European Medicines Agency
Evaluation of Medicines for Human Use

28 September 2004
EMEA/CHMP/269/2004

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
13-16 SEPTEMBER 2004 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its 4th plenary meeting from 13-16 September 2004.

Centralised procedures

The Committee adopted three positive opinions on initial marketing authorisation applications for:

- **Cymbalta** (duloxetine hydrochloride), from Eli Lilly Netherlands B.V., and **Xeristar** (duloxetine hydrochloride), from Boehringer-Ingelheim International GmbH, for treatment of major depressive episodes. EMEA review began on 23 October 2003, with an active review time of 210 days.
- **Kivexa** (abacavir/lamivudine), from Glaxo Group Limited, for the use in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection in adults and adolescents from 12 years of age. Kivexa is a fixed dose combination of two antiretroviral agents (abacavir and lamivudine) to be administered once a day. EMEA review began on 22 December 2003, with an active review time of 197 days.

Summaries of these opinions, including the full indications for each product, are available on the EMEA web site: http://www.emea.eu.int

The Committee adopted two positive opinions on the extension of indication for medicinal products that are already authorised in the EU:

- **Pegasys** (peginterferon alfa-2a), Roche Registration Ltd, to extend its use in combination with ribavirin for the treatment of adult patients with chronic hepatitis C and persistently normal alanine aminotransferase (ALT) levels. Pegasys was first authorised in the European Union on 20 June 2002.
- **Taxotere** (docetaxel), Aventis, to extend its use in combination with prednisone or prednisolone for the treatment of patients with hormone refractory metastatic prostate cancer. Taxotere was first authorised in the European Union on 27 November 1995.

Further information on these extensions will be included in the European Public Assessment Report (EPAR) once the European Commission has granted final approvals.

The Committee also adopted five Lists of Questions on initial applications.

An overview of centralised procedures since 1995 is given in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CHMP plenary meeting in July 2004 is provided in **Annex 2**. The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

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Referrals

The CHMP initiated a Community-wide review for **Rigevidon** (levonorgestrel and ethinylestradiol) from Gedeon Richter Ltd. This referral was made by the Netherlands under Article 29(2) of the Community Code on human medicines and relates to potential safety and efficacy concerns. A Rapporteur and a Co-Rapporteur were appointed and the review procedure has started.

CHMP Working Parties

The CHMP adopted the outcome of the discussions of the Scientific Advice Working Party (SAWP) meeting, which was held on 6-7 September 2004. For further details, please see **Annex 4**.

Invented Name Review Group

A joint EMEA/Interested Parties meeting, attended by representatives of AESGP, EFPIA, EGA, the European Commission, NRG members and the EMEA, took place on 13 September 2004. An update on the activities of the NRG since the last joint meeting in 2003 was presented. A detailed meeting report will be published on the EMEA website next month.

The CHMP adopted revision 4 of the 'Guideline on the Acceptability of invented names for human medicinal products processed through the centralised procedure (CPMP/328/98, Revision 4, available on the EMEA website: http://www.emea.eu.int/pdfs/human/regaffair/032898r4en.pdf.) . This revised guideline has been released for a 3-month consultation (See **Annex 5**). Comments should be sent to NRG@emea.eu.int by 6 December 2004.

Organisational Matters

The main topics addressed during the September 2004 CHMP meeting related to:

- A discussion on CHMP Working Parties mandates in the framework of Regulation (EC) No 726/2004 (see procedural announcements).
- A discussion on the draft European Regulation (EC) on conditional marketing authorisation for medicinal products falling within the scope of Regulation (EC) No 726/2004.
- The adoption of a procedure for the designation of (Co-)Rapporteurs for referral procedures.
- The presentation of the extension of the EMEA Post-Authorisation Guidance. The new guidance documents will be published for public consultation shortly after their adoption by the CHMP by written procedure in October.

Upcoming meetings following the September 2004 CHMP plenary meeting:

- The 5th meeting of the CHMP will be held on 18-21 October 2004.
- The next NRG meeting will be held on 18 October 2004.

PROCEDURAL ANNOUNCEMENTS

- **Publication of information related to designated Orphan Medicinal Products which have been the subject of a Centralised Application for Marketing Authorisation**

Three designated Orphan Medicinal Products have been the subject of a Centralised Application for Marketing Authorisation submitted since July 2003. As announced in the June 2004 CHMP Monthly Report and in accordance with a recommendation contained within the 'Commission Communication 2003/C 178/02 on Regulation (EC) No 141/2000, the active substance of those medicinal products, the applicant and the designated orphan indication are made available for the first time in **Annex 6.** This information is also published in the Press Release of the Committee for Orphan Medicinal Products (http://www.emea.eu.int/pdfs/human/comp/6539604en.pdf).

- **New mandate for the Scientific Advice Working Party (SAWP)**

The CHMP adopted at its September meeting a revised Mandate and Rules of procedures for the Scientific Advice Working Party (SAWP). A copy of this document will be published on the EMEA website by the end of September 2004. The composition of the new SAWP will be adopted at the October CHMP meeting.

The new mandate will apply to new requests for scientific advice or protocol assistance starting at the October SAWP meeting (11-13 October 2004).

Mutual Recognition procedure

The CHMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 13 September 2004. For further details, please see **Annex 7.**

Noël Wathion
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This CHMP Monthly Report and other documents are available on the Internet at the following address:
http://www.emea.eu.int

EMEA CENTRALISED PROCEDURES

	1995 - 2003	2004	Overall Total
Scientific Advice	367	46*	413
Follow-up to Scientific Advice	60	3	63
Protocol Assistance	30	19	49
Follow-up to Protocol Assistance	9	2	11

*Including two SA adopted via a written procedure in August

	1995-2003			2004			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	134	271	405	14	19	33	438
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	22	55	77	0	7	7	84
Positive opinions[2]	99	172	271	5	19	24	295[3]
Negative opinions[4]	2	5	7	0	0	0	7[5]
Marketing authorisations granted by the Commission	91	164	255	5	17	22	277[6]

	1995-2003			2004			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	771	1505	2276	47	320	367	2643
Positive opinions, variations type II	583	697	1280	129	100	229	1509
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	49	56	105	4	5	9	114

[1] Consultation in accordance with Council Directive 93/42/EEC concerning medical devices as amended by Directive 2000/70/EC as regards medical devices incorporating stable derivatives of human blood or plasma and Directive 2001/104/EC.
[2] 17 positive opinion corresponding to 17 Orphan Medicinal Products
[3] 295 positive opinions corresponding to 226 substances
[4] In case of appeal, the opinion will not be counted twice
[5] 7 negative opinions corresponding to 6 substances (2 of these negative opinions correspond to 2 Orphan Medicinal Products)
[6] 277 marketing authorisations corresponding to 211 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE JULY 2004 CHMP MONTHLY REPORT

Invented Name	Yentreve
INN	Duloxetine
Marketing Authorisation Holder	Eli Lilly Netherlands B.V
ATC code	Not yet assigned
Indication	YENTREVE is indicated for women for the treatment of moderate to severe Stress Urinary Incontinence (SUI
CPMP Opinion date	23 June 2004

Invented Name	Ariclaim
INN	Duloxetine
Marketing Authorisation Holder	Boehringer Ingelheim International GmbH
ATC code	Not yet assigned
Indication	YENTREVE is indicated for women for the treatment of moderate to severe Stress Urinary Incontinence (SUI
CPMP Opinion date	23 June 2004

OUTCOME OF THE SEPTEMBER 2004 CHMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
2 Extensions of indication	2 Positive opinions
19 SPC changes	19 Positive opinions
25 Quality changes	25 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Cystagon (mercaptamine) Orphan Europe SARL	Positive Opinion	The Marketing Authorisation will remain under exceptional circumstances
MabCampath (alemtuzumab) ILEX Pharmaceuticals Ltd	Positive Opinion	The Marketing Authorisation will remain under exceptional circumstances
Tracleer (bosentan) Actelion Registration Ltd	Positive Opinion	There were no remaining grounds to keep the Marketing Authorisation under exceptional circumstances

Opinions for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	---	---

OUTCOME OF THE SEPTEMBER 2004 CHMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Hepatocellular carcinoma*	X						X	
Chemical	Asthma*	X					X		
Chemical	Prostate cancer	X				X	X	X	
Chemical	Angioedema		X			X			
Chemical	Osteoarthritis and rheumatoid arthritis	X					X		
Chemical	Hypertension	X						X	
Chemical	Chronic myelogenous leukaemia		X					X	
Chemical	Breast cancer	X						X	
Chemical	Psoriasis	X						X	

* Adopted via a written procedure in August

SA: Scientific Advice

PA: Protocol Assistance

The above-mentioned 5 Scientific Advice letters and 2 Protocol Assistance letters were adopted at the 13-16 September 2004 CHMP meeting. 2 Scientific Advice letters* were adopted via a written procedure in August 2004.

In August 2004, the Committee accepted 4 Initial Scientific Advice Requests, 1 Follow-up Scientific Advice Requests and 2 Initial Protocol Assistance Requests.

In September 2004, the Committee accepted 6 Initial Scientific Advice Requests, 5 Follow-up Scientific Advice Requests and 3 Initial Protocol Assistance Requests.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE SEPTEMBER 2004 CHMP MEETING

INVENTED NAME REVIEW GROUP

Reference number	Document	Status
CPMP/328/98, Revision 4	Guideline on the Acceptability of invented names for human medicinal products processed through the centralised procedure.	Adopted. Released for 3 month consultation

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION SUBMITTED SINCE JULY 2003

Active substance	***Sponsor/applicant***	***EU Designation Number & Date of Orphan Designation***	***Designated Orphan Indication***
Autologous renal cell tumor vaccine (Reniale)	Liponova GmbH	EU/3/02/116 21/10/2002	Treatment of renal cell carcinoma
Rubitecan (Orathecin)	EuroGen Pharmaceuticals Limited	EU/3/03/145 10/06/2003	Treatment of pancreatic cancer
Sodium oxybate (Xyrem)	Celltech Pharmaceuticals Limited	EU/3/02/131 03/02/2003	Treatment of narcolepsy

Report from the meeting held on 13 September 2004

General Issues

Best Practice Guide on Cooperation between Mutual Recognition Facilitating Group and Pharmacovigilance Working Party

The above-mentioned document has been adopted at the Heads of Agencies meeting on 8 September 2004 and will be published on the website.

MRFG Best Practice Guides on Break-out sessions

An updated version of the document, to take account of the new assessment timescales for variations, has been adopted by the group and will be published on the website.

The Mutual Recognition Co-ordination Groups

The framework document for the Co-ordination Groups (Human and Veterinary) has been adopted at the Heads of Agencies meeting on 8 September 2004 and will be published on the Heads of Agencies website (http://heads.medagencies.org/).

Informal MRFG Meeting

An informal MRFG Meeting will be held in Scheveningen (NL) on 4-5 October 2004. It will be focused on the improvement of the current Mutual Recognition Procedure, preparation for the new Decentralised procedure and other requirements of the new pharmaceutical legislation. Questions in relation to pending applications in Member States after accession on 1 May 2004 will also be on the Agenda.

Implementation of the Commission Decision after a referral procedure

The SPC of the recently finalised referral for gemfibrozil has been published on the EMEA website (www.emea.eu.int/htms/human/referral/referral.htm).

Meeting schedule

The next MRFG meeting will be held on 18 October 2004.

Mutual Recognition Monitoring

The MRFG noted that **115** new mutual recognition procedures were finalised during the months of July and August 2004, as well as **620** type IA variations, **334** type IB variations and **187** type II variations.
1 arbitration from a New Application has been referred to CHMP in this period.

The status as of 31st of August of procedures under mutual recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures from Type IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CHMP
2004	458	215	2069	1328	706	2 N.A

119 new procedures (regarding **256** products) started in July and August 2004. The categories of these procedures are as follows:

7 new active substances (first authorisation in the European Community after RMS approval), including **1** multiple application and **3** repeat use.

18 known active substances (already authorised in at least one member state), including **6** repeat use.

83 abridged applications including **35** multiple applications and **6** repeat use.

11 line extension applications, including **1** repeat use.

The new procedures started related to **20** full dossiers, **70** generics, **7** bibliographic applications, **3** informed consent applications, **8** fixed combinations and **11** for different use, route or dose.

The procedures consisted of **114** chemical substances, **3** biological-vaccines, **1** biological-blood product and **1** biological-other[1].

117 of these procedures were prescription-only medicinal products in the reference Member State and **2** procedures were classified as a Non-prescription (including OTC) medicinal product[2].

1. As considered by RMS.
2. In this category products are classified as prescription-only or Non-prescription (OTC) products when the RMS has approved them accordingly, although the legal status is not part of the Mutual Recognition Procedure.

Number of countries involved in the new applications procedures started in July and August 2004

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (2)	1
BE (2)	1
BE (2)	1
BE (2)	10
BE (2)	1
BE (2)	1
DE (1)	13
DE (2)	10
DE (1)	2
DE (1)	2
DE (1)	1
DE (1)	4
DE (1)	5
DE (1)	20
DE (2)	4

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (2)	11
DE (4)	16
DE (4)	1
DE (4)	1
DE (4)	16
DK (1)	5
DK (1)	1
DK (2)	1
DK (2)	1
DK (1)	5
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (3)	3
DK (3)	1
DK (1)	1
DK (3)	1
DK (3)	1
DK (1)	2
DK (2)	1
DK (2)	1
ES (1)	15
FI (1)	13
FI (1)	1
FI (1)	1
FI (2)	1
FI (2)	1
FR (2)	1
FR (1)	1
FR (3)	2
FR (2)	2
FR (5)	17
FR (5)	13
NL (4)	13
NL (1)	1
NL (1)	6
NL (1)	1
NL (3)	7
NL (1)	9
NL (4)	9
NL (2)	1
NL (2)	2
NL (3)	6
NL (3)	4
NL (3)	6
NL (2)	2
NL (2)	1
NL (2)	1
NL (2)	1
NL (4)	2
NO (1)	4
SE (5)	2
SE (4)	3
SE (1)	12
SE (1)	2
SE (2)	17
SE (4)	2
SE (3)	8
SE (3)	5
SE (3)	3
SE (3)	3
SE (3)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
SE (3)	1
SE (3)	1
SE (3)	1
SE (3)	1
SE (3)	1
SE (3)	1
SE (3)	1
SE (2)	1
SE (2)	1
UK (1)	1
UK (1)	16
UK (1)	15
UK (2)	10
UK (1)	4
UK (3)	4
UK (2)	2
UK (1)	1
UK (1)	1
UK (2)	7
UK (2)	7
UK (1)	9
UK (1)	16
UK (1)	16
UK (1)	17
UK (1)	24
UK (4)	1
UK (1)	15
UK (4)	3
UK (4)	1
UK (3)	8
UK (1)	4
UK (1)	14
UK (1)	7
UK (6)	3
UK (3)	7
UK (3)	1
UK (2)	1
UK (1)	1
UK (1)	1
UK (1)	1
UK (1)	1

All documents mentioned in this press release can be found at the MRFG website at the European Medicines Authorities Windows under the heading MRFG Guidance.

Information on the above mentioned issues can be obtained from the presiding chair of the MRFG:

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