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

25 March 2002
CPMP/1110/02

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
19-21 MARCH 2002 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 80th plenary meeting from 19 to 21 March 2002.

The CPMP Chairman welcomed two new Members, Dr. Gonzalo Calvo Rojas, the new Spanish CPMP Member who replaces Dr. Fernando Garcia Alonso who resigned last month and the new Norwegian CPMP representative Prof. Eva Skovlund who is replacing Dr. Else Høibraaten.

Product related issues

Centralised procedures

The CPMP adopted two positive Opinions on initial marketing authorisation applications:

- For **Pegasys** (peginterferon alfa-2a) (Part A) from Roche Registration Ltd. indicated for the treatment of histologically proven chronic hepatitis C in adult patients with elevated transaminases and who are positive for serum HCV-RNA, including patients with compensated cirrhosis (for further details, please see the published Summary of Opinion (CPMP/0924/02)). The opinion was adopted by consensus on 21 March 2002, with an active review time of 206 days.
- For **Tamiflu** (oseltamivir) (Part B) from Roche Registration Ltd. indicated for the treatment and prophylaxis of influenza in adults and children one year of age or older, who present symptoms typical of influenza (for further details, please see the published Summary of Opinion (CPMP/715/02). The opinion was adopted by consensus on 21 March 2002, with an active review time of 203 days.

The Committee also noted the withdrawal of an application for an initial marketing authorisation and adopted three Lists of Questions (3 Part B) on initial marketing authorisation 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 CPMP plenary meeting in February 2002 is provided in **Annex 2**. The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Referrals

Referral under Article 30 of Directive 2001/83/EC (previously known as Article 11 of Council Directive 75/319/EEC, as amended)

Following a referral initiated by Italy under Article 30 of Directive 2001/83/EC, the CPMP adopted by consensus an opinion for a nationally authorised medicinal product containing captopril (Capoten and associated invented names), leading to a EU-wide harmonised SPC.

Referral under Article 31 of Directive 2001/83/EC (previously known as Article 12 of Council Directive 75/319/EEC, as amended)

The CPMP initiated a Community-level review on the risk-benefit of Sibutramine containing medicinal products, following a referral by Italy under Article 31 of Directive 2001/83/EC. A Rapporteur and Co-Rapporteur were appointed.

Referral under Article 36 of Directive 2001/83/EC (previously known as Article 15a of Council Directive 75/319/EEC, as amended)

On 19 September 2001, Portugal initiated a referral under Article 36 of Directive 2001/83/EC, regarding cerivastatin containing medicinal products (Lipobay and associated invented names) authorised via the Mutual Recognition procedure, following safety concerns related to the increased risk of rhabdomyolysis.

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Following review of all available data, including an oral explanation from the Marketing Authorisation Holder, regarding the safety and efficacy of cerivastatin containing medicinal products, the CPMP concluded the review with the adoption of an opinion by consensus recommending the withdrawal of all Marketing Authorisations for cerivastatin (Lipobay and associated invented names) containing medicinal products authorised under the Mutual Recognition Procedure.

Scientific Advice procedures

The CPMP was informed of the outcome of the discussions of the Scientific Advice Review Group (SciARG) meeting, which was held on Monday 18 March 2002. For further details, please see **Annex 4**.

Non-product related issues

CPMP Working Parties and Ad Hoc Groups

- Pharm Geert de Greef has been appointed as new Chairman of the Expert group on revision of the Guideline on Excipients, succeeding Dr. W. van der Giesen.
- The CPMP adopted European recommendations for Influenza Vaccines composition for the season 2002/2003. For further information, please see recommendations (CPMP/BWP/852/01) published on the EMEA Website.
- The CPMP adopted a revised position statement (CPMP/578/02 rev.1) with recommendations on the ability to drive and use machines for the Summary of Product Characteristics and Package Leaflets, which has been published on the EMEA Website. The revision concerns a clarification in the text for the package leaflet.

Upcoming meetings:

- There will be an Expert Workshop meeting on Human Transmissible Spongiform Encephalopathies (TSEs), including in particular variant Creutzfeldt-Jakobs disease (vCJD), which will be mainly focussing on medicinal products derived from blood and plasma and the review of the latest information on human TSEs. This workshop will take place on 19-21 June 2001.
- An antimicrobial resistance meeting will be organised under the Spanish Presidency on 21-22 June 2002 in Madrid.

An overview of guidance documents adopted during the meeting or released for consultation to Interested Parties is attached as **Annex 5**.

Organisational Matters

- The invented Name Review Group (NRG), held its 27th meeting on Monday 18 March 2002 and the conclusions of the group were subsequently adopted by the CPMP.
- The 11th CPMP ORGAnisational Matters (ORGAM) meeting took place on Monday 18 March 2002, chaired by Dr Daniel Brasseur. During the meeting the following topics were presented/discussed:
    - The CPMP Day-70 Assessment Report template: The template was presented and adopted by the CPMP. It will be used by CPMP Members and their Assessors for preparing their first Assessment Report at Day-70 of the centralised procedure. This report will be composed of four modules (Overview and List of Questions, clinical, non-clinical and quality modules); it will contain a preliminary benefit/risk assessment and the preliminary List of Questions classified in two types i.e. "Major Objections" for which applicants are expected to provide an answer or a proposal to solve the problem and "Other concerns" for which Applicants are expected to provide a satisfactory answer before approval. This template will be made available to CPMP Members/Experts mid-April and used for a 6-month trial period;
    - Rapporteur/Co-Rapporteur nomination: Rules for appointment of (Co-)Rapporteur appointment were discussed. CPMP Members expressed their concerns with regard to the impact of delay of application submissions in their planning, workload and resources. Applicants are therefore reminded that any delay in application submission should be announced (letter to be addressed to CPMP Chairman, Rapporteur and Co-Rapporteur) and that, upon CPMP agreement there could be (Co-)Rapporteur re-appointment. Appointments of (Co-)Rapporteurs take place every month and should be requested by applicants 3 to 4 months prior to submission.

- Review proposals of the Variation Regulation 542/95: The draft proposals and concept of new Type I (notification procedure), Type IIA "implicit variation" (30-days assessment procedure) and Type IIB "explicit variation" (60 days assessment procedure with possibility of clock-stops) were presented in advance of the European Commission Notice To Applicants meeting on 25-26 March 2002.
- Therapeutic Teams/Advisory Expert Groups: Preliminary discussions on such concept took place and will be further elaborated upon at an upcoming ORGAM meeting.
- EMEA Risk Management Strategy: Following a review on the current conduct of Pharmacovigilance at European level, the EMEA presented the outline of a Risk Management Strategy in order to provide a framework which will allow to reduce the risks associated with the placing on the market of new centralized medicinal products. Further discussions will take place at an upcoming ORGAM meeting.
- Consultation procedure for ancillary medicinal substances in medical devices: The EMEA/CPMP is in the process of defining the details of the consultation procedure for the above-mentioned medicinal substances. When available, guidelines will be published on the EMEA Website.

EMEA PROCEDURAL ANNOUNCEMENT

EMEA provides further guidance as to the interpretation of Commission Directive 2000/83/EC, i.e. in accordance with Volume 9 of "The Rules Governing Medicinal Products in the European Union", for nationally authorised products including those authorised through mutual recognition, MAHs should report to the EMEA, on an expedited basis all suspected serious unexpected adverse drug reactions occurring outside the EU, but **only electronically** using the EudraVigilance data-processing network, which has been made available as of 5 December 2001.

EMEA ANNOUNCEMENT

The EMEA is pleased to announce the appointment of the new Head of Sector Pharmacovigilance and Post-authorisation Safety and Efficacy for Human medicines, Dr Panos Tsintis with effect from 18 March 2002.

Mutual Recognition procedure

The CPMP noted the report from the MRFG, which was held on 18 March 2002. This report includes the list of the meetings organised under the Spanish Presidency. (For further details, please see **Annex 6**).

The 81st plenary meeting of the CPMP will be held from 23 to 25 April 2002.

Noël Wathion
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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

	1995-2001			2002			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	88	164	252	3	8	11	263
Follow-up to scientific advice	18	17	35	1	1	2	37
Protocol Assistance	0	2	2	2	0	2	4
Follow-up to Protocol Assistance	2	0	2	0	0	0	2

	1995-2001			2002			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	120	215	335	3	5	8	343
Withdrawals	15	45	60	1	2	3	63
Positive CPMP opinions	77	131	208	1	10	11	219[1]
Negative CPMP opinions[2]	1	4	5	0	0	0	5[3]
Marketing authorisations granted by the Commission	71	123	194	1	5	6	200[4]

	1995-2001			2002			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	448	806	1254	20	73	93	1347
Positive opinions, variations type II	285	362	647	24	30	54	701
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	38	36	74	0	1	1	75

ANNEX 2 to CPMP Monthly Report March 2002

[1] 219 positive opinions corresponding to 170substances
[2] In case of appeal the opinion will not be counted twice
[3] 5 negative opinions corresponding to 4 substances
[4] 200 marketing authorisations corresponding to 154 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE FEBRUARY 2002 CPMP MONTHLY REPORT

Brand name	Protopy
INN	tacrolimus
Marketing Authorisation Holder	Fujisawa GmbH
ATC code	D11AX14
Indication	Treatment of moderate to severe atopic dermatitis
CPMP Opinion date	18/10/2001
Date of Commission Decision	28/02/2002

Brand name	Protopic
INN	tacrolimus
Marketing Authorisation Holder	Fujisawa GmbH
ATC code	D11AX14
Indication	Treatment of moderate to severe atopic dermatitis
CPMP Opinion date	18/10/2001
Date of Commission Decision	28/02/2002

Brand name	Trisenox
INN	arsenic trioxide
Marketing Authorisation Holder	Cell Therapeutics (UK) Ltd
ATC code	L01XX27
Indication	Induction of remission and consolidation in adult patients with relapsed/refractory acute promyelocytic leukaemia (APL),
CPMP Opinion date	18/10/2001
Date of Commission Decision	08/03/2002

Brand name	Lumigan
INN	bimatoprost
Marketing Authorisation Holder	Allergan Sales Ltd
ATC code	S01EX
Indication	Reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension
CPMP Opinion date	15/11/2001
Date of Commission Decision	08/03/2002

Brand name	Kineret
INN	anakinra
Marketing Authorisation Holder	Amgen Europe B.V.
ATC code	L04AA14
Indication	Combination treatment of the signs and symptoms of rheumatoid arthritis
CPMP Opinion date	15/11/2001
Date of Commission Decision	08/03/2002

OUTCOME OF THE MARCH 2002 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
6 SPC changes	Positive opinions by consensus
4 quality changes	Positive opinions by consensus

Opinions for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Teslasan (mangafodipir), Nycomed Imaging A/S	Positive opinion by consensus	---

OUTCOME OF THE MARCH 2002 CPMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Substance	Intended indications(s)	Topic				
		Type of Request		Pharma-ceutical	Pre-Clinical	Clinical
		New	Follow-up			
Biological	Malignant melanoma	**X**			**X**	**X**
Biological	Influenza	**X**		**X**		
Chemical	Irritable Bowel Syndrome	**X**				**X**
Chemical	Ischemic cardiovascular disease	**X**				**X**
Biological	Non-Hodgkin's lymphoma	**X**				**X**
Chemical	Multiple basal cell carcinoma	**X**			**X**	**X**

In March 2002, the above-mentioned six final Scientific Advice letters were adopted. The Committee accepted eight new Scientific Advice requests and one follow-up request for Protocol Assistance.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE MARCH 2002 CPMP MEETING

QUALITY WORKING PARTY

Reference number	**Document**	**Status**
CPMP/QWP/2845/00	Note for Guidance on Requirements for pharmaceutical documentation for pressurised metered dose inhalation products	Adopted in March 2002

BIOTECHNOLOGY WORKING GROUP

Reference number	Document	Status
CPMP/BWP/852/02	Final EU recommendation for the influenza vaccine composition for the season 2002 / 2003	Adopted in March 2002

SAFETY WORKING GROUP

Reference number	Document	Status
CPMP/SWP/2600/01	Points to consider on the Need for assessment of reproductive toxicity of human insulin analogues	Adopted in March 2002
CPMP/SWP/668/02	Concept paper on the Development of a CPMP position paper on the Non-clinical safety studies to support low dose clinical screening studies in humans	Adopted in March 2002

EFFICACY WORKING GROUP

Reference number	Document	Status
CPMP/EWP/226/02	Concept paper on the Development of a CPMP Note for Guidance on the Clinical pharmacokinetic investigation of the pharmacokinetics of peptides and proteins	Adopted in March 2002
CPMP/EWP/225/02	Concept paper on the Development of a CPMP Note for Guidance on the Evaluation of the pharmacokinetics of medicinal products in patients with impaired renal failure	Adopted in March 2002

Report from the meeting held on 18 March 2002

General issues

The following meetings will take place under the Spanish presidency.

MEETINGS	PLACE	DAYS
Heads of European Medicinal Products Agencies (1st meeting)	Barcelona	12/13 February
CPMP informal (EMEA)	Málaga	7/8 May
MRFG (Mutual Recognition Facilitation Group)	Málaga	7/8 May
Committee for Orphan Medicinal Products	Málaga	7/8 May
EMACOLEX	Madrid Ministerio de Sanidad	22/23/24 May
Heads of European Medicinal Products Agencies/ Heads of European Veterinary Regulatory Agencies (2nd meeting)	Segovia	28/29 May
Joint meeting of CPMP/CVMP informal (EMEA)	Barcelona Universidad Autónoma	6/7 June
MRVFG (Mutual Recognition Veterinary Facilitation Group)	Barcelona Universidad Autónoma	6/7 June

Meeting schedule

The next MRFG meeting will be held on **22 April 2002**.

The MRFG noted that 20 new mutual recognition procedures were finalised during the month of February 2002, as well as 165 type I and 28 type II variations.

The status as of 28th February 2002 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 I variations pending	Procedures from Type II variations finalised	Procedures from Type II variations pending	Arbitrations referred to CPMP
2002	60	91	264	162	63	259	--

35 new procedures (regarding 71 products) started in February 2002. The categories of these procedures are as follows:

5 new active substances, including **1** multiple application and 2 repeat use.

8 known active substances (already authorised in at least one member state) including 1 repeat use.

22 abridged applications including **6** multiple applications.

The new procedures started last month relate to 8 full dossiers, 21 generics, 5 bibliographic applications and 1 for different use, route or dose.

The procedures consisted of 34 chemical substances and 1 biological blood product[1].

31 of these procedures were prescription-only medicinal products in the reference Member State and 4 were Non-prescription (including OTC) medicinal products[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 2002

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (1)	6
DE (2)	3
DE (3)	9
DE (3)	9
DE (3)	9
DE (3)	10
DE (3)	7
DK (2)	1
DK (2)	4
DK (2)	3
DK (2)	2
DK (2)	2
DK (1)	1
DK (3)	15
NL (1)	1
NL (1)	14
NL (2)	11
NL (1)	1
NL (1)	6
NL (1)	3
NL (1)	3
NL (1)	1
SE (1)	2
SE (4)	15
SE (4)	15
SE (4)	3
SE (3)	5
UK (1)	2
UK (1)	16
UK (3)	1
UK (1)	2
UK (2)	13
UK (2)	13
UK (1)	4
UK (2)	5

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

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

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