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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 2018

The Committee for Orphan Medicinal Products held its 206th plenary meeting on 4-6 December 2018.

Orphan medicinal product designation

Positive opinions

The COMP adopted 11 positive opinions recommending the following medicines for designation as orphan medicinal products to the European Commission:

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

- Acetylleucine for treatment of ataxia telangiectasia, Intrabio Limited;
- Benserazide hydrochloride for treatment of sickle cell disease, Isabelle Ramirez;
- Human glucagon-like peptide-2 analogue linked to a human immunoglobulin Fc fragment for treatment of short bowel syndrome, Hanmi Europe Limited;
- Miglustat for treatment of glycogen storage disease type II (Pompe's disease), Amicus Therapeutics UK Limited;
- Rozanolixizumab for treatment of immune thrombocytopenia, UCB Pharma;
- Vinorelbine tartrate for treatment of soft tissue sarcoma, TLC Biopharmaceuticals B.V.

2. Opinions adopted at the first COMP discussion:

- Synthetic double-stranded siRNA oligonucleotide directed against *TMPRSS6* mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues for treatment of beta-thalassaemia intermedia and major, Silence Therapeutics AG;
- Balipodect for treatment of Rett syndrome, Takeda Pharma A/S;

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- Melatonin for treatment of perinatal asphyxia, Therapicon S.r.l.;
- Ralinepag for treatment of pulmonary arterial hypertension, Arena Pharmaceuticals Limited;
- Mercaptamine-pantetheine disulfide for treatment of Rett syndrome, Thiogenesis Therapeutics S.A.R.L.

3. Opinion 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

1. Opinion adopted following the sponsor's response to the COMP list of questions:

None

2. Opinion following appeal procedures:

None

Lists of questions

The COMP adopted 9 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

10 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 9 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] Details of all orphan designations granted to date by the European Commission are entered in the EU Register of Orphan Medicinal Products

When a designated orphan medicinal product receives a positive opinion for marketing authorisation from EMA's Committee for Medicinal Products for Human Use (CHMP), the COMP has the responsibility to review whether or not the medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation.

1. Opinions adopted at time of CHMP opinion:

- Blincyto (blinatumomab) - Type II variation, for treatment of acute lymphoblastic leukaemia, Amgen Europe BV - The Netherlands (EU/3/09/650).

2. Opinion 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 207th meeting of the COMP will be held on 22-24 January 2019.

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]	Negative COMP opinions	EC designations	Orphan medicinal products[3] authorised	Orphan designations included in authorised therapeutic indication[4]
2018[5]	236	258	163 (63%)	92 (36%)	3 (1%)	169	22	28
2017	260	245	144 (59%)	100 (41%)	2 (1%)	147	14	15
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

[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.
[5] Revision of the figures for 2018

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
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	**3211**	**3043**	**2134 (70%)**	**881 (29%)**	**28 (1%)**	**2121**	**164**	**185**

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
3-(3-(3,5-dimethyl-1H-pyrazol-4-yl)propoxy)-4-fluorobenzoic acid	Treatment of ATTR amyloidosis	Pharma Gateway AB	11 October 2018	19 November 2018
5-{(1R,2R)-2-[(cyclopropylmethyl)amino]cyclopropyl}-N-(tetrahydro-2H-pyran-4-yl)thiophene-3-carboxamide monohydrochloride	Treatment of Kabuki syndrome	Takeda Pharma A/S	11 October 2018	19 November 2018
Anetumab ravtansine	Treatment of ovarian cancer	Bayer AG	11 October 2018	19 November 2018
Apraglutide	Treatment of short bowel syndrome	IQVIA RDS Ireland Limited	11 October 2018	19 November 2018
Autologous human adipose perivascular stromal cells genetically modified to secrete soluble tumour necrosis factor-related apoptosis-inducing ligand	Treatment of pancreatic cancer	Rigenerand S.r.l.	11 October 2018	19 November 2018
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-glutamyl-L-threonyl]acetate	Treatment of cystic fibrosis	Santhera Pharmaceuticals (Deutschland) GmbH	11 October 2018	19 November 2018
Glucagon	Treatment of noninsulinoma	Pharma Gateway AB	11 October 2018	19 November 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
	pancreatogenous hypoglycaemia syndrome			
Humanised IgG1 monoclonal antibody against GD2	Treatment of neuroblastoma	Y-mAbs Therapeutics A/S	11 October 2018	19 November 2018
Imlifidase	Treatment of anti-glomerular basement membrane disease	Hansa Medical AB	11 October 2018	19 November 2018
Larotrectinib	Treatment of glioma	Bayer AG	11 October 2018	19 November 2018
Larotrectinib	Treatment of papillary thyroid cancer	Bayer AG	11 October 2018	19 November 2018
Lisocabtagene maraleucel	Treatment of primary mediastinal large B-cell lymphoma	Celgene Europe Limited	11 October 2018	19 November 2018
Propagermanium	Treatment of focal segmental glomerulosclerosis	Quality Regulatory Clinical Ireland Limited	11 October 2018	19 November 2018
Allogeneic faecal microbiota, pooled	Treatment of graft-versus-host disease	MaaT PHARMA	11 October 2018	19 November 2018
Etamsylate	Treatment of hereditary heamorrhagic telangiectasia	Consejo Superior de Investigaciones Cientificas (CSIC)	11 October 2018	19 November 2018
Ex vivo fused normal allogeneic human myoblast with another normal allogeneic human myoblast	Treatment of Duchenne muscular dystrophy	Dystrogen Therapeutics S.A.	11 October 2018	19 November 2018
Ex vivo fused normal allogeneic human myoblast with autologous human myoblast derived from Duchenne muscular dystrophy affected donor	Treatment of Duchenne muscular dystrophy	Dystrogen Therapeutics S.A.	11 October 2018	19 November 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O_2)-NH_2-DOTA-213-bismuth	Treatment of glioma	Dr. Regenold GmbH	11 October 2018	19 November 2018
Human apotransferrin	Treatment of beta-thalassaemia intermedia and major	Sanquin Plasma Products B.V.	11 October 2018	19 November 2018
Ile-Ser-Ile-Thr-Glu-Ile-Lys-Gly-Val-Ile-Val-His-Arg-Ile-Glu-Thr-Ile-Leu-Phe-Lys-Lys-Lys-Lys-Glu-Met-Pro-Ser-Glu-Glu-Gly-Tyr-Gln-Asp	for treatment of multiple system atrophy	United Neuroscience Limited	11 October 2018	19 November 2018
Fidanacogene elaparvovec	Treatment of haemophilia B	Pfizer Europe MA EEIG	11 October 2018	19 November 2018
Setmelanotide	Treatment of leptin receptor deficiency	TMC Pharma Services Ltd.	11 October 2018	19 November 2018

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
Osilodrostat	Treatment of Cushing's syndrome	Novartis Europharm Limited	EU/3/14/1345