European Medicines Agency
Evaluation of Medicines for Human Use

London, 6th May 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
APRIL 2008 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its April plenary meeting from 21-24 April 2008.

CENTRALISED PROCEDURE

Initial applications for marketing authorisation

The CHMP adopted nine positive opinions by consensus on initial marketing authorisations and two for 'informed consent' applications:

- **Firazyr** (icatibant acetate), from Jerini AG, for the treatment of hereditary angioedema in adults with C1-esterase-inhibitor deficiency. Firazyr is the **47th orphan medicine** to receive a positive opinion. EMEA review began on 15 August 2007 with an active review time of 204 days.

- **Janumet/Velmetia/Efficib** (sitagliptin / metformin hydrochloride), from Merck Sharp & Dohme Ltd, for the treatment of type 2 diabetes mellitus. EMEA review of Janumet and Velmetia began on 23 May 2007 with an active review time of 204 days. EMEA review of Efficib began on 15 August 2007 with an active review time of 120 days.

- **Latixa** (ranolazine), from CV Therapeutics Europe Limited, for the treatment of stable angina pectoris. EMEA review began on 27 December 2006 with an active review time of 177 days.

- **Relistor** (methylnaltrexone bromide), from Wyeth Europa Limited, for the treatment of opioid-induced constipation in advanced illness patients who are receiving palliative care. EMEA review began on 23 May 2007 with an active review time of 204 days.

- **Tredaptive/Trevaclyn/Pelzont** (nicotinic acid/laropiprant), from Merck Sharp & Dohme Ltd, for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia and primary hypercholesterolaemia. EMEA review of Tredaptive began on 20 July 2007 with an active review time of 202 days. EMEA review of Trevaclyn and Pelzont began on 15 August 2007 with an active review time of 176 days.

Positive opinion for 'informed consent' applications

The CHMP adopted two positive opinions by consensus for **Clopidogrel Winthrop** (clopidogrel hydrogen sulphate), from Sanofi Pharma Bristol-Myers Squibb SNC, and **Clopidogrel BMS** (clopidogrel hydrogen sulphate), from Bristol-Myers Squibb Pharma EEIG, for which 'informed consent' applications were submitted, intended for the prevention of atherothrombotic events in adults. This type of application requires that reference is made to an authorised medicinal product and that the marketing authorisation holder of this reference product has given consent to the use of the dossier in the application procedure.

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Revised positive opinion for Tyverb

The CHMP adopted a revised positive opinion by majority for **Tyverb** (lapatinib), from GlaxoSmithKline, following a previous positive opinion issued on December 2007. Following reports of hepatobiliary events associated with the use of Tyverb in ongoing clinical trials, the European Commission stopped its decision-making process and requested that the CHMP re-assess its recommendation to grant a conditional marketing authorisation for this medicine.
Having reviewed the new data, the CHMP concluded that the benefit-risk-balance for the use of Tyverb in the treatment of patients with advanced or metastatic breast cancer whose tumours overexpress ErbB2 (HER2) and who have received prior therapy including anthracyclines, taxanes and trastuzumab was positive and recommended the granting of a marketing authorisation. The Committee recommended that the product information should be amended to add special warnings about the risk of hepatotoxicity.

Summaries of opinion for these medicinal products are available on the EMEA website http://www.emea.europa.eu/htms/human/opinion/opinion.htm. Further information will be included in the European Public Assessment Report (EPAR) once the European Commission has granted final approval.

Re-examination procedure under Article 9(2) of Regulation (EC) No. 726/2004

The EMEA has been formally requested by EpiCept GmbH, to re-examine the negative opinion for **Ceplene** (histamine dihydrochloride) to be used in combination with interleukin-2 for the maintenance of remission in patients with acute myeloid leukaemia in first remission, adopted during the CHMP meeting on 17-19 March 2008.

Post-authorisation procedures

Extensions of indication and other recommendations

The CHMP adopted seven positive opinions by consensus on applications for extensions of indication, adding new treatment options for the following previously approved medicines:

- **Abilify** (aripiprazole), from Otsuka Pharmaceutical Europe Ltd, to extend the indication for Abilify 7.5 mg/ml solution for injection for the rapid control of agitation and disturbed behaviours in patients with manic episodes in bipolar I disorder, when oral therapy is not appropriate. Abilify 7.5 mg/ml solution for injection is currently indicated for the rapid control of agitation and disturbed behaviours in patients with schizophrenia.

- **Apidra** (insulin glulisine), from Sanofi-Aventis Deutschland GmbH, to extend the indication to the paediatric population of six years or above. Apidra is currently authorised in the treatment of adult patients with diabetes mellitus.

- **Azopt** (brinzolamide), from Alcon Laboratories, to extend the indications to include adjunctive therapy with prostaglandin analogues. Azopt is currently indicated to decrease elevated intraocular pressure in ocular hypertension and open-angle glaucoma.

- **Mimpara** and **Parareg** (cinacalcet), from Amgen Europe B.V., to extend the indication to reduction of hypercalcaemia in patients with primary hyperparathyroidism for whom parathyroidectomy (surgery to remove parathyroid glands) would be indicated on the basis of serum calcium levels (as defined by relevant treatment guidelines) but in whom parathyroidectomy is not clinically appropriate or is contraindicated. Mimpara and Parareg are currently indicated for the treatment of secondary hyperparathyroidism in patients with chronic renal disease and for reduction of hypercalcaemia in patients with parathyroid carcinoma.

- **Neupro** (rotigotine), from SchwarzPharma Ltd, to extend the indication to include the symptomatic treatment of moderate to severe restless legs syndrome. Neupro is currently indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease.

- **Reyataz** (atazanavir sulphate), from Bristol Myers Squibb Pharma EEIG, to extend the indication to include adult patients who have not used antiretroviral treatment before. Reyataz is currently indicated for the treatment of HIV-1 infected adults, who previously received antiretroviral treatment.

Summaries of opinions for all mentioned products, including their full indication, can be found here.

Updated safety information

- Roche, the MAH for **Avastin** (bevacizumab) agreed with the CHMP on a Direct Healthcare Professional Communication concerning adverse events that occurred in an investigator-sponsored Phase I dose-escalation study combining Avastin and escalating doses of sunitinib malate in patients with metastatic renal cell carcinoma (mRCC). Five of 12 patients at the highest sunitinib malate dose level (50 mg once daily) exhibited laboratory findings consistent with microangiopathic haemolytic anaemia (MAHA). Prescribers are reminded that Avastin is not approved for use in combination with sunitinib malate for any indication.

- Elan Pharma International Ltd., the MAH for **Tysabri** (natalizumab) agreed with the CHMP on a Direct Healthcare Professional Communication concerning serious hepatic reactions (including elevated serum hepatic enzymes and total bilirubin) reported in the post-marketing phase in patients receiving TYSABRI. This communication follows the EMEA Press Release and question-and-answer document published on 20 March 2008.

- The CHMP recommended the exclusion of "reamed nail fixation in tibia fractures" from the therapeutic indications for **InductOs** (dibotermin alfa), from Wyeth Europe Ltd. This follows observations from a study which showed that the use of InductOs in acute open tibia fractures, as an adjunct to standard of care, using reamed intramedullary nails, has resulted in a higher number of localized cases of infections in the affected limb than standard of care alone. The CHMP and the MAH agreed on a Direct Healthcare Professional Communication concerning these reports of infections.
- The CHMP recommended that the product information of all centrally authorised **angiotensin II receptor antagonists** be harmonised, regarding their use during pregnancy. A separate press release and question-and-answer document with more information are available.

Withdrawals

The EMEA has been formally notified by Bioenvision Limited of its decision to withdraw the application for an extension of indication for the centrally authorised medicine **Evoltra** (clofarabine). Evoltra was expected to be used for the treatment of acute myeloid leukaemia. A separate press release and question-and-answer document with more information are available.

The EMEA has been formally notified by Wyeth Europe Ltd of its decision to withdraw the application for an extension of indication for the centrally authorised medicine **Tygacil** (tigecycline). Tygacil was expected to be used for the treatment of community-acquired pneumonia. A separate press release is avalable. The question-and-answer document will be published following the May CHMP meeting.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted eleven Lists of Questions on initial applications (including three under the mandatory scope, and eight under the optional scope).

Detailed information on the centralised procedure

An overview of centralised procedures since 1995 is given in **Annex 1**. The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 2**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CHMP plenary meeting in March 2008 is provided in **Annex 3.**

Applications for marketing authorisation for orphan medicinal products

Details of those orphan medicinal products that have been subject of a centralised application for marketing authorisation since the March 2008 CHMP plenary meeting are provided in **Annex 4**.

Name Review Group (NRG)

Statistical information on the outcome of the checking of acceptability of proposed invented names for medicinal products processed through the centralised procedure is provided in **Annex 5**.

REFERRAL PROCEDURES

Referral procedure concluded

The CHMP finalised a referral procedure under Article 29 of Directive 2001/83/EC for **Oracea** (doxycycline), from FGK Representative Service GmbH, intended to reduce inflammatory lesions in patients with rosacea. The CHMP concluded that the benefits of Oracea in the present indication outweigh the risk of potential harmful effects related to the development of resistance and therefore recommended the granting of a marketing authorisation by consensus, subject to certain changes in the product information and post-marketing obligations. The procedure was initiated by the United Kingdom due to efficacy and safety concerns in the proposed indication, in particular the potential induction of bacterial resistance by Oracea in its intended use.
Referral procedures under Article 29 of Directive 2001/83/EC are initiated by one or more Member States in cases where an agreement cannot be reached in the context of the mutual recognition procedure.

The CHMP finalised a number of referral procedures by consensus under Article 30 of Directive 2001/83/EC recommending the harmonisation of the product information across the European Union for the following medicines approved at the level of the Member States:

- **Cozaar** 25 mg, 50 mg, 100 mg film-coated tablets, (losartan potassium), from Merck Sharp & Dohme Inc, used as antihypertensive. The procedure was initiated by the European Commission.

- **Cozaar Comp** 50mg/12.5mg and 100mg/25mg film-coated tablets, (losartan potassium and hydrochlorothiazide), from Merck Sharp & Dohme Inc, used as antihypertensive. The procedure was initiated by Denmark.

- **Lamictal and associated names** (lamotrigine), from GlaxoSmithKline Research & Development Limited, used as anticonvulsant. The procedure was initiated by the marketing authorisation holder.

- **Singulair** 4mg chewable tablets and 4mg oral granules (montelukast sodium), from Merck Sharp & Dohme Inc, used as bronchodilator. The procedure was initiated by the marketing authorisation holder.

Referral procedures started

A harmonisation referral under Article 30 of the Directive 83/2001/EC as amended was started for **Diovan** (valsartan) from Novartis, in the therapeutic group of antihypertensives, at the request of the European Commission.
Article 30 referrals are initiated with a view to harmonising product information for medicinal products authorised at Member State level.

The Committee started a review of issues related to the administration and supply of medicinal products containing or derived from **heparin** under Article 5(3) of Regulation (EC) No 726/2004, following detection of a contaminant in a limited number of batches in some Member States of the European Union. The initiation of the procedure was requested by Germany.

MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 28th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 21-22 April 2008. For further details, please see the relevant press release on the CMD(h) website under the heading Press Releases: http://www.hma.eu/

CHMP WORKING PARTIES

The CHMP was informed of the outcome of the discussions of the Scientific Advice Working Party (SAWP) meeting, which was held on 31st March – 2nd April 2008. For further details, please see **Annex 6**.

Documents prepared by the CHMP Working Parties adopted during the April 2008 CHMP meeting are listed in **Annex 7**.

UPCOMING MEETINGS FOLLOWING THE APRIL 2008 CHMP PLENARY MEETING

- The 44th meeting of the CHMP will be held at the EMEA on 27-30 May 2008.
- The next Name Review Group meeting will be held at the EMEA on 14th May 2008.
- The 29th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the EMEA on 27-28 May 2008.

ORGANISATIONAL MATTERS

The main topics addressed during the April 2008 CHMP meeting related to:

- The re-election of Pr. Flamion as Chair of the Scientific Advice Working Party.
- The election of Dr. van Riet-Nales as Vice Chair of the Quality Working Party.
- The re-election of Dr. Abadie as Chair of the Pharmacogenomics Working Party and the re-election of Pr. Flamion as Vice Chair.
- The adoption of the guidance on Biomarkers Qualification Advice to applicants which will now be released for 2-month public consultation.
- An update from Dr. Arlett (European Commission) on the feedback received following the public consultation on the proposals for new Pharmacovigilance legislation.
- Follow-on discussion with regard to future interactions foreseen between the CHMP and the Committee for Advanced Therapies (CAT).
- The adoption of the Guideline on Safety and Efficacy Follow-up - Risk Management of Advanced Therapy Medicinal Products which will be released for 3-month public consultation.
- Preliminary discussion regarding the management of pharmacovigilance signals across the European Union.
- The adoption of the EMEA recommendation on the procedural aspects and dossier requirements for the consultation to the EMEA by Notified Body on an ancillary human blood derivative incorporated in a medical device.
- The adoption of a new assessment report template for safety and efficacy type II variations.
- The adoption of the final report on the pilot Joint EMEA/FDA Voluntary Genomic Data Submissions experience on Qualification of Nephrotoxicity biomarkers (EMEA/12956/2008).

PROCEDURAL ANNOUNCEMENT

- **Submission of applications for Type IA and Type IB variations**

Marketing Authorisation Holders are reminded that according to the guidelines on how to submit Type I Variation notification, as published on the EMEA website (http://www.emea.europa.eu/htms/human/postguidance/q03.htm), it is required to submit to the Central Information Group (CIG) one paper copy and one electronic copy (**CD-ROM or DVD**) of the Variation application form and supportive documentation. Should the application affect the Annexes of the Commission Decision, please be aware that the Product Information - SPC/Labels/Package Leaflet - is considered part of the supportive documentation. Deficient and missing documentation at the point of submission can lead to non-validation / rejection of the variation.

Eudralink is not considered as a valid means for submission of variations applications. It may only be used for the submission of Product Information in all EU languages, as foreseen in the published guideline (http://www.emea.europa.eu/htms/human/postguidance/q08.htm).

- CHMP meeting date for May 2008

Due to an EMEA public holiday on the 26th May 2008, the CHMP plenary session will be held from the 27th to 30th May.

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

ANNEX 1 TO CHMP MONTHLY REPORT APRIL 2008

PRE-AUTHORISATION: MARKETING AUTHORISATION APPLICATIONS

Activity	2008								1995 onwards
	Optional Scope				Mandatory scope			Total	Overall total
	NAS	Significant innovation	Interest of Patients	Generics	Biotech	Indications	Orphans		
Applications for MA submitted	10	1	0	0	4	3	3	21	689
Positive opinions	8	2	0	0	7	3	3	23	452
Negative opinions[1]	0	0	0	0	0	0	2	2	20
Withdrawals prior to opinion	1	0	0	0	3	0	1	5	121
Marketing authorisation granted by the Commission	6	3	0	2	0	0	2	13	430

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	2008	1995 onwards
Compassionate use applications	0	0
Art. 58 applications	0	4
Consultation for medical devices[2]	1	5
PMF (Click here for a list of PMF certifications)	1	12
VAMF	0	0

[1] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[2] 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 derivates of human blood or plasma and Directive 2001/104/EC

OUTCOME OF THE APRIL 2008 CHMP MEETING IN RELATION TO ACCELERATED ASSESMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Chemical	N/A	N/A	N/A
Biological	N/A	N/A	N/A

POST-AUTHORISATION: TYPE I AND II VARIATIONS, ANNEX II, RENEWALS AND ANNUAL RE-ASSESSMENT APPLICATIONS

Activity	2008	Overall total 1995 onwards
Type I Variations (positive notifications)	367	5569
Type II Variations (positive opinions)	103	3947
Type II Variations (negative opinions)	1	11
Annex II Applications (positive opinions)	19	188
Annual Re-assessment (positive opinions)	11	-
Opinion for renewals of conditional MA's (positive opinions)	0	2
5 Year Renewals (positive opinions)	16	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
8 Extensions of indication	8 Positive opinion
69 SPC changes	68 Positive opinions 1 Negative opinion
27 Quality changes	27 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
MabCampath (alemtuzumab) Genzyme B.V	Positive Opinion adopted	exceptional circumstances are being lifted
Reyataz (atazanavir sulphate) Bristol Myers Squibb Pharma EEIG	Positive Opinion adopted	exceptional circumstances are being lifted
Naglazyme (galsulfase) BioMarin Pharmaceutical Inc	Positive Opinion adopted	remaining under exceptional circumstances

Opinion for renewals of conditional MA's		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	N/A	N/A

Opinions for 5-Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Busilvex (busulfan) Pierre Fabre Medicament	Positive Opinion adopted	unlimited validity
Pylobactell (13C-urea) Torbet	Positive Opinion adopted	unlimited validity
Xenical (orlistat) Roche Registration Ltd	Positive Opinion adopted	unlimited validity
Fuzeon (enfuvirtide) Roche Registration Ltd	Positive Opinion adopted	unlimited validity
Plavix (clopidogrel) Sanofi Pharma Bristol Myers Squibb SNC	Positive Opinion adopted	unlimited validity
Iscover (clopidogrel) Bristol Myers Squibb Pharma EEIG	Positive Opinion adopted	unlimited validity
Optison (perfultren) GE Healthcare	Positive Opinion adopted in March	unlimited validity[3]

[3] The information published in the March CHMP Monthly Report regarding Optison was incorrect and has now been amended.

ANNEX 3 TO CHMP MONTHLY REPORT APRIL 2008

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE MARCH 2008 CHMP MONTHLY REPORT

Invented Name	Mycamine
INN	micafungin
Marketing Authorisation Holder	Astellas Pharma GmbH
Proposed ATC code	J02AX05
Indication	Mycamine is indicated for: Adults, adolescents ≥ 16 years of age and elderly: Treatment of invasive candidiasis. Treatment of oesophageal candidiasis in patients for whom intravenous therapy is appropriate. Prophylaxis of Candida infection in patients undergoing allogeneic haematopoietic stem cell transplantation or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells / µl) for 10 or more days. Children (including neonates) and adolescents < 16 years of age: Treatment of invasive candidiasis. Prophylaxis of Candida infection in patients undergoing allogeneic haematopoietic stem cell transplantation or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells / µl) for 10 or more days.
CHMP Opinion date	21.02.2008
Marketing Authorisation Date	25.04.2008

Invented Name	Adenuric
INN	febuxostat
Marketing Authorisation Holder	Ipsen Manufacturing Ireland Ltd
Proposed ATC code	M04AA03
Indication	Treatment of chronic hyperuricaemia in conditions where urate deposition has already occurred (including a history, or presence of, tophus and/or gouty arthritis)
CHMP Opinion date	21.02.2008
Marketing Authorisation Date	21.04.2008

Invented Name	Thalidomide Pharmion
INN	thalidomide
Marketing Authorisation Holder	Pharmion Ltd
Proposed ATC code	LO4AX 02
Indication	Thalidomide Pharmion in combination with melphalan and prednisone as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy. Thalidomide Pharmion is prescribed and dispensed according to the Thalidomide Pharmion Pregnancy Prevention Programme.
CHMP Opinion date	24.01.2008
Marketing Authorisation Date	16.04.2008

Invented Name	Pradaxa
Common Name	dabigatran etexilate mesilate
Marketing Authorisation Holder	Boehringer Ingelheim International GmbH
Proposed ATC code	B01AE07
Indication	Primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip replacement surgery or total knee replacement surgery.
CHMP Opinion date	24.01.2008
Marketing Authorisation Date	18.03.2008

Invented Name	Privigen
Common Name	human normal immunoglobulin (IVIg)
Marketing Authorisation Holder	CSL Behring GmbH
Proposed ATC code	J06BA02
Indication	<u>Replacement therapy in</u> • Primary immunodeficiency (PID) syndromes such as: – congenital agammaglobulinaemia and hypogammaglobulinaemia – common variable immunodeficiency – severe combined immunodeficiency – Wiskott Aldrich syndrome • Myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections. • Children with congenital AIDS and recurrent infections. <u>Immunomodulation</u> • Immune thrombocytopenic purpura (ITP), in children or adults

	at high risk of bleeding or prior to surgery to correct the platelet count. • Guillain-Barré syndrome. • Kawasaki disease. Allogeneic bone marrow transplantation **4.2 Posology and method of administration** *Posology* The dose and dosage regimen is dependent on the indication. In replacement therapy the dosage may need to be individualised for each patient depending on the pharmacokinetic and clinical response. The following dosage regimens are given as a guideline. Replacement therapy in primary immunodeficiency syndromes The dosage regimen should achieve a trough IgG level (measured before the next infusion) of at least 4 to 6 g/l. Three to six months are required after the initiation of therapy for equilibration to occur. The recommended starting dose is 0.4 to 0.8 g/kg body weight (bw) followed by at least 0.2 g/kg bw every three weeks. The dose required to achieve a trough level of 6 g/l is of the order of 0.2 to 0.8 g/kg bw/month. The dosage interval when steady state has been reached varies from two to four weeks. Trough levels should be measured in order to adjust the dose and dosage interval. Replacement therapy in myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections; replacement therapy in children with AIDS and recurrent infections The recommended dose is 0.2 to 0.4 g/kg bw every three to four weeks. Immune thrombocytopenic purpura For the treatment of an acute episode, 0.8 to 1 g/kg bw on day one, which may be repeated once within three days, or 0.4 g/kg bw daily for two to five days. The treatment can be repeated if relapse occurs. Guillain-Barré syndrome 0.4 g/kg bw/day for three to seven days. Experience in children is limited. Kawasaki disease 1.6 to 2.0 g/kg bw should be administered in divided doses over two to five days or 2.0 g/kg bw as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid. Allogeneic bone marrow transplantation: Human normal immunoglobulin treatment can be used as part of the conditioning regimen and after the transplantation. For the treatment of infections and prophylaxis of graft versus

	host disease, dosage is individually tailored. The starting dose is normally 0.5 g/kg bw/week, starting seven days before transplantation and continued for up to three months after the transplantation. In case of persistent lack of antibody production, a dose of 0.5 g/kg bw/month is recommended until antibody levels return to normal.
CHMP Opinion date	21.02.2008
Marketing Authorisation Date	25.04.2008

Invented Name	Effentora
Common Name	fentanyl citrate
Marketing Authorisation Holder	Cephalon Europe
Proposed ATC code	N02AB03
Indication	Effentora is indicated for the treatment of breakthrough pain (BTP) in adults with cancer who are already receiving maintenance opioid therapy for chronic cancer pain. BTP is a transitory exacerbation of pain that occurs on a background of otherwise controlled persistent pain**.** Patients receiving maintenance opioid therapy are those who are taking at least 60 mg of oral morphine daily, at least 25 micrograms of transdermal fentanyl per hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.
CHMP Opinion date	24.01.2008
Marketing Authorisation Date	04.04.2008

Invented Name	Volibris
Common Name	ambrisentan
Marketing Authorisation Holder	Glaxo Group Limited
Proposed ATC code	CO2KX02
Indication	Volibris is indicated for the treatment of patients with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III, to improve exercise capacity(see section 5.1). Efficacy has been shown in idiopathic PAH (IPAH) and in PAH associated with connective tissue disease
CHMP Opinion date	21.02.2008
Marketing Authorisation Date	21.04.2008

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION: UPDATE SINCE THE MARCH 2008 CHMP MEETING

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
N/A	N/A	N/A	N/A

ANNEX 5 TO CHMP MONTHLY REPORT APRIL 2008

INVENTED NAME REVIEW GROUP (NRG)

	April 2008		2008	
	Accepted	Rejected	Accepted	Rejected
Proposed invented names[1]	51	52	69	67
Justification for retention of invented name *[2]	3	1	6	2

*In case of objections to the proposed invented name(s), the applicant may justify the retention of the proposed invented name using the relevant justification form available on the EMEA website.

[1] None of the proposed invented name requests have been postponed to the May 2008 NRG meeting

[2] One of the justifications for retention of a proposed invented name has been postponed to the May NRG meeting

	April 2008		2008	
	Accepted	Rejected	Accepted	Rejected
Total number of objections raised	59	51	80	73
Criterion - Safety concerns				
Similarity with other Invented name	42	36	60	51
Conveys misleading therapeutic/pharmaceutical connotations	0	1	1	1
Misleading with respect to composition	0	1	0	1
Criterion - INN concerns				
Similarity with INN	2	0	3	1
Inclusion of INN stem	3	0	3	1
Criterion - Other public health concerns				
Unacceptable qualifiers	9	5	10	8
Conveys a promotional message	2	8	2	10
Appears offensive or has a bad connotation	0	0	0	0
Similarity between name of individual active substance and fixed combinations and/or between fixed combinations	1	0	1	0
Similarity between name of prodrug and related active substance	0	0	0	0

See Guideline on the Acceptability of Invented names for human medicinal products processed through the Centralised procedure (CPMP/328/98) for detailed explanations of criteria used.

ANNEX 6 TO CHMP MONTHLY REPORT APRIL 2008

PRE-AUTHORISATION: SCIENTIFIC ADVICE AND PROTOCOL ASSISTANCE EMEA CENTRALISED PROCEDURES

	1995 - 2007	2008	Overall Total
Scientific Advice	887	74	961
Follow-up to Scientific Advice	171	15	186
Protocol Assistance	198	17	215
Follow-up to Protocol Assistance	90	7	97
	1346	**113**	**1459**

OUTCOME OF THE APRIL 2008 CHMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Final 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	Treatment of gastro oesophageal reflux disease	X						X	
Biological	Treatment of diabetes mellitus	X				X		X	
Biological	Prevention of diabetes			X				X	
Biological	Management of weight in obese patients	X						X	
Chemical	Treatment of type 2 diabetes	X					X	X	
Chemical	Treatment of obesity	X						X	
Chemical	Treatment of chronic idiopathic constipation	X					X	X	
Chemical	Treatment of mantle cell lymphoma	X						X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Restoration of corneal sensitivity	X				X	X	X	
Chemical	Prevention of chronic rejection following lung transplantation		X					X	X
Biological	Treatment of neutropenias	X				X	X	X	
Biological	Treatment of neutropenias	X				X			
Chemical	Treatment of advanced or metastatic breast cancer			X				X	
Biological	Treatment of cutaneous melanoma	X						X	
Biological	Treatment of renal cell carcinoma		X			X		X	X
Chemical	Treatment of Non-small Cell Lung Cancer.	X						X	
Biological	Treatment of idiopathic thrombocytopenic purpura		X					X	
Biological	Treatment of relapsed or refractory Hodgkin's Lymphoma				X			X	
Chemical	Reduction of stroke/systemic embolic events	X						X	
Biological	Treatment of hereditary Factor X deficiency		X			X	X	X	X
Chemical	Treatment of hypertension	X					X	X	
Chemical	Treatment of diabetic nephropathy			X			X		

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of ischemic cardiomyopathy	X				X	X	X	
Chemical	Treatment of hypercholesterol-emia	X						X	
Chemical	Treatment of essential hypertension	X					X	X	
Biological	Treatment of eschar in burns				X			X	X
Chemical	Treatment of gram-negative pneumonia	X					X	X	
Chemical	Treatment of urinary tract infection	X						X	
Biological	Prevention of HPV related cervical cancer	X						X	
Chemical	Treatment of HIV-1 infections			X				X	
Biological	Prevention of herpes zoster and post-herpetic neuralgia	X					X	X	
Chemical	Treatment of lower urinary tract symptoms	X						X	
Chemical	Treatment of chronic low back pain	X						X	
Chemical	Reduction of risk of bone metastases in cancer patients			X				X	
Biological	Treatment of Alzheimer's disease			X				X	
Chemical	Treatment of asthma and chronic obstructive pulmonary disease	X					X	X	
Biological	Treatment of severe asthma			X				X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of cocaine addiction and prevention of recidivism	X						X	
Chemical	Treatment of hyperphosphat-aemia in end stage renal disease	X				X	X	X	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 26 Scientific Advice letters, 4 Protocol Assistance letters, 7 Follow-up Scientific Advice and 2 Follow-up Protocol Assistance letters were adopted at the 21-24 April CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 21 new Requests for which the procedure started at the SAWP meeting held on 31st March-2nd April. The new requests are divided as follows: 13 Initial Scientific Advice, 4 Follow-up Scientific Advice, 3 Initial Protocol Assistance and 1 Follow-up Protocol Assistance.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE FEBRUARY 2008 CHMP MEETING

WORKING PARTY ON SIMILAR BIOLOGICAL (BIOSIMILAR) MEDICINAL PRODUCTS (BMWP)

Reference number	Document	Status[4]
CHMP/BMWP/118264/ 2007	Guideline on Similar Biological Medicinal Products Containing Low Molecular Weight Heparins	Adopted for 6-month public consultation

PHARMACOGENOMICS WORKING PARTY (PgWP)

Reference number	Document	Status[4]
CHMP/56776/2006	Reflection Paper on Pharmacogenomics Experience in Oncology	Adopted for 3-month public consultation
CHMP/536201/2007	Overview of comments received on the Reflection Paper on Pharmacogenomic Samples, Testing and Data handling	Adopted
CHMP/125959/2008	Revised Mandate Pharmacogenomics Working Party	Adopted
EMEA/125958/2008	ICH Business Plan for Pharmaco Genomic (PG) Biomarker Qualification: Format and data standards	Adopted
EMEA/190395/2008	ICH Concept Paper on Pharmaco Genomic (PG) Biomarker Qualification: Format and data standards	Adopted

QUALITY WORKING PARTY (SWP)

Reference number	Document	Status[4]
EMEA/HMPC/CHMP/ CVMP/214869/2006	Guideline on Quality of Combination Herbal Medicinal Products / Traditional Herbal Medicinal Products	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[4]
CHMP/EWP/141412/2008	Concept Paper on the Revision of the Guideline on Clinical Investigation of Medicinal Products for Treatment of Osteoarthritis	Adopted for 3-month public consultation
CHMP/EWP/14377/2008	Addendum to the Note for Guidance on Evaluation of Medicinal Products Indicated for the Treatment of Bacterial Infections to Specifically Address the Clinical Development of New Agents to Treat Disease Due to Mycobacterium Tuberculosis	Adopted for 6-month public consultation

[4] Adopted or release for consultation documents can be found at the EMEA website (under "What's new-recent publications" or under Human Medicines-Guidance documents").

Reference number	Document	Status[4]
CHMP/EWP/30039/2008	Guideline on the Clinical Evaluation of Direct Acting Antiviral Agents Intended for Treatment of Chronic Hepatitis C	Adopted for 6-month public consultation
CHMP/EWP/12052/2008	Concept Paper on the harmonisation and update of the clinical aspects in the authorised conditions of use for radiopharmaceuticals and other diagnostic medicinal products	Adopted for 3-month public consultation