European Medicines Agency
Evaluation of Medicines for Human Use

London, 31st July 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
JULY 2008 PLENARY MEETING
MONTHLY REPORT

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

CENTRALISED PROCEDURE

Initial applications for marketing authorisation

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

New medicinal products

- **Evicel** (human fibrinogen / human thrombin), from Omrix Biopharmaceuticals S.A., fibrin sealant is used as supportive treatment in surgery where standard surgical techniques are insufficient for improvement of haemostasis, and as suture support for haemostasis in vascular surgery. EMEA review began on 15 August 2007 with an active review time of 207 days.
- **Xarelto** (rivaroxaban), from Bayer Health Care, for the prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery. EMEA review began on 23 November 2007 with an active review time of 181 days.

Generic medicinal products

- **Olanzapine Mylan** (olanzapine), from Generics (UK) limited, for the treatment of schizophrenia and the treatment of moderate to severe manic episodes. EMEA review began on 26 December 2007 with an active review time of 177 days. The reference product for Olanzapine Mylan is Zyprexa, from Eli Lilly Nederland B.V., which is already authorised in the European Union (EU), in the applied indication.

Positive opinion for 'informed consent' applications

This type of application requires that reference is made to an authorised medicine and that the marketing authorisation holder of this reference product has given consent to the use of the dossier in the application procedure. The medicines concerned are:

- **Duloxetine Boehringer Ingelheim** (duloxetine), from Boehringer Ingelheim International GmbH, for the treatment of moderate to severe stress urinary incontinence in women, and for the treatment of diabetic peripheral neuropathic pain in adults. EMEA review began on 30 March 2008 with an active review time of 89 days. Reference medicine is Ariclaim, from Eli Lilly Nederland B.V.
- **Fluticasone furoate GSK** (fluticasone furoate), from Glaxo Group Ltd., for the treatment of symptoms of allergic rhinitis in children aged 6 years or older, adolescents and adults. EMEA review began on 28 May 2008 with an active review time of 57 days. Reference medicine is Avamys, from Glaxo Group Ltd.

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- **Tadalafil Lilly** (tadalafil), from Eli Lilly Nederland B.V., for the treatment of erectile dysfunction. EMEA review began on 28 May 2008 with an active review time of 57 days. Reference medicine is Cialis, from Eli Lilly Nederland B.V.
- **Prepandemic influenza vaccine** GlaxoSmithKline Biologicals (pre-pandemic influenza vaccine (H5N1) [(split virion, inactivated, adjuvanted) A/Vietnam/1194/2004 NIBRG-14], from GlaxoSmithKline Biologicals S.A., for active immunisation against H5N1 subtype of influenza A virus. EMEA review began on 28 May 2008 with an active review time of 57 days. Reference medicine is Prepandrix (split inactivated, adjuvanted, H5N1 influenza vaccine containing antigens from A/VietNam/1194/2004 NIBRG-14), from GlaxoSmithKline Biologicals S.A.

Revised positive opinion

The CHMP adopted a revised positive opinion by consensus for **Ratiograstim** (filgrastim) from ratiopharm GmbH, **Biograstim** (filgrastim) from CT Arzneimittel GmbH, **Tevagrastim** (filgrastim) from Teva Generics GmbH and **Filgrastim ratiopharm** (filgrastim) from ratiopharm GmbH, following a previous positive opinion issued in February 2008.

The European Commission had requested that the CHMP evaluate whether data from a similar product (Grasalva), which has been marketed in Lithuania by Sicor Biotech UAB (part of Teva group), was relevant for the assessment of the marketing authorisation applications for the above products. Having reviewed these data, the CHMP concluded that the benefit-risk-balance for the use of Ratiograstim, Biograstim, Tevagrastim and Filgrastim ratiopharm in the treatment of neutropenia continues to be positive and recommended the granting of marketing authorisations.

Negative opinion

The CHMP adopted a negative opinion by consensus recommending the refusal of a marketing authorisation for **Sovrima,** from Santhera Pharmaceuticals (Deutschland) GmbH. Sovrima was intended to be used for treatment of Friedreich's Ataxia, an inherited condition that causes progressive damage to the nervous system and heart disease. It was designated as an orphan medicine. EMEA review began on 15 August 2007 with an active review time of 203 days

A separate question-and-answer document with more detailed information on the grounds for the negative opinion is available here.

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

Following the re-examination of the negative opinion adopted on 19 March 2008, the CHMP adopted a final positive opinion for **Ceplene** (histamine dihydrochloride), from EpiCept GmbH, intended to be used as maintenance treatment in combination with interleukin-2 in adults with acute myeloid leukaemia. Ceplene is **the 48th orphan medicine** to receive a positive opinion.

A separate question-and-answer document with more information about the re-examination procedure is available here.

The EMEA has been formally requested by Howmedica International S. de R.L, to re-examine the negative opinion for **Opgenra** (recombinant human osteogenic protein-1/eptotermin) intended to be used for posterolateral lumbar spinal fusion in adult patients with spondylolisthesis where autograft has failed, adopted during the CHMP meeting on 23-26 June 2008.

Withdrawal

The EMEA has been formally notified by IDEA AG of its decision to withdraw its application for a marketing authorisation application for **Diractin** (ketoprofen). Diractin was expected to be used for the symptomatic treatment of inflammation and pain from osteoarthritis. A separate press release with more information is available. The question-and-answer document will be released in the near future.

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.

Post-authorisation procedures

Extensions of indication and other recommendations

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

- **Aclasta** (zoledronic acid), from Novartis Europharm Ltd, to extend the indication to include treatment of osteoporosis in post-menopausal women and men at increased risk of fracture, including those with a recent low-trauma hip fracture. Aclasta is currently indicated for the treatment of osteoporosis in post-menopausal women at increased risk of fracture and treatment of Paget's disease of the bone.
- **Humira** (adalimumab), from Abbott Laboratories Ltd, to extend the indication to include treatment of active polyarticular juvenile idiopathic arthritis, in adolescents aged 13 to 17 years who have had an inadequate response to one or more disease-modifying anti-rheumatic medicines. Humira is currently indicated for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease and psoriasis.
- **Velcade** (bortezomib), from Janssen-Cilag International NV, to extend the indication for its use in combination with melphalan and prednisone for the treatment of patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with bone marrow transplant. Velcade is currently indicated as mono-therapy for the treatment of progressive multiple myeloma in patients who have received at least one prior therapy and who have already undergone or are unsuitable for bone marrow transplantation.

Negative opinion for extension of indication

The CHMP adopted a negative opinion for an extension of indication of **Taxotere** (docetaxel) and **Docetaxel Winthrop** (docetaxel), both from Aventis Pharma S.A. Both medicines were intended to be used to treat operable breast cancer whose tumours overexpress the protein HER2. Both medicines were expected to be used in addition to surgery to remove the tumour in combination with trastuzumab following treatment with doxorubicin and cyclophosphamide and in combination with trastuzumab and carboplatin. Taxotere and Docetaxel Winthrop are currently indicated for the treatment of advanced or metastatic breast cancer, in combination with other anticancer medicines, in patients previously or not previously treated with cytotoxic therapy and in breast cancer that can be treated with surgery. In these patients, Taxotere and Docetaxel Winthrop are used in addition to surgery to remove the tumour together with doxorubicin and cyclophosphamide. Taxotere and Docetaxel Winthrop are also indicated for the treatment of non-small cell lung cancer, prostate cancer, gastric adenocarcinoma and head and neck cancer.

A separate question-and-answer document with more detailed information on the grounds for the negative opinion is available here.

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

New contraindications

The CHMP recommended the addition of a new contraindication for **Rasilez / Enviage / Riprazo / Sprimeo / Tekturna** (aliskiren) from Novartis Europharm Ltd., stating that the concomitant use of aliskiren and cyclosporine, a highly potent P-gp inhibitor, and other potent P-gp inhibitors (quinidine,

verapamil) is contraindicated. The CHMP also recommended to vary the product information to add a warning regarding the co-administration of aliskiren with moderate P-gp inhibitors such as ketoconazole.

New safety information

The CHMP recommended the inclusion of a new warning in the prescribing information for the immunosuppressants **Advagraf** (tacrolimus), **CellCept** (mycophenolate mofetil) and **Rapamune** (sirolimus) related to cases of BK virus-associated nephropathy, as well as cases of JC virus-associated progressive multifocal leukoencephalopathy (PML) reported in patients treated with these immunosuppressants.

Withdrawals

The EMEA has been formally notified by Abbott Laboratories Ltd of its decision to withdraw its application for a line extension for **Humira** (adalimumab). The line extension referred to a 20 mg prefilled syringe to be used in juvenile idiopathic arthritis (JIA). In its official letter, the company stated that the withdrawal was based on the fact that the 20 mg formulation is not required based on the approval conditions for JIA in the European Union.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted eight Lists of Questions on initial applications (including two under the mandatory scope, and six under the optional scope) and five List of Questions on "line extension" application (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003).

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 June 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 June 2008 CHMP plenary meeting are provided in **Annex 4**.

REFERRAL PROCEDURES

Referral procedure concluded

The CHMP concluded a referral procedure under Article 31 of Directive 2001/83/EC, as amended, for oral **norfloxacin-containing medicines**.
A separate press release and a question-and-answer document with more detailed information are available on the EMEA website.

The CHMP concluded a number of referral procedures under Article 29 of Directive 2001/83/EC, as amended. This type of procedures is initiated by one or more Member States in cases where an agreement cannot be reached in the context of the mutual recognition procedure or the decentralised procedure. The medicines concerned are:

- **Lisonorm (**amlodipine / lisinopril), from Gedeon Richter Plc, indicated as therapy for patients with blood pressure adequately controlled with lisinopril and amlodipine given concurrently at

the same dose level. The procedure was initiated because of disagreement between the Member States on the grounds for approval of this medicine, in particular due to concerns over the bioequivalence with the reference product. The CHMP concluded that the benefits of Lisonorm outweigh its risks and recommended the granting of the marketing authorisation for Lisonorm.

- **Ribavirin "iQur"** (ribavirin), from iQur Pharmaceutical Ltd, is indicated for the treatment of chronic hepatitis C and to be used only in combination with peginterferon-α2a or interferon-α2a. The procedure was initiated because of disagreement between the Member States on the grounds for approval of this medicine. The concerns related to the application of the 'well established use' concept for the registration of Ribavirin due to its pharmacological characteristics. The CHMP considered that the company did not provide sufficient evidence for a systematic and documented use of the substance outside clinical trials, compassionate use and named patient supply to demonstrate the well established use of ribavirin in the claimed indication in the European Union. The Committee concluded that marketing authorisations should not be granted.

The CHMP finalised a number of referral procedures under Article 30 of Directive 2001/83/EC as amended. This type of procedure is initiated with a view to harmonising product information for medicinal products authorised at Member State level. The CHMP recommended for the three following medicines the amendment of the Summary of Product Characteristics, labelling and package leaflet:

- **Ciflox, Uniflox** (ciprofloxacin), from Bayer Pharma SA, used as antibacterial medicine. The procedure was initiated by France.
- **Efexor and associated names (venlafaxine) and Efexor Depot and associated names** (venlafaxine), from Wyeth Europa Ltd., intended for the treatment of major depressive episodes and prevention of recurrence of major depressive episodes. The procedure was initiated by the European Commission.
- **Risperdal and associated names** (risperidone), from Janssen-Cilag, intended for the treatment of schizophrenia, moderate to severe manic episodes associated with bipolar disorders, persistent aggression in patients with moderate to severe Alzheimer's dementia and persistent aggression in conduct disorder. The procedure was initiated by the European Commission.
- **Risperdal Consta and associated names** (risperidone), from Janssen-Cilag, intended for the maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics. The procedure was initiated by the European Commission.

Re-examination procedure for referral concluded

The CHMP confirmed its previous position and recommended the refusal of the marketing authorisation and, where appropriate, the suspension of the marketing authorisation of the following **Fentanyl-containing transdermal patches** (Fentastad, Fentador, Fentrans, Matrigesic, Matripain), from STADA Arzneimittel AG.
The CHMP had adopted a negative opinion in November 2007, because it concluded that the product failed to show adequate characteristics which are key requirements for a product of this type in order to guarantee its safety and efficacy. In a re-examination procedure, requested by the company, the CHMP confirmed this outcome for all dose forms concerned.
The European Commission referred the opinion back to the CHMP in April 2008, requesting the Committee provide more clarity on the arguments to refuse the marketing authorisation for the lowest patch-strength, 25 micrograms/h patch. A revised opinion was adopted accordingly.

Referral procedures started

The CHMP started a referral procedure under Article 30 of Directive 2001/83/EC as amended for **Losec (omeprazole)** from AstraZeneca, used in the gastrointestinal therapeutic area, at the request of the European Commission, with a view to harmonising the product information for the medicines authorised at the level of the Member States.

Review procedures under Article 107

The CHMP finalised a procedure under Article 107 of the Community code on human medicinal products (Directive 2001/83/EC as amended) for **oral moxifloxacin-containing medicines.**
A separate press release and a question-and-answer document with more detailed information are available on the EMEA website.

MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 31st CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 21-22 July 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 30 June-2 July 2008 For further details, please see **Annex 5**.

Documents prepared by the CHMP Working Parties adopted during the July 2008 CHMP meeting are listed in **Annex 6**.

UPCOMING MEETINGS FOLLOWING THE JULY 2008 CHMP PLENARY MEETING

- The 47th meeting of the CHMP will be held at the EMEA on 22-25 September 2008.
- The next Name Review Group meeting will be held at the EMEA on 30th September 2008.
- The 32nd CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the EMEA on 22-23 September 2008.

ORGANISATIONAL MATTERS

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

- The adoption of a Reflection paper on ethanol content in (traditional) herbal medicinal products used in children (EMEA/HMPC/85114/2008).
- The adoption of the ICH topic M3 (R2) on Non-Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals (CHMP/ICH/286/95).
- Follow up discussion on procedural advice for validation of new marketing authorisation application extension / variation application and compliance check to an agreed PIP.
- The adoption of a guidance document entitled "Procedural Advice to CHMP Members". This is a high level document describing the various duties of Rapporteurs, Co-Rapporteurs, Peer Reviewers, and EMEA staff in the context of activities related to approvals. This document will be published shortly on the EMEA website.
- The adoption for 2-month public consultation of proposed revisions to the guideline on Time allowed for Applicants to respond to Questions and Issues raised during the Assessment of new MAA in the Centralised Procedure (EMEA/352080/2008)[1].
- Follow up discussion on proposal for a revision of the European Commission Guideline on Summary of Product Characteristics.
- Follow up discussion on the Revision of Volume 9A of The Rules Governing Medicinal Products in the European Union following the autumn 2007 post-consultation.
- Coordination of input from the concerned Working Parties/Working Groups and the CHMP on the GCP guideline on Advanced Therapies published by the European Commission for public consultation until 15th October 2008.

[1] The previous document reference was EMEA/75401/2006 Rev. 1 and was originally published in March 2006

- Discussion of collaboration between EFSA and EMEA regarding the presence of the antibiotic resistance marker gene nptII in GM plants for food and feed uses. A meeting on this matter should be held late August 2008.
- Preliminary discussion regarding the draft agenda of the Informal CHMP meeting to be held early October under the French European presidency.

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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

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	18	4	0	6	12	9	9	58	726
Positive opinions	14	2	0	2	8	6	3	35	464
Negative opinions[2]	1	0	0	0	1	0	2	4	22
Withdrawals prior to opinion	4	1	0	0	4	0	4	13	129
Marketing authorisation granted by the Commission	13	3	0	2	3	4	3	28	462

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	2008	1995 onwards
Compassionate use applications	0	0
Art. 58 applications	0	4
Consultation for medical devices[3]	1	5
PMF (Click here for a list of PMF certifications)	0	11
VAMF	0	0

[2] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[3] 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 JULY 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

ANNEX 2 TO CHMP MONTHLY REPORT JULY 2008

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)	700	5902
Type II Variations (positive opinions)	386	4230
Type II Variations (negative opinions)	3	14
Annex II Applications (positive opinions)	21	190
Annual Re-assessment (positive opinions)	17	-
Opinion for renewals of conditional MA's (positive opinions)	0	2
5 Year Renewals (positive opinions)	33	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
5 Extensions of indication	3 Positive opinions 2 Negative opinions
38 SPC changes	38 Positive opinions
45 Quality changes	44 Positive opinions 1 Negative opinion

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Onsenal (celecoxib) Pfizer Limited	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**
Emend (aprepitant) Merck Sharp & Dohme	Positive Opinion adopted	unlimited validity
Emtriva (emtricitabine) Gilead Science International Limited	Positive Opinion adopted	unlimited validity
Karvezide (irbesartan hydrochlorothiazide) Bristol Myers Squibb Pharma EEIG	Positive Opinion adopted	unlimited validity
CoAprovel (irbesartan hydrochlorothiazide) Sanofi Pharma Bristol Myers Squibb SNC	Positive Opinion adopted	unlimited validity
Stalevo (levodopa, carbidopa, entacapone) Orion Corporation	Positive Opinion adopted	unlimited validity
Onsenal (celecoxib) Pfizer Limited	Positive Opinion adopted	recommending additional renewal

ANNEX 3 TO CHMP MONTHLY REPORT JULY 2008

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

Invented Name	Relistor
INN	methylnaltrexone bromide
Marketing Authorisation Holder	Wyeth Europa Limited
Proposed ATC code	not yet assigned
Indication	Treatment of opioid-induced constipation in advanced illness patients who are receiving palliative care when response to usual laxative therapy has not been sufficient.
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	02.07.2008

Invented Name	Tredaptive
INN	nicotinic acid / laropiprant
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	C10AD52
Indication	Tredaptive is indicated for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia (characterised by elevated levels of LDL-cholesterol and triglycerides and low HDL-cholesterol) and in patients with primary hypercholesterolaemia (heterozygous familial and non-familial). Tredaptive should be used in patients in combination with HMG-CoA reductase inhibitors (statins), when the cholesterol lowering effect of HMG-CoA reductase inhibitor monotherapy is inadequate. It can be used as monotherapy only in patients in whom HMG-CoA reductase inhibitors are considered inappropriate or not tolerated. Diet and other non-pharmacological treatments (e.g. exercise, weight reduction) should be continued during therapy with Tredaptive
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	03.07.2008

Invented Name	Trevaclyn
INN	nicotinic acid / laropiprant
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	C10AD52

Indication	Trevaclyn is indicated for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia (characterised by elevated levels of LDL-cholesterol and triglycerides and low HDL-cholesterol) and in patients with primary hypercholesterolaemia (heterozygous familial and non-familial). Trevaclyn should be used in patients in combination with HMG-CoA reductase inhibitors (statins), when the cholesterol lowering effect of HMG-CoA reductase inhibitor monotherapy is inadequate. It can be used as monotherapy only in patients in whom HMG-CoA reductase inhibitors are considered inappropriate or not tolerated. Diet and other non-pharmacological treatments (e.g. exercise, weight reduction) should be continued during therapy with Trevaclyn
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	03.07.2008

Invented Name	Pelzont
INN	nicotinic acid / laropiprant
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	C10AD52
Indication	Pelzont is indicated for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia (characterised by elevated levels of LDL-cholesterol and triglycerides and low HDL-cholesterol) and in patients with primary hypercholesterolaemia (heterozygous familial and non-familial). Pelzont should be used in patients in combination with HMG-CoA reductase inhibitors (statins), when the cholesterol lowering effect of HMG-CoA reductase inhibitor monotherapy is inadequate. It can be used as monotherapy only in patients in whom HMG-CoA reductase inhibitors are considered inappropriate or not tolerated. Diet and other non-pharmacological treatments (e.g. exercise, weight reduction) should be continued during therapy with Pelzont
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	03.07.2008

Invented Name	Latixa
INN	ranolazine
Marketing Authorisation Holder	CV Therapeutics Europe Limited
Proposed ATC code	C01EB18
Indication	Latixa is indicated as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists).

CHMP Opinion date	24.04.2008
Marketing Authorisation Date	09.07.2008

Invented Name	Firazyr
INN	icatibant acetate
Marketing Authorisation Holder	Jerini AG
Proposed ATC code	not yet assigned
Indication	Firazyr is indicated for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults (with C1-esterase-inhibitor deficiency).
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	11.07.2008

Invented Name	Janumet
INN	sitagliptin / metformin hydrochloride
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	A10BD07
Indication	For patients with type 2 diabetes mellitus: Janumet is indicated as an adjunct to diet and exercise to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of metformin alone or those already being treated with the combination of sitagliptin and metformin. Janumet is also indicated in combination with a sulphonylurea (i.e., triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	16.07.2008

Invented Name	Velmetia
INN	sitagliptin / metformin hydrochloride
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	A10BD07
Indication	For patients with type 2 diabetes mellitus: Velmetia is indicated as an adjunct to diet and exercise to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of metformin alone or those already being treated with the combination of sitagliptin and metformin.

	Velmetia is also indicated in combination with a sulphonylurea (i.e., triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	16.07.2008

Invented Name	Efficib
INN	sitagliptin / metformin hydrochloride
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	A10BD07
Indication	For patients with type 2 diabetes mellitus: Efficib is indicated as an adjunct to diet and exercise to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of metformin alone or those already being treated with the combination of sitagliptin and metformin. Efficib is also indicated in combination with a sulphonylurea (i.e., triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	16.07.2008

Invented Name	Clopidogrel BMS
INN	clopidogrel hydrogen sulphate
Marketing Authorisation Holder	Bristol-Myers Squibb Pharma EEIG
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. Patients suffering from acute coronary syndrome: Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA).ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	16.07.2008

Invented Name	Clopidogrel Winthrop
INN	clopidogrel hydrogen sulphate
Marketing Authorisation Holder	Sanofi Pharma Bristol-Myers Squibb SNC
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. Patients suffering from acute coronary syndrome: Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA).ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy
CHMP Opinion date	24.04.2008
Marketing Authorisation Date	16.07.2008

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

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
1, 1'-[1,4- phenylenebis (methylene)]-bis-1,4,8,11-tetraazacyclotetradecane	Genzyme BV	EU/3/04/227	Treatment to mobilize progenitor cells prior to stem cell transplantation
3,4 diaminopyridine phosphate	EUSA PHARMA SAS	EU/3/02/124	Treatment of Lambert-Eaton myasthenic syndrome

ANNEX 5 TO CHMP MONTHLY REPORT JULY 2008

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

	1995 - 2007	2008	Overall Total
Scientific Advice	887	134	1021
Follow-up to Scientific Advice	171	34	205
Protocol Assistance	198	29	227
Follow-up to Protocol Assistance	90	11	101
	1346	**208**	**1554**

OUTCOME OF THE JULY 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	In Vivo Diagnosis Of Solid-Phase Gastric Half Emptying Time In Gastric Motility	X						X	
Biological	Treatment Of Diabetes	X					X	X	
Biological	Treatment Of Diabetes	X				X	X	X	
Biological	Treatment Of Type 1 Diabetes Mellitus	X					X	X	
Biological	Treatment Of Primary Hyperoxaluria				X		X	X	
Innovative product	Treatment Of Breast Cancer and Non-Small Cell Lung Cancer	X					X		
Chemical	Treatment Of Hepatocellular Cancer			X				X	
Chemical	Treatment Of Relapsing Forms Of Multiple Sclerosis			X				X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Sentinel Lymph Node Mapping For Breast Cancer And Melanoma	X						X	
Chemical	Treatment Of Acute Lymphoblastic Leukaemia	X				X	X	X	
Chemical	Metastatic And/Or Unresectable Gastrointestinal Stromal Tumors		X					X	
Chemical	Chronic Lymphocytic Leukaemia		X					X	
Chemical	Treatment Of Non Small Cell Lung Cancer	X						X	
Chemical	Treatment of Severe Sepsis	X						X	
Chemical	Prophylaxis Of Organ Rejection In Solid Organ Transplant Patients	X						X	
Biological	Treatment Of Acute Myocardial Infarction	X						X	
Chemical	Reduction Of The Risk Of Cardiovascular Events	X						X	
Chemical	Reduction Of Ldl-C, Total Cholesterol, And Non-Hdl Cholesterol	X					X	X	
Biological	Treatment Of Hepatitis C	X				X	X		
Biological	Prophylaxis Of Early Childhood Wheezing In Infants At High Risk For Serious Rsv	X						X	
Chemical	Treatment Of HIV Infection			X				X	
Biological	Systemic-Onset Juvenile Idiopathic Arthritis		X					X	
Chemical	Treatment Of Epilepsy	X					X	X	
Chemical	Treatment Of Major Depressive Disorder	X						X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Treatment Of Sleep Disorders In Children With Neurodevelopmental Disabilities	X				X	X	X	
Chemical	Treatment Of Mild To Moderately Severe Dementia Of The Alzheimer	X				X	X	X	
Chemical	Treatment Of Tinnitus	X					X	X	
Biological	Smoking Cessation / Abrogation Of Nicotine Addiction	X					X	X	
Chemical	Treatment Of Fibromyalgia	X						X	
Chemical	Treatment of Asthma	X					X	X	
Chemical	Treatment of Asthma and COPD			X		X	X		
Biological	Efficacy Of Recombinant Antibody Products Enhancer	X				X			
Chemical	Prevention Of Rejection For Corneal Implant				X			X	
Biological	Treatment Of Growth Hormone Deficiency	X				X	X	X	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 25 Scientific Advice letters, 3 Protocol Assistance letters, 4 Follow-up Scientific Advice and 2 Follow-up Protocol Assistance letters were adopted at the 21-24 July 2008 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 22 new Requests for which the procedure started at the SAWP meeting held from 30 June to 3 July 2008. The new requests are divided as follows: 12 Initial Scientific Advice, 4 Follow-up Scientific Advice, 4 Initial Protocol Assistance and 2 Follow-up Protocol Assistance.

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

BIOLOGICS WORKING PARTY (BWP)

Reference number	Document	Status[4]
EMEA/BWP/398498/2008	Guideline on virus safety evaluation of biotechnological investigational medicinal products	Adopted
EMEA/CHMP/BWP/ 48316/2006	Guideline on quality of biological active substances produced by stable transgene expression in higher plants.	Adopted
EMEA/CHMP/BWP/ 125826/2007	Overview of comments received on draft Guideline on quality of biological active substances produced by stable transgene expression in higher plants	Adopted

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

Reference number	Document	Status[4]
EMEA/CHMP/BMWP/ 170734/2008	Revised Concept Paper on the revision of the guidance on similar biological medicinal products containing recombinant erythropoietins	Adopted for 3-month public consultation

QUALITY WORKING PARTY (QWP)

Reference number	Document	Status[4]
EMEA/138931/2008	Concept Paper on the development of a quality guideline on pharmaceutical development of medicines for paediatric use	Adopted for 3-month public consultation

SAFETY WORKING PARTY (SWP)

Reference number	Document	Status[4]
EMEA/CHMP/203927/ 2005	Guideline on Risk Assessment of Medicinal Products on Human Reproductive and Developmental Toxicities: from Data to Labelling	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[4]
CHMP/EWP/263148/2006	Guideline on Clinical Investigation of Immunosuppressants for Solid Organ Transplantation	Adopted
CPMP/EWP/2284/99/ Rev.1	Guideline on the Development of New Medicinal Products for the Treatment of Crohn's disease	Adopted
CHMP/EWP/517497/07	Addendum to the Guideline on the Clinical Evaluation of Medicinal Products Used in Weight Control	Adopted

[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]
	(CPMP/EWP/281/96 Rev. 1) for Weight Control in Children	
CPMP/EWP/563/95 Rev.1	Guideline on Parkinson's Disease	Adopted
CPMP/EWP/553/95 Rev.1	Guideline on Alzheimer's Disease	Adopted
CHMP/EWP/352438/2008	Addendum to the Guideline on Anti-Arrhythmics (CPMP/EWP/237/95) on Atrial Fibrillation	Adopted for 6-month public consultation.
CHMP/EWP/1401/98 Rev. 1	Guideline on the Investigation of Bioequivalence	Adopted for 6-month public consultation.
CHMP/EWP/297931/2008	Concept Paper on the Need for Revision of the Note for Guidance on the Investigation of Drug Interactions	Adopted for 3-month public consultation
CHMP/EWP/358650/2008	Guideline on Clinical Investigation of Medicinal Products in the Treatment of Post-Traumatic Stress Disorder	Adopted