European Medicines Agency
Evaluation of Medicines for Human Use

1 April 2005
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
MARCH 2005 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its March plenary meeting from 14 - 17 March 2005.

Centralised procedure

Opinions

The CHMP adopted two positive opinions on the extension of indication for medicinal products that are already authorised in the European Union (EU):

- **Emend** (aprepitant), Merck Sharp & Dohme, to extend its indication to the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy. Emend was first authorised in the EU on 11 November 2003.
- **Velcade** (bortezomib), Janssen-Cilag International N.V., to extend its use to patients with progressive multiple myeloma who have received at least one prior therapy and who have already undergone or are unsuitable for bone marrow transplantation. Velcade was first authorised in the EU on 26 April 2004.

Summaries of opinion for Emend and Velcade are available on the EMEA website: http://www.emea.eu.int

The Committee also gave positive opinions on new contra-indications for medicinal products that are already authorised in the EU:

- **Carbaglu** (Carglumic acid), Orphan Europe, to contra-indicate breast-feeding during the use of carglumic acid.
- **CellCept** (mycophenolate mofetil), Roche Registration Ltd, to contra-indicate breastfeeding.

A summary of opinion on Carbaglu and CellCept is available on the EMEA website: http://www.emea.eu.int. Further information on these extensions will be included in the European Public Assessment Report (EPAR) once the European Commission has granted final approval.

The Committee also adopted a positive opinion on a "line extension" application (Part B) (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003)

Lists of Questions

The Committee adopted four Lists of Questions on initial applications.

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Applications for marketing authorisation for orphan medicinal products

There has been no application through the centralised procedure for a marketing authorisation for any orphan medicinal product since the January 2005 meeting.

Detailed information on the centralised procedure

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 CHMP plenary meeting in February 2005 is provided in **Annex 2.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Referrals

The CHMP initiated a referral procedure under Article 30 of the Community code on human medicines (Directive 2001/83/EC as amended) for **Agopton and associated names** (INN: lanzoprazole) from Takeda Pharma GmbH. The referral was initiated by Germany because the medicinal products do not have the same SPC across all EU Member States, Iceland and Norway with respect to e.g. therapeutic indications and posology. A Rapporteur and a Co-Rapporteur were appointed and the review procedure has started.

CHMP Working Parties

The CHMP was informed of the outcome of the discussions of the Scientific Advice Working Group (SAWG) meeting, which was held on 28 February – 1 March 2005. For further details, please see **Annex 4**.

Documents prepared by the CHMP Working Parties adopted during the March 2005 CHMP meeting are listed in **Annex 5**.

Upcoming meetings following the March 2005 CHMP plenary meeting:

- The 11th meeting of the CHMP will be held at the EMEA on 18-21 April 2005.
- The next Invented Name Review Group meeting will be held at the EMEA on 18 April 2005.
- A Gene Therapy Working Party meeting on Insertional Oncogenesis will be held on 21-22 April 2005.

Organisational matters

The main topics addressed during the March 2005 CHMP related to:

- The adoption of the Composition of the following Working Parties:
  Blood Products Working Party (BPWP), Vaccine Working Party (VWP), Gene Therapy Working Party (GTWP), Working Party on Similar Biological (Biosimilar) Medicinal Products (BMWP) and Working Party on Cell-Based Products (CPWP).

- The adoption of the Composition of the Oncology and Anti-Infectives Scientific Advisory Groups (SAG).
  The Committee adopted the Mandate, Objectives and Rules of Procedure of the Diabetes/Endocrinology SAG. The Committee also agreed to the amendment of the mandate, objections and Rules of Procedure for all SAGs, with respect to the participation of an expert in clinical trials methodology (to be always considered for participation).

- The election of the Chairperson and the Vice Chairperson of the following Working Parties:

  Working Party on Cell-Based Products (CPWP): Dr. Kurki was elected as Chairperson of the CPWP.

  Biologics Working Party (BWP): Dr. Trouvin was elected as Chairperson and Dr. Haase as Vice-Chairperson.

  Blood Products Working Party (BPWP): Dr Haase was elected as Chairperson.

  Efficacy Working Party (EWP): Dr. van Zwieten-Boot was elected as Chairperson and Dr. Bertil Jonsson as Vice-Chairperson.

  Gene Therapy Working Party (GTWP): Prof. Cichutek was elected as Chairperson and Dr. Sol Ruiz as Vice-Chairperson.

  CHMP Pharmacogenetics Working Party (PgWP): Dr. Abadie was elected as Chairperson and Dr. Flamion as Vice-Chairperson.

  Working Party on Similar Biological (Biosimilar) Medicinal Products (BMWP): Dr. Kurki was elected as Chairperson of the BMWP.

  Scientific Advice Working Party (SAWP): Dr Flamion was elected as Chairperson.

  Vaccine Working Party (VWP): Dr. Dobbelaer was elected as Chairperson and Dr. M. Pfleiderer as Vice-Chairperson.

- A discussion on general rules for clock stops during the evaluation of medicinal products.
  A guideline on this aspect is under preparation and upon finalisation will be sent for external consultation.

- The adoption of a Correlation Table between previous and new CHMP Working Parties/Scientific Advisory Groups.

- A further discussion on the Peer Review procedure. This procedure will be implemented as a pilot phase, starting with the procedures scheduled for Rapporteur appointment at the April 2005 CHMP meeting.

EMEA Implementation of the New EU Pharmaceutical Legislation

- The second CHMP/EMEA Implementation Task Force (CEITAF) meeting took place on Monday 14th March 2005.
  Follow-up discussions on the following review implementation topics took place:
  - Main principles of the mandatory scope of the centralised procedure
  - Main principles of the Compassionate Use procedure

  Initial discussions took place on the following review implementation topics: Optional scope of the centralised procedure, Exceptional circumstances, Conditional Marketing Authorisations, Data protection, Guideline on monitoring and inspection of compliance with Pharmacovigilance obligations.

- A new section of the EMEA website has been created to highlight the Agency's activities relating to its implementation of the new EU Pharmaceutical Legislation (http://www.emea.eu.int.).
  This section provides overview information and a release schedule for documents being drafted during the year as part of the implementation process.
  The EMEA Stakeholders and Interested Parties will be requested to provide their comments on these draft documents during the consultation periods specified. Consultations are expected to start from March 2005. Unless otherwise specified, the consultation period for each document will be four weeks.

Mutual Recognition procedure

The CHMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 14 March 2005. For further details please see **Annex 6.**

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

EMEA CENTRALISED PROCEDURES

	1995 - 2004	2005	Overall Total
Scientific Advice	433	27	460
Follow-up to Scientific Advice	71	1	72
Protocol Assistance	59	11	70
Follow-up to Protocol Assistance	12	2	14

	1995-2004			2005			
	Part A	Part B	Total	Part A	Part B	Total	
Applications submitted	153	303	456	3	6	9	465
Consultation for Medical Device[1]	0	1	1	0	1	1	2
Withdrawals	22	62	84	0	2	2	86
Positive opinions[2]	107	197	304	0	2	2	306[3]
Negative opinions[4]	2	5	7	0	0	0	7[5]
Marketing authorisations granted by the Commission	98	190	288	3	7	10	298[6]

	1995-2004			2005			Overall Total
	Part A	Part B	Total	Part A	Part B	Total	
Variations type I	863	1937	2800	31	89	120	2920
Positive opinions, variations type II	758	886	1644	73	60	133	1777
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	53	63	116	1	2	3	119

[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] 19 positive opinion corresponding to 19 Orphan Medicinal Products
[3] 306 positive opinions corresponding to 237 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] 298 marketing authorisations corresponding to 229 substances

ANNEX 2 to CHMP Monthly Report March 2005

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE FEBRUARY 2005 CHMP MONTHLY REPORT

Invented Name	Quintanrix
INN	Diphtheria toxoid ≥ 30 IU Tetanus toxoid ≥ 60 IU Inactivated Bordetella pertussis strain ≥ 4 IU Hepatitis B virus surface antigen recombinant (S protein)10 micrograms Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate) 2.5 micrograms conjugated to tetanus toxoid as a carrier 5-10 micrograms
Marketing Authorisation Holder	GlaxoSmithKline Biologicals
Proposed ATC code	JO7CA10
Indication	Prophylaxis against diphtheria, tetanus, pertussis, hepatitis B and invasive disease caused by Haemophilus influenzae type b
CPMP Opinion date	21/10/2004
Marketing Authorisation Date	17/02/2005

Invented Name	Truvada
INN	tenofovir / emtricitabine
Marketing Authorisation Holder	Gilead Science International Limited
Proposed ATC code	J05AF30
Indication	Indicated in antiretroviral combination therapy for the treatment of HIV-1 infected adults.
CPMP Opinion date	18/11/2004
Marketing Authorisation Date	21/02/2005

Invented Name	Orfadin
INN	nitisinone
Marketing Authorisation Holder	Swedish Orphan International AB
Proposed ATC code	A16AX04
Indication	Treatment of patients with confirmed diagnosis of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine
CPMP Opinion date	18/11/2004

Marketing Authorisation Date	21/02/2005

Invented Name	Azilect
INN	rasagiline
Marketing Authorisation Holder	Teva Pharma GmbH
Proposed ATC code	N04BD02
Indication	Treatment of idiopathic Parkinson's disease (PD) as monotherapy (without levodopa) or as adjunct therapy (with levodopa) in patients with end of dose fluctuations
CPMP Opinion date	18/11/2004
Marketing Authorisation Date	21/02/2005

Invented Name	Prialt
INN	ziconotide
Marketing Authorisation Holder	Elan Pharma International Ltd
Proposed ATC code	N02BG (pending)
Indication	Treatment of severe, chronic pain in patients who require intrathecal (IT) analgesia.
CPMP Opinion date	18/11/2004
Marketing Authorisation Date	21/02/2005

Invented Name	Zonegran
INN	zonisamide
Marketing Authorisation Holder	Eisai Ltd
Proposed ATC code	N03AX15
Indication	Indicated as adjunctive therapy in the treatment of adult patients with partial seizures, with or without secondary generalisation
CPMP Opinion date	15/12/2004
Marketing Authorisation Date	10/03/2005

OUTCOME OF THE MARCH 2005 CHMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
2 Extensions of indication	2 Positive opinions
18 SPC changes	18 Positive opinions
29 Quality changes	29 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Zavesca (miglustat) Actelion Ltd,	Positive Opinion	The Marketing Authorisation will remain under exceptional circumstances.
Onsenal (celecoxib) Pharmacia-Pfizer EEIG	Positive Opinion	The Marketing Authorisation will remain under exceptional circumstances.

Opinions for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Forcaltonin (recomb salmon calcitonin) Unigene UK Limited	Positive Opinion.	---
Pegintron (peginterferon alfa-2b) SP Europe	Positive Opinion.	---
Viraferon PEG (peginterferon alfa-2b) SP Europe	Positive Opinion.	---

ANNEX 4 to CHMP Monthly Report March 2005

OUTCOME OF THE MARCH 2005
CHMP 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				
Biological	Prevention of HPV infection	X				X		X	
Chemical	Pancreatic cancer		X				X	X	X
Biological	Psoriatic arthritis	X				X		X	
Chemical	Fibromyalgia	X						X	
Biological	Renal cell carcinoma	X						X	
Chemical	Cardiogenic shock	X						X	
Chemical	Ovarian cancer				X			X	
Chemical	Cutaneous T cell lymphoma		X			X	X	X	X
Chemical	Chronic idiopathic constipation	X						X	
Chemical	Opioid-induced bowel dysfunction	X						X	
Chemical	Mobilisation of progenitor cells prior to stem cell transplantation in Non-Hodgkin's lymphoma and multiple myeloma		X					X	X
Biological	Multiple Sclerosis	X				X	X	X	
Chemical	Asthma	X						X	

SA: Scientific Advice

PA: Protocol Assistance

PA: Protocol Assistance

The above-mentioned 9 Scientific Advice letters, 3 Protocol Assistance letters, and 1 Follow-up Protocol Assistance letter were adopted at the 15-17 March CHMP meeting.

The Committee accepted 5 Initial Scientific Advice Requests, and 7 Initial Protocol Assistance Requests, 2 Follow Up Scientific Advice Requests.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE MARCH 2005 CHMP MEETING

BIOLOGICS WORKING PARTY

Reference number	Document	Status
CHMP/BWP/49348/2005	Guideline on similar medicinal products containing biotechnology-derived proteins as active substances: Quality issues	Released for 3 months consultation
CPMP/4548/03/Rev. 1	Guideline on requirements for Vaccine Antigen Master File (VAMF) certification	Adopted

BLOOD PRODUCTS WORKING PARTY

Reference number	Document	Status
CHMP/BPWG/151426/ 2004	Concept paper on revision of: • Note for Guidance on the Clinical Investigation of Human Normal Immunoglobulin for Intravenous Administration (IVIg) (CHMP/BPWG/388/95 rev. 1) • Core SPC for Human Normal Immunoglobulin for Intravenous Administration (IVIg) (CHMP/BPWG/859/95 rev. 2).	Released for 3 months consultation
CPMP/PhVWP/BPWG/2 231/99 rev. 1	Core SPC for Human Albumin solution	Adopted

EFFICACY WORKING PARTY

Reference number	Document	Status
CHMP/EWP/83561/05	Guideline on clinical trials in small populations	Released for 6 months consultation
CPMP/EWP/205/95/ Rev.3	Guideline on the evaluation of anticancer medicinal products in man	Released for 3 months consultation

PHARMACOGENETICS WORKING PARTY

Reference number	Document	Status
CHMP/6806/05	Concept Paper for the development of a Guideline on Biobanks issues relevant to pharmacogenetics	Released for 3 months consultation
CHMP/20227/04	Note for Guidance on Pharmacogenetics briefing meetings	Released for 6 months consultation

SAFETY WORKING PARTY

Reference number	Document	Status
CPMP/SWP/1094/04	Guideline on Evaluation of Control Sample for Toxicokinetic Parameters in Toxicology Studies: Checking for Contamination with the Test Substance	Adopted

Report from the MRFG meeting held on 14 March 2005

General Issues

Workshop on package leaflet

The workshop on package leaflet was held on the Tuesday following the MRFG plenary session with participants from the MRFG, the QRD and the EMEA to discuss the structure and content of package leaflets in different Member States for medicinal products with the same SPC, approved through the MRP or which have undergone a referral procedure.

The aim of the meeting was to compare the package leaflets in order to develop a harmonised view regarding the assessment of the package leaflet, since with the revision of the Pharmaceutical legislation the package leaflet of medicinal products approved through the MRP or DCP will have to be identical in all MS concerned by the procedures. Suggestions for improving the package leaflet will be further discussed by the Working Group on patient information.

Questions & Answers list for the submission of Variations according to Commission Regulation (EC) 1084/2003

Following the Variation sub-group meeting held on February, the MRFG has adopted an updated version of the Q&A document, to include 5 additional Q&A and to update Q&A 3, 5, 13, 16 and 18.

The Q&A document will be published on the website.

Proposal for the Decentralised procedure Member States' SOP – Consultation procedure

The MRFG has agreed on the SOP for the Decentralised procedure and has decided to publish it for a 6 week consultation period with Interested parties.

Any comments or proposals on the SOP for the Decentralised procedure should be sent by 29 April 2005 to the MRFG secretariat (sonia.ribeiro@emea.eu.int) in order to be discussed at the May MRFG meeting.

Fludeoxyglucose (^{18}F) Core SPC

The MRFG has adopted a Core SPC for Fludeoxyglucose (^{18}F). The Core SPC will be published on the website.

The Core SPC is based on the scientific literature published for more than 10 years. However, applications for marketing authorisation for Fludeoxyglucose (^{18}F) should be submitted with the necessary data in order to be considered valid. The MRFG recommends the use of the Fludeoxyglucose (^{18}F) Core SPC.

Best Practice Guide for Mutual Recognition Procedure and template for CMS comments in the MRP

The updated version of the BPG for MRP will be published on the website with the template for CMS comments in the MRP included as an annex to the Best Practice Guide.

Meeting schedule

The next MRFG meeting will be held on 18 April 2005.

Mutual Recognition Monitoring

The MRFG noted that **62** new mutual recognition procedures were finalised during the month of February 2005, as well as **324** type IA variations, **118** type IB variations and **72** type II variations.

The status as of 28th February of procedures and for the whole year under mutual recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures from Type IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CHMP
2005	113	220	487	230	145	--

59 new procedures (regarding **132** products) started in February 2005. The categories of these procedures are as follows:

9 known active substances (already authorised in at least one member state), including **1** multiple application and **5** repeat use.

39 abridged applications including **5** multiple applications and **6** repeat use.

11 line extension applications including **6** multiple applications.

The new procedures started related to **13** full dossiers, **36** generics, **3** bibliographic applications and **7** for different use, route or dose.

The procedures consisted of **57** chemical substances, **1** biological – blood product and **1** biological-vaccine[1].

56 of these procedures were prescription-only medicinal products in the reference Member State and **3** procedures were classified as a Non-prescription (including OTC) medicinal product[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 February 2005

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (1)	4
CZ (2)	5
CZ (4)	3
CZ (1)	5
DE (1)	16
DE (1)	16
DE (1)	6
DE (1)	8
DE (1)	5
DE (1)	7

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	2
DK (3)	1
DK (3)	13
DK (4)	2
DK (3)	4
DK (2)	2
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
FI (1)	4
FI (1)	1
FI (1)	1
FI (1)	1
FI (2)	8
FI (1)	1
FI (3)	16
FI (4)	6
FI (3)	6
FI (6)	13
FI (6)	1
FI (6)	2
FI (5)	12
FI (5)	8
FR (7)	10
HU (4)	4
NL (6)	9
NL (5)	7
NL (1)	10
NL (1)	6
NL (1)	6
NL (1)	6
SE (2)	4
SE (1)	13
SE (1)	3
SE (1)	2
SE (1)	2
SE (2)	1
SE (2)	1
SE (1)	2
SE (2)	16
UK (1)	2
UK (1)	7
UK (1)	1
UK (1)	12
UK (3)	8
UK (1)	6
UK (1)	8
UK (1)	7

All documents mentioned in this press release can be found at the MRFG website at the European Medicines Authorities Windows under the heading MRFG Guidance.

Information on the above mentioned issues can be obtained from the chair of the MRFG on behalf of the Luxembourg Presidency:

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*Or you could visit the **MRFG web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*
http://heads.medagencies.org/