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

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CPMP/1817/99

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 50th plenary meeting from 22 June to 23 June 1999.

An extraordinary meeting of the CPMP was held on 10 June 1999, during the course of which opinions recommending the suspension of the marketing authorisation of TROVAN/TROVAN IV and TURVEL/TURVEL IV were adopted. This was due to increasing concerns over 152 documented reports of serious hepatic events, including 9 cases where patients died or required a liver transplant. The background to this procedure and the grounds for the suspension are provided in a public statement, which is available on the EMEA website (Document reference: EMEA/18046/99).

Centralised Procedures

The Committee adopted:

- One revised positive opinion under exceptional circumstances by consensus for a product which was already the subject of a positive opinion under exceptional circumstances by consensus; this was further to a request from the European Commission for further scientific clarification. This product contains a new active substance (Part B), an iron chelating agent indicated for the treatment of iron overload in patients with thalassemia major for whom deferoxamine therapy is contra-indicated or who present serious toxicity with deferoxamine therapy.

- Three positive opinions by consensus for centralised type I variations following the type II procedure.

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

- One positive opinion by consensus following the annual re-assessment for a medicinal product (Part A) indicated for the treatment of ambulatory patients with relapsing-remitting multiple sclerosis. The CPMP recommended that the marketing authorisation for this product should remain "under exceptional circumstances".

Since the CPMP meeting in May 1999, the Committee noted the withdrawal of one application (Part B), from the centralised procedure because of major deficiencies in the clinical part of the dossier, particularly relating to efficacy.

The CPMP adopted five list of questions (three part A/two part B) concerning four active substances of which three products were considered to become approvable provided that satisfactory answers are provided to the questions raised and two non approvable based on the information available to the CPMP at this time.

The CPMP considered six GMP inspection requests (four new applications and two variations) and confirmed that no inspections are needed to complete the assessment of the applications.

The Committee heard one oral presentation from the applicant concerning a centralised procedure and one oral presentation from a company regarding a referral procedure.
An overview of centralised applications is given in Annex I.

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Since the CPMP meeting in May 1999, the European Commission has granted marketing authorisations for:

- Sustiva/Stocrin (efavirenz), indicated for treatment of HIV-1 infected adults, adolescents and children of 3 years of age and older.

See Annex II for details.

Scientific Advice

The Committee adopted the following scientific advice letters:

Part	Indication	Topic
A	Fabry's disease	Quality, pre-clinical and clinical programmes
A	Anaemia	Clinical development
A	Thrombolytic therapy in acute myocardial infarction	Pre-clinical and clinical development
B	Perennial allergic rhinitis and atopic dermatitis	Clinical development
B	Acute stroke (ischemic and intracerebral haemorrhagic)	Clinical development

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

The Committee heard three oral presentations regarding scientific advice.

From now on the scientific advice given by the CPMP stating the name of the co-ordinators will be included in the EPAR of the subsequent marketing authorisation.

Referrals

Referral under Article 7(5) of Commission Regulation (EC) No 541/95
The Committee noted the referral from France and Sweden to the CPMP of a type II variation relating to efficacy concerning a medicinal product already authorised through a mutual recognition procedure. A Rapporteur and a Co-Rapporteur were assigned.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

The CPMP heard reports from its Quality, Biotechnology, Safety, Efficacy and Pharmacovigilance Working Parties and the Ad Hoc Working Group on Blood Products.

SAFETY WORKING PARTY

One document was adopted*:*

- Revised workplan for the CPMP Safety Working Party 1999 (CPMP/SWP/2623/98 rev. 1)

EFFICACY WORKING PARTY

One document was released for two months' consultation*:*

- Concept Paper on the development of a Committee for Proprietary Medicinal Products Position Paper on Biostatistical/methodological issues arising from recent CPMP discussions on licensing applications: missing data (CPMP/EWP/1776/99)

PHARMACOVIGILANCE WORKING PARTY

One document was adopted:

- Revised workplan for the CPMP Pharmacovigilance Working Party 1999 (CPMP/PhVWP/1632/99)

AD HOC WORKING GROUP ON BLOOD PRODUCTS

The following documents were released for 6 months' consultation:

- Note for guidance on the clinical investigation of human anti-D immunoglobulin and human anti-D immunoglobulin for intravenous use (CPMP/BPWG/575/99)
- Note for guidance on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg) (CPMP/BPWG/388/95 rev. 1)
- Note for guidance on the clinical investigation of plasma derived factor VIII and IX products (CPMP/BPWG/198/95 rev. 1)
- Note for guidance on the clinical investigation of recombinant factor VIII and IX products (CPMP/BPWG/1561/99)
- Core SPC for human anti-D immunoglobulin and Human anti-D immunoglobulin for intravenous use (CPMP/BPWG/574/99)
- Core SPC for human normal immunoglobulin for intravenous administration (IVIg) (CPMP/BPWG/859/95 rev. 1)
- Core SPC for human plasma derived and recombinant coagulation factor VIII products (CPMP/BPWG/1619/99)
- Core SPC for human plasma derived and recombinant coagulation factor IX products (CPMP/BPWG/1625/99)

ORGANISATIONAL MATTERS

The following document was adopted:

- Calendar for CPMP meetings in 2001 (EMEA/CPMP/1375/99)

ICH

The following ICH guideline was released for 6 months' consultation:

- ICH topic E10: Note for guidance on choice of control group in clinical trials (CPMP/ICH/364/96)

Mutual Recognition

The CPMP noted the report from the mutual recognition facilitation group (MRFG) 21 June 1999, which is circulated together with this Press Release (Annex III).

Prof. Rolf 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

EMEA CENTRALISED PROCEDURES

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	33	45	78	15	16	31	109
Follow-up to scientific advice	9	4	13	1	1	2	15

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	62	115	177	9	12	21	198
Withdrawals	11	19	30	1	4	5	35
Positive CPMP opinions	35	65	100	5	11	16	116[1]
Negative CPMP opinions[2]	1	2	3	0	0	0	3[3]
Marketing authorisations granted by the Commission	28	60	88	9	9	18	106[4]

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	99	168	267	32	96	128	395
Positive opinions, variations type II	41	77	118	25	18	43	161
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	25	6	31	1	7	8	39

[1] 116 positive opinions corresponding to 90 substances
[2] In case of appeal the opinion will not be counted again
[3] 3 negative opinions corresponding to 2 substances
[4] 106 marketing authorisations corresponding to 82 substances

Medicinal products granted a Community Marketing Authorisation under the Centralised Procedure since the May 1999 Press Release

Brand name	Sustiva Stocrin
INN	Efavirenz
Marketing Authorisation Holders	DuPont Pharmaceuticals Limited, UK Merck Sharp & Dohme Limited, UK
ATC code	J05A G 03
Indication	Treatment of HIV-1 infected adults, adolescents and children of 3 years of age and older.
Opinion receipt date	24 February 1999
Date of Commission decision	28 May 1999

Report from the meeting held on 21 June 1999

The MRFG noted that 14 new mutual recognition procedures were finalised during the month of May 1999, as well as 63 type I and 26 type II variations.

The status as of 31 may 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	44	61	299	87	121	135	1 var.

20 new procedures (regarding 41 products) started in May 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]
0	1	1	10	0	0	0	0	8

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 other eight categories.

Each application can be classified in only one category.

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

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

General issues

- The document "Applications under Annex II of Regulation (EC) No. 541/95 in Mutual Recognition Procedures, Member States Recommendations", (including "line extensions") has been adopted and will be published on the Heads of Agencies Website as indicated below.

- The MRFG agreed that a pilot phase in the work on Mutual Recognition SPC (MR-SPC) could start in July 1999.

- Comments concerning specific products in the MRP index should be generally addressed to the reference member state directly. In addition, comments regarding the product name and marketing authorisation holder should be addressed directly to the respective concerned member state.

- As already stated in the Break-out session protocol, the latest time for the confirmation of a break-out session should be the Wednesday before the plenary MRFG meeting via the RMS.

- The June MRFG meeting was the last under German Presidency. Finland will take over the Chairmanship from the beginning of July 1999. Dr. Veijo Saano will be the next chairman. He should be contacted in future for details of the MRFG procedure.

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/