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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

February 2018

The Committee for Orphan Medicinal Products held its 197th plenary meeting on 13-15 February 2018.

Orphan medicinal product designation

Positive opinions

The COMP adopted 18 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:

- (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 C3 glomerulopathy, FGK Representative Service GmbH;
- Dimethyl fumarate for treatment of Friedreich's ataxia, PharmaBio Consulting;
- Ivosidenib for treatment of biliary tract cancer, QRC Consultants Ltd;
- Larotrectinib for treatment of salivary gland cancer, Loxo Oncology Limited;
- Patidegib for treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome), Blue-Reg Europe;
- Tazemetostat for treatment of diffuse large B-cell lymphoma, Quintiles Ireland Limited;
- Tazemetostat for treatment of follicular lymphoma, Quintiles Ireland Limited.

2. Opinions adopted at the first COMP discussion:

- Docosahexaenoic acid ethyl ester for treatment of sickle cell disease, TurnKey PharmaConsulting Ireland Limited;
- Efgartigimod alfa for treatment of myasthenia gravis, argenx BVBA;

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- Gemfibrozil for treatment of neuronal ceroid lipofuscinosis, Quintiles Ireland Limited;
- Melatonin for treatment of neonatal encephalopathy, Therapicon Srl;
- Miransertib for treatment of Proteus syndrome, QRC Consultants Ltd;
- Recombinant adeno-associated viral vector containing a codon-optimized Padua derivative of human coagulation factor IX cDNA for treatment of haemophilia B, uniQure biopharma B.V.
- Recombinant human acid alpha-glucosidase for treatment of glycogen storage disease type II (Pompe's disease), Amicus Therapeutics UK Ltd;
- Recombinant modified ricin toxin A-chain subunit for prevention of ricin poisoning, Soligenix UK Ltd.;
- Ribavirin for treatment of Crimean-Congo haemorrhagic fever, Pharmadev Healthcare Ltd;
- Ribavirin for treatment of Lassa fever, Pharmadev Healthcare Ltd;
- Tazemetostat for treatment of malignant mesothelioma, Quintiles Ireland Limited.

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 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

14 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 by the sponsor before adoption of the COMP opinion.

[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 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)

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

The COMP adopted 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:

- Mylotarg (gemtuzumab ozogamicin) for treatment of acute myeloid leukaemia (AML), Pfizer Limited (EU/3/00/005). The opinion was adopted by written procedure after the February meeting.
- Amglidia (glibenclamide) for treatment of neonatal diabetes, Ammtek (EU/3/15/1589). The opinion was adopted by written procedure after the February 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 198th meeting of the COMP will be held on 13-15 March 2018.

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	32	58	35 (60%)	21 (36%)	1 (2%)	34	3	3
2017	260	245	144 (59%)	100 (41%)	3 (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
2003	87	96	54 (56%)	37 (40%)	1 (1%)	55	5	5

[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
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	**3007**	**2843**	**2006 (71%)**	**810 (28%)**	**27 (1%)**	**1986**	**145**	**160**

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
(R)-2-(5-cyano-2-(6-(methoxycarbonyl)-7-methyl-3-oxo-8-(3-(trifluoromethyl)phenyl)-2,3,5,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-yl)phenyl)-N,N,N-trimethylethanaminium methanesulfonate dehydrate	Treatment of cystic fibrosis	Chiesi Farmaceutici S.p.A.	18 January 2018	22 February 2018
1-[[[4-(4-fluoro-2-methyl-1H-indol-5-yloxy)-6-methoxyquinolin-7-yl]oxy]methyl]cyclopropanamine-dihydrochloride	Treatment of soft tissue sarcoma	CATS Consultants GmbH	18 January 2018	22 February 2018
2'-O-(2-methoxyethyl)-modified antisense oligonucleotide targeting exon 13 in the *USH2A* gene	Treatment of retinitis pigmentosa	ProQR Therapeutics IV BV	18 January 2018	22 February 2018
6-{[(1R,2S)-2-aminocyclohexyl]amino}-7-fluoro-4-(1-methyl-1H-pyrazol-4-yl)-1,2-dihydro-3H-pyrrolo[3,4-c]pyridine-3-one monocitrate	Treatment of acute myeloid leukaemia	Takeda Pharma A/S	18 January 2018	22 February 2018
Adenovirus-associated viral vector serotype 8 containing the human *RPGR* gene	Treatment of retinitis pigmentosa,	Nightstar Therapeutics plc	18 January 2018	22 February 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Allogeneic CD4+ and CD25+ T lymphocytes ex vivo incubated with GP120	Treatment in haematopoietic stem cell transplantation	Universitätsmedizin der Johannes Gutenberg-Universität Mainz	18 January 2018	22 February 2018
Cannabidivarin	Treatment of fragile X syndrome	GW Research Ltd	18 January 2018	22 February 2018
Flucytosine	Treatment of glioma	Richardson Associates Regulatory Affairs Ltd	18 January 2018	22 February 2018
Human monoclonal IgG2 antibody against tissue factor pathway inhibitor	Treatment of haemophilia A	Bayer AG	18 January 2018	22 February 2018
Levosimendan	Treatment of amyotrophic lateral sclerosis	Orion Corporation	18 January 2018	22 February 2018
Mertansine functionalised gold nanoconjugate	Treatment of hepatocellular carcinoma	Midatech Pharma Plc	18 January 2018	22 February 2018
N-(tert-butylcarbamoyl)-5-cyano-2-((4'-(difluoromethoxy)-[1,1'-biphenyl]-3-yl)oxy)benzenesulfonamide	Treatment of pulmonary arterial hypertension	ATXA Therapeutics Limited	18 January 2018	22 February 2018
Pyridoxal 5'-phosphate	Treatment of pyridoxamine 5'-phosphate oxidase deficiency	Medicure Pharma Europe Limited	18 January 2018	22 February 2018
Recombinant human monoclonal antibody against mannan-binding lectin-associated serine protease-2	Treatment of primary IgA nephropathy	Omeros London Limited	18 January 2018	22 February 2018
Rusalatide acetate	Treatment of acute radiation syndrome	Raremoon Consulting Ltd	18 January 2018	22 February 2018
Seletalisib	Treatment of activated phosphoinositide 3-kinase delta syndrome	UCB Biopharma SPRL	18 January 2018	22 February 2018
Vocimagene amiretrorepvec	Treatment of glioma	Richardson Associates Regulatory Affairs Ltd.	18 January 2018	22 February 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
Asparaginase	Treatment of acute lymphoblastic leukemia	ERYTECH Pharma S.A.	EU/3/06/409
Cannabidiol	Treatment of Dravet syndrome	GW Research Ltd	EU/3/14/1339
Treosulfan	Conditioning treatment prior to haematopoietic progenitor cell transplantation	medac Gesellschaft fur klinische Spezialpraparate mbH	EU/3/04/186
Patisiran	Treatment of familial amyloid polyneuropathy	Alnylam UK Limited	EU/3/11/857