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Procedure Management and Committees Support Division

Committee for Orphan Medicinal Products (COMP) meeting report on the review of applications for orphan designation

January 2016

The Committee for Orphan Medicinal Products held its 174th plenary meeting on 19-21 January 2016.

Orphan medicinal product designation

Positive opinions

The COMP adopted 14 positive opinions recommending the following medicines for designation as orphan medicinal products to the European Commission (EC):

1. Opinions adopted at the second COMP discussion, following the sponsor's response to the COMP list of questions:

- Arsenic trioxide for treatment of acute myeloid leukaemia, Orsenix Holdings BV;
- Ex-vivo-expanded autologous fibroblasts transduced with lentiviral vector containing the *COL7A1* gene for treatment of epidermolysis bullosa, Dr Waseem Qasim;
- Humanised IgG4 monoclonal antibody against total complement component 1, subcomponent s for treatment of autoimmune haemolytic anaemia, Assign Group Development UK Ltd;
- Methyl 3-((2R)-2-hydroxy-4-(((((S)-1-methoxy-1-oxopropan-2-yl) amino)(phenoxy)phosphoryl)oxy)-3,3-dimethylbutanamido)propanoate for treatment of pantothenate-kinase-associated neurodegeneration, Retrophin Europe Limited;
- S3,S13-cyclo(D-tyrolsyl-L-isoleucyl-L-cysteinyl-L-valyl-1-methyl-L-tryptophyl-L-glutaminyl-L-aspartyl-L-tryptophyl-N-methyl-L-glycyl-L-alanyl-L-histidyl-L-arginyl-L-cysteinyl-N-methyl-L-isoleucinamide) for treatment of C3 glomerulopathy, Amyndas Pharmaceuticals S.A..

2. Opinions adopted at the first COMP discussion:

[1] Minor correction under Positive opinions

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- 2-ethylbutyl (2S)-2-{[(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy}(phenoxy)phosphoryl]amino}propanoate for treatment of Ebola virus disease, Gilead Sciences International Ltd;
- Allogeneic fetal human retinal progenitor cells expanded ex vivo for treatment of retinitis pigmentosa, Voisin Consulting S.A.R.L.;
- Delta-9-tetrahydrocannabinol and cannabidiol from extracts of the *Cannabis sativa* L. plant for treatment of glioma, GW Research Ltd;
- Diclofenamide for treatment of periodic paralysis, Prof Michael Hanna;
- DNA plasmid encoding a recombinant fusion protein consisting of the extracellular domain of human TNFα p55 receptor linked to the human IgG1 Fc domain for treatment of non-infectious uveitis, Eyevensys SA;
- N-(4-Methoxyphenyl)-N,2,6-trimethylfuro[2,3-d]pyrimidin-4-amine for treatment of glioma, FLAG Therapeutics Ltd;
- Tolfenamic acid for treatment of progressive supranuclear palsy, RV Developpement;
- Tolfenamic acid for treatment of behavioural variant frontotemporal dementia, RV Developpement;
- Venetoclax for treatment of acute myeloid leukaemia, Abbvie Ltd.

Public summaries of opinions will be available on the EMA website following adoption of the respective decisions on orphan designation[2] by the European Commission.

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

7 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.

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 given by the European Commission since the last COMP meeting is provided in Annex 2.

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

Applications for marketing authorisation for orphan medicinal products

Details of those designated orphan medicinal products that have been subject of a new European Union (EU) marketing authorisation application through the centralised procedure since the last COMP plenary meeting 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 175th meeting of the COMP will be held on 16-18 February 2016.

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

Year	Applications submitted	Applications discussed in reporting year	Positive COMP opinions	Applications withdrawn	Final negative COMP opinions	EC designations	Orphan medicinal products[3] authorised	Orphan designations included in authorised therapeutic indication
2016	3	19	14 (74%)	5 (26%)	0	9	0	0
2015	258	272	177 (65%)	94 (35%)	1 (1%)	190	14	21
2014	329	259	196 (76%)	61 (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%)	41 (43%)	1 (1%)	55	5	5
2002	80	75	43 (57%)	30 (40%)	2 (3%)	49	4	4
2001	83	90	62 (70%)	27 (29%)	1 (1%)	64	3	3
2000	72	32	26 (81%)	6 (19%)	0 (0%)	14	0	0
Total	**2388**	**2259**	**1621 (72%)**	**617 (27%)**	**21 (1%)**	**1605**	**114**	**128**

[3] Number of authorised orphan medicinal products may cover more than one orphan designation

Annex 2

Medicinal products granted a European Union designation as orphan medicinal product by the European Commission since the December 2015 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propanediol hydrochloride	Prevention of graft-versus-host disease	Novartis Europharm Limited	12 November 2015	14 December 2015
2-(2-chlorobenzylidene)hydrazinecarboximidamide acetate	Treatment of Charcot-Marie-Tooth disease	Inflectis Bioscience	12 November 2015	14 December 2015
[4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17)	Treatment of pseudohypoaldosteronism type 1B	Apeptico Forschung und Entwicklung GmbH	12 November 2015	14 December 2015
Adeno-associated viral vector serotype rh10 containing the human factor IX gene	Treatment of haemophilia B	Pharma Gateway AB	12 November 2015	14 December 2015
Bilayer engineered collagen hydrogel-based skin graft composed of autologous keratinocytes and fibroblasts	Treatment of partial deep dermal and full thickness burns	Voisin Consulting S.A.R.L.	12 November 2015	14 December 2015
Combretastatin A1 diphosphate	Treatment of acute myeloid leukaemia	Diamond BioPharm Limited	12 November 2015	14 December 2015
Glibenclamide	Treatment of neonatal diabetes	AMMTeK	12 November 2015	15 January 2016
Imetelstat sodium	Treatment of myelofibrosis	Janssen-Cilag International N.V.	12 November 2015	14 December 2015
Live attenuated Listeria monocytogenes bioengineered with a chimeric human epidermal	Treatment of osteosarcoma	Coté Orphan Consulting UK Limited	12 November 2015	14 December 2015

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
growth factor receptor 2 fused to a truncated form of the Lm protein listeriolysin O				
Live attenuated Listeria monocytogenes delta actA/delta inlB strain expressing human mesothelin	Treatment of malignant mesothelioma	Medpace Germany GmbH	12 November 2015	14 December 2015
Recombinant human nerve growth factor	Treatment of neurotrophic keratitis	Dompé farmaceutici S.p.A.	12 November 2015	14 December 2015
(R)-1-[1-(4-acetoxy-3,3-dimethyl-2-oxo-butyl)-2-oxo-5-(pyridin-2-yl)-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-(3-methylamino-phenyl)-urea	Treatment of gastro-entero-pancreatic neuroendocrine tumours	Trio Medicines Ltd	12 November 2015	14 December 2015
Recombinant human monoclonal IgG1 antibody against programmed death ligand-1	Treatment of Merkel cell carcinoma	Merck KGaA	12 November 2015	14 December 2015
Sirolimus	Treatment of beta-thalassaemia intermedia and major	Rare Partners srl Impresa Sociale	12 November 2015	14 December 2015
Sodium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methyl phosphate	Treatment of acute myeloid leukaemia	Otsuka Pharmaceutical Europe Ltd	12 November 2015	14 December 2015
Synthetic peptide L-cysteine, L-cysteinylglycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-, cyclic (1.fwdarw.17)-disulfide	Treatment of pseudohypoaldosteronism type 1B	Apeptico Forschung und Entwicklung GmbH	12 November 2015	14 December 2015
Variant of recombinant human fibroblast growth factor 19	Treatment of primary sclerosing cholangitis	Diamond BioPharm Limited	12 November 2015	14 December 2015

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Live attenuated *Listeria monocytogenes* delta *actA*/delta *inlB* strain expressing human mesothelin	Treatment of pancreatic cancer	Medpace Germany GmbH	10 December 2015	11 January 2016
Sodium benzoate	Treatment of hyperargininaemia	Syri Limited	10 December 2015	11 January 2016
Sodium benzoate	Treatment of arginosuccinic aciduria	Syri Limited	10 December 2015	11 January 2016
Two allogenic irradiated pancreatic tumour cell lines	Treatment of pancreatic cancer	Medpace Germany GmbH	10 December 2015	11 January 2016
Entolimod	Treatment of acute radiation syndrome	TMC Pharma Services Ltd	10 December 2015	11 January 2016
Live attenuated *Listeria monocytogenes* transfected with plasmids encoding the HPV-16E7 protein fused to a truncated fragment of the Lm protein listeriolysin O	Treatment of anal cancer	Dr Ulrich Granzer	10 December 2015	11 January 2016
Synthetic double-stranded oligomer specific to the *SERPINA1* gene and containing a cholesterol-conjugated, acyclic nucleobase analogue	Treatment of congenital alpha-1 antitrypsin deficiency	Pharma Gateway AB	10 December 2015	11 January 2016
(S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide hydrogen sulfate	Treatment of soft tissue sarcoma	TMC Pharma Services Ltd	10 December 2015	11 January 2016

Annex 3

Designated orphan medicinal products that have been subject of a new European Union marketing authorisation application under the centralised procedure since the November 2015 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Obinutuzumab	Treatment of follicular lymphoma	Roche Registration Limited	EU/3/15/1504
Trientine tetrahydrochlorid	Treatment of Wilson's disease	GMP-Orphan SA	EU/3/15/1471
Vosaroxin	Treatment of acute myeloid leukaemia	Sunesis Europe Ltd	EU/3/12/990