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

October 2015

The Committee for Orphan Medicinal Products held its 171th plenary meeting on 6-8 October 2015.

Orphan medicinal product designation

Positive opinions

The COMP adopted 16 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:

- 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-biphenyl]-2-sulfonamide for treatment of focal segmental glomerulosclerosis, Retrophin Europe Limited;
- Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor for treatment of acute lymphoblastic leukaemia, Kite Pharma UK, Ltd;
- Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor for treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma, Kite Pharma UK, Ltd;
- Azacitidine for treatment of nasopharyngeal carcinoma, Celgene Europe Limited;
- Humanised fusion protein consisting of extracellular domain of CD24 linked to IgG1 Fc domain for prevention of graft-versus-host disease, Enpharma Ltd;
- Interferon alfa-n3 for treatment of Middle East respiratory syndrome, NV Hemipsherx BioPharma Europe;
- Pentetrazol for treatment of idiopathic hypersomnia, Dr Jens Steinbrink;

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- Recombinant human interleukin-3 truncated diphtheria toxin fusion protein for treatment of blastic plasmacytoid dendritic cell neoplasm, Spector Consulting SAS.

2. Opinions adopted at the first COMP discussion:

- (5S,8S,10aR)-N-benzhydryl-5-((S)-2-(methylamino)propanamido)-3-(3-methylbutanoyl)-6-oxodecahydropyrrolo[1,2-a][1,5]diazocine-8-carboxamide for treatment of ovarian cancer, ASPHALION, SL;
- Adeno-associated viral vector serotype 8 encoding the human *ATP7B* gene under the control of the human alpha-1 antitrypsin promoter for treatment of Wilson's disease, Aligen Therapeutics S.L.;
- Adenovirus associated viral vector serotype 5 containing the human *RPE65* gene for treatment of Leber's congenital amaurosis, Athena Vision Ltd;
- Adenovirus associated viral vector serotype 8 containing the human *CNGB3* gene for treatment of achromatopsia caused by mutations in the *CNGB3*[1] gene, Alan Boyd Consultants Ltd;
- Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor for treatment of follicular lymphoma, Kite Pharma EU B.V.;
- Humanised monoclonal antibody of the IgG4 kappa isotype targeting CD47 for treatment of acute myeloid leukaemia, The Chancellor, Masters and Scholars of the University of Oxford;
- N-[5-(3,5-difluorobenzyl)-1H-indazol-3-yl]-4-(4 methylpiperazin-1-yl)-2-(tetrahydro-2H-pyran-4-ylamino)benzamide for treatment of neuroblastoma, Pharma Gateway AB;
- Sodium phenylbutyrate for treatment of pyruvate dehydrogenase complex deficiency, Fondazione Telethon.

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 19 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.

[1] Condition amended
[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.

Article 5(12) (b) of Regulation (EC) No 141/2000 of the European Parliament and of the Council

In line with its responsibility to review whether or not a designated orphan medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation, the COMP adopted 9 opinions recommending to the European Commission that the following orphan medicinal products be kept in the EU registry of orphan medicinal product:

- Blincyto (blinatumomab) for treatment of acute lymphoblastic leukaemia, Amgen Europe B.V. (EU/3/09/650);
- Kolbam (cholic acid) for treatment of inborn errors of primary bile acid synthesis responsive to treatment with cholic acid, Retrophin Europe Ltd (EU/3/09/683);
- Kyprolis (carfilzomib) for treatment of multiple myeloma, Amgen Europe B.V. (EU//3/08/548);
- RAVICTI (glyceryl tri-(4-phenylbutyrate)) for treatment of argininosuccinic aciduria, Horizon Therapeutics Limited (EU/3/10/736);
- RAVICTI (glyceryl tri-(4-phenylbutyrate)) for treatment of carbamoyl-phosphate synthase-1 deficiency, Horizon Therapeutics Limited (EU/3/10/733);
- RAVICTI (glyceryl tri-(4-phenylbutyrate)) for treatment of citrullinaemia type 1, Horizon Therapeutics Limited (EU/3/10/735);
- RAVICTI (glyceryl tri-(4-phenylbutyrate)) for treatment of hyperargininaemia, Horizon Therapeutics Limited (EU/3/10/737);
- RAVICTI (glyceryl tri-(4-phenylbutyrate)) for treatment of ornithine carbamoyltransferase deficiency, Horizon Therapeutics Limited (EU/3/10/734);
- RAVICTI (glyceryl tri-(4-phenylbutyrate)) for treatment of ornithine translocase deficiency (hyperornithinaemia-hyperammonaemia homocitrullinuria (HHH) syndrome), Horizon Therapeutics Limited (EU/3/10/738).

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 172st meeting of the COMP will be held on 10-12 November 2015

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
2015	190	221	152 (69%)	68 (31%)	1 (1%)	158	10	11
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	**2317**	**2189**	**1582 (72%)**	**586 (27%)**	**21 (1%)**	**1564**	**110**	**118**

[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 September 2015 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Autologous human peripheral blood Vdelta1+ T lymphocytes activated in vitro by cytokine and monoclonal antibody	Treatment for treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma, Lymphact	Lymphocyte Activation Technologies S.A.	3 September 2015	9 October 2015
Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor	Treatment of mantle cell lymphoma	Kite Pharma UK, Ltd	3 September 2015	9 October 2015
Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor	Treatment of primary mediastinal large B-cell lymphoma	Kite Pharma UK, Ltd	3 September 2015	9 October 2015
Nimodipine	Treatment of aneurysmal subarachnoid haemorrhage	Dr Stefan Blesse	3 September 2015	9 October 2015
Ovine-specific immunoglobulin (Fab) fragments raised against *Vipera berus* venom	Treatment of snakebite envenomation	MicroPharm Limited	3 September 2015	9 October 2015
Recombinant human IgG1 kappa light chain monoclonal antibody targeting plasma kallikrein	Treatment of hereditary angioedema	Dyax Ltd	3 September 2015	9 October 2015
Synthetic hepcidin	Treatment of beta thalassaemia intermedia and major	Emas Pharma Ltd	3 September 2015	9 October 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 primary graft dysfunction following lung transplantation	Apeptico Forschung und Entwicklung GmbH	3 September 2015	9 October 2015

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione	Treatment of systemic sclerosis	GenKyoTex Innovation S.A.S	3 September 2015	9 October 2015
2-chloro-N6-(3-iodobenzyl) adenosine-5'-N-methyluronamide	Treatment of hepatocellular carcinoma	PBS Regulatory Consulting Group Limited	3 September 2015	9 October 2015
3-pentylbenzeneacetic acid sodium salt	Treatment of idiopathic pulmonary fibrosis	ProMetic BioTherapeutics Ltd	3 September 2015	9 October 2015
A highly purified formulation of *Staphylococcus aureus* protein A	Treatment of immune thrombocytopenia	Coté Orphan Consulting UK Limited	3 September 2015	9 October 2015
Ataluren	Treatment of aniridia	PTC Therapeutics International Limited	3 September 2015	9 October 2015
Dronabinol and cannabidiol	Treatment of glioma	GW Research Ltd	3 September 2015	9 October 2015
Mazindol	Treatment of narcolepsy	NeuroLifeSciences	3 September 2015	9 October 2015
N-(2-((4Z,7Z,10Z,13Z,16Z,19Z)-docosa-4,7,10,13,16,19-hexaenamido)ethyl)-2-hydroxybenzamide	Treatment of Duchenne muscular dystrophy	FGK Representative Service GmbH	3 September 2015	9 October 2015
Recombinant adeno-associated viral vector expressing the human *CNGA3* gene	Treatment of achromatopsia caused by mutations in the *CNGA3* gene	TMC Pharma Services Ltd	3 September 2015	9 October 2015
Recombinant human interleukin-3 truncated diphtheria toxin fusion protein	Treatment of acute myeloid leukaemia	Spector Consulting SAS	3 September 2015	9 October 2015
Sirolimus	Treatment of tuberous sclerosis	Desitin Arzneimittel GmbH	3 September 2015	9 October 2015
Three chimeric human/murine monoclonal antibodies against the Ebola (Zaire) surface glycoprotein	Treatment for Ebola virus disease	Dr Stefan Blesse	3 September 2015	9 October 2015

Annex 3

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

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Aceneuramic acid	Treatment of hereditary inclusion body myopathy (New adopted indication: treatment of GNE myopathy)	Ultragenyx UK Limited	EU/3/12/972
Daratumumab	Treatment of plasma cell myeloma	Janssen-Cilag International N.V.	EU/3/13/1153
Eryaspase	a) Treatment of acute lymphoblastic leukaemia b) Treatment of acute myeloid leukaemia	ERYTECH Pharma S.A.	EU/3/06/409 EU/3/13/1106