12 November 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

November 2018

The Committee for Orphan Medicinal Products held its 205th plenary meeting on 6-8 November 2018.

Orphan medicinal product designation

Positive opinions

The COMP adopted 21 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:

- Acetylcysteine for treatment of pseudomyxoma peritonei, MUCPharm Pty Ltd;
- Adeno-associated viral vector expressing human 21-hydroxylase for treatment of congenital adrenal hyperplasia, Pharma Gateway AB;
- Afatinib for treatment of Fanconi anaemia, Consorcio Centro de Investigación Biomédica en Red, M.P.;
- Bromelain for treatment of pseudomyxoma peritonei, MUCPharm Pty Ltd;
- Human anti-promyostatin monoclonal antibody for treatment of spinal muscular atrophy, Yes Pharmaceutical Development Services GmbH;
- Ivacaftor, N-(1,3-dimethyl-1H-pyrazole-4-sulfonyl)-6-[3-(3,3,3-trifluoro-2,2-dimethylpropoxy)-1H-pyrazol-1-yl]-2-[(4S)-2,2,4-trimethylpyrrolidin-1-yl]pyridine-3-carboxamide, tezacaftor for treatment of cystic fibrosis, Vertex Pharmaceuticals (Europe) Limited;
- Ivacaftor, potassium(benzenesulfonyl)({[6-(3-{2-[1-(trifluoromethyl) cyclopropyl]ethoxy}-1H-pyrazol-1-yl)-2-[(4S)-2,2,4-trimethylpyrrolidin-1-yl]pyridin-3-yl]carbonyl})azanide, tezacaftor for treatment of cystic fibrosis, Vertex Pharmaceuticals (Europe) Limited;

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- Sodium 2-hydroxylinoleate for treatment of biliary tract cancer, Ability Pharmaceuticals SL;
- Venglustat for treatment of autosomal dominant polycystic kidney disease, Genzyme Europe BV.

2. Opinions adopted at the first COMP discussion:

- (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-yl]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid for treatment of biliary atresia, Albireo AB;
- (4-{(2S,4S)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoic acid-hydrogen chloride(1/1)) for treatment of C3 glomerulopathy, Novartis Europharm Limited;
- 6,8-bis(benzylthio)octanoic acid for treatment of pancreatic cancer, IQVIA RDS Ireland Limited;
- 6,8-bis(benzylthio)octanoic acid for treatment of acute myeloid leukaemia, IQVIA RDS Ireland Limited;
- 6-fluoro-9-methyl-9H-pyrido[3,4-b]-indole for treatment of sudden sensorineural hearing loss, AudioCure Pharma GmbH;
- Adeno-associated virus serotype HSC15 expressing human phenylalanine hydroxylase for treatment of phenylanaline hydroxylase deficiency, Yes Pharmaceutical Development Services GmbH;
- Allogeneic ABCB5-positive limbal stem cells for treatment of limbal stem cell deficiency, Rheacell GmbH & Co. KG;
- Bifunctional fusion protein composed of two extracellular domains of transforming growth factor beta receptor II fused with a human immunoglobulin G1 monoclonal antibody against programmed death ligand 1 for treatment of biliary tract cancer, Merck Europe B.V.;
- C1 esterase inhibitor (human) for treatment in solid organ transplantation, Shire Pharmaceuticals Ireland Limited;
- Lonafarnib for treatment of Hutchinson-Gilford progeria syndrome, Eiger Biopharmaceuticals Europe Limited;
- Marizomib for treatment of glioma, Celgene Europe B.V.;
- Pevonedistat for treatment of myelodysplastic syndromes, Takeda Pharma A/S.

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:

- Diacerein for treatment of epidermolysis bullosa, Therapicon Srl.

[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 following appeal procedures:

None

Lists of questions

The COMP adopted 15 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

4 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that no 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)

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:

- Namuscla - mexiletine hydrochloride for treatment of myotonic disorders, LUPIN (EUROPE) LIMITED (EU/3/14/1353).
- Takhzyro - lanadelumab for treatment of hereditary angioedema, Shire Pharmaceuticals Ireland Limited (EU/3/15/1551). The opinion was adopted by written procedure after the October meeting.

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 206th meeting of the COMP will be held on 4-6 December 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	203	234	152 (66%)	79 (34%)	3 (1%)	126	12	15
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	**3178**	**3019**	**2123 (70%)**	**868 (29%)**	**28 (1%)**	**2078**	**154**	**172**

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
(6aR,10aR)-3-(1,1-dimethylheptyl)-delta8-tetrahydro-cannabinol-9-carboxylic acid	Treatment of dermatomyositis	Accelsiors CRO and Consultancy Services Ltd	13 September 2018	26 October 2018
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	Treatment of medullary thyroid carcinoma	Loxo Oncology Limited	13 September 2018	26 October 2018
6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate	Treatment of cystic fibrosis	FGK Representative Service GmbH	13 September 2018	26 October 2018
Autologous CD34+ haematopoietic stem and progenitor cells genetically modified with the lentiviral vector IDUA LV, encoding for the alpha-L-iduronidase cDNA	Treatment of mucopolysaccharidosis type I	Fondazione Telethon	13 September 2018	26 October 2018
Avapritinib	Treatment of mastocytosis	PhaRA bvba	13 September 2018	26 October 2018
Gefinitib	Treatment of Fanconi anaemia	Consorcio Centro de Investigación Biomédica en Red, M.P.	13 September 2018	26 October 2018
Glycine, L-alanine, L-arginine, L-aspartic acid, L-cysteine, L-cystine, L-glutamic acid, L-histidine,	Treatment of maple syrup urine disease	Orphan Europe SARL	13 September 2018	26 October 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
L-lysine monohydrate, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine, taurine				
Melatonin	Treatment of acute radiation syndrome	Worphmed Srl	13 September 2018	26 October 2018
Peptides YMFPNAPYL, SGQAYMFPNAPYLPSCLES, RSDELVRHHNMHQRNMTKL and PGCNKRYFKLSHLQMHSRKHTG	Treatment of multiple myeloma	Sellas Life Sciences Limited	13 September 2018	26 October 2018
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	Treatment of haemophilia A	Spark Therapeutics Ireland Ltd	13 September 2018	26 October 2018
Recombinant adeno-associated viral vector serotype S3 containing codon-optimised expression cassette encoding human coagulation factor IX variant	Treatment of haemophilia B	Freeline Therapeutics Ltd.	13 September 2018	26 October 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
Quizartinib	Treatment of acute myeloid leukaemia	Daiichi Sankyo Europe GmbH	EU/3/09/622
Onasemnogene abeparvovec	Treatment of spinal muscular atrophy	AveXis Netherlands B.V.	EU/3/15/1509