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Committee for Orphan Medicinal Products (COMP)

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

September 2014

The Committee for Orphan Medicinal Products held its 159th plenary meeting on 2-4 September 2014.

Orphan medicinal product designation

Positive opinions

The COMP adopted 19 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:

- (S)-2-(1-((6-amino-5-cyanopyrimidin-4-yl)amino)ethyl)-4-oxo-3-phenyl-3,4-dihydropyrrolo[2,1-f][1,2,4]triazine-5-carbonitrile for treatment of pemphigus; Almirall S.A.
- (S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride for treatment of Leigh syndrome; Khondrion BV
- Cannabidiol for treatment of Dravet syndrome; GW Pharma Ltd
- Cultured allogeneic corneal limbal stem cells for treatment of limbal stem cell deficiency; NHS National Services Scotland Trading as Scottish National Blood Transfusion Service
- Cysteamine hydrochloride for treatment of cystinosis; Lucane Pharma SA
- Immunoglobulin G1, anti-(human tumour-associated calcium signal transducer 2)(human-Mus musculus monoclonal hRS7 heavy chain), disulfide with human-Mus musculus monoclonal hRS7 κ-chain, dimer, hexakis(thioether) with (4S)-4-[[[[4-[[(2S)-2-(4-aminobutyl)-2-[[2-[2-[[26-[4-[[[[4-[(3-mercapto-2,5-dioxo-1-pyrrolidinyl)methyl]cyclohexyl]carbonyl]amino]methyl]-1H-1,2,3-triazol-1-yl]-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl]amino]-2-oxoethoxy]acetyl]amino]-1-oxoethyl]amino]phenyl]methoxy]carbonyl]oxy]-4,11-diethyl-9-hydroxy-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione for treatment of pancreatic cancer; Immunomedics GmbH

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- Osilodrostat for treatment of Cushing's syndrome; Novartis Europharm Limited
- *Oxalobacter formigenes* strain HC-1 for treatment of short bowel syndrome; OxThera AB
- Recombinant human monoclonal antibody of the IgG1 kappa class against human macrophage colony-stimulating factor for treatment of tenosynovial giant cell tumour, localised and diffused type; Novartis Europharm Limited

2. Opinions adopted at the first COMP discussion:

- (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one for treatment of fragile X syndrome; Centre National de la Recherche Scientifique (CNRS)
- Acamprosate calcium for treatment of fragile X syndrome; Real Regulatory Limited
- Adeno-associated viral vector serotype 8 containing the human *UGT1A1* gene for treatment of Crigler-Najjar syndrome; Généthon
- Glucagon for treatment of congenital hyperinsulinism; S-Cubed Limited
- Nitric oxide for treatment of cystic fibrosis; PD Dr.med. Joachim Riethmüller
- Pyridoxal 5'-phosphate for treatment of pyridoxamine 5'-phosphate oxidase deficiency; Great Ormond Street Hospital Foundation Trust
- Raxibacumab for treatment of inhalation anthrax disease; GlaxoSmithKline Trading Services Limited
- Recombinant human bone morphogenetic protein 4 for treatment of glioma; STEMGEN S.p.A
- Recombinant human insulin receptor monoclonal antibody-fused-α-L-iduronidase for treatment of mucopolysaccharidosis type I; Voisin Consulting S.A.R.L.
- Recombinant human monoclonal IgG1 antibody for fibroblast growth factor 23 for treatment of X-linked hypophosphataemia; NDA Group AB

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 18 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.

Withdrawals of applications for orphan medicinal product designation

The COMP noted that 5 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 2 opinions recommending to the European Commission that the following orphan medicinal product be kept in the EU registry of orphan medicinal product:

Imbruvica (1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H- pyrazolo [3,4-d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one); Janssen-Cilag International N.V.

a) for treatment of mantle cell lymphoma (EU/3/13/1115)

b) for treatment of chronic lymphocytic leukaemia (EU/3/12/984)

Other matters

The main topics addressed during the meeting related to:

- Protocol assistance advice

Upcoming meetings

- The 160th meeting of the COMP will be held on 7-9 October 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
2014	207	158	118 (75%)	39 (25%)	1 (1%)	112	10[5]	10[5]
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[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	**2005**	**1867**	**1352 (72%)**	**496 (27%)**	**19 (1%)**	**1331**	**95**	**101**

[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
[5] One product with two indications removed as it was not a new MA application

Annex 2

Medicinal products granted a European Union designation as orphan medicinal product by the European Commission since the July 2014 COMP monthly report

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
(3S)-1-azabicyclo[2.2.2]oct-3-yl{2-[2-(4-fluorophenyl)-1,3-thiazol-4-yl]propan-2-yl}carbamate	Treatment of Fabry disease	Genzyme Europe BV	10 July 2014	22 August 2014
(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide	Treatment of acute myeloid leukaemia	Clinipace GmbH	10 July 2014	22 August 2014
(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide	Treatment of diffuse large B-cell lymphoma	Clinipace GmbH	10 July 2014	22 August 2014
[5-amino-1-(4-fluoro-phenyl)-1H-pyrazol-4-yl]-[3-(2,3-dihydroxy-propoxy)-phenyl]-methanone	Treatment of pancreatic cancer	Synovo GmbH	21 July 2014	22 August 2014
17α,21-dihydroxy-16α-methyl-pregna-1,4,9(11)-triene-3,20-dione	Treatment of Duchenne muscular dystrophy	NDA Group AB	10 July 2014	22 August 2014
2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethylsulfamide	Treatment of small cell lung cancer	DualTpharma B.V.	10 July 2014	22 August 2014
4-{[(2R,3S,4R,5S)-4-(4-chloro-2-fluoro-phenyl)-3-(3-chloro-2-fluoro-phenyl)-4-cyano-5-(2,2-dimethyl-propyl)-pyrrolidine-2-carbonyl]-amino}-3-methoxy-benzoic acid	Treatment of acute myeloid leukaemia	Roche Registration Limited	10 July 2014	22 August 2014
Adeno-associated viral vector serotype 8 containing the human *UGT1A1* gene	Treatment of Crigler-Najjar syndrome	Fondazione Telethon	10 July 2014	22 August 2014
Adeno-associated viral vector serotype 9 containing the human cardiac calsequestrin	Treatment of catecholaminergic polymorphic ventricular	Fondazione Salvatore Maugeri Clinica del Lavoro e	27 June 2014	29 July 2014

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
gene	tachycardia	della Riabilitazione		
Carboxy pyrrolidine hexanoyl pyrrolidine carboxylate	Treatment of AL amyloidosis	GlaxoSmithKline Trading Services Limited	12 June 2014	29 July 2014
Cediranib	Treatment of ovarian cancer	AstraZeneca AB	12 June 2014	29 July 2014
Cysteamine bitartrate	Treatment of Huntington's disease	Raptor Pharmaceuticals Europe BV	12 June 2014	29 July 2014
Eculizumab	Treatment of myasthenia gravis	Alexion Europe SAS	12 June 2014	29 July 2014
Gevokizumab	Treatment of Schnitzler syndrome	Les Laboratoires Servier	10 July 2014	22 August 2014
Humanised anti-alpha v beta 6 monoclonal antibody	Treatment of idiopathic pulmonary fibrosis	Biogen Idec Limited	12 June 2014	29 July 2014
Humanised IgG1 monoclonal antibody against human KIR3DL2	Treatment of cutaneous T-cell lymphoma	Innate Pharma S.A.	10 July 2014	22 August 2014
Humanised recombinant monoclonal antibody against epidermal growth factor receptor conjugated to maleimidocaproyl monomethylauristatin F	Treatment of glioma	AbbVie Ltd	12 June 2014	29 July 2014
Lentiviral vector containing the human liver and erythroid pyruvate kinase (*PKLR*) gene	Treatment of pyruvate kinase deficiency	Centro de Investigación Biomédica en Red (CIBER)	10 July 2014	22 August 2014
Lumacaftor/ivacaftor	Treatment of cystic fibrosis	Vertex Pharmaceuticals (U.K.) Limited	10 July 2014	22 August 2014
Macromolecular conjugate of heparin sodium on a polymer backbone	Prevention of ischaemia reperfusion injury associated with solid organ transplantation	Corline Systems AB	10 July 2014	22 August 2014
Marizomib	Treatment of plasma cell myeloma	Richardson Associates Regulatory Affairs Ltd	12 June 2014	29 July 2014

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Obinutuzumab	Treatment of diffuse large B-cell lymphoma	Roche Registration Limited	10 July 2014	22 August 2014
Oxytocin	Treatment of Prader-Willi syndrome	Maïthé Tauber	12 June 2014	29 July 2014
Recombinant factor VIIa modified with three terminal repeats derived from the β chain of human chorionic gonadotropin	Treatment of congenital factor VII deficiency	Richardson Associates Regulatory Affairs Ltd	10 July 2014	22 August 2014
Recombinant factor VIIa modified with three terminal repeats derived from the β chain of human chorionic gonadotropin	Treatment of haemophilia A	Richardson Associates Regulatory Affairs Ltd	10 July 2014	22 August 2014
Recombinant factor VIIa modified with three terminal repeats derived from the β chain of human chorionic gonadotropin	Treatment of haemophilia B	Richardson Associates Regulatory Affairs Ltd	10 July 2014	22 August 2014
Recombinant fusion protein consisting of a modified form of the extracellular domain of human activin receptor IIB linked to the human IgG1 Fc domain	Treatment of beta-thalassaemia intermedia and major	IDEA Innovative Drug European Associates Limited	12 June 2014	29 July 2014
Recombinant fusion protein consisting of a modified form of the extracellular domain of human activin receptor IIB linked to the human IgG1 Fc domain	Treatment of myelodysplastic syndromes	IDEA Innovative Drug European Associates Limited	10 July 2014	22 August 2014
Recombinant human apolipoprotein A-I in a complex with phospholipids	Treatment of ATP-binding cassette transporter A1 deficiency	Cerenis Therapeutics Holding SA	21 July 2014	22 August 2014
Recombinant human apolipoprotein A-I in a complex with phospholipids	Treatment of apolipoprotein A-I deficiency	Cerenis Therapeutics Holding SA	10 July 2014	22 August 2014
Recombinant human diamine oxidase	Treatment of mastocytosis	Medical University of Vienna	10 July 2014	22 August 2014
Recombinant monoclonal antibody to human	Treatment of AL amyloidosis	GlaxoSmithKline Trading	12 June 2014	29 July 2014

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
serum amyloid P component		Services Limited		
Retinol	Prevention of bronchopulmonary dysplasia	Dr Philipp Heinrich Novak	10 July 2014	22 August 2014
Rilotumumab	Treatment of gastric cancer	Amgen Europe BV	12 June 2014	29 July 2014
Riociguat	Treatment of systemic sclerosis	Bayer Pharma AG	12 June 2014	29 July 2014
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)	Treatment of paroxysmal nocturnal haemoglobinuria	Amyndas Pharmaceuticals S.A.	10 July 2014	22 August 2014
Sodium acetate salt of the synthetic peptide H-D-Ala-Ser-Pro-Met-Leu-Val-Ala-Tyr-Asp-D-Ala-OH	Treatment for necrotising soft tissue infections	Dr Ulrich Granzer	12 June 2014	29 July 2014
Sodium ascorbate and menadione sodium bisulfite	Treatment of autosomal dominant polycystic liver disease	JJGConsultancy Ltd	10 July 2014	22 August 2014
Synthetic double-stranded siRNA oligonucleotide directed against antithrombin mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues	Treatment of haemophilia A	Alnylam UK Limited	12 June 2014	29 July 2014
Synthetic double-stranded siRNA oligonucleotide directed against antithrombin mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues	Treatment of haemophilia B	Alnylam UK Limited	12 June 2014	29 July 2014
Ulinastatin	Treatment of acute pancreatitis	BSV BioScience GmbH	10 July 2014	22 August 2014
Variant of recombinant human fibroblast growth factor 19	Treatment of primary biliary cirrhosis	Diamond BioPharm Limited	21 July 2014	22 August 2014

Active substance	Orphan indication	Sponsor	COMP opinion date	EC designation date
Vector based on an adeno-associated virus serotype 2 backbone, pseudo-serotyped with a type 8 capsid, which carries the coding sequence of the human *TYMP* gene under the control of the human thyroxine binding globulin promoter	Treatment of mitochondrial neurogastrointestinal encephalomyopathy	Vall d'Hebron Institute of Research	10 July 2014	22 August 2014

Annex 3

Designated orphan medicinal products that have been subject of a new European Union marketing authorisation application under the centralised procedure since the July 2014 COMP monthly report

Active substance	Designated orphan indication	Sponsor/applicant	EU designation number
Recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein (Asfotase alfa)	Treatment of hypophosphatasia	Alexion Europe SAS	EU/3/08/594
Recombinant porcine factor VIII (Susoctocog alfa)	Treatment of haemophilia A	Baxter AG	EU/3/10/784