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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

July 2018

The Committee for Orphan Medicinal Products held its 202nd plenary meeting on 17-19 July 2018.

Orphan medicinal product designation

Positive opinions

The COMP adopted 15 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:

- (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 for treatment of glioma, IQVIA RDS Ireland Limited;
- 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 for treatment of acute myeloid leukaemia, Pharm Research Associates (UK) Limited;
- Adeno-associated viral vector serotype hu68 containing the human *SMN1* gene for treatment of spinal muscular atrophy, Biogen Idec Limited;
- Copanlisib for treatment of marginal zone lymphoma, Bayer AG;
- Recombinant human monoclonal antibody against mannan-binding lectin-associated serine protease-2 for treatment in haematopoietic stem cell transplantation, Omeros London Limited;
- Somapacitan for treatment of growth hormone deficiency, Novo Nordisk A/S;
- Tilorone for treatment of idiopathic pulmonary fibrosis, Professor Marjukka Myllärniemi.

2. Opinions adopted at the first COMP discussion:

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- (S)-(−)-3-(4-aminophenyl)-2-methoxypropanoic acid for treatment of idiopathic pulmonary fibrosis, Nogra Pharma Limited;
- 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 - for treatment of beta-thalassaemia intermedia and major, IQVIA RDS Ireland Limited;
- Acetylleucine for treatment of spinocerebellar ataxia, IntraBio Ltd;
- Autologous glioma tumour cells treated with antisense molecule directed against the insulin-like growth factor type 1 receptor for treatment of glioma, Pharma Gateway AB;
- Bertilimumab for treatment of bullous pemphigoid, IQVIA RDS Ireland Limited;
- CD34+ haematopoietic stem and progenitor cells with CD3+ T-cells for treatment in solid organ transplantation, IQVIA RDS Ireland Limited;
- Obiltoxaximab for treatment of inhalational anthrax disease, SFL Regulatory Services GmbH;
- Pemigatinib for treatment of biliary tract cancer, Incyte Biosciences Distribution B.V.

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 11 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

6 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. Opinions adopted at time of CHMP opinion:

- Cablivi (caplacizumab) for treatment of thrombotic thrombocytopenic purpura, Ablynx NV (EU/3/09/629).
- Kymriah (autologous t cells transduced with lentiviral vector containing a chimeric antigen receptor directed against cd19) for treatment of diffuse large B-cell lymphoma, Novartis Europharm Limited (EU/3/16/1745).
- Kymriah (autologous t cells transduced with lentiviral vector containing a chimeric antigen receptor directed against cd19) for treatment of B-lymphoblastic leukaemia/lymphoma, Novartis Europharm Limited (EU/3/14/1266).
- Mepsevii (vestronidase alfa) for treatment of mucopolysaccharidosis type VII (Sly syndrome), Ultragenyx Germany GmbH (EU/3/12/973). The opinion was adopted by written procedure after the June meeting.
- Vyxeos (cytarabine: daunorubicin) liposome for injection –daunorubicin/ cytarabine for treatment of adults with high-risk acute myeloid leukaemia (AML), Jazz Pharmaceuticals Ireland (EU/3/11/942). The opinion was adopted by written procedure after the June meeting.
- Yescarta (axicabtagene ciloleucel) for treatment of diffuse large B cell lymphoma, Kite Pharma EU B.V. (EU/3/14/1393).
- Yescarta (axicabtagene ciloleucel) for treatment of primary mediastinal large B-cell lymphoma, Kite Pharma EU B.V. (EU/3/15/1553).

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 203rd meeting of the COMP will be held on 11-13 September 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	150	139	98 (64%)	54 (39%)	2 (2%)	86	9	9
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	**3125**	**2924**	**2069 (70%)**	**843 (29%)**	**27 (1%)**	**2038**	**151**	**166**

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)-1-(3-(aminomethyl) phenyl)-N-(5-((3-cyanophenyl)(cyclopropylmethylamino)methyl)-2-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide dihydrochloride	Treatment of hereditary angioedema	BioCryst UK Ltd	24 May 2018	27 June 2018
2-[(2S)-2-methyl-1,4-dioxa-8-azaspiro[4.5]dec-8-yl]-8-nitro-6-trifluoromethyl-4H-1,3-benzothiazin-4-one	Treatment of tuberculosis	Klinikum der Universität München	24 May 2018	27 June 2018
20-hydroxyecdysone	Treatment of Duchenne muscular dystrophy	Biophytis	24 May 2018	27 June 2018
Argon	Treatment of perinatal asphyxia	Air Liquide Santé (International)	24 May 2018	27 June 2018
Carmustine	Treatment in haematopoietic stem cell transplantation	ADIENNE S.r.l.S.U.	24 May 2018	27 June 2018
Codon-optimised human ornithine transcarbamylase mRNA complexed with lipid-based nanoparticles	Treatment of ornithine transcarbamylase deficiency	Real Regulatory Limited	24 May 2018	27 June 2018
Deferiprone	Treatment of neurodegeneration with brain iron accumulation	Apotex Europe B.V.	24 May 2018	27 June 2018
Efpegsomatropin	Treatment of growth hormone	Hanmi Europe Limited	24 May 2018	27 June 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
	deficiency			
L-cystine bis(N'-methylpiperazide)	Treatment of cystinuria	PharmaKrysto Ltd.	24 May 2018	27 June 2018
Omaveloxolone	Treatment of Friedreich's ataxia	Dr Stefan Blesse	24 May 2018	27 June 2018
Palovarotene	Treatment of multiple osteochondromas	PPD Global Ltd	24 May 2018	27 June 2018
Recombinant adeno-associated viral vector serotype 9 containing human iduronidase gene	Treatment of mucopolysaccharidosis type I	REGENXBIO EU Limited	24 May 2018	27 June 2018
Recombinant human placental growth factor	Treatment of pre-eclampsia	IQVIA RDS Ireland Limited	24 May 2018	27 June 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
Enasidenib	Treatment of acute myeloid leukaemia	Celgene Europe Limited	EU/3/16/1640