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Product Development Scientific Support

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

December 2013

The Committee for Orphan Medicinal Products held its 151st plenary meeting on 10-12 December 2013.

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 (EC):

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

- **(2*R*,3*R*,4*S*,5*R*)-2-(6-amino-9*H*-purin-9-yl)-5-((((1*r*,3*S*)-3-(2-(5-(*tert*-butyl)-1*H*-benzo[*d*]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl) amino)methyl)tetrahydrofuran-3,4-diol** for treatment of acute myeloid leukaemia; Voisin Consulting S.A.R.L.
- **(2*R*,3*R*,4*S*,5*R*)-2-(6-amino-9*H*-purin-9-yl)-5-((((1*r*,3*S*)-3-(2-(5-(*tert*-butyl)-1*H*-benzo[*d*]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl) amino)methyl)tetrahydrofuran-3,4-diol** for treatment of acute lymphoblastic leukaemia; Voisin Consulting S.A.R.L.
- **Adenovirus-specific T-cells derived from allogeneic donor leukocytes, expanded ex vivo** for treatment of adenovirus infection in allogeneic haematopoietic stem cell transplant recipients; Cell Medica Ltd.
- **Allantoin** for treatment of epidermolysis bullosa; ORS Oxford Ltd
- **Allogeneic bone-marrow derived adherent ex-vivo expanded multipotent adult progenitor cells** for prevention of graft-versus-host disease; ReGenesys BVBA
- **Autologous dendritic cells pulsed with allogeneic tumour cell lysate** for treatment of malignant mesothelioma; Amphera BV

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- **Inecalcitol** for treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma; Hybrigenics SA
- **Lonafarnib** for treatment of hepatitis delta virus infection; Eiger Biopharmaceuticals Europe Limited
- **Obeticholic acid** for treatment of primary sclerosing cholangitis; Intercept Italia S.R.L.
- **Sodium nitrite** for treatment of aneurysmal subarachnoid haemorrhage; Hope Pharmaceuticals Ltd.

2. Opinions adopted at the first COMP discussion:

- **(6aS)-1,10-dimethoxy-6-methyl-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinoline-2,9-diol** for treatment of dystrophic myotonia; Valentia BioPharma S.L.
- **Amatuximab** for treatment of malignant mesothelioma; Eisai Europe Limited
- **N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino)phenyl)acrylamide benzenesulfonic acid salt** for treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma; Celgene Europe Limited

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 10 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

12 oral hearings took place.

Appeal

The COMP noted the sponsor's letter of intention to appeal to a negative opinion for the following product:

- **5-Chloro-N2-[2-isopropoxy-5-methyl-4-(4-piperidinyl)phenyl]-N4-[2-(isopropylsulfonyl)phenyl]-2,4-pyrimidinediamine** for treatment of non-small cell lung carcinoma (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive; Novartis Europharm Limited

The negative opinion was adopted via written procedure on 18 November 2013 following the 5-6 November 2013 COMP meeting. Detailed grounds for appeal must be submitted within 90 days of receipt of the opinion.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 7 applications for orphan medicinal product designation were withdrawn.

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

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.

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 an opinion recommending to the European Commission that the following orphan medicinal product be kept in the EU registry of orphan medicinal product:

- **Cholic Acid FGK** for treatment of inborn errors of primary bile acid synthesis responsive to treatment with cholic acid; FGK Representative Service GmbH (EU/3/09/683).

Other matters

The main topics addressed during the meeting related to:

- 7 protocol assistance letters were adopted.

Upcoming meetings

- The 152nd meeting of the COMP will be held on 7-9 January 2014.

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
2013	201	195	136 (70%)	59 (29%)	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[3] (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[4] (3%)	49	4	4
2001	83	90	62[4] (70%)	27 (29%)	1 (1%)	64	3	3
2000	72	32	26 (81%)	6 (19%)	0 (0%)	14	0	0
Total	**1798**	**1707**	**1234 (72%)**	**456 (27%)**	**18 (1%)**	**1219**	**85**	**91**

[2] Number of authorised orphan medicinal products may cover more than one orphan designation
[3] Negative opinion adopted in 2009 was revised and finalised in 2010, therefore it is not included in 2009 listing
[4] Following a quality assurance exercise it was identified that this figure needed correction

Annex 2

Medicinal products granted a European Union designation as orphan medicinal product by the European Commission since the November 2013 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
(4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride	Treatment of primary biliary cirrhosis	Lumena Pharma UK Limited	6 November 2013	18 December 2013
(4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride	Treatment of Alagille syndrome	Lumena Pharma UK Limited	6 November 2013	18 December 2013
(4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride	Treatment of primary sclerosing cholangitis	Lumena Pharma UK Limited	6 November 2013	18 December 2013
(4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride	Treatment of progressive familial intrahepatic cholestasis	Lumena Pharma UK Limited	6 November 2013	18 December 2013

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Allogeneic and autologous haptenised and irradiated cells and cell lysates derived from glioma	Treatment of glioma	ERC Belgium	6 November 2013	18 December 2013
Autologous ex-vivo-expanded leucocytes treated with 5-aza-2'-deoxycytidine	Treatment of glioma	CytoVac A/S	10 October 2013	13 November 2013
Defibrotide	Prevention of graft-versus-host disease	Gentium S.p.A.	10 October 2013	13 November 2013
Fenfluramine hydrochloride	Treatment of Dravet syndrome	Brabant Pharma Limited	6 November 2013	18 December 2013
Human monoclonal antibody against human interleukin 13	Treatment of eosinophilic oesophagitis	Novartis Europharm Limited	10 October 2013	13 November 2013
Humanised monoclonal modified IgG4 antibody with bispecific structure targeting factors IX, IXa, X and Xa	Treatment of haemophilia A	Chugai Pharma Europe Ltd	6 November 2013	18 December 2013
Ibrutinib	Treatment of diffuse large B-cell lymphoma	Janssen-Cilag International N.V.	10 October 2013	13 November 2013
Ibrutinib	Treatment of follicular lymphoma	Janssen-Cilag International N.V.	6 November 2013	18 December 2013
Lactobacillus acidophilus* and *Bifidobacterium bifidum	Prevention of necrotising enterocolitis	Laboratorio Farmaceutico S.I.T. s.r.l.	6 November 2013	18 December 2013
Poly[2-[(4-{[1-carboxy-2-(hexadecylcarbamoyl)ethyl]sulfanyl}-2,3-bis({2-[((2S)-2-(2-{[(2R)-2-carbamoyl-(2-{[(2S)-1-ethoxy-3-(3-hydroxy-4oxo-1,4-dihydropyridin-1-	Treatment of dengue	Coté Orphan Consulting UK Limited	6 November 2013	18 December 2013

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
yl)-1-oxopropan-2-yl]carbamoyl}ethyl]sulfanyl}-3-{[(2S)-1-ethoxy-3-(3-hydroxy-4-oxo-1,4-dihydropyridin-1-yl)-1-oxopropan-2-yl]carbamoyl}propanamido)-3-(3-hydroxy-4-oxo-1,4-dihydropyridin-1-yl)propanoyl Ethyl ester))-methoxy]acetyl}oxy)butyl)sulfanyl]-3-(hexadecylcarbamoyl)propanoic acid]-poly(ethylene glycol)-ester]				
Recombinant human insulin receptor monoclonal antibody-fused iduronate 2-sulfatase	Treatment of mucopolysaccharidosis type II (Hunter's syndrome)	Voisin Consulting S.A.R.L.	10 October 2013	13 November 2013
Recombinant human parathyroid hormone	Treatment of hypoparathyroidism	NPS Phama UK Ltd.	6 November 2013	18 December 2013
Recombinant human type I pancreatic elastase	Prevention of arteriovenous access dysfunction in haemodialysis patients	Proteon Therapeutics Limited	6 November 2013	18 December 2013
Sirolimus	Prevention of arteriovenous access dysfunction in patients undergoing surgical creation of an arteriovenous access for haemodialysis	S-Cubed Limited	10 October 2013	13 November 2013
Sorafenib tosylate	Treatment of follicular thyroid cancer	Bayer HealthCare AG (Leverkusen)	10 October 2013	13 November 2013
Sorafenib tosylate	Treatment of papillary thyroid cancer	Bayer HealthCare AG (Leverkusen)	10 October 2013	13 November 2013
Soraprazan	Treatment of Stargardt's disease	Katairo GmbH	10 October 2013	13 November 2013

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Synthetic 12 amino acids peptide designed after subcommissural organ spondin	Treatment of spinal cord injury	Neuronax SAS	10 October 2013	13 November 2013
Tivantinib	Treatment of hepatocellular carcinoma	Daiichi Sankyo Development Ltd	10 October 2013	13 November 2013
Trebananib	Treatment of ovarian cancer	Amgen Europe BV	10 October 2013	13 November 2013

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 2013 COMP monthly report

Active substance	Invented name	Sponsor/applicant	EU designation number	Designated orphan indication
Ketoconazole	Ketoconazole AID-SCFM	Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare	EU/3/12/1031	Treatment of Cushing's syndrome