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

30 July, 1999
CPMP/2137/99

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 51st plenary meeting from 27 July, 1999 to 29 July, 1999.

Centralised Procedures[1]

The Committee adopted:

- Three positive opinions on initial centralised applications:
  - One positive opinion was adopted by consensus relating to one medicinal product containing a new active substance (Part A), a diagnostic agent indicated for the detection of thyroid remnants and well-differentiated thyroid cancer in post-thyroidectomy patients maintained on hormone suppression therapy.
  - One positive opinion was adopted by consensus relating to one medicinal product containing a new active substance (Part B), a product indicated as adjunctive therapy in the chronic management of urea cycle disorders, involving deficiencies of carbamylphosphate synthetase, ornithine transcarbamylase, or argininosuccinate synthetase.
  - One positive opinion was adopted by consensus relating to one medicinal product containing a new active substance (Part B), an antiarrhythmic, class III, indicated for:
    - Conversion of persistent atrial fibrillation or atrial flutter to normal sinus rhythm in patients in whom cardioversion by electrical means is not appropriate and in whom the duration of the arrhythmic episode is less than 6 months.
    - Maintenance of sinus rhythm (after conversion) in patients with persistent atrial fibrillation or atrial flutter.

- Three positive opinions on line extension applications (in accordance with Annex II of the Commission Regulation (EC) No 542/95):
  - One positive opinion was adopted by consensus relating to one application for a new pharmaceutical form concerning an already centrally authorised medicinal product containing a direct acting antiviral substance (Part B), indicated for the treatment of HIV-1 infected patients with advanced or progressive immunodeficiency.
  - Two revised positive opinions were adopted by consensus relating to two applications for an additional strength concerning an already centrally authorised medicinal product containing a dopaminergic agent (Part B), indicated for symptomatic treatment of advanced idiopathic Parkinsons's disease in combination with levodopa.

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

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

Three of the variations and two of the line extensions are a follow-up to three urgent safety restrictions concerning serious cases of sudden onset of sleep observed in patients treated with pramipexole

[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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(Sifrol/Daquiran/Mirapexin). Details of the previous urgent safety restrictions were described in the EMEA Public Statement dated 19 July, 1999 (EMEA/20642/99) which is available on the Internet.

Following assessment of the 20 cases of sudden onset of sleep associated with the administration of pramipexole-containing medicinal products (Sifrol/Daquiran/Mirapexin), the changes introduced in relevant sections of the SPC concerning safety information have been reinforced at the request of the marketing authorisation holders; **patients being treated with pramipexole must be informed not to drive or engage in other activities where impaired alertness could put themselves or others at risk of serious injury or death (e.g. operating machines).** Additional information is available on the Internet in a Public Statement addressing this issue (EMEA/23380/99).

Since the CPMP meeting in June 1999, the Committee noted the withdrawal of one application (Part B) from the centralised procedure because of major deficiencies in the pharmaco-toxicological and clinical parts of the documentation, particularly relating to safety and efficacy for the sought indication.

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

The CPMP considered the need for GMP inspections for six medicinal products (five Part A/one Part B) and requested an inspection for one of them.

The Committee considered the need for GLP inspections for one medicinal product (Part B) and requested an inspection.

The Committee heard three oral presentations/clarifications from applicants concerning ongoing procedures.

Rapporteurs and Co-Rapporteurs were assigned for nine applications forthcoming in the centralised procedure within the next four months (three Part A/six Part B).

An overview of centralised applications is given in Annex I.

For marketing authorisations granted by the European Commission since the last CPMP in June 1999, see Annex II.

Since the CPMP meeting in June 1999, the European Commission has refused a marketing authorisation for Rescupase (saruplase), an antithrombotic agent.

Scientific Advice

The Committee adopted the following scientific advice:

Part	Indication	Topic
B	Depression	Pre-clinical and clinical development programme
B	Hypercalcaemia and Paget's disease	Pre-clinical and clinical development programme
B	Septic shock	Quality and clinical development programme
A	Rheumatoid arthritis	Quality, pre-clinical and clinical development programme
B	Sudden hearing loss	Clinical development programme
A	Hepatic fibrosis	Clinical development programme

The Committee adopted one follow-up scientific advice on the clinical development programme

concerning one new medicinal product (Part B) intended for chronic constipation and opioid-induced constipation.

The Committee accepted six new requests and one follow-up request from companies for scientific advice. Co-ordinators were appointed.

The Committee adopted a discussion paper on oral explanation (CPMP/1299/99).

Referrals

Referral under Article 10 of Council Directive 75/319/EEC, as amended
The Committee noted the referral for arbitration to the CPMP from Germany of an antifibrinolytic agent. A Rapporteur and a Co-Rapporteur were assigned.

Working Parties and Ad Hoc Expert Groups

The CPMP heard reports from its Quality, Biotechnology, Efficacy and Pharmacovigilance Working Parties and from the Multidisciplinary Group on Thiomersal, the Ad Hoc Working Group on Blood Products and the Ad Hoc Expert Group on Update of the Guideline on the excipients on the label and package leaflet of medicinal products for human use.

QUALITY WORKING PARTY

The following document was adopted for coming into operation in January 2000:

- Note for guidance on quality of modified release products: A: Oral dosage forms, B: Transdermal dosage forms, *Section I (Quality)* (CPMP/QWP/604/96)

BIOTECHNOLOGY WORKING PARTY

Three documents were adopted*:*

- Plasma-derived medicinal products: Position paper on ALT testing (CPMP/BWP/385/99)
- Concept paper on the development of a Committee for Proprietary Medicinal Products (CPMP) Points to consider on cell-derived influenza vaccines (CPMP/BWP/1764/99)
- Concept paper on the development of a Committee for Proprietary Medicinal Products (CPMP) Points to consider on live attenuated influenza vaccines (CPMP/BWP/1765/99)

EFFICACY WORKING PARTY

The following document was adopted for coming into operation in January 2000:

- Note for guidance on modified release oral and transdermal dosage forms: *Section II (pharmacokinetic and clinical evaluation)* (CPMP/EWP/280/96)

The following document was released for 3 months' consultation:

- Points to consider concerning endpoints in clinical studies with haematopoietic growth factors for mobilisation of stem cells (CPMP/EWP/197/99)

The following document was released for 6 months' consultation:

- Note for guidance on clinical investigation of medicinal products for the treatment of multiple sclerosis (CPMP/EWP/561/98)

The following documents were adopted:

- Electronic exchange of pharmacovigilance information for human and veterinary medicinal products in the European Union (CPMP/PhVWP/2056/99) (to be released after CVMP approval at the August 1999 meeting)

- Revised Note for guidance on the Rapid Alert System (RAS) and Non-Urgent Information System (NUIS) in human pharmacovigilance (CPMP/PhVWP/005/96 Rev. 1)

- Joint pilot plan for the implementation of the electronic transmission of Individual Case Safety Reports between the EMEA, national competent authorities and pharmaceutical industry (CPMP/PhVWP/2058/99)

Mutual Recognition

The CPMP noted the report from the mutual recognition facilitation group (MRFG) 26 July 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	17	20	37	115
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	12	13	25	202
Withdrawals	11	19	30	1	5	6	36
Positive CPMP opinions	35	65	100	6	13	19	119[1]
Negative CPMP opinions[2]	1	2	3	0	0	0	3[3]
Marketing authorisations granted by the Commission	28	60	88	9	11	20	108[4]

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	99	168	267	48	113	161	428
Positive opinions, variations type II	41	77	118	32	30	62	180
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	25	6	31	1	8	9	40

[1] 119 positive opinions corresponding to 93 substances
[2] In case of appeal the opinion will not be counted again
[3] 3 negative opinions corresponding to 2 substances
[4] 108 Marketing Authorisations corresponding to 84 substances

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

Brand name	Ziagen
INN	Abacavir sulfate
Marketing Authorisation Holder	Glaxo Group Limited, UK
ATC code	J05AF06
Indication	Antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults
Opinion receipt date	25 March 1999
Date of Commission decision	8 July 1999

Brand name	Paxene
INN	Paclitaxel
Marketing Authorisation Holder	Norton Health Care Limited, UK
ATC code	L01CD01
Indication	Treatment of patients with advanced AIDS-related Kaposi's sarcoma (KS) who have failed prior liposomal anthracycline therapy
Opinion receipt date	27 January 1999
Date of Commission decision	19 July 1999

ANNEX III to CPMP July 1999
Press Release

Report from the meeting held on 26 July 1999

The MRFG noted that 14 new mutual recognition procedures were finalised during the month of June 1999, as well as 57 type I and 30 type II variations.

The status as of 30 June 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	58	66	356	54	151	129	1 var.

21 new procedures (regarding 43 products) started in June 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	9	0	0	0	0	10

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 June 1999:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	4
DE (1)	13
DE (1)	13
DE (1)	13
DE (1)	10
DE (1)	9
DE (1)	3
DK (3)	14

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (3)	1
DK (3)	1
DK (3)	1
DK (3)	1
DK (3)	1
DK (3)	1
DK (2)	2
NL (1)	2
SE (3)	5
UK (1)	2
UK (1)	1
UK (4)	9
UK (3)	14

General issues

- An in-depth analysis of the reasons for withdrawals from the Mutual Recognition Procedure was agreed by the MRFG and will start as of 1 September 1999. The aim of this project is to identify the real causes of withdrawals and to suggest solutions by which similar withdrawals could be prevented.

- A single document to record what has occurred during the whole Mutual Recognition Procedure will be prepared by the respective RMS as of 1 October 1999. This updated assessment report will help to facilitate repeat use MR procedures and granting of Marketing Authorisations by countries belonging to the PER-scheme and CADREAC countries.

- A project was started to streamline the handling of variations in the Mutual Recognition Procedure by RMS and CMS. A 'best practice guide' is currently being drafted.

- Updated MR statistics relating to the period 01.01.95 to 30.6.99 have been added to the MRFG Website.

- After its plenary meeting, the MRFG met with representatives of trade associations of pharmaceutical industry (EFPIA, AESGP, EGA).

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/