European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

8 October 2008
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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS
OCTOBER 2008 PLENARY MEETING
MONTHLY REPORT

The Committee for Orphan Medicinal Products (COMP) held its ninety-forth plenary meeting on 6-7 October 2008. The Committee welcomed Dr Albert Cilia Vincenti as the new COMP member for Malta. The Committee also discussed the publication of the two guidelines from the European Commission concerning the application of Articles 8(1), (2) and (3) of Regulation (EC) No 141/2000 on orphan medicinal products.

ORPHAN MEDICINAL PRODUCT DESIGNATION

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

For the following medicines the EMEA review began on 11 July 2008 with an active review time of 90 days.

- **Palifosfamide,** from Ziopharm Oncology Limited, for treatment of soft tissue sarcoma.
- **Daunorubicin (liposomal)** from Diatos S.A., for treatment of acute myeloid leukaemia.

For the following medicines the EMEA review began on 8 August 2008 with an active review time of 62 days.

- **2-[[3-({4-[(5-{2-[(3-Fluorophenyl)amino]-2-oxoethyl}- 1H-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](ethyl)amino]ethyl dihydrogen phosphate trihydrate ,** from AstraZeneca AB, for treatment of acute myeloid leukaemia.
- **5-(ethylsulfonyl)-2-(naphthalen-2-yl)benzo[d]oxazole,** from Summit (Oxford) Limited, for treatment of Duchenne muscular dystrophy.
- **RNA, [P-deoxy-P-(dimethylamino)] (2',3'-dideoxy-2',3'-imino-2',3'-seco) (2'a→5') (C-m^{5}U-C-C-A-A-C-A-m^{5}U-C-A-A-G-G-A-A-G-A-m^{5}U-G-G-C-A-m^{5}U-m^{5}U-m^{5}U-C-m^{5}U-A-G), P-[4-[[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]carbonyl]-1-piperazinyl]-N,N-dimethylaminophosphonamidate,** from AVI BioPharma Inernational Ltd, for treatment of Duchenne muscular dystrophy.
- **Cenersen,** from EleosInc Limited, for treatment of chronic lymphocytic leukaemia.
- **Gadodiamide (liposomal),** from Dr Matthias Luz, for treatment of glioma.
- **Monoclonal antibody against human CD30 covalently linked to the cytotoxin monomethylauristatin E,** from Seattle Genetics UK, Limited, for treatment of anaplastic large cell lymphoma.
- **Monoclonal antibody against human CD30 covalently linked to the cytotoxin monomethylauristatin E,** from Seattle Genetics UK, Limited, for treatment of Hodgkin lymphoma.
- **Murine anti-CD22 antibody variable region fused to truncated Pseudomonas exotoxin 38,** from MedImmune Ltd, for treatment of hairy cell leukaemia.

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- **N2'-Deacetyl-N2'-[4-methyl-4-(oxobuthyldithio)-1-oxopentyl]-maytansine-chimerized anti-CD138 IgG4 monoclonal,** for Biotest AG, for treatment of multiple myeloma.
- **Recombinant human ADAMTS-13,** for Baxter AG, for treatment of thrombotic thrombocytopenic purpura.
- **Recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein,** from Europa Rx Limited, for treatment of hypophosphatasia.
- **Yttrium (^{90}Y) edotreotide,** from Molecular Insight Limited, for treatment of gastro-entero-pancreatic neuroendocrine tumours.

Public summaries of opinion will be available on the EMEA website which the Agency updates following adoption of the respective decisions on orphan designation by the European Commission.

OTHER INFORMATION ON THE ORPHAN MEDICINAL PRODUCT DESIGNATION

Lists of questions

The COMP adopted 8 lists of questions on initial applications. These applications will be discussed again at the next COMP plenary meeting prior to adoption of the opinion.

Oral hearing

One oral hearing took place.

Withdrawals of application for orphan medicinal product designation

The COMP noted that no application for orphan medicinal product designation was withdrawn.

Detailed information on the orphan designation procedure

An overview of orphan designation procedures since 2000 is provided in **Annex 1**.

The list of medicinal products for which decisions on orphan designation[1] have been given by the European Commission since the last COMP plenary 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 community marketing authorisation application through the centralised procedure since the last COMP plenary meeting are provided in **Annex 3**.

Details on the opinions for marketing authorisation for orphan medicinal products adopted by the Committee for Medicinal Products for Human Use (CHMP) can be found in the CHMP Monthly Report on the EMEA website.

Article 5 (12) 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 one opinion recommending to the European Commission that the following orphan medicinal product be kept in the Community registry of orphan medicinal prouducts:

- **Tetrahydrobiopterin,** from Merck KGaA, for treatment of hyperphenylalaninemia.

[1] Details of all orphan designations granted to date by the European Commission are entered in the Community Register of Orphan Medicinal Products (http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm)

UPCOMING MEETINGS FOLLOWING THE OCTOBER 2008 COMP PLENARY MEETING

- EPPOSI workshop will be held in Paris, France on the 16-17 October 2008
- The ninety-fifth meeting of the COMP will be held on 4-5 November 2008.

ORGANISATIONAL MATTERS

The main topics addressed during the October 2008 COMP meeting related to:

- Discussion on the revision on the draft Recommendation on the 'Elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation' (COMP/1527/03).
- Discussion on the published two guidelines from the European Commission concerning the application of Articles 8(1), (2) and (3) of Regulation (EC) No 141/2000 on orphan medicinal products. These relate to:

  - the possibility for Member States to inform the European Medicines Agency that the criteria on which market exclusivity was granted may no longer be met (potentially resulting in the market exclusivity period for the medicine concerned being shortened); and

  - assessment of the similarity of medicinal products, which is a requirement for accepting marketing authorisations when orphan medicinal products have been authorised for similar indications.

  The guidelines are available on the European Commission website as follows: Review of the period of market exclusivity of orphan medicinal products - C(2008) 4051 final Assessing similarity of medicinal products versus authorised medicinal products - C(2008) 4077 final
- Discussion on the EMEA strategy paper: Acceptance of clinical trials conducted in third countries, for evaluation in Marketing Authorisation Applications.
- One Protocol Assistance letter was adopted.

NOTE: This Monthly Report and other documents may be found on the internet at the following location: http://www.emea.europa.eu

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OVERVIEW FOR ORPHAN MEDICINAL PRODUCT DESIGNATION PROCEDURE SINCE 2000

Year	Applications submitted	Positive COMP Opinions	Applications withdrawn	Final negative COMP Opinions	Designations granted by Commission
2008	88	70	22	-	49
2007	125	97	19	1	98
2006	104	81	20	2	80
2005	118	88	30	0	88
2004	108	75	22	4	72
2003	87	54	41	1	55
2002	80	43	30	3	49
2001	83	64	27	1	64
2000	72	26	6	0	14

MEDICINAL PRODUCTS GRANTED A COMMUNITY DESIGNATION AS ORPHAN MEDICINAL PRODUCT SINCE THE SEPTEMBER 2008 COMP PLENARY REPORT BY THE EUROPEAN COMMISSION

Active substance	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate
Sponsor	KeyNeurotek Pharmaceuticals AG
Orphan Indication	Treatment of moderate and severe closed traumatic brain injury
COMP Opinion date	11/06/2008
Orphan Designation date	05/09/2008

Active substance	Avian polyclonal IgY antibody against Pseudomonas aeruginosa
Sponsor	Immunsystem I.M.S. AB
Orphan Indication	Treatment of cystic fibrosis
COMP Opinion date	09/07/2008
Orphan Designation date	23/09/2008

Active substance	Bosentan
Sponsor	Actelion Registration Limited
Orphan Indication	Treatment of idiopathic pulmonary fibrosis
COMP Opinion date	11/06/2008
Orphan Designation date	05/09/2008

Active substance	Donor lymphocyte preparation depleted of functional alloreactive T-cells
Sponsor	Kiadis Pharma Netherlands B.V
Orphan Indication	Prevention of Graft-versus-Host Disease
COMP Opinion date	11/06/2008
Orphan Designation date	05/09/2008

Active substance	Levofloxacin hemihydrate
Sponsor	Mpex London Ltd
Orphan Indication	Treatment of cystic fibrosis
COMP Opinion date	09/07/2008
Orphan Designation date	23/09/2008

Active substance	Miltefosine
Sponsor	ExperGen Drug Development GmbH

Orphan Indication	Treatment of cutaneous T-cell lymphoma
COMP Opinion date	09/07/2008
Orphan Designation date	22/09/2008

Active substance	Pegylated L-asparaginase
Sponsor	Enzon (UK) Limited
Orphan Indication	Treatment of acute lymphoblastic leukaemia
COMP Opinion date	09/07/2008
Orphan Designation date	22/09/2008

Active substance	Recombinant derivative of C3 transferase
Sponsor	Triskel EU Services
Orphan Indication	Treatment of traumatic spinal cord injury
COMP Opinion date	11/06/2008
Orphan Designation date	05/09/2008

Active substance	Recombinant human CXCL8 mutant
Sponsor	ProtAffin Biotechnologie AG
Orphan Indication	Prevention of delayed graft function after solid organ transplantation
COMP Opinion date	09/07/2008
Orphan Designation date	22/09/2008

Active substance	Recombinant human minibody against complement component C5
Sponsor	Adienne S.r.l
Orphan Indication	Treatment of atypical Haemolytic Uraemic Syndrome (aHUS) associated with an inherited abnormality of the complement system
COMP Opinion date	09/07/2008
Orphan Designation date	22/09/2008

Active substance	Topotecan hydrochloride (liposomal)
Sponsor	Dr Matthias Luz
Orphan Indication	Treatment of glioma
COMP Opinion date	11/06/2008
Orphan Designation date	05/09/2008

Active substance	N'-(5-chloro-2-hydroxy-3-methylbenzylidene)-2,4-dihydroxybenzhydrazide
Sponsor	Innate Pharmaceuticals AB

Orphan Indication	Treatment of partial deep dermal and full thickness burn wounds
COMP Opinion date	09/07/2008
Orphan Designation date	22/09/2008

DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN SUBJECT OF A NEW COMMUNITY MARKETING AUTHORISATION APPLICATION UNDER THE CENTRALISED PROCEDURE SINCE THE SEPTEMBER 2008 COMP MONTHLY REPORT

Active substance	Invented name	Sponsor/applicant	EU Designation Number	Designated Orphan Indication
Mepolizumab	Bosatria	Glaxo Group Limited UK	EU/3/04/213	Treatment of hypereosinophilic syndrome
Temsirolimus	Torisel	Wyeth Europa Ltd.	EU/3/06/420	Treatment of mantle cell lymphoma