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

24 November 1998
CPMP/2572/1998

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 43rd plenary meeting from 17 November to 19 November 1998.

The quarterly regular meeting with the Interested Parties was held in the afternoon of the 19 November 1998.

On 20 November 1998 a Joint EFPIA/EMEA Information Day on Performance Assessment for the European Registration Systems was held.

The CPMP welcomed Prof. Cristina Sampaio from Portugal as a new member, replacing Prof. Miguel Forte. In addition to Dr. Gro Ramsten Wesenberg from Norway, two further observers have joined the CPMP: Dr. Lars Gramstad from Norway and Dr. Sigurdur Thorsteinson from Iceland.

An extraordinary meeting of CPMP members and experts was convened on 10 November 1998 to discuss the benefit / risk profile of Tasmar (Tolcapone). Following this meeting, the CPMP adopted an Opinion on 12 November 1998 recommending the suspension of the marketing authorisation for Tasmar, and an EMEA Press Release (CPMP/2457/98) was issued on 17 November 1998 and is published on the Internet.

Centralised Procedures

The Committee adopted:

- Four positive Opinions[1] on Centralised Applications:
  - One positive Opinion was adopted by consensus relating to a Medicinal Product containing a new active substance (Part A), an immuno-modulating agent to be used in combination as an adjunct to prevent or delay amputation in irresectable soft tissue sarcoma of the limbs.
  - One positive Opinion was adopted by consensus relating to a Medicinal Product containing a new active substance (Part A), an immuno-suppressive agent indicated for prophylaxis of acute organ rejection in patients receiving renal transplants.
  - Two positive Opinions were adopted by majority of votes relating to two Medicinal Products containing the same new active substance (Part B), indicated as a short-acting hypnotic.

- Two positive Opinions on Applications (line extensions) in accordance with Annex II of the Commission Regulation (EC) No 542/95:
  - One positive Opinion was adopted by consensus relating to one Application in accordance with Annex II (an additional pharmaceutical form) for an already Centrally Authorised Medicinal Product, containing an ovulation stimulating agent (Part A), indicated for the treatment of infertility.

[1] Note for Editors:
Applicants may appeal any CPMP opinion, provided they notify the EMEA in writing of their intention to appeal within 15 days of receipt of the Opinion. In line with the decision of the Management Board at its 30 September 1998 meeting, further information on Opinions adopted by the CPMP will be made available 60 days after adoption of the final Opinion.

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- One positive Opinion was adopted by consensus relating to one Application in accordance with Annex II (an additional pharmaceutical form) for an already Centrally Authorised Medicinal Product containing an immuno-suppressive agent (Part B), indicated for prophylaxis of acute transplant reaction in patients receiving allogeneic renal or cardiac transplants.

- Six positive Opinions by consensus for Centralised Type II Variations.

- Two negative Opinions by majority of votes for Centralised Type II Variations.

- Two positive Opinions by consensus following the annual re-assessment for Medicinal Products (one Part A and one Part B) indicated for the treatment of haemophilic B factor IX deficiency, and treatment of HIV infected patients, respectively. The Marketing Authorisations for these products will remain "under exceptional circumstances".

An Urgent Safety Restriction concerning Comtess/Comtan (Entacapone) to include a warning on the possibility to develop Neuroleptic Malignant-like Syndrome (NMS) or rhabdomyolysis has been published (Press Release EMEA/39582/98 Entacapone (Comtess/Comtan) - Update of Product Information) and is available on the Internet.

Since the CPMP meeting in October 1998, the Committee noted the withdrawal of four applications (three Part A, one Part B) from the Centralised Procedure.

The CPMP adopted six lists of questions (Part B) (concerning five active substances) of which three Medicinal Products were considered to be approvable and three non-approvable based on the information available to the CPMP.

The Committee heard three Oral Presentations/Clarifications from Applicants concerning ongoing Centralised Procedures.

Rapporteurs and Co-Rapporteurs were assigned for four applications forthcoming in the Centralised Procedure within the next four months, two for Part A and two for Part B. A Rapporteur was also assigned for Extension Applications for two already Centrally Authorised Medicinal Products (Part B).

An overview of Centralised Applications is given in Annex I.

Scientific Advice

The Committee:

- Accepted three new and two follow-up requests from companies for Scientific Advice. Co-ordinators were appointed.
- Adopted two opinions for Scientific Advice by consensus on clinical development concerning two new Medicinal Products (one for Part A, one for Part B), intended for:
  - treatment of urinary stress incontinence
  - treatment of relapsing-remitting Multiple Sclerosis

Referrals

Referral under Article 10 of Council Directive 75/319/EEC, as amended
The Committee noted the Referral for Arbitration to the CPMP from France concerning a platelet aggregating inhibitor regarding efficacy issues. A Rapporteur and a Co-Rapporteur were assigned.

Referral under Article 15 of Council Directive 75/319/EEC, as amended
Further to the suspension of the marketing in the Netherlands, the Netherlands made a Referral under Article 15 of Council Directive 75/319/EEC, as amended, concerning a neuroleptic Medicinal Product regarding Pharmacovigilance issues, namely an increased risk of sudden or cardiac death. A Rapporteur and a Co-Rapporteur were assigned.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

The CPMP heard reports from its Quality, Safety, Efficacy, and Pharmacovigilance Working Parties.

QUALITY WORKING PARTY

Three documents were adopted:

- Concept Paper to revise the Note for Guidance "European Drug Master File Procedure for Active Substances" (CPMP/QWP/2430/98)
- Concept Paper to develop a guideline on parametric release (CPMP/QWP/2431/98)
- Concept Paper to develop a guideline on in-use stability testing of non-sterile human Medicinal Products (CPMP/QWP/2570/98)

EFFICACY WORKING PARTY

One document was adopted:

- Note for Guidance on clinical investigation of medicinal products in the treatment of hypertension, revision 1, incorporating an addendum (CPMP/EWP/238/95, Rev. 1)

In addition the following EMEA guidance document was released on the EMEA website:

- EMEA Pre-submission Guidance for Users of the Centralised Procedure (EMEA/H/38179/1998)

ICH

The following document was adopted for coming into operation in May 1999:

- Note for Guidance on the duration of chronic toxicity testing in animals (rodent and non-rodent toxicity testing) (CPMP/ICH/300/95) - ICH topic S4.

Mutual Recognition

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) 19 November 1998, which is circulated together with this Press Release (Annex II).

Prof. R. Bass
Head of Human Medicines Evaluation Unit

This press release and other documents are available on the Internet at the following address: http://www.eudra.org/emea.html

CENTRALISED APPLICATIONS TO THE EMEA

	Part A	**Part B**	**Total**
Scientific Advice	30	45	75
Follow-up to Scientific Advice	9	2	11

	Part A	**Part B**	**Total**[1]
Applications submitted since 1 January 1995	62	110	172
Withdrawn	10	16	26
Positive CPMP Opinions	33	64	97[2]
Negative CPMP Opinions	1	2	3[3]
Marketing Authorisations granted by the Commission	28	56	84[4]

	Part A	**Part B**	**Total**
Variations Type I	95	157	252
Positive Variations Type II	40	68	108
Negative Variations Type II	0	2	2[5]
Extensions	25	6	30

[1] These figures include the 18 ex-concertation procedures submitted before January 1995 of which 14 have been authorised and 4 withdrawn before end 1996
[2] 97 positive Opinions corresponding to 73 substances
[3] 3 negative Opinions corresponding to 2 substances
[4] 84 Marketing Authorisations corresponding to 65 substances
[5] 2 negative Type II Variations corresponding to 1 substance

MRFG
Mutual Recognition Facilitation Group

Report from the meeting held on 16 November 1998

The MRFG noted that 6 new mutual recognition procedures have been finalised during the month of October 1998 as well as 32 type I and 24 type II variations.
The status as of 31 October 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
1998	148	33	266	80	181	119	1 N.A. 4 var.

6 new procedures (regarding 24 products) have been started in October 1998. The categories of these procedures are as follows:

New active substance[1]	Line extensions[2]	Fixed combinations	Generics	Herbal products[3]	OTC[4]	Others[5]
2	1	0	2	0	0	1

1. When in one of the involved Member States it concerns a new active substance according to the definition in the Notice to Applicants Part IIA;
2. Line extensions are those applications which extend a range of products, e.g. an additional strength, or a new pharmaceutical form from the same Marketing Authorisation Holder;
3. In this category products are classified as herbals when the RMS has considered them as herbal product;
4. In this category products are classified as OTC products when the RMS has approved it for OTC use, although the legal status is not part of the Mutual Recognition Procedure;
5. When the product is not classified in the previous six categories.

Each application can be classified in only one category.

Number of countries involved in the started new applications procedures in October 1998

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (3)	8
FR (1)	3
NL (3)	7
SE (13)	1
SE (2)	2
UK (1)	2

General issues

- The Group adopted the *Article 7a of Directive 65/65/EEC Member States' Standard Operating Procedure* (MS SOP Art. 7a). It will be put on the MRFG Website for information.

- Concerning line extensions
  the general rules are:

  - If the first product has been authorised via MRP, the line extensions have also to follow MRP.
  - For line extensions of not harmonised nationally authorised products the national procedure is still possible to apply. Alternatively the MRP for line extensions can be followed if a harmonisation of the SPC was achieved in advance. But these procedures cannot be used in parallel.

  There is a particular issue for products, which have been authorised nationally in some MS's and via MRP in the remaining MS's for which more consideration has to be foreseen. In the meantime for line extensions of national authorised products the national procedure still can be followed in parallel to the MRP, which is mandatory for those line extensions where the products have been authorised via MRP.

- The Group noted the relatively low number of procedures started in October 98. This probably reflects Companies reassessing their strategic options in the light of the Commission Communication.

- Concerning variations, Companies should contact the RMS in advance of the submission of a variation dossier in order to receive the MRP variation number. This number should be used in all the forms so that the variation is clearly identified among the Member States.

- The Group and a representative from the European Commission met with the European Association of Plasma Products Industry (EAPPI) and had a depth discussion on several items, especially focusing on the MRP in relation with this special kind of products.

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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*Or you could visit the **MRFG web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*
http://heads.medagencies.org/