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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

November 2015

The Committee for Orphan Medicinal Products held its 172th plenary meeting on 10-12 November 2015.

Orphan medicinal product designation

Positive opinions

The COMP adopted 17 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:

- 2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propanediol hydrochloride for prevention of graft-versus-host disease, Novartis Europharm Limited;
- Combretastatin A1 diphosphate for treatment of acute myeloid leukaemia, Diamond BioPharm Limited.
- Recombinant human nerve growth factor for treatment of neurotrophic keratitis, Dompé farmaceutici S.p.A.;
- (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 for treatment of gastro-entero-pancreatic neuroendocrine tumours, Trio Medicines Ltd;
- Sirolimus for treatment of beta-thalassaemia intermedia and major, Rare Partners srl Impresa Sociale;
- Variant of recombinant human fibroblast growth factor 19 for treatment of primary sclerosing cholangitis, Diamond BioPharm Limited.

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2. Opinions adopted at the first COMP discussion:

- 2-(2-chlorobenzylidene)hydrazinecarboximidamide acetate for treatment of Charcot-Marie-Tooth disease, Inflectis Bioscience;
- [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) for treatment of pseudohypoaldosteronism type 1B, Apeptico Forschung und Entwicklung GmbH
- Adeno-associated viral vector serotype rh10 containing the human factor IX gene for treatment of haemophilia B, Pharma Gateway AB;
- Bilayer engineered collagen hydrogel-based skin graft composed of autologous keratinocytes and fibroblasts for treatment of partial deep dermal and full thickness burns, Voisin Consulting S.A.R.L.;
- Glibenclamide for treatment of neonatal diabetes, AMMTeK;
- Imetelstat sodium for treatment of myelofibrosis, Janssen-Cilag International N.V.;
- Live attenuated *Listeria monocytogenes* bioengineered with a chimeric human epidermal growth factor receptor 2 fused to a truncated form of the Lm protein listeriolysin O for treatment of osteosarcoma, Coté Orphan Consulting UK Limited;
- Live attenuated *Listeria monocytogenes* delta *actA*/delta *inlB* strain expressing human mesothelin for treatment of malignant mesothelioma, Medpace Germany GmbH;
- Recombinant human monoclonal IgG1 antibody against programmed death ligand-1 for treatment of Merkel cell carcinoma, Merck KGaA;
- 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 for treatment of acute myeloid leukaemia, Otsuka Pharmaceutical Europe Ltd;
- 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 for treatment of pseudohypoaldosteronism type 1B, Apeptico Forschung und Entwicklung GmbH.

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.

Lists of questions

The COMP adopted 12 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

13 oral hearings took place.

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

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 13 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.

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 173st meeting of the COMP will be held on 8-10 December 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[2] authorised	Orphan designations included in authorised therapeutic indication
2015	213	254	169 (67%)	84 (33%)	1 (1%)	175	11	13
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	**2340**	**2222**	**1599 (72%)**	**602 (27%)**	**21 (1%)**	**1581**	**111**	**120**

[2] 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 October 2015 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
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	Treatment of focal segmental glomerulosclerosis	Retrophin Europe Limited	8 October 2015	11 November 2015
(5S,8S,10aR)-N-benzhydryl-5-((S)-2-(methylamino)propanamido)-3-(3-methylbutanoyl)-6-oxodecahydropyrrolo[1,2-a][1,5]diazocine-8-carboxamide	Treatment of ovarian cancer	ASPHALION, SL	8 October 2015	11 November 2015
Adeno-associated viral vector serotype 8 encoding the human ATP7B gene under the control of the human alpha-1 antitrypsin promoter	Treatment of Wilson's disease	Aligen Therapeutics S.L.	8 October 2015	11 November 2015
Adenovirus associated viral vector serotype 5 containing the human RPE65 gene	Treatment of Leber's congenital amaurosis	Athena Vision Ltd	8 October 2015	11 November 2015
Adenovirus associated viral vector serotype 8 containing the human CNGB3 gene	Treatment of achromatopsia caused by mutations in the CNGB3 gene	Alan Boyd Consultants Ltd	8 October 2015	11 November 2015
Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor	Treatment of follicular lymphoma	Kite Pharma EU B.V	8 October 2015	11 November 2015
Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor	Treatment of acute lymphoblastic leukaemia	Kite Pharma UK, Ltd	8 October 2015	11 November 2015
Autologous T cells transduced with retroviral	Treatment of chronic lymphocytic	Kite Pharma UK, Ltd	8 October 2015	11 November 2015

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor	leukaemia / small lymphocytic lymphoma			
Azacitidine	Treatment of nasopharyngeal carcinoma	Celgene Europe Limited	8 October 2015	11 November 2015
Humanised fusion protein consisting of extracellular domain of CD24 linked to IgG1 Fc domain	Prevention of graft-versus-host disease	Enpharma Ltd	8 October 2015	11 November 2015
Humanised monoclonal antibody of the IgG4 kappa isotype targeting CD47	Treatment of acute myeloid leukaemia	The Chancellor, Masters and Scholars of the University of Oxford	8 October 2015	11 November 2015
Interferon alfa-n3	Treatment of Middle East respiratory syndrome	NV Hemipsherx BioPharma Europe	8 October 2015	11 November 2015
N-[5-(3,5-difluorobenzyl)-1H-indazol-3-yl]-4-(4 methylpiperazin-1-yl)-2-(tetrahydro-2H-pyran-4-ylamino)benzamide	Treatment of neuroblastoma	Pharma Gateway AB	8 October 2015	11 November 2015
Pentetrazol	Treatment of idiopathic hypersomnia	Dr Jens Steinbrink	8 October 2015	11 November 2015
Recombinant human interleukin-3 truncated diphtheria toxin fusion protein	Treatment of blastic plasmacytoid dendritic cell neoplasm	Spector Consulting SA	8 October 2015	11 November 2015
Sodium phenylbutyrate	Treatment of pyruvate dehydrogenase complex deficiency	Fondazione Telethon	8 October 2015	11 November 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 October 2015 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Chenodeoxycholic acid	Treatment of inborn errors of primary bile acid synthesis	Sigma-tau Arzneimittel GmbH	EU/3/14/1406
Elotuzumab	Treatment of multiple myeloma	Bristol-Myers Squibb Pharma EEIG	EU/3/12/1037
Gallium (68Ga)-edotreotide	Diagnosis of gastro-entero-pancreatic neuroendocrine tumours	Advanced Accelerator Applications	EU/3/15/1450
Murine monoclonal antibody against CD26	Treatment of graft-versus-host disease	ADIENNE S.r.l. S.U	EU/3/10/808
3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Treatment of cystic fibrosis	PTC Therapeutics International Limited	EU/3/05/277

Annex 4

COMP opinions on amendment of existing orphan drug designations since October 2015 COMP monthly report

Active substance	Initial orphan indication	Amended orphan indication	Sponsor/applicant	COMP opinion date	EC designation date
Sialic acid	Treatment of hereditary inclusion body myopathy	Treatment of GNE myopathy	Ultragenyx UK Limited	3 September 2015	16 October 2015