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

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EMEA/CPMP/1238/04

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
MARCH 2004 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 102nd plenary meeting from 23-24 March 2004.

Product related issues

Centralised procedures

The CPMP adopted five opinions on initial marketing authorisation applications at this meeting:

- A positive opinion on the marketing authorisation for **Erbitux** (cetuximab), from Merck KGaA, for the treatment of metastatic colorectal cancer. EMEA review began on 21 July 2003 and the opinion was adopted on 24 March 2004, with an active review time of 201 days.
- A positive opinion on the marketing authorisation for **Lyrica** (pregabalin), from Pfizer Ltd, for the treatment of neuropathic pain and epilepsy. EMEA review began on 24 March 2003 and the opinion was adopted on 24 March 2004, with an active review time of 200 days.
- A positive opinion on the marketing authorisation for **Telzir** (fosamprenavir), from Glaxo Group Limited, intended for the treatment, with low dose of ritonavir, of human immunodeficiency virus type 1 (HIV-1) infected adults in combination with other antiretroviral medicinal products. EMEA review began on 20 January 2003 and the opinion was adopted on 24 March 2004, with an active review time of 201 days.
- A positive opinion on the marketing authorisation for **Yentreve** (duloxetine), from Eli Lilly Netherlands B.V., for the treatment of stress urinary incontinence. EMEA review began on 24 February 2003 and the opinion was adopted on 24 March 2004, with an active review time of 178 days.
- A positive opinion on the marketing authorisation for **Ariclaim** (duloxetine), from Boehringer Ingelheim International GmbH, for the treatment of stress urinary incontinence. EMEA review began on 23 June 2003 and the opinion was adopted on 24 March 2004, with an active review time of 60 days.

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

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The Committee also gave positive opinions on the extension of indication for two medicinal products that are already authorized in the EU:

- **Arava** (leflunomide), Aventis Pharma Deutschland GmbH, to extend its use for the treatment of adult patients with active psoriatic arthritis (PsA). Arava was first authorised in the European Union on 2 September 1999.
- **Cancidas** (caspofungin), Merck Sharp & Dohme Ltd, to include empirical therapy for presumed fungal infections (such as *Candida* and *Aspergillus*) in febrile, neutropaenic adult patients. Cancidas was first authorised in the European Union on 24 October 2001.
- **Ferriprox** (deferiprone), Apotex Europe Ltd, to extend its use to include the treatment of patients with thalassaemia major when deferoxamine therapy is inadequate. Ferriprox was first authorised in the European Union on 25 August 1999.

Further information on the above extensions of indications will be included in the public assessment report (EPAR) once the European Commission has granted final approval.

The Committee also adopted 2 Lists of Questions (Part B) on initial Marketing Authorisation applications and one List of Questions (Part A) on a "line extension" application (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003).

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 CPMP plenary meeting in February 2004 is provided in **Annex 2.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Referrals

The Committee finalised its EU-wide review for **Lopid** (gemfibrozil) and associated product names from Pfizer. The referral was made by the European Commission in January 2003 under Article 30 of the Community Code on human medicines as part of the concerted action by EU regulatory authorities to harmonise the marketing conditions of a number of European brand leaders in major therapeutic areas.

The CPMP recommended that Lopid should be indicated as an adjunct to diet and other non-pharmacological treatment (e.g. exercise, weight reduction) in the treatment of dyslipidaemia in mixed dyslipidaemia characterised by hypertriglyceridaemia and/or low HDL-cholesterol. In addition, the Committee recommended that Lopid should be indicated in primary prevention, in the reduction of cardiovascular morbidity in males with increased non-HDL cholesterol and at high risk for a first cardiovascular event, particularly when a statin is considered inappropriate or is not tolerated.

Non-product related issues

CPMP Working Parties, Ad Hoc Groups and Therapeutic Advisory Groups

- The CPMP was informed of the outcome of the discussions of the **Scientific Advice Working Group** (SAWG) meeting, which was held on 08-09 March 2004. For further details, please see **Annex 4**.
- Documents prepared by the **CPMP Working Parties and Ad Hoc Groups** adopted during the March 2004 CPMP meeting are listed in **Annex 5**.
- The **CPMP Therapeutic Advisory Group on Anti-Infectives (TAG AI)**, chaired by Professor Jaap van Dissel from Leyden, The Netherlands, was held on 08 March 2004. The Group discussed specific aspects on the "CPMP Note for Guidance on the evaluation of medicinal products intended for treatment of bacterial infections" (CPMP /EWP/558/95 rev 1). The proposals from the TAG AI will be further considered by the Efficacy Working Party and the CPMP before final adoption and publication of the CPMP Note for Guidance.

Organisational Matters

The 31st CPMP Organisational Matters meeting took place on Monday 22 March 2004, chaired by Dr Daniel Brasseur. During the meeting the following principle topics were presented/discussed:

- Issues related to **CPMP Working Parties/Ad Hoc Working Groups** (Guidelines, Concept Papers, Core SPCs, Interim Recommendations etc) (see **Annex 5**).

Upcoming meetings following the March 2004 CPMP plenary meeting:

- The 103rd plenary meeting of the CPMP will be held from 20-22 April 2004.
- The next CPMP Organisational Matters meeting will be held on Monday 19 April 2004.
- The next Invented Name Review Group meeting is scheduled to take place on Monday 19 April 2004.

PROCEDURAL ANNOUNCEMENT

- **Update on the Appointment of Rapporteur and Co-Rapporteur**

  Applicants are reminded that decisions to assign CPMP Rapporteur and CPMP Co-Rapporteur for the evaluation of upcoming centralised applications are taken at every CPMP meeting.
  Further to the receipt of the letter of intention to submit a centralised application, future Applicants are advised that requests on (Co-) Rapporteur appointment optimally should be provided six months before the intended submission date. These requests should be sent to the EMEA at least 2 weeks in advance of the CPMP meeting. (See scheduled dates of CPMP meetings: http://www.emea.eu.int/htms/human/presub/q25-2.htm).

  Applicants are reminded and strongly advised to express three to four preferences for CPMP Members coming from three to four different Member States. Names of Members should be mentioned rather than delegations.

  It is recommended that future Applicants liaise with the CPMP Secretariat (email: cpmpdl@emea.eu.int)/Product Team Leader when planning such requests.

  The EMEA will notify the Applicant of the name of the Rapporteur and the Co-Rapporteur appointed by the CPMP directly after the CPMP meeting.

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 22 March 2004. For further details, please see **Annex 6.**

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This CPMP 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	14	381
Follow-up to Scientific Advice	60	0	60
Protocol Assistance	30	7	37
Follow-up to Protocol Assistance	9	1	10

	1995-2003			2004			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	134	271	405	5	5	10	415
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	22	55	77	0	1	1	78
Positive CPMP opinions[2]	99	172	271	3	7	10	281[3]
Negative CPMP opinions[4]	2	5	7	0	0	0	7[5]
Marketing authorisations granted by the Commission	91	164	255	0	3	3	258[6]

	1995-2003			2004			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	771	1505	2276	20	103	123	2399
Positive opinions, variations type II	583	697	1280	29	31	60	1340
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	49	56	105	0	1	1	106

[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] 15 positive opinion corresponding to 15 Orphan Medicinal Products
[3] 281 positive opinions corresponding to 216 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] 258 marketing authorisations corresponding to 195 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE FEBRUARY 2004 CPMP MONTHLY REPORT

Invented Name	Bonviva
INN	ibandronic acid
Marketing Authorisation Holder	Roche Registration Ltd
ATC code	M05BA06
Indication	Treatment of osteoporosis in postmenopausal women, in order to reduce the risk of vertebral fractures. Efficacy on femoral neck fractures has not been established. Prevention of osteoporosis in postmenopausal women who are at risk of developing osteoporosis
CPMP Opinion date	22.10.2003

Invented Name	Ibandronic acid Roche 2.5 mg film-coated tablet
INN	ibandronic acid
Marketing Authorisation Holder	Roche Registration Ltd
ATC code	M05BA06
Indication	Treatment of osteoporosis in postmenopausal women, in order to reduce the risk of vertebral fractures. Efficacy on femoral neck fractures has not been established. Prevention of osteoporosis in postmenopausal women who are at risk of developing osteoporosis
CPMP Opinion date	22.10.2003

Invented Name	Reyataz
INN	atazanavir sulphate
Marketing Authorisation Holder	Bristol Myers Squibb Pharma EEIG
ATC code	J05AE
Indication	Treatment of HIV-1 infected, antiretroviral treatment experienced adults, in combination with other antiretroviral medicinal products
CPMP Opinion date	20.11.2003

OUTCOME OF THE MARCH 2004 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
3 Extensions of indications	3 Positive opinions
16 SPC changes	16 Positive opinions
16 Quality changes	16 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Renagel (sevelamer) Genzyme B.V.	Positive opinion	Marketing Authorisation will remain under exceptional circumstances

Opinions for Renewal applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Cetrotide (cetrorelix) Ares Serono (Europe) Ltd	Positive opinion	---
Procomvax (haemophilus b conjugated and hepatitis B vaccine) Pasteur Merieux MSD	Positive opinion	---
Refacto (moroctocog alfa) Wyeth Europe Ltd	Positive opinion	---

OUTCOME OF THE MARCH 2004 CPMP 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	Neurotoxicity associated with taxane and/or platinum type chemotherapeutic agents	**X**						**X**	
Biological	Rotavirus disease	**X**				**X**	**X**	**X**	
Chemical	Osteoporosis	**X**						**X**	
Biological	Uveitis	**X**				**X**		**X**	
Chemical	Angioedema		**X**				**X**		
Biological	Scarring in glaucoma filtration surgical procedures		**X**				**X**		

SA: Scientific Advice

PA: Protocol Assistance

In March 2004, the above-mentioned 4 Scientific Advice letters and 2 Protocol Assistance letters were adopted.
The Committee accepted 5 Initial Scientific Advice new Requests and 3 Initial Protocol Assistance new Requests.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD HOC GROUPS ADOPTED DURING THE MARCH 2004 CPMP MEETING

BIOTECH WORKING PARTY

Reference number	Document	Status
CPMP/BWP/1104/04	Interim EU Recommendations for the Influenza Vaccine Composition for the season 2004/2005	Adopted and released on the EMEA website

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/4937/03	Concept paper on the development of a CPMP Points to consider on investigations of medicinal products for the treatment of chemotherapy induced nausea and vomiting	Adopted

SAFETY WORKING PARTY

Reference number	Document	Status
CPMP/SWP/1094/04	Guideline on the evaluation of control samples for Toxicokinetic parameters in toxicology studies: checking for contamination with the test substance	Released for 6 months consultation

VACCINES EXPERT GROUP

Reference number	Document	Status
CPMP/VEG/17/03	Draft Guideline on Adjuvants in Vaccines	Released for 6 months consultation
CPMP/VEG/1194/04 v02	Revised Public Statement on Thiomersal in vaccines for Human Use	Adopted

BLOOD PRODUCTS WORKING GROUP

Reference number	Document	Status
CPMP/BPWG/859/95 rev 2	Core SPC for Human normal immunoglobulin for intravenous administration	Released for 1 month consultation
CPMP/BPWG/3732/02	Core SPC for human tick-borne encephalitis immunoglobulin for intramuscular use	Adopted and released on the EMEA website
CPMP/BPWG/3730/02	Core SPC for human tetanus immunoglobulin for intramuscular use	Adopted and released on the EMEA website
CPMP/BPWG/3728/02	Core SPC for human rabies immunoglobulin for intramuscular use	Adopted and released on the EMEA website

CPMP / EMEA WORKING GROUP WITH PATIENTS' ASSOCIATIONS

Reference number	Document	Status
CPMP/5819/04	Recommendations and Proposals for action	Released for 3 months consultation

Report from the meeting held on 22 March 2004

General Issues

Core SPC for HRT products
The updated version of the core SPC has been adopted by the group and will be published on the website.

Timetable for Mutual Recognition Procedure
A Mutual Recognition Procedure Timetable to avoid key dates in the procedure during the Christmas period has been agreed. The document on starting dates for MRFG published on the website will be updated accordingly.

Best practice guide for Mutual Recognition Procedure
An updated version of the document has been adopted by the group and will be published on the website.

Questions/Answers on Mutual Recognition Procedure
Four additional questions and the related answers were agreed and will be added to the Questions/Answers document on the website.

Variation subgroup meeting, London, 24 February 2004
An MRFG subgroup meeting on variations was held on 24 February 2004. It was agreed that:

- validation requirements for variations will be strictly applied and that the timetable of Type IA procedures starts only when the list of Dispatch Dates has been received by the RMS;
- submission should be made as far as possible simultaneously to the RMS and CMSs and excessive delays avoided;
- after referrals, applicants are strongly encouraged to submit a Type II variation for the harmonization of the quality section of the dossier to a "single quality dossier".

Meeting schedule
The next MRFG meeting will be held on 19 April 2004.

Mutual Recognition Monitoring

The MRFG noted that **57** new mutual recognition procedures were finalised during the month of February 2004, as well as **13** type I variations, **289** type IA variations, **125** type IB variations and **54** type II variations.

The status as of 29th February 2004 of procedures under mutual recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures from Type I variations finalised	Procedures from Type IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CPMP
2004	87	127	32	497	267	106	--

39 new procedures (regarding **89** products) started in February 2004. The categories of these procedures are as follows:

5 new active substance (first authorisation in the European Community after RMS approval), of which **2** are classified as repeat use.

5 known active substances (already authorised in at least one member state), of which **1** is classified as multiple application.

27 abridged applications including **4** multiple applications and **2** repeat use.

2 line extension applications.

The new procedures started related to **6** full dossiers, **22** generics, **5** bibliographic applications, **1** fixed combination and **5** for different use, route or dose.

The procedures consisted of **38** chemical substances and **1** biological-blood product[1].

36 of these procedures were prescription-only medicinal products in the reference Member State and 3 procedures was 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 February 2004

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	14
DE (4)	4
DK (1)	7

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (1)	1
DK (2)	3
DK (2)	1
DK (6)	16
DK (2)	6
DK (2)	1
DK (3)	1
DK (3)	8
DK (4)	8
ES (3)	4
ES (3)	1
FI (4)	1
FI (2)	1
FR (1)	16
FR (1)	16
IE (3)	1
IT (1)	11
NL (1)	2
NL (1)	2
NL (2)	11
NL (2)	1
SE (1)	10
SE (1)	11
SE (3)	5
SE (1)	3
UK (2)	4
UK (1)	1
UK (3)	1
UK (3)	1
UK (3)	1
UK (3)	1
UK (4)	1
UK (1)	3
UK (1)	1
UK (4)	1
UK (3)	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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http://heads.medagencies.org/