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

25 October 1999
CPMP/2769/99

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 53rd plenary meeting from 19 October 1999 to 21 October 1999.

The quarterly regular meeting with the Interested Parties was held in the afternoon of 20 October 1999 (see Annex II).

This meeting was followed by a joint EMEA/EFPIA information day on 22 October 1999.

The CPMP welcomed a new Spanish member, Dr. Cristina Avendaño, who succeeds Prof. José Félix Olalla Marañón.

Centralised Procedures[1]

The Committee adopted:

- Three positive opinions on initial centralised applications:
  - Two positive opinions were adopted by consensus relating to two medicinal products containing the same active substance (Part A), an interferon indicated for the treatment of
    - chronic hepatitis B and C.
    - chronic hepatitis B and C, as well as a number of cancers.
  - One positive opinion was adopted by consensus relating to a new medicinal product concerning a new pharmaceutical form for an already licensed active substance (Part B), an antipsychotic indicated for the treatment of schizophrenia.

- Three negative opinions were adopted by majority vote, relating to three medicinal products containing the same new active substance (Part B), indicated for the treatment of diabetes mellitus.

- One positive opinion by consensus for a centralised type I variation following the type II procedure.

- Eight positive opinions by consensus for centralised type II variations.

- Two positive opinions following annual re-assessment:
  - One positive opinion by consensus for a medicinal product (Part A) indicated for the treatment of relapsing multiple sclerosis. The CPMP recommended that the marketing authorisation for this product should remain “under exceptional circumstances”.
  - One positive opinion by consensus for a medicinal product (Part B) indicated for the treatment of nephropathic cystinosis. The CPMP recommended that the marketing authorisation for this product should remain “under exceptional circumstances”.

[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.

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- One opinion by majority vote recommending the renewal of the suspension of the marketing authorisation for Tasmar (tolcapone) for a further year.

The Committee agreed on an urgent safety restriction initiated by the marketing authorisation holder for Arava to include a warning on the possibility of serious side effects including pancytopenia and serious skin reactions. An EMEA Public Statement has been published [EMEA Public Statement on Leflunomide (Arava) – Pancytopenia and Serious Skin Reactions, EMEA/31637/99] and is available on the Internet.

The CPMP adopted three lists of questions (two Part A/one Part B) concerning three active substances of which two products were considered to be approvable and one non-approvable, based on the information available to the CPMP at this time.

The Committee considered the need for GMP inspections for eight medicinal products (five Part A/three Part B) and requested three inspections for two products (Part A): two inspections for an assessment of a new application and one inspection for a variation. Furthermore the CPMP requested one GCP inspection due to non-compliance with Pharmacovigilance reporting requirements.

The Committee heard two oral presentations from applicants concerning ongoing procedures and one oral presentation regarding a type II variation, as well as two oral presentations on Pharmacovigilance issues.

An overview of centralised applications is given in Annex I.

The CPMP strongly reminds applicants to comply with declared submission dates for initial applications for marketing authorisation, as failure to comply with such dates causes significant workflow difficulties for the Rapporteurs, Co-Rapporteurs and their assessment teams, potentially requiring re-assignment of Rapporteurship.

Scientific Advice

The Committee adopted the following scientific advice letters:

Part	Indication	Topic
A	For use in cardiac surgery in heparin resistant patients	Clinical development programme
A	Treatment of advanced non-small cell lung cancer and advanced colorectal cancer	Clinical development programme
A	Gene therapy for the treatment of a variety of cancers	Clinical development programme
B	Adjunctive therapy of epilepsy	Clinical development programme

The Committee accepted four new requests from companies for scientific advice. Co-ordinators were appointed.

Referrals

Referral under Article 12 of Council Directive 75/319/EEC, as amended
The Committee noted the referral initiated by Belgium for sibutramine-containing medicinal products, regarding efficacy and safety issues. A Rapporteur and a Co-Rapporteur were assigned.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

The CPMP heard reports from its Biotechnology, Efficacy, Safety, and Pharmacovigilance Working Parties, as well as from the Multidisciplinary Group on Thiomersal and the Ad Hoc Expert Working Group on Update of Guidance of SPCs.

The Steering Committee for the evaluation of the metabolic complications of highly active antiretroviral therapy (HAART), constituted in March 1999 following a request by the CPMP gave a presentation on their strategies to study the short and long-term consequences of lipodystrophy.

BIOTECHNOLOGY WORKING PARTY

The following document was adopted by the CPMP for coming into operation in April 2000:

- Note for Guidance on Development pharmaceutics for biotechnological and biological products/Annex to Note for Guidance on Development pharmaceutics (CPMP/BWP/328/99)

EFFICACY WORKING PARTY

The following document was released for 6 months' consultation:

- Note for guidance on Clinical investigation of medicinal products in the treatment of epileptic disorders (CPMP/EWP/566/98)

AD HOC EXPERT WORKING GROUP ON UPDATE OF GUIDANCE OF SPCS

The CPMP adopted a document for transmission to the Commission for the upcoming discussion at the Notice to Applicants Working Party [Final consolidated proposal for the wording of the SPC (CPMP/1697/98, draft 4, Rev. 4)]

ICH

The following document was released for 6 months' consultation:

- ICH Topic E11: Note for guidance on Clinical investigation of medicinal products in the paediatric population (CPMP/ICH/2711/99)

ORGANISATIONAL MATTERS

The following revised SOP was adopted by the CPMP to replace the previous document as of 1 November 1999 (subject to the outcome of the Management Board meeting of 1 December 1999)*:*

- SOP on Scientific Advice to be given by the CPMP for innovative medicinal products (CPMP/2072/99)

MULTIDISCIPLINARY GROUP ON THIOMERSAL

The Committee adopted a position paper (CPMP/2612/99) on the warning statements relating to sensitisation which should be implemented in the Summary of Product Characteristics and Package Leaflets of medicinal products where Thiomersal is used.

Consultation with Interested Parties

Continuing the cycle of meetings with Interested Parties, the CPMP and the EMEA Secretariat held discussions with European representatives of health professionals and trade associations from the pharmaceutical industry on 20 October 1999.

Mutual Recognition

The CPMP noted the report from the mutual recognition facilitation group (MRFG) 18 October 1999, which is circulated together with this Press Release (Annex III).

Prof. Rolf Bass
Head of Unit
Evaluation of Medicines for Human Use

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

EMEA CENTRALISED PROCEDURES

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific advice	33	45	78	23	24	47	125
Follow-up to scientific advice	9	4	13	1	2	3	16

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	62	115	177	18	27	45	222
Withdrawals	11	19	30	1	5	6	36
Positive CPMP opinions	35	65	100	8	16	24	124[1]
Negative CPMP opinions [2]	1	2	3	0	3	3	6[3]
Marketing authorisations granted by the Commission	28	60	88	12	16	28	116[4]

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	99	168	267	56	144	200	467
Positive opinions, variations type II	41	77	118	40	42	82	200
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	25	6	31	7	8	15	46

[1] 124 positive opinions corresponding to 96 substances
[2] In case of appeal the opinion will not be counted again
[3] 6 negative opinions corresponding to 3 substances
[4] 116 Marketing Authorisations corresponding to 92 substances

ANNEX II to CPMP October 1999
Press Release

INTERESTED PARTY MEETING HELD ON 20 OCTOBER 1999

In continuation of the cycle of quarterly meetings with European Interested Parties, discussions were held on 20 October 1999 with representatives of Association Européenne des Spécialités Grand Public (AESGP), Standing Committee of European Doctors (CP), European Federation of Pharmaceutical Industries Associations (EFPIA) and Groupement des Pharmaciens de l'Union Européenne (GPUE).

Rolf Bass and Noël Wathion from the Secretariat presented the main results of the still ongoing October 1999 meeting. A number of CPMP members and experts also participated in the meeting together with Secretariat staff.

It was noted that some Marketing Authorisation Holders still fail to comply with the fulfilment of post-marketing commitments. Another difficulty arises when submissions in the Centralised Procedure have to be postponed and (Co-) Rapporteur teams have to be rescheduled for review.

A number of scientific issues were discussed, including the modular European Public Assessment Report (EPAR) structure. For the extension of the scientific content of the EPAR, a more comprehensive template is under development and was outlined to Interested Parties. Furthermore, the Guideline on the Readability of the Label and Package Leaflet of Medicinal Products for Human Use was discussed, with special emphasis on the user testing recommendations.

The Executive Director of the EMEA, Mr Fernand Sauer, presented the EMEA Code of Conduct adopted by the Management Board at its 29 September 1999 meeting. Intended to complement the Code of Conduct currently being developed by the European Commission, the EMEA Code incorporates and develops existing practice and provides specific guidance concerning conflicts of interest, confidentiality and discretion, and gifts and invitations. This document has been placed on the EMEA website for comments.

Interested Parties were asked to give feedback on the current format and organisation of the meetings with Interested Parties. There was general agreement that these meetings are extremely valuable and that the cycle of regular meetings should continue. Improvements suggested include more focused agendas, improved timing of meeting (Wednesday lunchtime) and availability of background information on the EMEA.

The next meeting is scheduled to take place in February 2000.

For further information please contact:

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Report from the meeting held on 18 October 1999

The MRFG noted that 22 new mutual recognition procedures were finalised during the month of September 1999, as well as 42 type I and 25 type II variations.

The status as of 30 September 1999 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
1999	126	103	476*+42= 518	45	250	98	1 N.A.+ 1 var.

* A typing error for this figure was reported from the September MRFG report.

49 new procedures (regarding 87 products) started in September 1999. The categories of these procedures are as follows:

New active substance[1]	Line extensions[2]	Fixed comb.	Generics	Herbal products[3]	OTC[4]	Blood products	Immuno-logicals	Others[5]
5	3	6	17	0	0	0	2	16

[1] When in one of the involved Member States it concerns a new active substance according to the definition in the Notice to Applicants Volume IIA; the number given includes multiple applications and repeat use procedures.
[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 other eight categories.

Each application can be classified in only one category.

Number of countries involved in the new applications procedures started in September 1999:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure	Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (1)	1	FR (1)	14
DE (3)	2	FR (2)	12
DE (1)	1	FR (1)	11
DE (1)	14	FR (1)	6
DE (1)	13	IR (2)	4
DE (1)	13	NL (3)	10
DE (1)	13	NL (3)	5
DE (1)	13	NL (3)	7
DE (1)	13	NL (3)	2
DE (1)	10	NL (3)	5
DE (1)	10	NL (1)	1
DE (1)	10	NL (1)	1
DE (3)	6	SE (2)	13
DE (3)	8	UK (1)	1
DE (3)	7	UK (1)	1
DE (3)	8	UK (2)	6
DE (1)	2	UK (1)	14
DK (2)	7	UK (1)	10
DK (2)	1	UK (2)	2
DK (2)	1	UK (1)	11
DK (2)	1	UK (1)	14
DK (3)	14	UK (2)	6
DK (1)	1	UK (1)	14
DK (3)	1	UK (4)	1

General issues

- Based on the initiative of the MRFG and discussions in the Pharmaceutical Committee, the European Commission clarified the interpretation of links between marketing authorisation holders. This will be reflected in the NTA and Part IA form.
- A survey to clarify legislation in member states concerning the acceptability of combination packs was initiated.
- An updated list of MRP contact points was made available on the Heads of Agencies WebSite.
- A working group to propose new categories for MR applications was created.

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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Alternatively, you could visit the ***MRFG website*** *at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*

http://heads.medagencies.org/