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

29 March, 1999
CPMP/841/99

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 47th plenary meeting from 23 March to 25 March 1999.

Centralised Procedures

The Committee adopted:

- Opinions[1] on initial centralised applications:

  - One positive opinion was adopted by consensus relating to a medicinal product (Part B), a nucleoside analogue reverse transcriptase inhibitor indicated in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults.

- Opinions on line extensions applications (in accordance with Annex II of the Commission Regulation (EC) No 542/95):

  - One positive opinion was adopted by consensus relating to an application for a new pharmaceutical form concerning an already centrally authorised medicinal product (Part B), containing an antiviral agent, indicated as part of combination therapy for the antiviral treatment of HIV-1 infected adult patients with advanced or progressive immunodeficiency.

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

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

- Appeals in centralised procedures :

  Three negative opinions adopted in October 1998 were confirmed in the appeal procedures:

  - Two negative opinions were adopted by majority of votes relating to two medicinal products containing the same new active substance (Part B), for the treatment of dementia.

  - One negative opinion was adopted by majority of votes relating to a medicinal product containing a new active substance (Part A), a thrombolytic agent.

Since the CPMP meeting in February 1999, the Committee noted the withdrawal of one application (Part B) from the centralised procedure because of unresolved problems related to interpretation of the results from pivotal equivalence trials, and safety concerns.

The CPMP adopted the GMP inspections requests for five medicinal products (Part B). Two inspections has been requested by the CPMP.

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

Rapporteurs and Co-Rapporteurs were assigned for 17 applications forthcoming in the centralised procedure within the next four months, six for Part A and eleven for Part B, including two double applications for the same active substance (one Part A and one Part B).

An overview of centralised applications is given in Annex I.

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

- Zaleplon-Wyeth Medica Ireland (zaleplon)
- Sonata (zaleplon)

both indicated for the treatment of patients with insomnia.

See Annexes II & III for details.

Scientific Advice

The Committee:

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

- Adopted nine scientific advice letters on quality, preclinical and/or clinical issues, and clinical development plans concerning nine medicinal products, three part A and six part B, intended for:

    - Relapsed acute myeloid leukaemia
    - Stable angina
    - Open angle glaucoma or raised intra-ocular pressure
    - Hepatitis C
    - Crohn's disease
    - Anorexia associated with AIDS, cancer chemotherapy and multiple sclerosis induced spasticity
    - Cystic fibrosis
    - Psychotic disorders and schizophrenia
    - Severe sepsis.

Referrals

Referrals under Article 10 of Council Directive 75/319/EEC, as amended
The Committee heard an oral presentation/clarification from the applicant and adopted by consensus a positive opinion following a referral for arbitration to the EMEA under the mutual recognition procedure and such opinion will be forwarded to the Commission.

Referrals under Article 15a of Council Directive 75/319/EEC, as amended
The Committee heard four oral explanations/clarifications from companies. The opinions are scheduled for adoption at the April CPMP meeting.

ICH

The following document was adopted:

- Note for guidance on specifications: Tests and procedures for biotechnological/biological products (CPMP/ICH/365/96) ICH Topic Q6B.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

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

QUALITY WORKING PARTY

The CPMP agreed to the proposal from the Quality Working Party on clarification of the operation of the two year transition period (agreed by the CPMP in October 1998) for application of the Note for Guidance on Residual Solvents (CPMP/ICH/283/95) to marketed products. This proposal will be published on the EMEA Website.

BIOTECHNOLOGY WORKING PARTY

The following document was released for 3 months' consultation:

- Explanatory note: the expiry date of products incorporating plasma-derived products as stabilisers or excipients. Addendum to Note for guidance on plasma-derived medicinal products (CPMP/BWP/305/99)

The following document was released for 6 months' consultation:

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

The following document was adopted:

- Preliminary EU recommendations for the influenza vaccine composition for the season 1999/2000 (CPMP/BWP/733/99)

The TSE Note for guidance was discussed at the BWP Meeting of March 1999. The comments from Directorate-General XXIV / Scientific Steering Committee were taken into account. The amendments were accepted by the CPMP. The amended guideline will be forwarded to the Commission before adoption at the April CPMP meeting.

ORGANISATIONAL MATTERS

Following the publication of Council Regulation (EC) No 2743/98 on 14 December 1998 (OJ L 345, 19.12.1999, p. 3) amending Regulation (EC) No 297/95 on fees payable to the EMEA, and following the adoption of the Implementing Rules by the EMEA Management Board on 10 February, the EMEA has published a summary of the new fees together with an explanatory note on the EMEA Website (Documents/Regulatory Affairs).

Mutual Recognition

The CPMP noted the report from the mutual recognition facilitation group (MRFG) 22 March 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

EMEA CENTRALISED PROCEDURES

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific advice	33	45	78	6	9	15	93
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	6	5	11	188
Withdrawals	11	19	30	0	3	3	33
Positive CPMP opinions	35	65	100[2]	2[3]	8[3]	10[4]	110[5]
Negative CPMP opinions[6]	1	2	3[7]	0	0	0	3[8]
Marketing authorisations granted by the Commission	28	60	88[9]	3	4[10]	7	95[11]

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	99	168	267	3	41	44	311
Positive opinions, variations type II	41	77	118	9	10	19	137
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	25	6	31	1	2	3	34

2 100 positive opinions corresponding to 76 substances
3 Correction to February Press Release, 2 products previously listed under Part A instead of B
4 10 positive opinions corresponding to 8 substances
5 110 positive opinions corresponding to 84 substances
6 In case of appeal the opinion will not be counted again.
7 3 negative opinions corresponding to 2 substances
8 3 negative opinions corresponding to 2 substances
9 88 marketing authorisations corresponding to 67 substances
10 4 marketing authorisations corresponding to 3 substances
11 95 marketing authorisations corresponding to 73 substances

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

PRODUCT	**Brand names**	**Sonata** **Zaleplon Wyeth Medica Ireland**
	INN	zaleplon
	Part A/B	Part B
COMPANY ORIGIN	**Country**	USA
MARKETING AUTHORISATION HOLDER	**Name**	Wyeth
THERAPEUTIC AREA	**ATC code**	N05CH01
	Indication	Short term treatment of insomnia
PRESENTATION	**Pharmaceutical form**	Capsules
	Strength	5mg, 10mg
	Number of presentations	6
EMEA/CPMP	**Validation**	30.01.1998
	Date of opinion	19.11.1998
	Active time	182
	Clock stop	113
COMMISSION DECISION	**Opinion receipt date**	13.01.1999
	Date of Commission decision	12.03.1999

Abstracts for Products granted a community Marketing Authorisation under the centralised procedure since the February 1999 Press Release

SONATA

International Nonproprietary Name (INN): Zaleplon

Abstract

On 12 March 1999, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Sonata, which contains zaleplon. This decision was based on the assessment report and on the favourable Opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 19 November 1998. The Marketing Authorisation Holder responsible for this medicinal product is Wyeth Europa Limited, UK.

The approved indication is for the treatment of patients with insomnia who have difficulty falling asleep. It is indicated only when the disorder is severe, disabling or subjecting the individual to extreme distress. 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 Sonata is zaleplon a hypnotic agent which binds selectively to the benzodiazepine type I receptor in the Central Nervous System (CNS). Zaleplon is rapidly absorbed after oral administration and peak concentrations are reached after 1 hour. Zaleplon is also rapidly metabolised with an elimination half-life of 1 hour.

In clinical trials zaleplon has been shown to be a safe and effective hypnotic with a rapid onset of action and a low propensity to cause carryover effects on the following day. However zaleplon did not show clinically significant differences from placebo for a series of sleep maintenance measures. Due to its short half-life alternative therapy should be considered if early morning awakening is experienced.

No major CNS or other side effects were associated with the recommended doses of 5 or 10mg studied and there was no evidence for the occurrence of rebound insomnia or other withdrawal effects following their abrupt discontinuation. The most apparent undesirable effects observed during clinical studies included mild headache, asthenia (weakness), somnolence and dizziness.

The CPMP, on the basis of efficacy and safety data submitted, considered that there was a favourable benefit to risk balance for Sonata and recommended that the Marketing Authorisation should be granted.

ZALEPLON-WYETH MEDICA IRELAND

International Nonproprietary Name (INN): Zaleplon

Abstract

On 12 March 1999, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Zaleplon-Wyeth Medica Ireland, which contains zaleplon. This decision was based on the assessment report and on the favourable Opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 19 November 1998. The Marketing Authorisation Holder responsible for this medicinal product is Wyeth Research (UK) Limited, UK.

The approved indication is for the treatment of patients with insomnia who have difficulty falling asleep. It is indicated only when the disorder is severe, disabling or subjecting the individual to extreme distress. 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 Zaleplon-Wyeth Medica Ireland is zaleplon a hypnotic agent which binds selectively to the benzodiazepine type I receptor in the Central Nervous System (CNS). Zaleplon is rapidly absorbed after oral administration and peak concentrations are reached after 1 hour. Zaleplon is also rapidly metabolised with an elimination half-life of 1 hour.

In clinical trials zaleplon has been shown to be a safe and effective hypnotic with a rapid onset of action and a low propensity to cause carryover effects on the following day. However zaleplon did not show clinically significant differences from placebo for a series of sleep maintenance measures. Due to its short half-life alternative therapy should be considered if early morning awakening is experienced.

No major CNS or other side effects were associated with the recommended doses of 5 or 10mg studied and there was no evidence for the occurrence of rebound insomnia or other withdrawal effects following their abrupt discontinuation. The most apparent undesirable effects observed during clinical studies included mild headache, asthenia (weakness), somnolence and dizziness.

The CPMP, on the basis of efficacy and safety data submitted, considered that there was a favourable benefit to risk balance for Zaleplon-Wyeth Medica Ireland and recommended that the Marketing Authorisation should be granted.

MRFG
Mutual Recognition Facilitation Group

Report from the meeting held on 22 March 1999

The MRFG noted that 8 new mutual recognition procedures were finalised during the month of February 1999, as well as 60 type I and 21 type II variations.

The status as of 28 February 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	16	25	98	74	51	119	--

14 new procedures (regarding 18 products) started in February 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]
1	1	1	4	0	0	0	0	7

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 February 1999:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (1)	5
FR (1)	1
FR (1)	14

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
FR (1)	10
FR (1)	11
NL (3)	8
SE (1)	12
SE (1)	2
SE (1)	12
SE (1)	9
UK (1)	1
UK (3)	9
UK (1)	1
UK (1)	1

General issues

- The Position Paper on "Duplicate Applications" ("Recommendations on duplicate applications in mutual recognition procedures") was finalised and will be available at the MRFG website [http://heads.medagencies.org/]
- Position Papers of the MRFG on informed consent applications, line-extensions and repeat use ("second wave") applications are currently under discussion.
- The MRP Index will be launched by 15 April 1999.

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/