20 September 2018
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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 2018

The Committee for Orphan Medicinal Products held its 203rd plenary meeting on 11-13 September 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:

- Avapritinib for treatment of mastocytosis, PhaRA bvba;
- Gefinitib for treatment of Fanconi anaemia, Consorcio Centro de Investigación Biomédica en Red, M.P.;
- Melatonin for treatment of acute radiation syndrome, Worphmed Srl;
- Peptides YMFPNAPYL, SGQAYMFPNAPYLPSCLES, RSDELVRHHNMHQRNMTKL and PGCNKRYFKLSHLQMHSRKHTG for treatment of multiple myeloma, Sellas Life Sciences Limited.

2. Opinions adopted at the first COMP discussion:

- (6aR,10aR)-3-(1,1-dimethylheptyl)-delta8-tetrahydro-cannabinol-9-carboxylic acid for treatment of dermatomyositis, Accelsiors CRO and Consultancy Services Ltd;
- 6-(2-hydroxy-2-methylpropoxy)-4-(6-(6-((6-methoxypyridin-3-yl)methyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)pyridin-3-yl)pyrazolo[1,5-a]pyridine-3-carbonitrile for treatment of medullary thyroid carcinoma, Loxo Oncology Limited;

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- 6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate for treatment of cystic fibrosis, FGK Representative Service GmbH;
- Autologous CD34+ haematopoietic stem and progenitor cells genetically modified with the lentiviral vector IDUA LV, encoding for the alpha-L-iduronidase cDNA for treatment of mucopolysaccharidosis type I, Fondazione Telethon;
- Glycine, L-alanine, L-arginine, L-aspartic acid, L-cysteine, L-cystine, L-glutamic acid, L-histidine, L-lysine monohydrate, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine, taurine for treatment of maple syrup urine disease, Orphan Europe SARL;
- Recombinant adeno-associated viral vector containing a bioengineered capsid and a codon-optimised expression cassette to drive the expression of the SQ form of a B-domain deleted human coagulation factor VIII for treatment of haemophilia A, Spark Therapeutics Ireland Ltd;
- Recombinant adeno-associated viral vector serotype S3 containing codon-optimised expression cassette encoding human coagulation factor IX variant for treatment of haemophilia B, Freeline Therapeutics Ltd.

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 25 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

5 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.

[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. Opinions adopted at time of CHMP opinion:

- Darzalex (daratumumab) – Type II variation, for treatment of plasma cell myeloma, Janssen-Cilag International N.V. (EU/3/13/1153). The opinion was adopted by written procedure after the July meeting.
- Kalydeco (ivacaftor) - Type II variation, for treatment of cystic fibrosis, Vertex Pharmaceuticals (EU/3/08/556).
- Onpattro (patisiran) for treatment of familial amyloid polyneuropathy, Alnylam UK Limited (EU/3/11/857). The opinion was adopted by written procedure after the July meeting.
- Symkevi (tezacaftor / ivacaftor) for treatment of cystic fibrosis, Vertex Pharmaceuticals (Europe) Ltd. (EU/3/17/1828).

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 204th meeting of the COMP will be held on 9-11 October 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	173	172	109 (63%)	61 (35%)	2 (1%)	115	11	14
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
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	**3148**	**2957**	**2080 (70%)**	**850 (29%)**	**27 (1%)**	**2067**	**153**	**171**

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
2'-O-(2-methoxyethyl) antisense oligonucleotide targeting microtubule-associated protein tau pre-mRNA	Treatment of behavioural variant frontotemporal dementia	Ionis USA Ltd	21 June 2018	31 July 2018
Combination of carboplatin and sodium valproate	Treatment of glioma	Dr Ulrich Granzer	21 June 2018	31 July 2018
Ex-vivo fused autologous human bone marrow-derived mesenchymal stem cell with allogenic human myoblast	Treatment of Duchenne muscular dystrophy	Dystrogen Therapeutics S.A.	21 June 2018	31 July 2018
Ex-vivo-expanded adult human allogeneic mesenchymal stromal cells	Treatment of graft-versus-host disease	medac Gesellschaft für klinische Spezialpräparate mbH (WEDEL)	21 June 2018	31 July 2018
Givinostat	Treatment of Becker muscular dystrophy	Italfarmaco S.p.A.	21 June 2018	31 July 2018
Liposomal mannose-1-phosphate	Treatment of phosphomannomutase-2 congenital disorder of glycosylation	Glycomine SARL	21 June 2018	31 July 2018
N-acetylgalactosamine-conjugated synthetic double-stranded oligomer specific to serpin	Treatment of congenital alpha-1 antitrypsin deficiency	Pharma Gateway AB	21 June 2018	31 July 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
family A member 1 gene				
Recombinant human ectonucleotide pyrophosphatase/phosphodiesterase 1 fused to the Fc fragment of IgG1	Treatment of ectonucleotide pyrophosphatase/phosphodiesterase 1 deficiency	Inozyme Pharma Ireland Ltd	21 June 2018	31 July 2018
Selumetinib	Treatment of neurofibromatosis type 1	AstraZeneca AB	21 June 2018	31 July 2018
Synthetic antisense oligonucleotide directed against human dystrophin pre-mRNA	Treatment of Duchenne muscular dystrophy	Wave life Sciences Ireland Limited	21 June 2018	31 July 2018
Synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues	Treatment of primary hyperoxaluria	Dicerna EU Limited	21 June 2018	31 July 2018
Tamibarotene	Treatment of acute myeloid leukaemia	Lakeside Regulatory Consulting Services Ltd	21 June 2018	31 July 2018
Tetracosactide	Treatment of Duchenne muscular dystrophy	Mallinckrodt Specialty Pharmaceuticals Ireland Limited	21 June 2018	31 July 2018
1-(2-hydroxyethyl)-8-{[5-(4-methylpiperazin-1-yl)-2-(trifluoromethoxy) phenyl]amino}-4,5-dihydro-1H-pyrazolo[4,3-h]quinazoline-3-carboxamide fumarate salt	Treatment of acute myeloid leukaemia	Pharm Research Associates (UK) Limited	19 July 2018	24 August 2018
Adeno-associated viral vector serotype hu68 containing the human *SMN1* gene	Treatment of spinal muscular atrophy	Biogen Idec Limited	19 July 2018	24 August 2018
Copanlsib	Treatment of marginal zone lymphoma	Bayer AG	19 July 2018	24 August 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Recombinant human monoclonal antibody against mannan-binding lectin-associated serine protease-2	Treatment in haematopoietic stem cell transplantation	Omeros London Limited;	19 July 2018	24 August 2018
Somapacitan	Treatment of growth hormone deficiency	Novo Nordisk A/S	19 July 2018	24 August 2018
Tilorone	Treatment of idiopathic pulmonary fibrosis	Professor Marjukka Myllärniemi	19 July 2018	24 August 2018
(S)-(−)-3-(4-aminophenyl)-2-methoxypropanoic acid	Treatment of idiopathic pulmonary fibrosis	Nogra Pharma Limited	19 July 2018	24 August 2018
1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate	Treatment of beta-thalassaemia intermedia and major	IQVIA RDS Ireland Limited	19 July 2018	24 August 2018
Acetylleucine	Treatment of spinocerebellar ataxia	IntraBio Ltd	19 July 2018	24 August 2018
Autologous glioma tumour cells treated with antisense molecule directed against the insulin-like growth factor type 1 receptor	Treatment of glioma	Pharma Gateway AB	19 July 2018	24 August 2018
Bertilimumab	Treatment of bullous pemphigoid	IQVIA RDS Ireland Limited	19 July 2018	24 August 2018
CD34+ haematopoietic stem and progenitor cells with CD3+ T-cells	Treatment in solid organ transplantation	IQVIA RDS Ireland Limited	19 July 2018	24 August 2018
Obiltoxaximab	Treatment of inhalational anthrax disease	SFL Regulatory Services GmbH	19 July 2018	24 August 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Pemigatinib	Treatment of biliary tract cancer	Incyte Biosciences Distribution B.V.	19 July 2018	24 August 2018
Adenovirus associated viral vector serotype 2/8 containing the human CNGA3 gene	Treatment of achromatopsia	MeiraGTx UK II Limited	21 June 2018	31 July 2018
(3R,3aS,9R,9aS,9bS)-3-((dimethylamino)methyl)-9-hydroxy-6,9-dimethyl-3,3a,4,5,7,8,9,9a-octahydroazuleno[4,5-b]furan-2(9bH)-one fumarate	Treatment of glioma	IQVIA RDS Ireland Limited	19 July 2018	24 August 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
Ravulizumab	Treatment of paroxysmal nocturnal haemoglobinuria	Alexion Europe SAS	EU/3/16/1661
Emapalumab	Treatment of haemophagocytic lymphohistiocytosis	Novimmune B.V.	EU/3/10/749