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

1 March, 1999
CPMP/566/1999

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 45th plenary meeting from 23 February to 25 February 1999.

Centralised Procedures

The Committee adopted:

- Five positive opinions[1] on centralised applications:

  - One positive opinion was adopted by consensus relating to one medicinal product containing a new active substance (Part B), an antithrombotic agent/platelet aggregation inhibitor which is indicated for the prevention of early new myocardial infarction within the first 3-4 days after onset of acute angina symptoms.
  - Two positive opinions were adopted by consensus relating to two medicinal products containing the same new active substance (Part A), where a reverse transcriptase inhibitor is indicated in combination with interferon alfa-2b in relation to certain chronic hepatitis C status.
  - Two positive opinions were adopted by consensus relating to two medicinal products containing the same new active substance (Part B), where a reverse transcriptase inhibitor is indicated in antiviral combination treatment of HIV-1 infected adults, adolescents and children of 3 years of age and older.

- Two positive opinions on applications in accordance with Annex II of the Commission Regulation (EC) No 542/95:

  - One positive opinion was adopted by majority vote relating to one application for a new pharmaceutical form concerning an already centrally authorised medicinal product containing an anticholinesterase (Part B) indicated for symptomatic treatment of mild to moderate severe Alzheimer's dementia.
  - One positive opinion was adopted by consensus relating to one application for an additional strength concerning an already centrally authorised medicinal product containing a hormonal ovulation stimulant (Part A), indicated for:
    (i) Anovulation (including polycystic ovarian disease, PCOD);
    (ii) Stimulation of multifollicular development in patients undergoing superovulation for assisted reproductive technologies (ART);
    (iii) Stimulation of spermatogenesis in men with hypogonadotrophic hypogonadism (Treatment in combination with concomitant human Chorionic Gonadotropin (hCG).

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

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

A public statement concerning Trovan IV and Turvel IV (alatrofloxacin mesylate) on additional physico-chemical incompatibility information is published on the Internet (CPMP/573/99).

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[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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Since the CPMP meeting in January 1999, the Committee noted the withdrawal of one application (Part B) from the centralised procedure because the risk/benefit ratio was unfavourable.

The CPMP finalised procedures concerning two inspections requests relating to four medicinal products (Part B) including one triple application for the same substance.

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

An overview of centralised applications is given in Annex I.

Since the CPMP meeting in January 1999, the European Commission has granted a marketing authorisation for:

- Infergen (Interferon-alphacon-1), indicated for the treatment of patients of 18 years and older with histologically proven chronic hepatitis and serum markers for hepatitis C virus (HCV) infection e.g. those who have elevated serum transaminase levels without decompensated liver disease.

See Annex II for details.

Scientific Advice

The Committee:

- Accepted seven new requests from companies for scientific advice. Co-ordinators were appointed.

- Adopted two scientific advice letters and two follow-up to scientific advice on quality and clinical development concerning four medicinal products, one Part A/three Part B, intended for:

    - Treatment of patients with coughs by chronic/severe diseases (lung cancer) and patients with cough due to acute upper respiratory tract infections.
    - Management of acute pain in patients requiring opioid analgesia.
    - Haemophilus influenza type b vaccine.
    - Treatment of urinary stress incontinence.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

The CPMP heard reports from its Quality, Biotechnology, Safety, Efficacy and Pharmacovigilance Working Parties and from the Ad Hoc Expert Working Group for revision of the guideline on excipients in the label and package leaflet of medicinal products for human use.

QUALITY WORKING PARTY

Two documents were adopted*:*

- The Quality Working Party Workplan for 1999/2000 (CPMP/QWP/583/99).
- Annex to the CPMP Note for Guidance on development pharmaceutics: Decision trees for the selection of sterilisation methods (CPMP/QWP/054/98).

BIOTECHNOLOGY WORKING PARTY

Two documents were adopted*:*

- A concept paper for the development of Points to consider on human somatic cellular therapy (CPMP/BWP/2257/98).
- EMEA Workshop on application to pharmaceuticals of assays for markers of TSE, held on 19-20 January 1999. Report to the CPMP from the Biotechnology Working Party (CPMP/BWP/257/99).

SAFETY WORKING PARTY

The Concept paper on revision of the CPMP Note for Guidance on carcinogenic potential (CPMP/SWP/166/99) was adopted.

EFFICACY WORKING PARTY

Two documents were adopted*:*

- Concept paper on the development of a CPMP points to consider concerning endpoints in clinical studies with haematopoietic growth factors for mobilisation of stem cells (CPMP/EWP/197/99).
- Concept paper on the development of a CPMP points to consider on biostatistical/methodological issues arising from recent CPMP discussions on licensing applications: superiority, non-inferiority and equivalence (CPMP/EWP/482/99).

The following documents were released for 3 months' consultation:

- Points to Consider on wording of Helicobacter Pylori eradication therapy in selected SPC sections (CPMP/EWP/863/98 draft).
- Points to Consider on clinical investigation of medicinal products for prophylaxis of intra- and post-operative venous thromboembolic risk (CPMP/EWP/707/98 draft).
- Points to Consider on the clinical investigation of new medicinal products for the treatment of unstable angina pectoris or non-Q-wave myocardial infarction (CPMP/EWP/570/98 draft).

The following documents were released for 6 months consultation:

- Note for Guidance on clinical investigation of medicinal products for the treatment of cardiac failure (CPMP/EWP/235/95 revision 1 draft).
- Note for Guidance on clinical investigation of medicinal products for the treatment of venous thromboembolic disease (CPMP/EWP/563/98 draft).

PHARMACOVIGILANCE WORKING PARTY

The Revised Note for Guidance on the procedure for competent authorities on the undertaking of pharmacovigilance activities (CPMP/PhVWP/175/95 revision 1) was adopted.

ORGANISATIONAL MATTERS

The following documents were adopted:

- Report to define the role and responsibilities of the Scientific Advice Review Group (CPMP/180/99).
- Procedure for developing CPMP guidelines and Points to consider documents (CPMP/2024/98).

Mutual Recognition

The CPMP noted the report from the mutual recognition facilitation group (MRFG) 22 February 1999, which is circulated together with this Press Release (Annex IV).

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

CENTRALISED APPLICATIONS TO THE EMEA

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	33	45	78	3	3	6	84
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	3	5	8	185
Withdrawals	11	19	30	0	2	2	32
Positive CPMP opinions	35	65	100[2]	4	5	9[3]	109[4]
Negative CPMP opinions	1	2	3[5]	0	0	0	3[6]
Marketing authorisations granted by the Commission	28	60	88[7]	3	2	5	93[8]

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	99	168	267	2	32	34	301
Positive opinions, variations type II	41	77	118	9	7	16	134
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	25	6	31	1	1	2	33

[2] 100 positive opinions corresponding to 76 substances
[3] 9 positive opinions corresponding to 7 substances
[4] 109 positive opinions corresponding 83 substances
[5] 3 negative opinions corresponding to 2 substances
[6] 3 negative opinions corresponding to 2 substances
[7] 88 marketing authorisations corresponding to 67 substances
[8] 93 marketing authorisations corresponding to 72 substances

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

PRODUCT	**Brand name**	**Infergen**
	INN	Interferon-alfacon-1
	Part A/B	A
COMPANY ORIGIN	**Country**	NL
MARKETING AUTHORISATION HOLDER	**Name**	Yamanouchi Europe BV
THERAPEUTIC AREA	**ATC code**	L03
	Indication	Treatment of patients of 18 years and older with histologically proven chronic hepatitis and serum markers for hepatitis C virus (HCV) infection e.g. those who have elevated serum transaminase levels without decompensated liver disease.
PRESENTATION	**Pharmaceutical form**	Solution for injection
	Strength	9 micrograms
	Number of presentations	3
EMEA/CPMP	**Validation**	25 July 1997
	Date of opinion	23 July 1998
	Active time	182
	Clock stop	181
COMMISSION DECISION	**Opinion receipt date**	3 December 1998
	Date of Commission decision	1 February 1999

Abstracts for Products granted a Community Marketing Authorisation under the centralised procedure since the January 1999 Press Release

INFERGEN

International Nonproprietary Name (INN): **Interferon alfacon-1**

Abstract[9]

On 1 February 1999 the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Infergen, which contains interferon alfacon-1. This decision was based on the assessment report on the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 23 July 1998. The Marketing Authorisation Holder responsible for this medicinal product is Yamanouchi Europe B.V. Netherlands.

The approved indication is for the treatment of adult patients with histologically proven chronic hepatitis with serum markers for hepatitis C virus (HCV) infection e.g. those who have elevated serum transaminase without decompensated liver disease. 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.

The active substance of Infergen, interferon alfacon-1 is a protein, an immunomodulator, and immunoregulator with antiviral and antiproliferative effects.

Clinical trials were designed to investigate the safety and efficacy of Infergen in the treatment of histologically proven chronic hepatitis in patients with serum markers for hepatitis C infection e.g. those who have elevated serum transaminase without decompensated livel disease. These studies showed that Infergen was comparable to interferon alfa-2b. During treatment the majority of patients experienced fever, fatigue, headache and myalgia.

The CPMP, on the basis of safety, quality and efficacy data submitted, considered that Infergen showed a favourable risk benefit ratio for the approved indications, and therefore recommended that the Marketing Authorisation should be granted.

[9] This text will be published as abstract of the full EPAR

MRFG
Mutual Recognition Facilitation Group

Report from the meeting held on 22 February 1999

The MRFG noted that 8 new mutual recognition procedures were finalised during the month of January 1999, as well as 38 type I and 30 type II variations.

The status as of 31 January 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	8	23	38	97	30	114	

5 new procedures (regarding 11 products) started in January 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	Vaccines	Others[5]
1	1	0	1	0	0	0	0	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 other eight categories.

Each application can be classified in only one category.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (4)	1
DK (1)	2

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
FR (1)	14
UK (2)	4
UK (3)	10

General issues

- The MRFG would like to remind applicants to state the European Procedure Number of the variation on all documentation submitted for the variation.
- Position Papers of the MRFG on "duplicate applications", line extensions and repeat use ("second wave") applications, are currently being elaborated and could be finalised shortly.
- Following the MRFG meeting, there was a meeting with representatives of PEFRAS (Pan European Federation of Regulatory Affairs Societies).

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/