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

20 November 1997
CPMP/1056/97

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 32nd plenary meeting on 18-19 November 1997. This meeting was followed on 19 November 1997 by a debriefing meeting with Interested Parties.

Centralised Procedures

The Committee adopted by consensus the following opinions:

- Two positive opinions on centralised applications:
  - One relating to a new fixed combination product (Part B) for the treatment of HIV infected patients. It was possible to conclude this review within a 118-day assessment period.
  - One relating to a product containing a new active substance (Part B) indicated for detection of Helicobacter pylori infection.
- Three positive opinions for centralised type I variations following the type II procedure and eight positive opinions for centralised type II variations.
- One positive opinion was given following an annual re-assessment for a product indicated in combination therapy for the treatment of HIV-infection.

The Committee noted the withdrawal of two applications.

For five (1 Part A and 4 Part B) applications forthcoming in the centralised procedure within the next four months rapporteurs and co-rapporteurs were assigned.

Since the CPMP meeting in October 1997, the European Commission has granted a marketing authorisation for DAQUIRAN (pramipexole), indicated for the treatment of idiopathic Parkinson's disease (27 October 1997). A summary concerning this product is given in Annex III.

An overview of the centralised applications is given in Annex I and II.

Statement on nvCJD and Blood Products

In the light of recent published information on new variant Creutzfeldt-Jakob Disease (nvCJD), the CPMP considered that there is a need to review all available information (including unpublished/preliminary data) on nvCJD and relevant transmissible spongiform encephalopathies (TSEs). CPMP is convening a further expert ad hoc meeting to examine the emerging information and to advise further on any implications for human plasma derived medicinal products.

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In the meantime, and as a precautionary measure, CPMP considers that it would be prudent to withdraw batches of plasma derived medicinal products from the market in the event that a donor to a plasma pool subsequently has a confirmed diagnosis of nvCJD. However, consequences for essential medicinal products where alternatives may be unavailable will need careful consideration.

A further CPMP statement will be made after consideration of the advice of the expert group.

Scientific Advice

The CPMP adopted by consensus one scientific advice on preclinical and clinical development for an antiviral agent intended for the treatment of eye infections. Four new requests for scientific advice were accepted as justified, and co-ordinators were appointed.

Referrals under Article 15(a) of Council Directive 75/319/EEC, as amended

Further to a referral to the CPMP at its October 1997 meeting of fenfluramine and dexfenfluramine containing medicinal products, a procedure was initiated by Belgium for phentermine and amphepramone containing medicinal products. Both referrals relate to pharmacovigilance concerns.

Working Parties and Ad Hoc Expert Groups

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

Biotechnology Working Party:

The principal issues of discussion were the 'Summary of the Provisional CPMP Report: Medicinal Products for Human Use Affected by Commission Decision 97/534/EC', and the 'Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents Via Medicinal Products (Revision October 1997)'. The CPMP is continuing to revise this Note for Guidance. However it cannot be finalised until proposed amendments to Commission Decision 97/534/EC and Council Directive 75/318/EEC have been adopted and taken into account.

Efficacy Working Party:

The following document was adopted:

- Points to Consider on Hormone Replacement Therapy (HRT) (CPMP/EWP/021/97)

The following document was released for six months consultation:

- Note for Guidance on Clinical Investigation of Medicinal Products in the Treatment of Parkinson's Disease (CPMP/EWP/563/95)

Ad Hoc Group of Experts on Antiretroviral Medicinal Products:

The following document was adopted:

- Points to Consider in the Assessment of Anti-HIV Medicinal Products (CPMP/602/95 Rev.1)

ICH

The CPMP agreed to participate in the Common Technical Document project.

Organisational Matters

Since the date of first release of Rapporteur's and Co-Rapporteur's assessment reports to the applicant seems to have given rise to some confusion, the CPMP highlighted that, as agreed, such release should take place at day 70 of the procedure. It further emphasised that, as stated in the Notice to Applicants, such assessment reports do not yet represent the position of the CPMP.

Mutual Recognition

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) (17 November 1997) which is circulated together with this press release.

CPMP Meeting Dates 1999

25-28 January	17-20 May	20-23 September
22-25 February	21-24 June	18-21 October
22-25 March	26-29 July	15-18 November
19-22 April	23-26 August	13-16 December

Prof. R. Bass
Head of Human Medicines Evaluation Unit

Annex I:	Centralised Applications: Statistics
Annex II:	New Community Marketing Authorisations
Annex III:	Product Summary for DAQUIRAN (pramipexole)

This press release and other documents are available on the Internet at the following address: http://www.eudra.org/emea.html

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ANNEX I to **CPMP - November 1997**
Press Release

CENTRALISED APPLICATIONSTO THE EMEA

	CENTRALISED		**TOTAL***
	Part A	***Part B***	
Applications submitted since 01.01.95	47	82	129
Withdrawn	2	8	10
Review ongoing	19	37	56
Opinions given by CPMP	26	37	63**
Marketing Authorisation granted by Commission	24	27	51***

* These figures include the 18 ex-concertation procedures submitted before January 1995 of which 14 have been authorised and 4 withdrawn before end 1996
** 63 Opinions corresponding to 48 substances
*** 51 Marketing Authorisations corresponding to 41 substances

	PENDING		**FINAL**		**TOTAL**
	Part A	***Part B***	***Part A***	***Part B***	
Variations type I	4	9	62	62	137
Variations type II	2	3	18	29	52
Extensions	16	2	10	2	30
Scientific advice	9		40		49

Update 20 November 1997

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ANNEX II to **CPMP – November 1997**
Press Release

Medicinal Products granted a Community Marketing Authorisation under the Centralised Procedure

Status: November 1997

Product a) Brandname b) INN c) Part A/B	**Company** a) Name b) Origin	**Therapeutic Area** a) ATC b) Indication	**Presentation** a) Form b) Dose c) Number of Presentations	**EMEA/CPMP** a) Validation b) Opinion c) Active Time d) Clock stop	**Commission** a) Trans-mission to COM b) Date of decision c) Date of notification d) OJ No.
a) **DAQUIRAN** b) pramipexole c) Part B	a) Dr. K. Thomae b) DE	a) N04BC b) Treatment of idiopathic Parkinson's disease	a) Tablets b) 0.125 mg, 0.25 mg, 1.0 mg, 1.25 mg, 1.5 mg c) 10 Presentations	a) 18.06.96 b) 18.06.97 c) 208 Days d) 141 Days	a) 05.08.97 b) 27.10.97 c) d)

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ANNEX III to **CPMP – November 1997**
Press Release

DAQUIRAN

International Non-proprietary Name (INN): **pramipexole**

On 27 October 1997, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product DAQUIRAN, which contains pramipexole. This decision was based on the favourable opinion and on the assessment report adopted by the Committee for Proprietary Medicinal Products (CPMP) on 18 June 1997. The Marketing Authorisation Holder responsible for this medicinal product is Dr. Karl Thomae GmbH, Germany.

The approved indication is for the treatment of signs and symptoms of advanced idiopathic Parkinson's disease (PD) in combination with levodopa i.e. over the course of the disease, when the effect of levodopa wears off or becomes inconsistent and fluctuations of the therapeutic effect occur (end of dose or "on off" fluctuations). Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in this EPAR and is available in all European Union official languages.

The active substance of DAQUIRAN, pramipexole is a amino-benzothiazole derivative. It has been shown to be a selective and specific full dopamine (DA) receptor agonist with high affinity and selectivity for the DA D2 receptor subfamily, and particularly the D_3 receptor subtype.

Clinical trials were performed in advanced idiopathic PD patients showing end-of-dose phenomena on optimized L-dopa therapy. In this patient population, a clinically relevant benefit of pramipexole was demonstrated for up to 6 months in comparison to placebo.

In general, the side-effect profile of pramipexole is typical of a DA agonist, including hallucinations, sleep disturbances and gastrointestinal effects. In addition, ophthalmologic monitoring is recommended at regular intervals or if vision abnormalities should occur due to a suspected potential of pramipexole to cause ocular toxicity. An increased dyskinesia frequency, particularly in women could not be excluded, and therefore L-dopa dose adjustments may be required. By these precautions and recommendations, which are included in the SPC, the potential safety concerns were considered to be adequately addressed.

The CPMP, on the basis of efficacy and safety data submitted, considered that DAQUIRAN 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 DAQUIRAN.

MRFG

Mutual Recognition Facilitation Group

Report from the meeting held on 17th November 1997

The MRFG noted that 13 new mutual recognition procedures have been finalised recently as well as 5 type I and 51 type II variations.
The status as of 17th November 1997 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
1997	126	47	80	23	145	56	1 N.A. + 1 Var.

18 new procedures (regarding 40 products) have been started since 20th October. 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]
1	2	2	7	0	0	6

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 strenght, 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 since 20th October 1997:

Reference Member State (number of products involved in the procedure)	Number of CMS involved in the procedure
DE (3)	3
DE (3)	1
DE (1)	1
DE (1)	5
DE (1)	2
DK (1)	6

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FR (1)	1
NL (3)	6
NL (2)	2
NL (2)	2
NL (2)	1
SE (1)	4
SE (2)	2
UK (1)	5
UK (1)	10
UK (1)	10
UK (6)	10
UK (8)	13

General issues

- EudraTrack. The MRFG received a report from its EudraTrack Sub-group which had met to monitor and review the first month of the live operation of the system. Operational and network problems had been noted. Progress was being made but the system was not yet in a position to generate the standard reports required by the MRFG. The sub-group would meet again in December.
- The MRFG agreed a format for the response document of the applicant after day 60. This template will be issued with the December MRFG report and should further enhance the operation of the procedure. It complements the template previously agreed for the reporting of the potentially serious public health objections and the SPC comments agreed by the MRFG in the spring.
- The arrangement for the authorisation of influenza vaccines through the MR procedure for the 1998/99 season were further reviewed. The MRFG plans to meet with the European Vaccines Manufacturers(EVM) in December. It was noted that the procedures for reviewing the five core dossiers through mutual recognition had commenced on schedule.
- The MRFG wishes to continue the fruitful dialogue with the European trade associations (EFPIA, AESGP, EGA). It proposes to hold two such meetings in the first six months of 1998.
- The MRFG has selected and adopted a logo which appears at the head of this report. This will give an important identity to the mutual recognition procedure and to the MRFG. It illustrates the significant progress which has been made for this important part of the single community system.
- The group also considered a series of procedual issues and classifications for individual products and gave responses to the companies concerned.
- Eight break-out meetings were held.
- The report shows that 18 procedures (regarding 40 applications) have been started since the October meeting.
- The MRFG considered how video conferencing could be used in future to assist break-out sessions. An inventory of video conferencing facilities in the member states will be made for the December meeting.

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

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