The European Agency for the Evaluation of Medicinal Products
Pre-authorisation Evaluation of Medicines for Human Use

17 March 2004
EMEA/COMP/134/04

PRESS RELEASE
Committee for Orphan Medicinal Products
March 2004 Meeting

The forty-fourth meeting of the Committee for Orphan Medicinal Products (COMP) took place on 16 March 2004.

On 8 March 2004 the Committee adopted two positive opinions via written procedure for the following conditions:

- Anaplastic thyroid cancer
- Atopic keratoconjunctivitis

Two positive opinions on the designation of orphan medicinal products were adopted by the Committee during this meeting, for the following conditions:

- Cutaneous T-cell lymphoma
- Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

One oral explanation took place during the meeting. The COMP noted that four applications for orphan medicinal product designation were withdrawn by sponsors.

The European Commission granted nine positive decisions on orphan designation[1] since the last COMP meeting on 4-5 February 2004 (see Annex 1). One negative decision on orphan medicinal product designation was also adopted by the European Commission on 1 March 2004. The grounds for the negative decision were based on the prevalence criterion. The sponsor had not established that the condition that was the subject of the designation application concerned, seizures which continue for at least five minutes, affected not more than 5 in 10,000 persons in the Community at the time the application was made and thus the designation criteria were not met.

The status of orphan designation procedures, to date for 2004, is summarised below:

Applications submitted	*Positive COMP Opinions*	*Applications withdrawn*	*Appeals ongoing*	*Final negative COMP Opinions*	*Designations granted by Commission*
20	13	6	-	-	12

An overview of orphan designation procedures for 2000-2003 is provided in Annex 2.

Further information on designated orphan medicinal products is publicly available in the form of summarised COMP Opinions[2], which the Agency routinely publishes following adoption of the respective decisions on orphan designation by the European Commission.

Dr. Kalle Hoppu (COMP member representing Finland) reported on the outcome of the meeting of Ad-hoc Experts on Prevalence, which was held at the EMEA on 25 February 2004. A report from this Workshop is provided in Annex 3.

The next COMP meeting will be held on 14 April 2004. A training session for new COMP members nominated from the accession countries will be held on 13 April 2004.

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[1] Details of all orphan designations granted to date by the European Commission are entered in the Community Register of Orphan Medicinal Products (http://pharmacos.eudra.org/F2/register/index.htm)

[2] These documents are available on the EMEA web-site.

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NOTE: This Press Release, together with other information about the work of the EMEA, may be found on the internet at the following location: http://www.emea.eu.int/

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Medicinal products Designated as Orphan Medicinal Products since the February 2004 COMP Meeting

Active substance	Treosulfan
Sponsor	Medac Gesellschaft für klinische Spezialpräparate mbH
Orphan Indication	Conditioning treatment prior to haematopoietic progenitor cell transplantation.
Opinion receipt date	21/1/2004
Date of Commission Decision	23/2/2004

Active substance	N-3[[4(aminoiminomethyl)benzoyl] amino]propyl]-1-[[2,4-dichloro-3-[[2,4-dimethyl-8-quinolinyl)oxy]methyl] phenyl]sulphonyl]-(2S)-2-pyrrolidinecarboxamide, di(methanesulfonate)
Sponsor	Laboratoires Fournier
Orphan Indication	Treatment of moderate and severe traumatic brain injury
Opinion receipt date	21/1/2004
Date of Commission Decision	23/2/2004

Active substance	Human monoclonal hepatitis B immunoglobulins
Sponsor	ICON Clinical Research (UK) Ltd.
Orphan Indication	Prevention of hepatitis B re-infection following liver transplantation.
Opinion receipt date	21/1/2004
Date of Commission Decision	23/2/2004

Active substance	3-(4´aminoisoindoline-1´-one)-1-piperidine-2,6-dione
Sponsor	Gregory Fryer Associates Limited
Orphan Indication	Treatment of myelodysplastic syndromes
Opinion receipt date	11/2/2004
Date of Commission Decision	8/3/2004

Active substance	Ethanol (96 per cent) (gel for injection)
Sponsor	Orfagen
Orphan Indication	Treatment of congenital venous malformations
Opinion receipt date	11/2/2004
Date of Commission Decision	8/3/2004

Active substance	Ethanol (96 per cent) (gel for injection)
Sponsor	Orfagen
Orphan Indication	Treatment of congenital lymphatic malformations
Opinion receipt date	11/2/2004
Date of Commission Decision	8/3/2004

Active substance	Adeno-associated viral vector expressing lipoprotein lipase
Sponsor	Mr. Aart Brouwer
Orphan Indication	Treatment of lipoprotein lipase deficiency
Opinion receipt date	11/2/2004
Date of Commission Decision	8/3/2004

Active substance	Idebenone
Sponsor	Promedipharm GmbH
Orphan Indication	Treatment of Friedreich's ataxia
Opinion receipt date	11/2/2004
Date of Commission Decision	8/3/2004

Active substance	Anti-epithelial cell adhesion molecule / anti-CD3 monoclonal antibody
Sponsor	Fresenius Biotech GmbH
Orphan Indication	Treatment of ovarian cancer
Opinion receipt date	11/2/2004
Date of Commission Decision	8/3/2004

Overview of Procedures for Orphan Medicinal Product Designation for 2000-2003

Year	*Applications submitted*	*Positive COMP Opinions*	*Applications withdrawn*	*Final negative COMP Opinions*	*Designations granted by Commission*
2003	87	54	35	1	55
2002	80	43	24	3	49
2001	83	64	25	1	64
2000	72	26	3	0	14

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Report from Meeting of Ad-hoc Experts on Prevalence held on 25 February 2004

In March 2002, the EMEA published a Points to Consider document on the Calculation and Reporting of the Prevalence of a Condition for Orphan Designation (COMP/436/01). Since almost two years have passed since the adoption of this guidance document by the Committee for Orphan Medicinal Products (COMP), the ad-hoc prevalence expert group involved in its drafting was reconvened to (i) review the document in light of experience and (ii) discuss specific issues that have arisen related to prevalence.

On 25 February 2004, prevalence experts met at the EMEA (see Annex 1 for list of participants). The meeting, which took the form of a Workshop on the determination of the prevalence of rare diseases, was co-chaired by Dr. Kalle Hoppu (COMP) and Dr. Agnès Saint Raymond (EMEA). Topics addressed during the meeting included: a review of COMP statistics, a presentation of case studies, and discussion of specific problems encountered in estimating the prevalence of conditions which are the subject of applications for orphan designation.

Dr. C. Debruyne (EMEA) updated the group on the work of the COMP. Since EU Legislation[3] on orphan medicinal products was implemented in 2000, 327 applications for orphan designation based on the prevalence criterion (i.e. that the condition affects not more than 5 in 10,000 persons in the Community) and 1 application based on the insufficient return on investment criterion have been filed in the European Union.

Dr. F. Pignatti (EMEA) highlighted the type of problems that have been encountered by COMP in reviewing the prevalence of conditions that are the subject of applications for orphan medicinal product designation. The importance of basing the prevalence calculation on a condition that is medically plausible was underlined. It was noted that problems encountered by sponsors in demonstrating medical plausibility and determining prevalence account for more than half of the withdrawn applications.

Specific issues that have arisen with prevalence estimates in applications for orphan medicinal product designation were illustrated in presentations of six individual case studies made by Dr. Antoniu, Dr. Llinares-Garcia, and Dr. Pignatti (EMEA). The particular issues addressed included: extrapolation of data, the use of weights when pooling data, the use of surrogate data, the handling of geographical differences in prevalence, borderline cases where the prevalence approaches the limit of 5 in 10,000, and how the concept of conditions being 'cured' should be handled in the prevalence calculation. The group also discussed a number of general issues related to prevalence estimates, including confidence intervals and the use of 'worst case' scenarios when estimating the point prevalence.

It was concluded that the following proposals will be taken forward by the EMEA for further consideration:

- revision of the COMP Prevalence Points to Consider document to include new elements such as the use of quality scores when pooling data, and the extrapolation of data to the entire Community;
- preparation of an article reviewing experience to date in estimating the prevalence of conditions, which are the subject of applications for orphan designation, with examples to illustrate particular issues;
- preparation of guidance for sponsors on issues to consider when determining the 'medical plausibility' of conditions which are the subject of applications for orphan medicinal product designation;
- liason with the European Commission DG Research and DG SANCO to highlight the need to support epidemiological research into rare diseases.

[3] Regulation (EC) No 141/2000 adopted of 16 December 1999 and Commission Regulation (EC) No 847/2000 of 27 April 2000

Annex

Meeting of Ad-hoc Experts on Prevalence held on 25 February 2004

List of attendees

Co-Chairpersons:
Dr Kalle Hoppu, COMP
Dr Agnès Saint-Raymond, EMEA

Experts and COMP members:
Prof. Gianmartino Benzi, COMP member
Dr. Fabrizio Bianchi, Epidemiology Unit, Consiglio Nazionale delle Ricerche (CNR), Italy
Prof Jørn Olsen, Danish Epidemiology Science Centre, University of Aarhus, Denmark
Dr Manuel Posada de la Paz, Rare Diseases Research Institute, Spain
Dr Domenica Taruscio, COMP member

Apologies:
Dr Paolo Bruzzi, Centro Biotecnologie Avanzate, Italy

EMEA:
Dr. Sabina Antoniu, EMEA
Dr Francesco Pignatti, EMEA
Dr. Channa Debruyne, EMEA
Dr. Jordi Llinares Garcia, EMEA
Ms Melanie Carr, EMEA
Dr. Eric Pelfrene, EMEA
Dr. Bettina Klug, EMEA
Ms. Dominique Doan Tran, EMEA
Mr. Henry Fitt, EMEA
Dr. Francois Maignen, EMEA