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

27 March 1998
CPMP/438/98

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 36th plenary meeting on 24-25 March 1998.

Centralised Procedures
The Committee adopted the following Opinions:

- Four positive Opinions on Centralised applications
  - One positive Opinion by consensus relating to a product containing a new active substance (Part B) indicated for ultrasound echocardiography investigations.
  - Two positive Opinions by consensus relating to two products containing the same new active substance (Part B) indicated for the reduction of atherosclerotic events in patients with a history of symptomatic atherosclerotic disease.
  - One positive Opinion by a majority of votes relating to a product containing a new active substance (Part B) indicated for the treatment of obesity.
- Four positive Opinions by consensus for Centralised type I Variations following the type II procedure and three positive Opinions by consensus for Centralised type II Variations.
- One positive Opinion by consensus following the annual re-assessment for a product indicated for the treatment of patients with locally advanced and metastatic breast cancer. The Marketing Authorisation for this product will no longer remain "under exceptional circumstances".

Rapporteurs and Co-rapporteurs were assigned for five applications forthcoming in the Centralised Procedure within the next four months two for Part A and three for Part B (one of them is a line extension to a product already approved)

An overview of Centralised Applications is given in Annex I.

Since the CPMP meeting in February 1998, the European Commission has granted a Marketing Authorisation for Combivir (combination of lamivudine and zidovudine) indicated for use in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults and adolescents over 12 years of age (Annexes II and III).

Scientific Advice
The CPMP adopted Scientific Advice in response to one request, by consensus, on manufacturing, biotechnology and clinical issues concerning one new product indicated for the treatment of patients with severe sepsis (Part A). Scientific Advice was also adopted on the follow-up for a product indicated for the treatment of chronic constipation (Part B).

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

<u>Biotechnology Working Party</u>
The following document was adopted and will come into operation in July 1999:

- Addendum to the Note for Guidance on Plasma Derived Medicinal Products:
  The introduction of Nucleic Acid Amplification Technology (NAT) for the Detection of Hepatitis C Virus RNA in Plasma Pools (CPMP/BWP/390/97)

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ICH
The following documents were adopted and will come into operation in September 1998:

- Note for Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data, ICH topic E5 (CPMP/ICH/289/95)
- Note for Guidance on Statistical Principles for Clinical Trials, ICH topic E9 (CPMP/ICH/363/96)

Mutual Recognition
The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) (23 March 1998) which is circulated together with this press release (Annex IV).

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.

Annex I to CPMP - March 1998
Press Release

CENTRALISED APPLICATIONS TO THE EMEA

	Part A	Part B	Total
Scientific Advice	26	26	52

	Centralised Applications		Total*
	Part A	Part B	
Applications submitted since 1 January 1995	52	95	147
Withdrawn	3	10	13
Opinions given by the CPMP	26	44	70**
Marketing Authorisations granted by the Commission	24	32	56***

	Final		Total
	Part A	Part B	A + B
Variations type I	72	106	178
Variations type II	19	40	59
Extensions	10	2	12

* These figures include the 18 ex-concertation procedures submitted before January 1995 of which 14 have been authorised and 4 withdrawn before end 1996

** 70 Opinions corresponding to 56 substances

*** 56 Marketing Authorisations corresponding to 47 substances

Medicinal Products granted a Community Marketing Authorisation under the Centralised Procedure since the February 1998 Press Release

Product	*Brandname:*	**Combivir**
	INN:	Lamivudine and Zidovudine
	Part A/B:	Part B
	Country of origin:	UK
Applicant	*Name:*	Glaxo Wellcome
	Country:	UK
Therapeutic Area	*ATC:*	J05AB20
	Indication:	Treatment of HIV infected adults and adolescents over 12 years of age
Presentation	*Form:*	Film coated tablets
	Dosage:	150 mg/300mg
	No. of presentations:	2 Presentations
EMEA/CPMP	*Validation:*	25.07.97
	Date of Opinion:	19.11.97
	Active time:	119 Days
	Clock stop:	None
Commission	*Opinion receipt date:*	05.01.98
	Date of Commission Decision:	18.03.98

COMBIVIR

International Non-proprietary Name (INN): **Lamivudine/zidovudine**

Abstract*

On 18 March 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product COMBIVIR, which contains lamivudine and zidovudine. This decision was based on the favourable opinion and on the assessment report adopted by the Committee for Proprietary Medicinal Products (CPMP) on 19 November 1997. The Marketing Authorisation Holder responsible for this medicinal product is Glaxo Group Limited.

The approved indication is for use in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults and adolescents over 12 years of age. Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

COMBIVIR is the first tablet to combine two known antiretroviral compounds in one tablet formulation. The two active substances contained in the tablet, lamivudine 150 mg and zidovudine 300 mg belong to the nucleoside reverse transcriptase inhibitors class. Individual formulations of lamivudine (150 mg tablets) and zidovudine (300 mg tablets) have already been authorised in the European Union for the treatment of HIV. This combined formulation aims to reduce the number of daily tablets and to improve the treatment compliance.

The clinical benefit of the combination was established based on the large experience gained with the association lamivudine/zidovudine, which was shown to be effective, and well tolerated in the treatment of HIV. In addition, a clinical study demonstrated the therapeutic equivalence between the combination and the two individual products.

COMBIVIR was found to be well tolerated. The type and severity of the adverse events associated with lamivudine and zidovudine may be expected with this combined formulation. The most frequent and significant adverse events observed during treatment of lamivudine in association with zidovudine are neutropenia and anaemia, occasionally severe.

The CPMP, on the basis of efficacy and safety data submitted considered that COMBIVIR showed adequate evidence of efficacy and a satisfactory safety profile and therefore recommended that the Marketing Authorisation should be granted.

* This text is also published as Abstract of the EPAR for Combivir

MRFG
Mutual Recognition Facilitation Group

Report from the meeting held on 23rd March 1998

The MRFG noted that 22 new mutual recognition procedures have been finalised during the month of February 1998 as well as 20 type I and 19 type II variations.
The status as of 28th February 1998 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	29	35	28	43	25	89	--

11 new procedures (regarding 24 products) have been started in February 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]
4	1	0	3	0	1	2

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 February 1998:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (2)	2
FR (5)	1
FR (5)	6
FR (1)	1
UK (2)	1
UK (1)	7
UK (1)	7
UK (4)	9
UK (1)	4
UK (1)	14
UK (1)	4

General issues

- The Group received a report from its Eudratrack subgroup. It was noted that progress has been made and that the tracking system should be operational by May.
  During April 1998 there will be a 1-month operational tracking with the usual fax support.
  The group noted that problems still remain with the extraction of statistical information from the database and this is being addressed further.

- The Group agreed the operational details for the Automatic Validation of MR Procedures for New Applications, which it had decided upon at its February meeting. This procedure will start from May the 1st for a six-month trial.

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

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