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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

May 2018

The Committee for Orphan Medicinal Products held its 200th plenary meeting on 22-24 May 2018.

Orphan medicinal product designation

Positive opinions

The COMP adopted 13 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:

- (R)-1-(3-(aminomethyl) phenyl)-N-(5-((3-cyanophenyl)(cyclopropylmethylamino)methyl)-2-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide dihydrochloride for treatment of hereditary angioedema, BioCryst UK Ltd;
- 20-hydroxyecdysone for treatment of Duchenne muscular dystrophy, Biophytis;
- Carmustine for treatment in haematopoietic stem cell transplantation, ADIENNE S.r.l.S.U.;
- Deferiprone for treatment of neurodegeneration with brain iron accumulation, Apotex Europe B.V.;
- Efpegsomatropin for treatment of growth hormone deficiency, Hanmi Europe Limited;
- L-cystine bis(N'-methylpiperazide) for treatment of cystinuria, PharmaKrysto Ltd.

2. Opinions adopted at the first COMP discussion:

- 2-[(2S)-2-methyl-1,4-dioxa-8-azaspiro[4.5]dec-8-yl]-8-nitro-6-trifluoromethyl-4H-1,3-benzothiazin-4-one for treatment of tuberculosis, Klinikum der Universität München;
- Argon for treatment of perinatal asphyxia, Air Liquide Santé (International);
- Codon-optimised human ornithine transcarbamylase mRNA complexed with lipid-based nanoparticles for treatment of ornithine transcarbamylase deficiency, Real Regulatory Limited;

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- Omaveloxolone for treatment of Friedreich's ataxia, Dr Stefan Blesse;
- Palovarotene for treatment of multiple osteochondromas, PPD Global Ltd;
- Recombinant adeno-associated viral vector serotype 9 containing human iduronidase gene for treatment of mucopolysaccharidosis type I, REGENXBIO EU Limited;
- Recombinant human placental growth factor for treatment of pre-eclampsia, IQVIA RDS Ireland Limited.

3. Opinion following appeal procedures:

None

The COMP also recommended the amendment to 1 existing orphan designation:

- Interferon beta for treatment of acute respiratory distress syndrome, Faron Pharmaceuticals Limited (initially for treatment of acute lung injury).

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

5 oral hearings took place.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 5 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.

[1] Details of all orphan designations granted to date by the European Commission are entered in the EU Register of Orphan Medicinal Products

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:

- Myalepta (metreleptin) for treatment of Barraquer-Simons syndrome, Aegerion Pharmaceuticals Limited (EU/3/12/1023). The opinion was adopted by written procedure after the May meeting.
- Myalepta (metreleptin) for treatment of Berardinelli-Seip syndrome, Aegerion Pharmaceuticals Limited (EU/3/12/1025). The opinion was adopted by written procedure after the May meeting.
- Myalepta (metreleptin) for treatment of familial partial lipodystrophy, Aegerion Pharmaceuticals Limited (EU/3/12/1022). The opinion was adopted by written procedure after the May meeting.
- Myalepta (metreleptin) for treatment of Lawrence syndrome, Aegerion Pharmaceuticals Limited (EU/3/12/1024). The opinion was adopted by written procedure after the May meeting.
- Tegsedi (inotersen) for treatment of ATTR amyloidosis, IONIS USA Ltd (EU/3/14/1250). The opinion was adopted by written procedure after the May meeting.

2. Opinion following appeal procedures:

None

3. Revision of the COMP opinion:

The COMP adopted an opinion recommending to the European Commission that the following orphan medicinal product be kept in the Community Register of orphan medicinal products for human use:

- Verkazia (ciclosporin) for treatment of vernal keratoconjunctivitis, Santen Oy (EU/3/06/360). The opinion was adopted via written procedure after the May meeting.

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 201st meeting of the COMP will be held on 19-21 June 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	96	110	69 (63%)	39 (35%)	2 (2%)	73	8	8
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	**3071**	**2895**	**2040 (70%)**	**828 (29%)**	**27 (1%)**	**2025**	**150**	**165**

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
1-(3-{4-[3,4-difluoro-2-(trifluoromethyl)phenyl]piperidine-1-carbonyl}-1H,4H,5H,6H,7H-pyrazolo[3,4-c]pyridin-6-yl)ethan-1-one	Treatment of Stargardt's disease	IQVIA RDS Ireland Limited	19 April 2018	25 May 2018
Adeno-associated viral vector serotype 8 containing a functional copy of the codon-optimised F8 cDNA encoding the B-domain deleted human coagulation factor VIII	Treatment of haemophilia A	Baxalta Innovations GmbH	19 April 2018	25 May 2018
Adeno-associated viral vector serotype 9 containing the human *CLN1* gene	Treatment of neuronal ceroid lipofuscinosis	Abeona Therapeutics Europe SL	19 April 2018	25 May 2018
Ambroxol hydrochloride	Treatment of amyotrophic lateral sclerosis	Spedding Research Solutions SAS	19 April 2018	25 May 2018
Autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor	Treatment of follicular lymphoma	Celgene Europe Limited	19 April 2018	25 May 2018
Bardoxolone methyl	Treatment of Alport syndrome	Dr Stefan Blesse	19 April 2018	25 May 2018
Daratumumab	Treatment of AL amyloidosis	Janssen-Cilag International N.V.	19 April 2018	25 May 2018
Equine immunoglobulin F(ab')2 fragments	Prevention of haemolytic uraemic syndrome	Chemo Research S.L.	19 April 2018	25 May 2018

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
targeting Shiga toxin				
Glucagon analogue linked to a human immunoglobulin Fc fragment	Treatment of congenital hyperinsulinism	Hanmi Europe Limited	19 April 2018	25 May 2018
H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-2Thi-Gly-Leu-Met(O2)-NH2-DOTA-225-actinium	Treatment of glioma	Dr. Regenold GmbH	19 April 2018	25 May 2018
Itraconazole	Prevention of invasive aspergillosis	Galephar M/F	19 April 2018	25 May 2018
Modified mRNA encoding human methylmalonyl-coenzyme A mutase encapsulated into lipid nanoparticles	Treatment of methylmalonic acidaemia	Pharma Gateway AB	19 April 2018	25 May 2018
Synthetic double-stranded siRNA oligonucleotide targeted against transthyretin mRNA, with six phosphorothioate linkages in the backbone, and nine 2'-fluoro and thirty-five 2'-O-methyl nucleoside residues in the sequence, which is covalently linked via a phosphodiester group to a ligand containing three N-acetylgalactosamine residues	Treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis)	Alnylam UK Limited	19 April 2018	25 May 2018
Three human monoclonal antibodies against the Ebola virus glycoprotein	Treatment of Ebola virus disease	Regeneron Ireland U.C.	19 April 2018	25 May 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

No new designated orphan medicinal products that have been subject of a new European Union marketing authorisation application under the centralised procedure since last COMP plenary meeting.