European Medicines Agency
Evaluation of Medicines for Human Use

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SEPTEMBER 2006 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its September plenary meeting from 18-21 September 2006.

Centralised procedure

Initial marketing authorisation applications

The Committee for Medicinal Products for Human Use (CHMP) gave two positive opinions on initial marketing authorisation applications for new treatment options for patients suffering from diabetes or from cancer:

- **Byetta** (exenatide), from Eli Lilly and Company Limited, received a positive opinion for the treatment of patients with type 2 diabetes. EMEA review began on 23 November 2005 with an active review time of 208 days.
- **Sprycel** (dasatinib), from BMS pharma EEIG, received a positive opinion for the treatment of chronic myeloid leukaemia in patients with resistance or intolerance to prior therapy including imatinib mesylate, and acute lymphoblastic leukaemia in patients with resistance or intolerance to prior therapy. Sprycel is the 31st orphan medicinal product to receive a positive opinion from the Committee. EMEA review began on 1 February 2006 with an active review time of 177 days.

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.

Scientific opinion for medicinal products for use outside the European Union

The Committee adopted a positive opinion for **Aluvia** (lopinavir/ritonavir), from Abbott Laboratories Limited (UK). Aluvia is intended for the treatment of HIV-1 infected adults and children above the age of 2 years, in combination with other antiretroviral agents. The opinion was adopted in accordance with Article 58 of Regulation (EC) No 726/2004, which allows the CHMP, in the context of cooperation with the World Health Organization (WHO), to adopt scientific opinions for medicinal products intended exclusively for markets outside of the European Union. Aluvia is the third medicinal product to receive a positive opinion under Article 58.

Extensions of indication and other recommendations

The Committee adopted four positive opinions on extensions of indication of medicinal products that are already authorised in the European Union in the area of cancer, diabetes, infectious and cardiovascular diseases:

- **Taxotere** (docetaxel), from Aventis Pharma S.A., received a positive opinion to include the use of Taxotere in combination with cisplatin and 5-fluorouracil for the induction treatment of patients with inoperable locally advanced squamous cell carcinoma of the head and neck. Taxotere was first granted a marketing authorisation in the European Union on 27 November 1995 and is authorised for the treatment of breast cancer, non-small cell lung cancer, prostate cancer and gastric adenocarcinoma.

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- **Actos** (pioglitazone), from Takeda Europe R&D Centre Ltd., received a positive opinion to add triple oral combination therapy with metformin and sulphonylurea. Actos was first granted a marketing authorisation in the European Union on 13 October 2000 and is authorised as monotherapy or as dual oral therapy with other medicinal products for the treatment of type 2 diabetes.

- **Noxafil** (posaconazole) and **Posaconazole SP** (posaconazole), from Schering Plough Europe, received a positive opinion to extend the indication to include prophylaxis of invasive fungal infections in high-risk patients and to add treatment of oropharyngeal candidiasis in adults. Noxafil and Posaconazole SP were first granted marketing authorisation in the European Union on 25 October 2005 and are currently indicated for several invasive fungal infections in adults.

- **Tracleer** (bosentan), from Actelion Registration Ltd, received a positive opinion to extend the indication to pulmonary arterial hypertension patients associated with congenital systemic-to-pulmonary shunts and Eisenmenger's physiology. Tracleer was first granted marketing authorisation in the European Union on 15 May 2002 and is currently indicated for treatment of pulmonary arterial hypertension (PAH) in selected patient populations with grade-III functional status.

Summaries of opinion for these five products are available and can be found here.

New contraindications

The Committee recommended to add a contraindication for **Ketek** (telithromycin) and **Levviax** (telithromycin), from Aventis Pharma S.A., stating that, in patients with severely impaired renal and/or hepatic functions, the two medicinal products should not be administered concomitantly with strong CYP3A4 inhibitors, such as protease inhibitors or ketoconazole. Ketek and Levviax were first granted marketing authorisations on 9 July 2001 and are currently authorised for a number of respiratory-tract infections.

Summaries of opinion for these two products are available and can be found here.

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

Lists of Questions

The Committee adopted ten Lists of Questions on initial applications (four under the mandatory scope and six under the optional scope).

Withdrawals

The European Medicines Agency has been formally notified by Sanofi-Aventis of their decision to withdraw their application for a centralised marketing authorisation for the medicinal product **Multaq** (dronedarone hydrochloride).

The indication applied was for rhythm and rate control in patients with atrial fibrillation or atrial flutter (abnormalities of the heartbeat), to maintain normal sinus rhythm or to decrease ventricular rate. The application for marketing authorisation for Multaq was submitted to the EMEA on 20 July 2005. At the time of the withdrawal, it was under review by the CHMP. In its official withdrawal letter, the company stated that the withdrawal of Multaq was due to the fact that the additional clinical data requested by the CHMP cannot be provided within the timeframe of the current procedure. More information about Multaq and the current state of the scientific assessment at the time of withdrawal will be made available in a question and answer document. This document, together with the withdrawal letter from the company, will be published on the EMEA website www.emea.europa.eu/htms/human/withdraw/withdrawapp.htm, in the very near future.

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 July 2006 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 July 2006 CHMP plenary meeting are provided in **Annex 4**.

Referral procedures

- The Committee concluded a referral procedure for **Glucomed** (glucosamine hydrochloride) and associated names, from Navamedic ASA, recommending the granting of a marketing authorisation for the relief of symptoms in mild to moderate osteoarthritis of the knee. The procedure was initiated under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) because of disagreement regarding the benefit-risk profile in this indication among the Member States during the mutual recognition procedure.

- The Committee concluded a referral procedure for **Agopton** (lansoprazole) and associated names, from Takeda Pharma GmbH, with a recommendation to harmonise the product information, in particular therapeutic indications and posology, across the EU. The procedure was initiated by Germany under Article 30 of the Community code on human medicinal products (Directive 2001/83/EC as amended), which is triggered in order to harmonise differences between product information across the EU for nationally authorised products.

- The European Commission asked the Committee to look at the risk-benefit profile of **veralipride**-containing medicinal products. This follows concerns regarding psychiatric and neurological reactions reported with veralipride. The procedure was initiated under Article 31 of Directive 2001/83/EC as amended. Veralipride is indicated for the treatment of hot flushes and psycho-functional symptoms such as anxiety, depression or irritability of confirmed menopause.

- The European Commission has asked the Committee to look at the risk-benefit profile of **Piroxicam**. This follows concerns that piroxicam may have a less favourable gastrointestional safety profile and a higher risk of skin reactions than other non-selective NSAIDs. The procedure was initiated under Article 31 of Directive 2001/83/EC as amended. Piroxicam is a non-selective NSAID that is widely used in the treatment of inflammatory conditions, such as arthritis and other painful conditions. A separate question and answers document with more detailed information about the referral concerning piroxicam is available.

- The Committee started a referral procedure for a generic medicinal product called **Simvastatine** (simvastatine) from Neo Pharma Ltd because of concerns over the reliability of a bioequivalence study used to demonstrate comparability with the originator product. The procedure was initiated by the Netherlands under Article 36 of the Community code on human medicinal products (Directive 2001/83/EC as amended). Article 36 procedures are initiated where a Member State considers that there are public health issues relating to a product that may require regulatory action.

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

The European Medicines Agency has been formally requested by Les Laboratoires Servier to re-examine the negative opinion for **Valdoxan** (agomelatine) and **Thymanax** (agomelatine) adopted during the CHMP meeting that took place on 24-27 July 2006.

Re-examination procedure under Article 32(4) of Directive 2001/83/EC

The CHMP confirmed its previous opinion adopted at the May 2006 meeting, to suspend the marketing authorisation for a number of generic medicines containing **cetirizine dihydrochloride 10 mg** (film coated tablets). The Committee recommended the suspension of these products in the context of a referral procedure under Article 36 of Directive 2001/83/EC as amended, because of concerns regarding compliance with good clinical practices (GCP) and good laboratory practices (GLP) that impact on the quality and reliability of bioequivalence studies supporting the marketing authorisations.

Other procedures

- **Review of NSAIDs**

The French national medicines agency, Agence Française de Sécurité Sanitaire des Produits de Santé (Afssaps), has asked the Committee to review the cardiovascular safety of non-selective non-steroidal anti-inflammatory drugs (NSAIDs) in the context of their overall benefit-risk profile. New data and analyses are now available on the cardiovascular safety of NSAIDs stemming from clinical and epidemiological studies, which signal a potential increased thrombotic risk (such as heart attack or stroke) for some of these NSAIDs especially when used in long-term treatment. This review procedure has been initiated under Article 5(3) of Regulation (EC) No 726/2004 and will result in a CHMP scientific opinion, which will be made publicly accessible.

A separate Press Release and question and answers document with more detailed information about the review of NSAIDs is available.

- **Adequacy of guidance on use of medicinal products in the elderly**

The European Commission made a request to the CHMP to provide an opinion on the adequacy of guidance on the elderly regarding medicinal products for human use according to the provisions set out in the Regulation (EC) No 726/2004. This review procedure has been initiated on the basis of Articles 5(3) and 57(p) of Regulation (EC) No 726/2004 and will result in a CHMP scientific opinion, which will be made publicly accessible.

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 29-31 August 2006. For further details, please see **Annex 5**.

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

Invented Name Review Group (NRG)

- **Joint EMEA (NRG)/EFPIA Workshop on invented names:**

A Joint EMEA (NRG)/EFPIA Workshop took place in the morning of 11 September 2006 with the purpose of exchanging information on the trade marking creation/development process as well as on the NRG review process with the aim of improving the predictability of the NRG outcome.

- **Joint EMEA (NRG)/Interest parties meeting on invented names:**

A Joint EMEA (NRG)/Interested parties meeting took place in the afternoon of 11 September 2006 to discuss proposed amendments to the Guideline on invented names with a view to eliminate restrictions which are not justified based on public health grounds as well as to address the specificities in relation to the naming of the non-prescription and generics medicinal products.

The meeting reports and presentations will shortly be made available on the EMEA website.

Statistical information on the outcome of the checking of acceptability of proposed invented names for medicinal products processed through the centralised procedure are provided in **Annex 7.**

Upcoming meetings following the September 2006 CHMP plenary meeting:

- The 26th meeting of the CHMP will be held at the EMEA on 16-19 October 2006.
- The next Invented Name Review Group meeting will be held at the EMEA on 16 October 2006.
- The 11th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the EMEA on 16-17 October 2006.
- The first meeting of the Working Group with Health Care Professionals will take place on the 17th November 2006.
- A SAG Central Nervous System will take place on the 8th November 2006.
- A SAG Endocrinology meeting will take place on the 20th November 2006.
- A SAG Oncology meeting will take place on the 30th November 2006.

Organisational matters

The main topics addressed during the September 2006 CHMP meeting related to:

- Follow-on discussions with regard to the publication of information related to withdrawals or refusals of applications.
- The adoption of draft work plans for all CHMP Working Parties.
- Discussions with regards to the application of Article 107 of Directive 2004/27/EC.
- The innovative drug development approaches-project and the interim report from the EMEA/CHMP think-tank group dated 18th September 2006.
- The interim report published by the UK Department of Health on phase I clinical trials related to the TGN1412 trial. The CHMP discussed the report and requested its Working Parties to consider whether their recommendations and other initiatives at a European level should be further addressed in EU guidance.

PROCEDURAL ANNOUNCEMENT

- Advisory note on Dossier requirements for Bulgaria and Romania Accession to the EU

In view of the anticipated enlargement of the EU with Bulgaria and Romania on 1st January 2007[1], Marketing Authorisation Holders and Applicants are advised that they should consider to provide Modules 1-2 of pending applications to the Contact Points of the New Member States that can be found below in view of upcoming adoption of CHMP opinions in 2007.

The EMEA proposes the following:

Centralised Procedure:

New Full Applications:

After positive validation of the MAA, in addition to the normal submission to the CHMP Members, as per the published EMEA dossier requirements, Module 1 and Module 2 (electronically and/or hard copies) can be presented to the Contact Points of the New Member States*

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Ongoing Full Applications:

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

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

Type II variations (only Extensions of Indication):

After positive validation of the variation application, in addition to the normal submission to the CHMP Members, as per the published EMEA Post-Authorisation guide, Module 1 and Module 2 can be presented to the Contact Points of the New Member States*.

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

[1] Accession date to be confirmed by the European Council in fourth quarter of 2006. Therefore, this guidance and in particular the timelines for submission of documents, cannot be considered as final and may need to be adjusted accordingly.

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

- The publication of the detailed CMD(h) report in Annex 8 will no longer appear in next month's CHMP monthly report and will be replaced by a link to the Heads of Agencies website where the report will be found.

- Update on the Appointment of Rapporteurs and Co-Rapporteurs

Following the publication of the Paper on the "CHMP Rapporteur /Co-Rapporteur appointment: Principles, objective criteria and methodology" early July 2006, Applicants are reminded that they should still indicate in a letter of intent their request for appointment of Rapporteur and Co-Rapporteur. These requests should be received approximately seven months prior to the intended submission date and at least one week prior to a CHMP meeting so that appointment can optimally take place six months prior to submission. It is recommended that future Applicants liaise with the respective Product Team Leader when planning such requests.

Mutual Recognition procedure and Decentralised procedures-Human

The CHMP noted the report from the 10th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 18 September 2006. For further details, please see **Annex 8**.

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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	Dec 2005/2006[2]							1995 onwards
	Optional Scope			Mandatory scope			Total	Overall total
	NAS	Significant innovation	Interest of Patients	Biotech	Indications	Orphans		
Applications for MA submitted[3]	25	6	0	14	6	10	61	596
Positive opinions[4]	17	2	0	6	0	7	32	358[5]
Negative opinions[6]	3	0	0	2	0	0	5	12[6]
Withdrawals prior to opinion	2	1	0	1	0	3	7	106
Marketing authorisation granted by the Commission	19	1	0	10	0	8	38	349

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	Dec 2005/2006	1995 onwards
Compassionate use applications	0	0
Art. 58 applications	1	3
Consultation for medical devices[7]	1	5
PMF	2	9
VAMF	0	0

[2] Starting point for operation of the new eligibility criteria to the centralised procedure
[3] Number of accelerated reviews requested and number of accelerated reviews granted (3/0)
[4] Subdivided by conditional and exceptional (0/0)
[5] 358 positive Opinions corresponding to 284 substances
[6] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[7] 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 SEPTEMBER 2006 CHMP MEETING IN RELATION TO ACCELERATED ASSESMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Chemical	Treatment of advanced renal cell carcinoma		X
Chemical	Treatment of HIV-1 infection in adults		X

ANNEX 2 TO CHMP MONTHLY REPORT SEPTEMBER 2006

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

Activity	2006	Overall total 1995 onwards
Type I Variations (positive notifications)	538	3978
Type II Variations (positive opinions)	488	2670
Type II Variations (negative opinions)	1	8
Annex II Applications (positive opinions)	14	141
Annual Re-assessment (positive opinions)	17	-
Opinion for renewals of conditional MA's (positive opinions)	0	0
5 Year Renewals (positive opinions)	45	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
7 Extensions of indication	7 Positive opinions
51 SPC changes	51 Positive opinions
33 Quality changes	33 Positive opinions

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

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**
Foscan (temoporfin) Biolitec Pharma Limited	Positive Opinion adopted	The Marketing Authorisation will remain under exceptional circumstances and one further renewal would be required in 5 years time
Protopic (tacrolimus) Astellas Pharma GmbH	Positive Opinion adopted	Unlimited validity
Protopy (tacrolimus) Astellas Pharma GmbH	Positive Opinion adopted	Unlimited validity

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE JULY 2006 CHMP MONTHLY REPORT

Invented Name	Atryn
INN	antithrombin alfa
Marketing Authorisation Holder	Genzyme Europe B.V.
Proposed ATC code	B01AB02
Indication	Atryn is indicated for the prophylaxis of venous thromboembolism in surgery of patients with congenital antithrombin deficiency. ATryn is normally given in association with heparin or low molecular weight heparin.
CHMP Opinion date	01.06.2006
Marketing Authorisation Date	28.07.2006

Invented Name	Livensa
INN	testosterone
Marketing Authorisation Holder	Procter & Gamble Pharmaceuticals – Germany, GmbH
Proposed ATC code	G03BA03
Indication	Livensa is indicated for the treatment of hypoactive sexual desire disorder (HSDD) in bilaterally oophorectomised and hysterectomised (surgically induced menopause) women receiving concomitant estrogen therapy.
CHMP Opinion date	01.06.2006
Marketing Authorisation Date	28.07.2006

Invented Name	Intrinsa
INN	testosterone
Marketing Authorisation Holder	Procter & Gamble Pharmaceuticals – Germany, GmbH
Proposed ATC code	G03BA03
Indication	Intrinsa is indicated for the treatment of hypoactive sexual desire disorder (HSDD) in bilaterally oophorectomised and hysterectomised (surgically induced menopause) women receiving concomitant estrogen therapy.
CHMP Opinion date	01.06.2006
Marketing Authorisation Date	28.07.2006

Invented Name	Luminity
INN	perflutren
Marketing Authorisation Holder	Bristol-Myers Squibb Pharma Belgium Sprl
Proposed ATC code	V08D A04
Indication	Luminity is an ultrasound contrast-enhancing agent for use in patients in whom non-contrast echocardiography was suboptimal (suboptimal is considered to indicate that at least two of six segments in the 4- or 2-chamber view of the ventricular border were not evaluable) and who have suspected or established coronary artery disease, to provide opacification of cardiac chambers and improvement of left ventricular endocardial border delineation at both rest and stress.
CHMP Opinion date	27.07.2006
Marketing Authorisation Date	20.09.2006

Invented Name	Competact
INN	Pioglitazone / metformin
Marketing Authorisation Holder	Takeda Global R&D Centre (Europe) Ltd
Proposed ATC code	Not yet assigned.
Indication	Competact is indicated in the treatment of type 2 diabetes mellitus patients, particularly overweight patients, who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone.
CHMP Opinion date	01.06.2006
Marketing Authorisation Date	28.07.2006

Invented Name	Exjade
INN	deferasirox
Marketing Authorisation Holder	Novartis Europharm Limited
Proposed ATC code	V03AC03
Indication	EXJADE is indicated for the treatment of chronic iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older. EXJADE is also indicated for the treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups: - in patients with other anaemias, - in patients aged 2 to 5 years, in patients with beta thalassaemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells).
CHMP Opinion date	28.06.2006
Marketing Authorisation Date	28.08.2006

Invented Name	Thelin
INN	sitaxentan sodium
Marketing Authorisation Holder	Encysive (UK) Limited
Proposed ATC code	Not yet assigned
Indication	Treatment of patients with pulmonary arterial hypertension classified as WHO functional class III, to improve exercise capacity. Efficacy has been shown in primary pulmonary hypertension and in pulmonary hypertension associated with connective tissue disease.
CHMP Opinion date	01.06.2006
Marketing Authorisation Date	10.08.2006

Invented Name	Savene
INN	dexrazoxane
Marketing Authorisation Holder	Topo Target A/S
Proposed ATC code	V03AF02
Indication	Savene is indicated for the treatment of anthracycline extravasation.
CHMP Opinion date	01.06.2006

Marketing Authorisation Date	28.07.2006

Invented Name	Gardasil
INN	Human Papillomavirus Vaccine [Types 6, 11, 16, 18] (Recombinant, adsorbed)
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	J07BM01
Indication	Gardasil is a vaccine for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high-grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18. The indication is based on the demonstration of efficacy of Gardasil in adult females 16 to 26 years of age and on the demonstration of immunogenicity of Gardasil in 9- to 15-year old children and adolescents.—Protective efficacy has not been evaluated in males (see section 5.1). The use of Gardasil should be in accordance with official recommendations.
CHMP Opinion date	27.07.2006
Marketing Authorisation Date	20.09.20069

Invented Name	Silgard
INN	Human Papillomavirus Vaccine [Types 6, 11, 16, 18] (Recombinant, adsorbed)
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	J07BM01
Indication	Silgard is a vaccine for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high-grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18. The indication is based on the demonstration of efficacy of Silgard in adult females 16 to 26 years of age and on the demonstration of immunogenicity of Silgard in 9- to 15-year old children and adolescents.—Protective efficacy has not been evaluated in males (see section 5.1). The use of Silgard should be in accordance with official recommendations.
CHMP Opinion date	27.07.2006
Marketing Authorisation Date	20.09.2006

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION: UPDATE SINCE THE JULY 2006 CHMP MEETING

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
Recombinant human C1-inhibitor (Rhucin)	Pharming Group N.V.	EU/3/01/036 11/05/2001	Treatment of angioedema by C1 inhibitor deficiency
Ecteinascidin 743(Yondelis)	PharmaMar SA Sociedad Unipersonal	EU/3/01/039 30/05/2001	Treatment of soft tissue sarcoma

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

	1995 - 2005	2006	Overall Total
Scientific Advice	558	114	672
Follow-up to Scientific Advice	94	25	119
Protocol Assistance	107	39	146
Follow-up to Protocol Assistance	26	8	34
	785	**186**	**971**

OUTCOME OF THE SEPTEMBER 2006 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	Gastro-intestinal stromal tumor				X			X	
Chemical	Multiple myeloma		X					X	
Chemical	Acute myeloid leukaemia		X					X	X
Biological	Neutropenias	X				X	X	X	
Chemical	Acute lymphocytic leukaemia (T-ALL)/lymphoblastic lymphoma (T-LBL)	X						X	
Chemical	Chronic myeloid leukaemia		X				X	X	
Chemical	Chronic myeloid leukaemia	X				X		X	
Chemical	Non-hodgkin's lymphoma	X						X	
Chemical	Glioblastoma		X					X	X

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Parkinson's disease		X			X	X	X	X
Chemical	Insomnia	X						X	
Chemical	Multiple sclerosis	X						X	
Chemical	Pain			X				X	
Chemical	Bipolar disorder and schizophrenia	X						X	
Biological	Neuromyelitis Optica	X						X	
Chemical	Schizophrenia			X				X	
Chemical	Pain			X				X	
Chemical	Epilepsy			X				X	
Chemical	Prevention of deep vein thrombosis			X				X	
Chemical	Adrenal insufficiency		X					X	X
Chemical	Obesity	X						X	
Chemical	Atrial fibrillation			X				X	
Chemical	Type 2 diabetes	X					X	X	
Chemical	Acute coronary syndrome, cardiovascular secondary prevention		X				X		
Chemical	Febrile neutropenia	X						X	
Chemical	HIV-1 infection	X				X		X	
Chemical	HCV infection			X				X	
Chemical	Mastocytosis			X				X	
Biological	Alpha1-antitrypsin deficiency		X					X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Disfiguring scar appearance	X				X	X	X	
Chemical	Cystic fibrosis		X				X	X	
Chemicals	Prevention of aspirin-associated peptic ulcers	X					X	X	
Chemical	Osteoarthritis			X				X	
Chemical	Infantile hemangioma	X					X	X	
Biological	ANCA-associated vasculitis and systemic lupus erythematosus	X						X	
Biological	Acute graft-versus-host-disease				X		X		
Chemical	Gastro-oesophagal reflux disease	X					X	X	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned Scientific Advice letters, Protocol Assistance letters, Follow-up Scientific Advice letters and Follow-up Protocol Assistance letters were adopted at the 18-21 September CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 14 Initial Scientific Advice Requests, 4 Follow-up Scientific Advice Requests, 3 Initial Protocol Assistance Requests and 5 Follow-up Protocol Assistance Requests started at the SAWP meeting that took place on 29-31 August 2006.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE SEPTEMBER 2006 CHMP MEETING

BIOLOGICS WORKING PARTY

Reference number	Document	Status[8]
CHMP/BWP/48316/2006	Guideline on the Quality of Biological Active Substances Produced by Stable Transgene Expression in Higher Plants	Release for 6 months
CHMP/BWP/298388/2005	Guideline on validation of immunoassay for the detection of antibody to human immunodeficiency virus (Anti-HIV) in plasma pools	Adopted
CHMP/BWP/94182/2006	Overview of comments received on draft guideline on validation of immunoassay for the detection of antibody to human immunodefiency virus (Anti-HIV) in plasma pools	Adopted
CHMP/BWP/298390/2005	Guideline on validation of immunoassay for the detection of hepatitis B virus surface antigen (HBsAg) in Plasma Pools	Adopted
CHMP/BWP/94181/2006	Overview of comments received on draft guideline on validation of immunoassay for the detection of hepatitis B virus surface antigen (HbsAg) in Plasma Pools	Adopted

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/504/97 Rev. 1	Guideline on Clinical Investigation of Medicinal Products in the Treatment of Patients with Acute Respiratory Distress Syndrome	Adopted
CHMP/EWP/358390/ 2006	Overview of comments received on the Guideline on Clinical Investigation of Medicinal Products in the Treatment of Patients with Acute Respiratory Distress Syndrome	Adopted
CHMP/EWP/358650/2006	Concept Paper on the Development of a Note for Guidance on the Development of Medicinal Products for the Treatment of Post-Traumatic Stress Disorder	Release for 3 months
CHMP/EWP/346228/2006	Overview of comments received on the draft guideline on the role of pharmacokinetics in the development of medicinal products in the paediatric population	Adopted
CHMP/EWP/358487/ 2006	Concept Paper on the Need for Revision of the Note for Guidance on Antiarrhythmics	Adopted
CHMP/EWP/358529/ 2006	Concept Paper on the Need for Regulatory Guidance in the Evaluation of Medicinal Products for a First-Line Indication of Fixed Combination Medicinal Products in Therapeutic Doses in the Treatment of Hypertension	Adopted

[8] 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").

ANNEX 7 TO CHMP MONTHLY REPORT SEPTEMBER 2006

INVENTED NAME REVIEW GROUP (NRG)

	September 2006			2006	
	Accepted	Rejected	Pending	Accepted	Rejected
Proposed invented names	14	13	78[1]	83	109
Justification for retention of invented name *	2	2	7[2]	13	21

*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] Two proposed invented names requests have been postponed from the September NRG meeting.
[2] Three justification requests have been postponed from the September NRG meeting.

Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

Report from the CMD(h) meeting held on 18th and 19th September 2006

List of medicinal products for SPC harmonisation – Consultation with Interested Parties

The CMD(h) has agreed a list of medicinal products for which a harmonised SPC should be drawn up, in accordance with Article 30(2) of Directive 2001/83/EC, as amended and has forwarded the list to the European Commission.

The list of medicinal products for SPC harmonisation will be published on the website for an eight week period for public consultation.

Any comments on the list of medicinal products for SPC harmonisation should be sent to the CMD(h) secretariat **(sonia.ribeiro@emea.europa.eu)** by 30 November 2006, coordinated where possible by trade associations.

Usage Patents – Implementation within the framework of the Mutual Recognition and Decentralised Procedures

The CMD(h) has agreed a Q&A document to address the implementation of usage patents within the framework of MRP and DCP, in accordance with Article 11(12), second paragraph of Directive 2001/83/EC, as amended.

Change in the product information of a generic medicinal product following an Article 30 referral procedure for the originator – Use of Variation No. 46, Type IB

The CMD(h) has agreed that Applicants can use variation No. 46, type IB to change the SPC, package leaflet and labelling following a Commission Decision for a referral for an original medicinal product in accordance with Article 30 of Directive 2001/83/EC, as amended.

The proposed SPC, package leaflet and labelling should be identical for the concerned sections to that annexed to the Commission Decision on the referral procedure for the original product.

CMD(h) Standard Operating Procedure – Disagreement in Procedures – Referral to CMD(h) & Guidance on oral explanations to CMD(h)

In order to make optimal use of the 60 days timeline in case of disagreement between Member States in a particular mutual recognition or decentralised procedure, the CMD(h) agreed, at the February CMD(h) meeting, to change the timelines for the procedure and to work with the new timelines for a pilot period of 6 months.

The CMD(h) has revised at the September CMD(h) meeting the CMD(h) SOP – Disagreement in Procedures – Referral to CMD(h) & Guidance on oral explanations to CMD(h), to reflect the currently agreed timetable for the 60 days procedure in the CMD(h).

New Question and Answer on CMD(h) SOP –Disagreement in Procedures – Referral to CMD(h)

The CMD(h) has agreed a new Q&A to clarify that if on Day 210 of a DCP there is consensus among the RMS and the CMS(s) that the application is not approvable, this will not be referred to the CMD(h) for the 60 days referral procedure. An application can only be referred to the CMD(h) if the MSs involved in the procedure cannot reach consensus.

Manufacturing authorisation in the Decentralised procedure

With a view to avoiding delays in the start of the procedure, the CMD(h) has agreed that in exceptional cases it should be possible to validate a decentralised procedure application, where an inspection of sites outside the EU has not yet been carried out. The manufacturing authorisation has to be available for the restart of the procedure on Day 106.

Information on applications referred to the CMD(h) in accordance with Article 29(1) of Directive 2001/83/EC, as amended

Please find below information on the Name of the products in the RMS, active substances, pharmaceutical forms, procedure numbers, CMS, legal basis, grounds for referral to CMD(h), Day 60 and outcome of the procedures, for the referrals to the CMD(h) finalised on 4 August 2006 and on 17 August 2006.

Name of the product in the RMS	Protaminsulfat Leo Pharma
Active substance	Protamine sulfate
Pharmaceutical form	Solution for injection
Procedure number	SE/H/562/01/MR
CMS	AT, BE, DE, DK, EE, EL, ES, FI, FR, IE, IS, LT, LU, NL, NO, PT, SI, UK
Legal basis	Article 10.1(a)(ii), Directive 2001/83/EC - Bibliographic
Grounds for referral to CMD(h)	Potential serious risk to public health concerns were raised by one CMS, especially relating to the posology and the declaration of the strength.
Day 60	04.08.06
Outcome	Agreement reached

Name of the product in the RMS	Matrifen
Active substance	Fentanyl
Pharmaceutical form	Transdermal patch
Procedure number	SE/H/568/01-05/MR
CMS	BE, CZ, DK, EE, EL, ES, FI, HU, IE, IT, LT, LU, LV, NL, NO, PL, PT, SI, SK, UK
Legal basis	Article 10.1, Directive 2001/83/EC – Generic
Grounds for referral to CMD(h)	Potential serious risk to public health concerns were raised by one CMS regarding the wording of the indication.
Day 60	04.08.06
Outcome	Agreement reached

Name of the product in the RMS	Fentanyl ratiopharm 25, 50, 75, 100 mcg/h Matrixpflaster Fentanyl CT 25, 50, 75, 100 mcg/h Matrixpflaster Ribofentanyl 25, 50, 75, 100 mcg/h Matrixpflaster
Active substance	Fentanyl
Pharmaceutical form	Transdermal patch

Procedure number	DE/H/634/01-04/MR DE/H/635/01-04/MR DE/H/636/01-03/MR
CMS	CZ, DK, FI, HU, IT, NO, PL, SE, SK
Legal basis	Article 10.1, Directive 2001/83/EC – Generic
Grounds for referral to CMD(h)	Potential serious risk to public health concerns were raised by one CMS regarding the wording of the indication.
Day 60	25.09.06
Outcome	Agreement reached

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **114** new Mutual Recognition Procedures were finalised during the months of July and August 2006. **14** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period. **2** Mutual Recognition Procedure for a new application were referred to CHMP in this period.

The status as of 31st August of procedures under Mutual Recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures referred to CMD(h)	Agreement reached in the CMD(h)	Arbitrations referred to CHMP
2006	367	167	57 N.A.	29	17

132 Mutual Recognition Procedures (regarding **334** products) started in July and August 2006. The categories of these procedures are as follows:

2 new active substances (classified as a multiple application), including **1** repeat use.

15 known active substances (already authorised in at least one member state).

105 abridged applications, including **42** multiple and **6** repeat use applications.

10 line extension applications, including **3** repeat use applications.

The new procedures started in July and August related to **9** full dossiers, **110** generics, **3** hybrid applications, **2** fixed combination applications and **8** bibliographic applications.

These procedures consisted of **129** chemical substance applications and **2** biological blood product and **1** biological other products.

All of these procedures were prescription-only medicinal products in the reference Member State[1].

Number of countries involved in the new applications in Mutual Recognition procedure started in July and August 2006.

[1] 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.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	12
DE (1)	8
DE (1)	11
DE (8)	1
DE (2)	13
DE (2)	9
DE (3)	1
DE (2)	10
DE (1)	4
DE (1)	13
DE (1)	3
DE (1)	1
DE (1)	13
DE (1)	2
DE (6)	16
DE (4)	5
DE (4)	5
DK (1)	2
DK (1)	3
DK (4)	3
DK (2)	3
DK (3)	1
DK (2)	11
DK (4)	2
DK (3)	11
DK (3)	1
DK (3)	1
DK (4)	16
DK (3)	1
DK (3)	1
DK (3)	1
DK (4)	1
DK (4)	1
DK (3)	9
DK (2)	1
DK (3)	1
DK (3)	4
DK (3)	19
DK (5)	2
DK (4)	18
DK (4)	1
DK (4)	1
DK (4)	20
DK (4)	1
DK (4)	1
DK (1)	5
DK (3)	1
DK (3)	1
DK (3)	2
DK (4)	1
DK (1)	1
DK (3)	1
DK (3)	1
DK (3)	1
ES (1)	8
FI (4)	1
FI (5)	1
FI (3)	7
FI (4)	5
FI (2)	9
FI (2)	2
FI (2)	1
FI (2)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
FR (1)	10
FR (1)	18
HU(1)	6
HU(1)	2
HU(1)	3
HU(1)	5
HU(1)	2
IT (1)	6
IT (1)	7
IT (1)	4
IT (1)	3
IT (1)	6
NL (4)	14
NL (4)	2
NL (4)	3
NL (4)	1
NL (1)	2
NL (2)	3
NL (1)	11
NL (2)	9
NL (4)	1
NL (2)	5
NL (2)	3
NL (4)	9
NL (3)	10
NL (1)	7
NL (2)	15
NL (2)	1
NL (3)	1
NL (3)	1
NL (3)	1
NL (3)	1
NL (3)	2
NL (2)	1
NL (2)	1
NL (2)	1
NL (1)	7
PT (3)	2
PT (1)	17
PT (1)	15
PT (1)	19
SE (2)	9
SE (3)	1
SE (4)	13
SE (1)	1
SE (1)	9
SE (1)	6
SE (1)	5
SE (1)	7
SE (1)	7
SE (1)	11
SE (4)	2
SE (3)	1
SE (3)	1
SE (4)	7
SE (4)	1
SE (4)	1
SE (4)	1
SE (4)	1
SE (4)	3
UK (2)	1
UK (4)	4
UK (4)	5

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
UK (1)	6
UK (4)	3
UK (1)	12
UK (2)	6
UK (4)	17
UK (1)	1

Decentralised Procedure

The CMD(h) noted that **10** new Decentralised Procedures were finalised during the months of July and August 2006.

The status as of 31st August of procedures under Decentralised Procedure is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures referred to CMD(h)	Agreement reached in the CMD(h)	Arbitrations referred to CHMP
2006	10	273	--	--	--

84 Decentralised Procedures (regarding **215** products) started in July and August 2006. The categories of these procedures are as follows:

1 new active substance application (first application in the European Community).

74 abridged applications, including **23** multiple applications.

6 known active substance applications.

3 line extension applications.

The new Decentralised procedures started related to **4** full dossier, **74** generic, **1** hybrid and **5** bibliographical applications.

These procedures consisted of **81** chemical substance and **3** biological vaccine applications.

These procedures related to **81** prescription-only and **3** non-prescription medicinal products in the reference Member State[2].

Number of countries involved in the new applications in Decentralised procedures started in July and August 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
CZ (3)	5
CZ (3)	8
DE (1)	8
DE (3)	7
DE (2)	13
DE (1)	2
DE (4)	17
DE (1)	21
DE (1)	11
DE (4)	15

[2] In this category products are classified as prescription-only or Non-prescription (OTC) products as applied for in the RMS, although the legal status is not part of the Decentralised Procedure.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (4)	13
DE (3)	2
DE (1)	4
DE (1)	4
DE (1)	4
DE (4)	3
DE (6)	6
DE (1)	1
DE (1)	9
DE (3)	3
DE (2)	1
DE (3)	11
DE (3)	8
DE (1)	6
DE (1)	1
DE (1)	9
DE (2)	1
DK (2)	14
DK (4)	3
DK (1)	10
DK (1)	10
DK (1)	9
DK (1)	9
DK (5)	7
DK (6)	13
DK (4)	2
DK (4)	1
DK (6)	8
DK (4)	2
DK (5)	13
DK (5)	3
DK (5)	2
DK (3)	5
DK (3)	15
DK (2)	6
DK (6)	2
FI (3)	6
FI (3)	1
FR (1)	18
NL (2)	19
NL (2)	21
NL (1)	2
NL (4)	1
NL (4)	2
NL (4)	4
NL (4)	1
NL (4)	3
SE (1)	1
SE (1)	1
SE (4)	4
SE (1)	23
UK (1)	1
UK (2)	13
UK (1)	22
UK (4)	11
UK (2)	1
UK (2)	1
UK (2)	1
UK (2)	2
UK (4)	11
UK (1)	22
UK (1)	22
UK (1)	20

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
UK (1)	1
UK (1)	5
UK (1)	5
UK (2)	21
UK (4)	15
UK (1)	1
UK (4)	1
UK (4)	1
UK (1)	3
UK (1)	1
UK (4)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **814** type IA variations, **329** type IB variations and **382** type II variations were finalised during the months of July and August 2006. **84** renewals were finalised in this period.

The status as of 31st August of variations and renewals under Mutual Recognition is as follows:

Year	Procedures from Type IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Renewals finalised	Arbitrations referred to CHMP
2006	2933	1431	1213	232	--

All documents mentioned in this press release can be found at the CMD(h) website at the European Medicines Authorities Windows under the heading *Press Releases*.

Information on the above mentioned issues can be obtained from the chair of the CMD(h):

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