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

24 October 2003
EMEA/CPMP/5020/03/Rev 0

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
21-22 OCTOBER 2003 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 97th plenary meeting from 21-22 October 2003.

The CPMP Chairman, on behalf of the Committee, welcomed Prof. Pavel Svec from the Slovak Republic, who was attending the CPMP for the first time.

Product related issues

Centralised procedures

The CPMP adopted four positive opinions on initial marketing authorisation applications at this meeting:

- A positive opinion on the marketing authorisation application for **Advate** (octocog alfa), from Baxter AG, which is intended for the treatment and prophylaxis of bleeding in haemophilia A patients. EMEA review began on 21 October 2002 and the opinion was adopted on 22 October 2003, with an active review time of 200 days.
- Two positive opinions on the marketing authorisation applications for **Bonviva** (ibandronic acid) and **Ibandronic acid Roche 2.5 mg film-coated tablet** (ibandronic acid), from Roche Registration Ltd, intended for the treatment and prevention of osteoporosis in post-menopausal women. EMEA review began on 22 July 2002 and the opinion was adopted on 22 October 2003, with an active review time of 175 days.
- A positive opinion on the marketing authorisation application for **Litak** (cladribine), from Lipomed GmbH, intended for the treatment of hairy cell leukaemia. EMEA review began on 22 July 2002 and the opinion was adopted on 22 October 2003, with an active review time of 201 days.
  Litak was designated an orphan medicinal product on 18 September 2001 and is the **fourteenth orphan medicinal product** to receive a positive CPMP opinion.

Summaries of these opinions are available on the EMEA web site: http://www.emea.eu.int

The Committee also adopted the following positive opinions on the extension of indication for three medicinal products that are already authorised in the EU:

- **Infergen** (interferon alfacon-1), from Yamanouchi Europe, to include results of studies investigating combination therapy with Ribavirin. Infergen was first authorised in the European Union on 1 February 1999.
- **Lumigan** (bimatoprost), from Allergan Pharmaceuticals Ireland, to include its use as first line therapy in the reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension (as monotherapy or as adjunctive therapy to beta-blockers). Lumigan was first authorised in the European Union on 8 March 2002.

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- **NovoSeven** (eptacog alfa (activated)), from Novo Nordisk, to include its use in the treatment of Glanzmann's thrombasthenia and also in factor VII deficiency. NovoSeven was first authorised in the European Union on 23 February 1996.

Further information on these extensions will be included in the public assessment report (EPAR) once the European Commission has granted final approval.

The Committee also adopted four opinions (4 Part B) by consensus for 4 "line extension" applications (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003 (previously known as Commission Regulation (EC) No. 542/95, as amended)) and four Lists of Questions on initial Marketing Authorisation applications (4 Part B).

Furthermore 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 2003 is provided in **Annex 2.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Invented Name Review Group

The Invented Name review Group held its 42^{d} meeting on 20 October 2003, and the conclusions of the group were subsequently adopted by the CPMP.

The next meeting of the Invented Name review Group will take place on 17 November 2003 where a review of all the comments received from the Accession Countries on invented names for already authorised medicinal products and for on-going centralised applications will be discussed. Relevant Applicants and MAHs will thereafter be informed directly (by the end of the year 2003).

Non-product related issues

CPMP Working Parties and Ad Hoc Groups

- The CPMP was informed of the outcome of the discussions of the Scientific Advice Working Group (**SAWG**) meeting, which was held on 6 - 7 October 2003. For further details, please see **Annex 4**. The EMEA has given its scientific advice in the first parallel EMEA-FDA scientific advice procedure. This is the first such parallel procedure following the 12 September 2003 signature of a confidentiality agreement with the FDA. The advice was adopted by the CPMP on 22 October 2003. For further details please see the EMEA Web site: http://www.emea.eu.int/htms/hotpress/d2872703.htm
- Documents prepared by the **CPMP Working Parties and Ad Hoc Groups** adopted during the October 2003 CPMP meeting are listed in **Annex 5**.
- Dr. Daniel Brasseur, Chairman of the Paediatric Expert Group (**PEG**), reported on the last meeting, which took place on 26 September 2003. The Group discussed several topics related to the development of medicinal products in children, in particular the impact of renal immaturity when investigating medicinal products in neonates. In addition the Group progressed the work initiated to assess paediatric needs in different therapeutic classes, focusing the discussion on pain. The next PEG meeting is scheduled to take place on Friday 21 November 2003.
- A meeting of the **Ad Hoc Expert Group on Pharmacogenetics** (Chairperson Dr E. Abadie) was held on 15 October 2003. Amongst other topics, the document related to lay language terminology was discussed. Briefing sessions with Industry also took place during the meeting where general issues relevant to Pharmacogenetics case studies were discussed. An update was given on the activities of the group, in preparation of the 4th EMEA/ DIA/EFPIA Pharmacogenetics Workshop "Moving Toward Clinical Application", which took place on 29-30 October 2003 in London (Web link: http://www.emea.eu.int/pdfs/conferenceflyers/diaphgen.pdf).

Interested Parties meeting:

- An EMEA-EFPIA Info Day took place at the EMEA on 24 October 2003 where exchange of results/analysis of the 2003 Performance Indicators exercise on pre- and post-authorisation activities were presented.

Upcoming meetings following the October 2003 CPMP plenary meeting:

- The next Ad Hoc Expert Group on Antiretroviral Medicinal Products (Chairperson Dr. Nilsson) will be held on 16 January 2004.

Organisational Matters

The 27th CPMP Organisational Matters (**ORGAM**) meeting took place on Monday 20 October 2003, chaired by Dr D. Brasseur. Topics addressed during the meeting related to:

- Issues related to Working Parties on proposed new Efficacy and Quality Concept papers and other Guidelines **(**see **Annex 5)**.

- Training activities: details of the upcoming **New National Competent Authorities' assessors' training** which will be held at the EMEA on 27-28 November 2003.

- The Group discussed the outcome of **Performance Indicators** for the centralised procedure (post-authorisation applications). This analysis on post activities was focussed on variations/line extensions related to new indications.

- Updates on the status of enlargement and **participation of Accession Countries representatives** in EMEA meetings as observers. The group was informed that a National Authority general framework confidentiality undertaking agreement has been signed off by the Heads of Agencies of the 10 Acceding Countries and that Accession Countries are invited to participate as observers until 1st May 2004 in Committee meetings (CxMP), Working Party meetings and meetings of the Quality Review of Documents.

The next CPMP Organisational Matters meeting is scheduled to take place on Monday 17th November 2003.

Procedural announcement

Marketing Authorisation Applications (MAAs) transitional requirements for the New Member States

In view of the EU Enlargement and in order to facilitate a smooth transitional phase for the evaluation activities of the CPMP, the EMEA request Applicants to also submit their Applications, namely Module 1 and Module 2, to the Contact Points of the New Member States that can be found in the attached table.
This will enable the CPMP Observers of the Accession Countries to have an increased awareness of the supporting documentation that will be discussed by the CPMP during their monthly meetings between now and the 1st May 2004.

The EMEA proposes the following:

Centralised Procedure:

New Full Applications:
After positive validation of the MAA, in addition to the normal submission to the CPMP Members, as per the published EMEA dossier requirements, Module 1 and Module 2 (electronically and/or hard copies) can be presented to the Contact Points of the New Member States* (see attached Table in Annex 6).

Ongoing Full Applications:
It is thought preferable to stage the supply of these MAAs at specific milestones in the centralised procedure as follows:

- At the time of submission of the Responses to Day 120 List of Questions, Module 1 and Module 2 should be forwarded to the Contact Points of the New Member States*
- At the time of submission of the Responses to Day 180 List of Outstanding Issues, Module 1 and Module 2 should be forwarded to the Contact Points of the New Member States

Type II variations (only Extensions of Indication):
After positive validation of the variation application, in addition to the normal submission to the CPMP Members, as per the published EMEA Post-Authorisation guide, Module 1 and Module 2 can be presented to the Contact Points of the New Member States*.

In parallel with the above process, which the applicants are recommended to follow, the EMEA will also forward relevant assessment reports to the Nominated CPMP Observers. If there are any queries regarding this proposed process, please forward them to: CIG2@emea.eu.int

* **It is important to state the purpose of such a submission in a clear letter accompanying the documentation.**

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 20 October 2003. For further details, please see **Annex 7**.

The 98th plenary meeting of the CPMP will be held from 18-20 November 2003.

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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 - 2002	2003	Overall Total
Scientific Advice	302	53	355
Follow-up to Scientific Advice	50	8	58
Protocol Assistance	13	16	29
Follow-up to Protocol Assistance	4	2	7

	1995-2002			2003			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	127	239	366	6	29	35	401
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	20	53	73	2	2	4	77
Positive CPMP opinions[2]	92	155	247	7	12	19	266[3]
Negative CPMP opinions[4]	1	4	5	1	1	2	7[5]
Marketing authorisations granted by the Commission	88	146	234	3	14	17	251[6]

	1995-2002			2003			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	585	1132	1717	156	307	463	2180
Positive opinions, variations type II	405	511	916	150	138	288	1204
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	44	44	88	5	12	17	105

[1] Consultation in accordance with Council Directive 93/42/EEC concerning medical devices as amended by Directive 2000/70/EC as regards medical devices incorporating stable derivatives of human blood or plasma and Directive 2001/104/EC.
[2] 14 positive opinion corresponding to 14 Orphan Medicinal Products
[3] 266 positive opinions corresponding to 202 substances
[4] In case of appeal, the opinion will not be counted twice
[5] 7 negative opinions corresponding to 6 substances (2 of these negative opinions correspond to 2 Orphan Medicinal Products)
[6] 251 marketing authorisations corresponding to 189 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE SEPTEMBER 2003 CPMP MONTHLY REPORT

Invented Name	Avandamet
INN	rosiglitazone/metformin
Marketing Authorisation Holder	SmithKline Beecham plc
ATC code	A10BH01
Indication	Treatment of Type 2 diabetes mellitus
CPMP Opinion date	26/06/2003

Invented Name	Onsenal
INN	celecoxib
Marketing Authorisation Holder	Pharmacia-Pfizer EEIG
ATC code	L01XX
Indication	Treatment of familial adenomatous Polyposis (FAP), as an adjunct to usual care
CPMP Opinion date	26/06/2003

OUTCOME OF THE SEPTEMBER 2003 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
4 Extension of indication	4 Positive opinion
9 SPC changes	9 Positive opinions
12 Quality changes	12 Positive opinions

Opinion for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Fabrazyme (agalsidase beta) Genzyme B.V	Positive opinion	Marketing Authorisation to remain under exceptional circumstances
Replagal (agalsidase alfa) TKT Europe-5S AB	Positive opinion	Marketing Authorisation to remain under exceptional circumstances

Opinions for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	N/A	---

OUTCOME OF THE OCTOBER 2003 CPMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Schizophrenia and manic episodes	X				X		X	
Biological	Acute lung injury				X		X		
Chemical	Delayed graft function in renal transplantation		X			X	X	X	X
Biological	Anemia	X				X	X	X	
Chemical	Delayed graft function after solid organ transplantation		X				X	X	
Biological	Mucopolysaccharidosis I		X					X	
Biological	Anemia	X				X	X	X	
Chemical	Sickle cell syndrome		X			X			
Biological	Invasive candidosis		X			X	X	X	X
Biological	Niemann-Pick		X			X	X	X	
Biological	Malabsorption	X						X	

SA: Scientific Advice

PA: Protocol Assistance

In October 2003, the above-mentioned 4 Scientific Advice letters, 6 Protocol Assistance letters and 1 Follow-up Protocol Assistance letter were adopted.
The Committee accepted 4 Initial Scientific Advice Requests.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE OCTOBER 2003 CPMP MEETING

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/4891/03	Concept Paper on the Development of a Committee for Proprietary Medicinal Products (CPMP) points to consider on clinical investigation of medicinal products for the treatment of ankylosing spondylitis.	Adopted

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/4814/03	Concept Paper on the development of a Note for Guidance on stability of active substances and finished products manufactured in and distributed from climatic zones 3 and 4.	Adopted
CPMP/QWP/4815/03	Concept Paper on the revision of Note for Guidance on plastic primary packing materials (3AQ10A).	Adopted
CPMP/QWP/4812/03	Concept paper on the revision of Note for Guidance on stability testing for a Type II Variation to a Marketing Authorisation.	Adopted

BIOTECH WORKING PARTY

Reference number	Document	Status
EMEA/410/01 rev 2	TSE Revision of Joint CPMP/CVMP Note for Guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products.	Adopted. This Note for Guidance will be forwarded to the Commission for publication in the Official Jounal.
CPMP/BPWG/BWP/561/03	Note for Guidance on the Warning on transmissible agents in SPCs and Package Leaflets for Plasma-Derived Medicinal Products.	Adopted
CPMP/BWP/5180/03	Note for Guidance on Assessing the risk for Virus Transmission - New Chapter 6 of the Note for Guidance on Plasma-derived medicinal products.	Released for 3 months consultation

SAFETY WORKING PARTY

Reference number	Document	Status
CPMP/SWP/3833/03	Discussion paper on contraindications in pregnancy concerning sections 4.3, 4.6 and 5.3 of the SPC	Released for 3 months consultation

ANNEX 6 to CPMP Monthly Report October 2003

CONTACT POINTS OF THE NEW MEMBER STATES

COUNTRY	MEMBER	ADDRESS	TELEPHONE	FAX	E-MAIL
Cyprus	Panayiota Kokkinou	Ministry of Health (Cyprus) 7 Larnacos Avenue CY - 1475 Lefkosia, Nicosia Cyprus	+ 357 22 40 71 03	+ 357 22 40 71 49	Rocphc3@cytanet.com.cy
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COUNTRY	MEMBER	ADDRESS	TELEPHONE	FAX	E-MAIL
Czech Republic	Prof. Milan Smid	State Institute for Drug Control Srobarova 48 100 41 Prague 10 Czech Republic	+420 272 185 835	+420 272 739 995	smid@sukl.cz
Poland	To be confirmed	Office for Registration of Medicinal Products, Medical Devices and Biocides 30/34 Chelmska str. PL-00-725 Warsaw Poland	+48 22 8514381	+48 22 8515243	firstname.surname@urpl.gov.pl
Lithuania	Vladas Volbekas	Drug Registration Commission State Medicines Control Agency in Lithuania Traku 14 LT - 2001 Vilnius Lithuania	+370 37 22 28 23	+370 37 22 28 23	volbekas@kaunas.omnitel.net
Slovenia	Dr Vesna Koblar	Agency for Medicinal Products Kersnikova UL.2 SI - 1000 Ljubljana Slovenia	+386 1 478 62 43	+386 1 478 62 60	Vesna.Koblar@gov.si

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ANNEX 7 to CPMP Monthly Report October 2003

Report from the meeting held on 20 October 2003

General Issues

Best practice guide for the exchange of regulatory and administrative information regarding orphan medicinal products between the EMEA and national competent authorities

The Best practice guide for the exchange of regulatory and administrative information regarding orphan medicinal products between the EMEA and national competent authorities was adopted and will be published on the website.

Processing of Renewals in the post-Referral phase

The documents 'Recommendation for Mutual Recognition Procedure after finalisation of an arbitration procedure with a positive opinion by the CPMP and a positive Decision by the EU Commission' and 'MRFG Best Practice Guide for handling Renewals in the Mutual Recognition Procedure' Rev. 2 were adopted and will be published on the website

Guidance on submission dates for applicants of the MRP for the year 2004

The document was adopted and will be published on the website.

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Mutual Recognition Monitoring

The MRFG noted that **46** new mutual recognition procedures were finalised during the months of September 2003, as well as **225** type I variations and **69** type II variations.

The status as of 30 September 2003 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
2003	313	234	2059	378	556	195	1 N.A. and 1 Variation

90 new procedures (regarding **202** products) started in September 2003. The categories of these procedures are as follows:

4 new active chemical substances.

15 known active substances (already authorised in at least one member state), including **2** multiple and **1** repeat uses.

61 abridged applications; including **32** multiple applications and **1** repeat use.

10 line extension application and

The new procedures started related to **17** full dossiers, **51** generics, **9** bibliographic applications, **3** fixed combinations and **10** other.

The procedures consisted of **87** chemical substances, **1** biological-other and **2** biological blood products[1] .

84 of these procedures were prescription-only medicinal products in the reference Member State and **6** 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 2003

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (1)	7
DE (1)	4
DE (1)	1
DE (1)	3
DE (1)	4
DE (4)	7
DK (3)	13
DK (2)	3
DK (2)	2
DK (2)	1
DK (2)	3

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	3
DK (1)	1
DK (1)	1
DK (2)	2
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	2
DK (2)	3
DK (2)	7
DK (2)	9
DK (2)	1
DK (2)	7
DK (2)	1
DK (3)	1
FI (1)	6
FI (1)	12
FI (2)	3
FI (1)	2
FI (1)	1
FI (1)	1
FI (2)	12
FI (2)	1
FI (2)	10
FI (2)	1
FI (2)	1
FI (1)	7
FI (2)	3
FI (2)	2
FI (2)	1
FI (2)	1
NL (3)	6
SE (2)	2
SE (1)	1
SE (1)	15
SE (1)	1
SE (2)	7
SE (1)	2
SE (1)	1
SE (1)	1
SE (2)	11
SE (1)	10
SE (3)	3
SE (4)	5
SE (4)	10
SE (4)	10
SE (4)	3
SE (4)	2
SE (4)	2

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
SE (4)	1
SE (6)	16
SE (1)	3
SE (2)	10
SE (2)	1
Se (2)	1
SE (6)	3
SE (4)	1
SE (4)	1
SE (4)	2
SE (4)	1
SE (4)	1
SE (4)	1
SE (4)	1
SE (4)	1
SE (4)	3
SE (4)	3
SE (4)	1
SE (6)	1
SE (1)	1
SE (1)	1
UK (2)	1
UK (1)	11
UK (1)	11
UK (1)	1
UK (40	14
UK (1)	16

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 from 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/