cutaneous T-cell lymphoma	Kyowa Kirin Limited	EU/3/16/1756
Pegylated B-domain-deleted sequence-modified recombinant human factor VIII	Treatment of haemophilia A	Bayer AG	EU/3/10/847