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

21 November 2001
CPMP/3536/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
13-15 NOVEMBER 2001 PLENARY MEETING

MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 76th plenary meeting from 13-15 November 2001.

Product related issues

Centralised procedures

The CPMP adopted five positive Opinions by consensus (four Part B and one Part A) on initial marketing authorisation applications:

- For the triple application **Dynastat** (parecoxib sodium), **Rayzon** (parecoxib sodium) and **Xapit** (parecoxib sodium), (three Part B), from Pharmacia Europe EEIG indicated for the short-term treatment of postoperative pain. Review by the EMEA began on 31 October 2000 and the opinion was adopted on 15 November 2001, with an active review time of 204 days. For further details, please see the published Summary of Opinions (CPMP/2465/01), (CPMP/3653/01) and (CPMP/3654/01).
- For **Lumigan** (bimatoprost) (Part B) from Allergan Pharmaceuticals (Ireland) Ltd. indicated for the reduction of elevated intraocular pressure in chronic open angle glaucoma and ocular hypertension. As monotherapy in patients insufficiently responsive to first-line therapy or intolerant or contraindicated to first-line therapy. As adjunctive therapy to beta-blockers. Review by the EMEA began on 26 December 2000 and the opinion was adopted on 15 November 2001, with an active review time of 178 days. For further details, please see the published Summary of Opinion (CPMP/3463/01).
- For **Kineret** (anakinra) from Amgen Europe B.V. (The Netherlands) indicated for the treatment of the signs and symptoms of rheumatoid arthritis in combination with methotrexate, in patients with an inadequate response to methotrexate alone. Kineret treatment should be initiated and supervised by specialist physicians experienced in the treatment and diagnosis of rheumatoid arthritis. Review by the EMEA began on 18 July 2000 and the opinion was adopted on 15 November 2001, with an active review time of 204 days. For further details, please see the published Summary of Opinion (CPMP/3364/01).

The CPMP adopted two positive opinions by consensus on "line extension" applications (in accordance with Annex II of Commission Regulation (EC) No 542/95 as amended) related to two active substances (two Part A).

Furthermore, the Committee adopted fourteen Lists of Questions (five Part A and nine Part B) for initial marketing authorisation applications.

Following a number of reports involving Metalyse (tenecteplase) suggesting that the instructions for use of the medicinal product may not have been followed appropriately, which could result in greater than the required dose of Metalyse being administered, the EMEA published on 12 November 2001 a public statement highlighting the importance of correct product handling (see EMEA Website: http://www.emea.eu.int/pdfs/human/press/pus/347801en.pdf). Thereafter the CPMP initiated and finalised during its plenary meeting an Urgent Safety Restriction (USR) procedure in order to emphasise the need to correctly follow the instructions for use and handling of Metalyse (tenecteplase). This revised wording will be included in the Summary Product Characteristics and in the medicinal product labelling and package leaflet. Metalyse is indicated for the thrombolytic treatment of acute myocardial infarction and the Marketing Authorisation Holder is Boehringer Ingelheim International GmbH.

An overview of centralised procedures since 1995 is given in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CPMP plenary meeting in September 2001 is provided in **Annex 2** (none were granted in October 2001). The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

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Referrals

Referral under Article 10(2) of Council Directive No 75/319/EEC, as amended

A Referral for Arbitration under Article 10(2) of Council Directive No 75/319/EEC, as amended was initiated by France on Dacarbazine Faulding from Faulding Pharmaceuticals Plc. A Rapporteur and Co-Rapporteur were appointed and the review procedure has been started.

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 12 November 2001. For further details, please see **Annex 4**.

Non-product related issues

CPMP Working Parties and Ad Hoc Groups

- The Committee was informed of the outcome of the second meeting of the Ad Hoc Working Group on comparability of biotechnology products, (Pre-)Clinical and Clinical issues, chaired by Dr Markku Toivonen, which took place on 5 October 2001. As announced in the last CPMP monthly report, the next meeting will take place on 18 January 2002.
- The Ad Hoc Expert Group on Pharmacogenetics, chaired by Dr Eric Abadie, was held on 5 November 2001. During the meeting the comments on the proposal for a CPMP Points to Consider document on terminology in pharmacogenetics were discussed and this document is expected to be released for external consultation in the next couple of months.

The Committee was informed of up-coming Ad Hoc Expert Group meetings:

- The first expert meeting on paediatric oncology of the Ad Hoc Group on Oncology, to be chaired by Dr Frances Rotblat, is scheduled to take place on 3 December 2001.
- As previously announced, the second meeting of the Paediatric Expert Group is scheduled to take place on 14 December 2001.

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

Organisational Matters

- A workshop on communication issues was held on Wednesday 14 November 2001, with representatives of the European Commission, the EMEA Management Board chair, the CPMP and pharmacovigilance Working Party chairs and vice-chair, the Troika of Heads of Agencies and the EMEA. This workshop, which was convened by the European Commission, was established in order to examine the possibility to set-up new structures/processes of communication between all the Competent Authorities in the European Union, especially in the field of pharmacovigilance.
- The Committee heard a report on the ICH Steering Committee video conference held on 24 October 2001.
- The 9th meeting of the CPMP Ad Hoc Group on Organisational Matters (ORGAM) was held on 12 November 2001. The following topics were discussed:
    - Revision of the status and composition of the Scientific Advice Review Group (SciARG): It was agreed that two Members of the Committee on Orphan Medicinal Product (COMP) will be nominated by the COMP to participate to the SciARG activities related to Protocol Assistance. Existing Scientific Advice guidance documents for sponsors will be updated in the near future.
    - Renewal procedure and proposed changes to be considered during the renewal assessment or via a variation procedure.

- Proposals from the EMEA Product Information Process Improvement Team (PIPIT) group for a revised and simplified product information checking process.
- The amount/type of data which could be accepted by EMEA/CPMP as part of the responses to the list of questions/outstanding issues.

PROCEDURAL ANNOUNCEMENT

- **Marketing Authorisation Holders** are reminded not to include as part of a **renewal application**, any changes to the dossier or product information which are not related to the renewal assessment and which require a separate variation application. For further details, please refer to the "Guideline on the processing of Renewals in the Centralised Procedure – June 2001" (http://pharmacos.eudra.org/F2/eudralex/vol-2/C/299000en_2.pdf)). Marketing Authorisation Holders are invited to request a pre-submission meeting well in advance of the expected renewal filing to discuss the content of the application, possible overlap with variation procedures and any other regulatory procedural aspects.
- **Applicants/Marketing Authorisation Holders** are informed that when **filing/dispatching** full/Annex II or Type II Variations **applications** to the mail room of National Competent Authorities, they should also directly notify Rapporteur/Co-Rapporteur of these deliveries to ensure a timely start of the review.
- **Applicants** are informed that should they wish to have a **Scientific Advice procedure** started at the January 2002 CPMP meeting, **notification of intent** should be submitted to the EMEA by **17 December 2001.**

- The Tradename Ad Hoc Review Group (TRAHG) held its 23rd meeting on Monday 12 November 2001 and the conclusions of the group were subsequently adopted by the CPMP.
- The third meeting of the joint CPMP/Mutual Recognition Facilitation Group (MRFG) Working Group on the Harmonisation of Summary Product Characteristics (SPCs) chaired by Dr Tomas Salmonson took place on Monday 12 November 2001. For further details see MRFG Press Release (**Annex 6**).

The 77th plenary meeting of the CPMP will be held from 11 to 13 December 2001.

Mutual Recognition procedure

The CPMP noted the report from the MRFG which was held on 12 November 2001 (**Annex 6**).

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

EMEA CENTRALISED PROCEDURES

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	74	122	196	13	44*	57	253
Follow-up to scientific advice	15	11	26	4**	5	9	35

* Including two Protocol Assistance advice.
** Including one Protocol Assistance advice.

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	97	182	279	23	32	55	334
Withdrawals	12	37	49	2	8	10	59
Positive CPMP opinions	64	112	176	10	18	28	204[1]
Negative CPMP opinions [2]	1	3	4	0	1	1	5[3]
Marketing authorisations granted by the Commission	56	95	151	15	27	42	193[4]

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	265	551	816	157	246	404	1220
Positive opinions, variations type II	159	224	383	113	123	236	619
Negative opinions, variations type II	0	2	2	1	4	5	7
Extensions (Annex II applications)	34	20	54	3	6	9	63

[1] 204 positive opinions corresponding to 159 substances
[2] In case of appeal the opinion will not be counted twice
[3] 5 negative opinions corresponding to 4 substances
[4] 193 marketing authorisations corresponding to 148 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE SEPTEMBER 2001 CPMP MONTHLY REPORT

Brand name	Caspofungin MSD
INN	caspofungin
Marketing Authorisation Holder	Merck Sharp & Dohme
ATC code	J 02 AX 04
Indication	Treatment of invasive aspergillosis in adult patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B and/or itraconazole
CPMP Opinion date	26.07.2001
Date of Commission Decision	24.10.2001

Brand name	Foscan
INN	temoporfin
Marketing Authorisation Holder	Scotia Pharmaceuticals
ATC code	L01XX
Indication	Treatment of patients with advanced head and neck squamous cell carcinoma failing prior therapies and unsuitable for radiotherapy, surgery or systemic chemotherapy.
CPMP Opinion date	28.06.2001
Date of Commission Decision	24.10.2001

Brand name	Glivec
INN	imatinib
Marketing Authorisation Holder	Novartis Europharm Ltd
ATC code	To be determined
Indication	Treatment of adult patients with Philadelphia chromosome (bcr-abl) positive chronic myeloid leukaemia (CML) in chronic phase after failure of interferon- alpha therapy, or in accelerated phase or blast crisis
CPMP Opinion date	26.07.2001
Date of Commission Decision	07.11.2001

Note: No European Commission Decision was issued in October 2001.

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

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
11 (SPC/PL update)	Positive by consensus
8 (Pharmaceutical Aspects)	Positive by consensus

Opinion for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Avonex (interferon beta-1a) – Biogen France S.A.	Positive by consensus	Marketing Authorisation to remain under exceptional circumstances.
BeneFIX (nonacog alfa) – Generics Institute of Europe B.V.	Positive by consensus	Marketing Authorisation to remain under exceptional circumstances.

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

Substance	Intended indications(s)	Topic				
		Type of Request		Pharma-ceutical	Pre-Clinical	Clinical
		New	Follow-up			
Biological	Congenital factor IX deficiency	**X**				**X**
Chemical	Non-infectious uveitis	**X**				**X**
Chemical	Dependent alcoholism	**X**				**X**
Chemical	Osteoporosis	**X**			**X**	
Chemical	Irritable bowel syndrome	**X**				**X**
Chemical	Osteoporosis/Paget's disease	**X**			**X**	**X**
Chemical	Essential thrombocythaemia	**X**				**X**

In November 2001, the above mentioned seven final Scientific Advice letters were adopted. The Committee accepted three new requests for Scientific Advice.

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

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/158/01	Note for guidance on Quality of water for pharmaceutical use	Adopted in November 2001
CPMP/QWP/3309/01	Note for guidance on the Use of near infared spectroscopy by the pharmaceutical industry and the data to be forwarded in Part II of the dossier for a Marketing Authorisation	Released in November 2001 for 6 months consultation

SAFETY WORKING PARTY

Reference number	Document	Status
CPMP/SWP/372/01	Points to consider on the Non-clinical assessment of the carcinogenic potential of insulin analogues	Adopted in November 2001
CPMP/SWP/3404/01	Draft concept paper on the Development of a CPMP Note for guidance on the Need for testing toxic potential in juvenile animals	Adopted in November 2001

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/1119/98	Points to consider on the Evaluation of diagnostic agents	Adopted in November 2001
CPMP/EWP/2991/01	Concept paper on the Development of an Addendum on the Clinical requirements of modified release medicinal products submitted as a line-extension of an existing marketing authorisation to the CPMP Note for guidance on Modified release oral and transdermal dosage forms: section II (pharmacokinetic and clinical evaluation) (CPMP/EWP/280/96)	Adopted in November 2001
CPMP/EWP/1776/99	Points to consider on Missing data	Adopted in November 2001
CPMP/EWP/18/01	Note for guidance on the Clinical investigation of medicinal products for the treatment of urinary incontinence in women	Released in November 2001 for 6 months consultation
CPMP /EWP/612/00 draft	Note for guidance on Clinical investigation of medicinal products for treatment of pain	Released in November 2001 for 6 months consultation
CPMP/EWP/2922/00 draft	Note for guidance on the Clinical investigation of medicinal products in the treatment of asthma	Released in November 2001 for 6 months consultation

Report from the meeting held on 12 November 2001

General issues

Revision of MRFG documents

The MRFG adopted the revision of the following documents that will be published on the Heads of Agencies Website:

- MRFG Best practice Guide for the Reference Member State in the Mutual recognition Procedure
- SOP on Automatic Validation of Mutual Recognition Procedure for New Applications
- SOP on Procedure for Validation of Mutual Recognition Procedures for Variations

MRFG Frequently Asked Questions (FAQ)

The MRFG agreed to install the Frequently Asked Questions -feature in the Heads of Agencies Website.

Meeting schedule

The next MRFG meeting will be held on **10 December 2001**.

Joint CPMP / MRFG Working Group on harmonisation of SPC's

The second meeting of the "Joint CPMP / MRFG Working Group on Harmonisation of SPCs" took place on Monday, 12 November 2001. All questions pointed out by the Heads of Agencies have been considered now. A report will be presented to the Heads of Agencies meeting on 29–30 November 2001.

Mutual Recognition Monitoring

The MRFG noted that 50 new mutual recognition procedures were finalised during the month of October 2001, as well as 91 type I and 33 type II variations.

The status as of 30 October 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	345	137	1182 *	187	384	243	1 N.A. 2 var.

* as there was a mistake on the calculation of the September 2001 Report, the number has been revised accordingly.

41 new procedures (regarding 83 products) started in October 2001. The categories of these procedures are as follows:

2 new active substances.

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

22 abridged applications including **4** multiple applications.

The new procedures started this month relate to 4 full dossiers, 21 generics, 6 bibliographic applications, 3 fixed combinations and 7 informed consent.

The procedures consisted of 40 chemical substances and 1 herbal medicinal product[1].

33 of these procedures were prescription-only medicinal products in the reference Member State and 8 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 September 2001

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (3)	10
DE (3)	10
DE (1)	3
DK (2)	1
DK (2)	1
DK (2)	1
DK (1)	2
FI (2)	1
FI (2)	1
FI (2)	1
FI (2)	1
FI (2)	1
FI (2)	1
FR (1)	14
FR (1)	14
FR (2)	16
FR (2)	15
FR (2)	14
IR (2)	2
NL (2)	2
NL (2)	2
NL (2)	1
NL (2)	1
NL (2)	1
NL (2)	1
NL (2)	1
NL (2)	2
NL (2)	2
NL (2)	2
NL (3)	11
NL (3)	1
NL (3)	2
NL (3)	1
NL (3)	1
NL (1)	12
NL (1)	1
NL (1)	13

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
UK (4)	9
UK (2)	4
UK (1)	1
UK (2)	15

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/