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

2 May 2001
CPMP/1252/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
MEETING REPORT

24 to 25 APRIL 2001

The Committee for Proprietary Medicinal Products (CPMP) held its 70th plenary meeting from 24 to 25 April 2001.

The CPMP welcomed Dr. Peter Arlett as a new member from the United Kingdom, succeeding Prof. Alasdair Breckenridge. On behalf of the CPMP, the CPMP Chairman expressed his thanks to Prof. Alasdair Breckenridge's contribution to the work of the Committee.

Product related issues

Centralised procedures

The CPMP adopted two opinions on initial marketing authorisation applications:

- One positive opinion by consensus for the medicinal products Liprolog, Liprolog-Pen, Liprolog Mix25, Liprolog Mix50, Liprolog Mix25 Pen and Liprolog Mix50 Pen, intended for the treatment of diabetes mellitus. The applicant for these medicinal products is Eli Lilly Nederland BV. The active substance of Liprolog is insulin lispro, a fast acting human insulin analogue medicinal product which regulates glucose metabolism (for further details please see Summary of Opinion published on the EMEA Website: http://www.emea.eu.int/pdfs/human/opinion/114001en.pdf).
- One negative opinion by consensus recommending the refusal of the granting of a marketing authorisation for the medicinal product EVOXAC, 15 and 30 mg, hard capsules, intended for the treatment of symptoms of dry mouth in patients with primary Sjögren's syndrome or with secondary Sjögren's syndrome associated with rheumatoid arthritis, polymyositis, systemic lupus erythematosus or systemic sclerosis. The applicant for this medicinal product is Snow Brand France S.A.R.L. The active substance of EVOXAC is cevimeline, a cholinergic agonist medicinal product, which has specificity for the muscarinic M_1 and M_3 receptors (for further details please see Summary of Opinion published on the EMEA Website: http://www.emea.eu.int/pdfs/human/opinion/220300en.pdf).

Further to the renewed suspension of the marketing authorisations of Trovan/Trovan IV and Turvel/Turvel IV, the CPMP was informed of the notification to the European Commission from the Marketing Authorisation Holders (Pfizer Ltd. and Roerig Farmaceutici Italiana S.p.A.) to voluntarily withdraw their Marketing Authorisations of the above mentioned medicinal products (for further information, please see http://www.emea.eu.int/pdfs/human/press/pus/233501en.pdf).

An appeal procedure under article 8 of Council Regulation (EEC) No 542/95 was initiated and Rapporteur and Co-Rapporteur were appointed.

The CPMP agreed to an accelerated evaluation request for a medicinal product indicated in HIV infections in heavily pre-treated patients.

The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 1** and an overview of centralised procedures since 1995 is given in **Annex 2**.

For marketing authorisations granted by the European Commission since the last CPMP plenary meeting in March 2001, see **Annex 3**.

Referral procedure

One harmonisation procedure was started under article 11 of Council Directive 75/319/EEC, as amended. This referral was initiated by the French National Competent Authority.

Scientific Advice procedures

The CPMP was informed of the outcome of the discussions of the Scientific Advice Review Group (SciARG) meeting, which was held on Monday 23 April 2001. For further details, please see **Annex 4**.

Other product related issues

As part of the Committee's ongoing scientific review on cardiovascular risks and third generation oral contraceptives, the CPMP heard an oral explanation from marketing authorisation holders. The CPMP will continue its discussions at its next meeting on 29 to 31 May 2001.

Non-product related issues

CPMP Working Parties and Ad-Hoc Groups

A meeting between the CPMP Chairman and Vice-Chairman, the CPMP Working Parties' the Chairpersons, European Commission and EMEA representatives took place on Tuesday 24 April 2001 in order to discuss CPMP/ICH activities, Working Parties' meetings with Interested Parties and the Working Parties' mandates.

The CPMP adopted the Joint Pharmacovigilance plan for the implementation of the ICH E2B, M1 and M2 requirements related to the electronic transmission on individual case safety reports in the Community.

In relation to the European paediatric medicines initiative, the Committee heard a presentation regarding the FDA's implementation of the paediatric exclusivity and paediatrics rules regarding medicines in children in the United-States. The CPMP decided to establish an ad hoc Expert Group on Paediatrics under the chairmanship of Dr Daniel Brasseur, Chairman of the CPMP.

The CPMP heard a report from the ad hoc Expert Group meeting on radio-pharmaceuticals which was held on 2 April 2001 and it was agreed that the discussion will continue at the May 2001 plenary meeting.

An overview of guidance documents adopted during the meeting or released for consultation to Interested Parties is attached as **Annex 5**.

Organisational Matters

CPMP Members were informed and invited to the informal CPMP meeting which is going to take place in Sweden (Uppsala) on 17 and 18 May 2001. During this meeting, there will also be joint CPMP/MRFG and CPMP/COMP sessions.

The third CPMP Ad-Hoc Group on Organisational Matters (ORGAM) was held on 23 April 2001. During the meeting the following topics were discussed: Scientific Advice Review Group (SciARG) meeting schedule and provision of Protocol Assistance regarding scientific issues, Transparency/ CPMP Summary of Opinions, CPMP Variations activities and involvement of Rapporteur and Co-Rapporteur in the post-authorisation assessment phase.

The CPMP endorsed a procedure for provision of Protocol Assistance regarding scientific issues. In particular, it was agreed that two COMP representatives will participate in the SciARG meetings for discussion of all matters related to Protocol Assistance procedures. The details of this procedure will be made public in the near future.

Due to the increasing number of Scientific Advice requests and the subsequent need to schedule more oral explanations with companies, potential changes to the SciARG meetings' schedule were discussed. It was agreed that both SciARG meetings and SciARG oral explanations will continue to be organised during the CPMP week, on Monday afternoon and that any additional oral explanations could be held on Thursday of the CPMP plenary meeting, if required. The process will be closely monitored and revised at a later stage, if necessary.

PROCEDURAL UPDATE

- Applicants are informed that any request for Part B status should be submitted within a maximum timeframe of **18 months** from the expected date of submission of the application.
- MAHs are requested to systematically inform the EMEA (letter of intent to be sent by e-mail to Dr Antony Humphreys, Head of Sector Regulatory Affairs and Organisational Support: Antony.Humphreys@emea.eudra.org) of any upcoming variation applications for new clinical indications, at least **2 months** before the submission date. This is to allow the CPMP to discuss the need to involve the Co-Rapporteur in the review of such applications. The letter of intent for Annex II applications should also be submitted within the same timeframe. Pre-submission meetings to discuss any of these submission can also be requested.
- The CPMP discussed the introduction of Near Infra-Read Spectroscopy methods as variations to marketing authorisations. It was agreed that such changes should be submitted as Type II Variation applications to allow adequate evaluation time.

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 26 March 2001, which is circulated together with this Press Release (see **Annex 6**), including the status of the activities of the sub-group on harmonisation of Summary of Product Characteristics.

Next meetings

The next CPMP ad hoc Expert Group on clinical efficacy of beta-interferons on multiple sclerosis treatment will take place on 25 May 2001.

The 71th plenary meeting of the CPMP will be held from 28 May 2001 until 31 May 2001.

Noël Wathion
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This Press Release and other documents are available on the Internet at the following address:
http://www.emea.eu.int

OUTCOME OF THE APRIL 2001 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type I Variation applications following Type II Procedure	
Number of Opinions	**Outcome**
4	Positive by consensus

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
5 (Extension of the Indication)	Positive by consensus
12 (SPC/PL update)	Positive by consensus
18 (Pharmaceutical Aspects)	Positive by consensus

Opinions for Annual Re-Assessment		
Name of Medicinal Product	**Outcome**	**Comments**
Viramune	Positive by consensus	Marketing Authorisation to remain under exceptional circumstances
Viracept	Positive by consensus	Marketing Authorisation to remain no longer under exceptional circumstances

Opinions for Renewal applications		
Name of Medicinal Product	**Outcome**	**Comments**
Bondronat	Positive by consensus	----
Bonviva	Positive by consensus	----
Rilutek	Positive by consensus	----

EMEA CENTRALISED PROCEDURES

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	74	122	196	6	20*	19	215
Follow-up to scientific advice	15	11	26	3**	0	3	29

* Including two Protocol Assistance requests.

** Including one Protocol Assistance request.

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	97	182	279	7	13	20	299
Withdrawals	12	37	49	0	4	4	53
Positive CPMP opinions	64	112	176	9	7	16	192[1]
Negative CPMP opinions[2]	1	3	4	0	2	2	6[3]
Marketing authorisations granted by the Commission	56	95	151	6	17	23	174[4]

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	265	551	816	77	99	176	992
Positive opinions, variations type II	159	224	383	36	58	94	477
Negative opinions, variations type II	0	2	2	0	1	1	3
Extensions (Annex II applications)	34	20	54	0	2	2	56

[1] 192 positive opinions corresponding to 150 substances
[2] In case of appeal the opinion will not be counted twice
[3] 6 negative opinions corresponding to 4 substances
[4] 174 Marketing Authorisations corresponding to 134 substances

Medicinal products granted a Community Marketing Authorisation under the Centralised Procedure since March 2001 Press Release

Brand name	Targretin
INN	bexarotene
Marketing Authorisation Holder	Ligand Pharmaceuticals Ltd
ATC code	L01XX25
Indication	Treatment of skin manifestations of advanced stage of cutaneous T-cell Lymphoma
CPMP Opinion date	16.11.2000
Date of Commission Decision	29.03.2001

Brand name	Starlix
INN	nateglinide eflorithine
Marketing Authorisation Holder	Novartis Europharm Ltd
ATC code	A10BX03
Indication	Combination treatment of diabetes mellitus Type II
CPMP Opinion date	14.12.2000
Date of Commission Decision	03.04.2001

Brand name	Trazec
INN	nateglinide eflorithine
Marketing Authorisation Holder	Novartis Europharm Ltd
ATC code	A10BX03
Indication	Combination treatment of diabetes mellitus Type II
CPMP Opinion date	14.12.2000
Date of Commission Decision	03.04.2001

OUTCOME OF THE APRIL 2001 CPMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Substance	Intended indication(s)	Topic				
		Type of Request		Pharma-ceutical	Pre-Clinical	Clinical
		New	Follow-up			
Biological	Treatment of acute myocardial infarction.	**X**		**X**	**X**	**X**
Chemical	Conditioning treatment prior to hematopoietic progenitor cell transplantation.	**X** (Protocol Assistance)				**X**
Chemical	Treatment of insomnia.	**X**			**X**	**X**
Chemical	Treatment of invasive fungal infections.	**X**				**X**
Chemical	Treatment of male erectile dysfunction.	**X**				**X**
Biological	Treatment of follicular non-hodgkin's lymphoma.	**X**				**X**
Biological	Treatment of patients undergoing primary or repeat coronary artery bypass and/or valve surgery with a CPB pump.	**X**			**X**	**X**

In addition to the adoption of the above final Scientific Advice letters, the Committee accepted two new requests from companies for Scientific Advice.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE APRIL 2001 CPMP MEETING

BIOTECHNOLOGY WORKING PARTY

Reference number	Document	Status
CPMP/BWP/819/01	Vaccines and the use of the bovine material: Questions and answers on the evaluation of bovine spongiform encephalopathies (TSE)-risk via the use of materials of animal origin in or during the manufacture of vaccines.	Adopted in April 2001
CPMP/BWP/2517/00	Points to consider on the Reduction, elimination or substitution of thiomersal in vaccines.	Adopted in April 2001
CPMP/BWP/3088/99	Note for guidance on the Quality pre-clinical and clinical aspects of gene transfer medicinal products.	Adopted in April 2001

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/567/98 rev. 1	Note for guidance on Clinical investigation of medicinal products for the treatment and prevention of bipolar disorder.	Adopted in April 2001
CPMP/EWP/518/97 rev. 1	Note for guidance on Clinical investigation of medicinal products in the treatment of depression.	Released in April 2001 for 6-month consultation

PHARMACOVIGILANCE WORKING PARTY

Reference number	Document	Status
EMEA/H/2058/01	Joint Pharmacovigilance plan for the implementation of the ICH E2B, M1 and M2 requirements related to the electronic transmission on individual case safety reports in the Community.	Adopted in April 2001

Report from the meeting held on 23 April 2001

General issues

Sub-group meeting on harmonisation of SPCs

The fourth sub-group meeting on harmonisation of SPCs was held on Monday 23 April 2001. Letters to the trade associations and the MAHs of the 36 candidate medicinal products have been sent out and responses are awaited by 1 May 2001. Based on the information obtained from the MAHs and other sources, the MRFG will suggest a final shorter list of products that could be harmonised through an Article 11 procedure. This proposal together with justifications will be presented to the Heads of Agencies meeting in June 2001.

TSE and Mutual Recognition Procedure

MRFG discussed several procedural questions concerning TSE and clarification on specific issues will shortly be published on the Heads of Agencies website.

MRFG documents released for a consultation to the interested parties

Further to the MRFG's decision during the March 2001 MRFG meeting to release selected documents for consultation, it was decided that these documents will be sent directly to the trade associations (EFPIA, AESGP and EGA), who will be asked to co-ordinate the consultation among their members.

Participation of Liechtenstein to the MRFG meetings

The MRFG was informed that a representative from Liechtenstein, Ms Brigitte Batliner, will be involved in the MRFG as an observer from now on.

Meeting schedule

An informal MRFG meeting will take place on 17 and 18 May 2001 in Uppsala, Sweden.

The next MRFG meeting will be held on 28 May 2001.

Mutual Recognition Monitoring

The MRFG noted that 24 new mutual recognition procedures were finalised during the month of March 2001, as well as 108 type I and 28 type II variations.

The status as of 31 March 2001 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
2001	69	96	282	113	87	213	--

39 new procedures (regarding 72 products) started in March 2001. The categories of these procedures are as follows:

9 new active substances (first authorisation in the European Community after RMS approval) including **2** repeat use and **4** multiple applications.

7 known active substances (already authorised in at least one member state), including **1** repeat use and **1** multiple applications.

14 abridged applications including **4** repeat use and **3** multiple applications.

9 line extension applications including **1** repeat use application.

The new procedures started this month relate to 17 full dossiers, 9 generics, 2 bibliographic applications, 2 fixed combination applications, 3 informed consent and 6 for different use, route or dose.

The procedures consisted of 35 chemical substances, 1 biological-blood product, 2 biological-others and 1 biological-vaccine[1].

37 of these procedures were prescription-only medicinal products in the reference Member State and 2 were Non-prescription (including OTC) medicinal products[2].

1. As considered by RMS.
2. In this category products are classified as prescription-only or Non-prescription (OTC) products when the RMS has approved them accordingly, although the legal status is not part of the Mutual Recognition Procedure.

Number of countries involved in the new applications procedures started in March 2001

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (3)	6
DE (1)	7
FR (1)	14
FR (1)	14
FR (1)	11
FR (1)	1
FR (1)	1
FR (1)	1
IR (3)	1
IR (3)	1
NL (1)	1
NL (1)	3
NL (1)	1
NL (1)	2
NL (1)	1
NL (1)	1
NL (1)	3
NL (1)	5
NL (2)	1
NL (1)	13
NL (1)	16
NO (2)	3
SE (2)	1
SE (2)	1
SE (2)	1
SE (1)	16
SE (1)	3
UK (2)	14
UK (1)	9
UK (1)	5
UK (2)	8
UK (3)	2
UK (6)	16
UK (1)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
UK (3)	16
UK (3)	4
UK (4)	16
UK (4)	4
UK (4)	2

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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http://heads.medagencies.org/