22 March 2010
EMA/CHMP/190774/2010

Monthly Report

Committee for Medicinal Products for Human Use (CHMP)

15-19 March 2010

CENTRALISED PROCEDURE

Update on pandemic medicines

The Committee reviewed further results from clinical studies and post-marketing experience for all three centrally authorised pandemic influenza vaccines, **Celvapan, Focetria** and **Pandemrix.** The data confirm the expected immunogenicity and safety profile for the vaccines. For Celvapan, the Committee recommended changes to the product information to include additional information on the vaccine's immunogenicity and safety. The latest data on the safety of Celvapan show no unexpected serious safety issue. The most frequent adverse reactions that have been reported are non-serious and as expected.

The Agency will continue to evaluate all information that becomes available and make further recommendations as necessary. The most recent pandemic influenza pharmacovigilance update report was published on 10 March 2010 and can be found here.

Initial applications for marketing authorisation

Positive opinion for a biosimilar medicine adopted

The Committee adopted a positive opinion by consensus recommending the granting of a marketing authorisation for:

- **Nivestim** (filgrastim), from Hospira UK Ltd, intended for the treatment of neutropenia. This medicine has shown to be similar to the reference medicinal product Neupogen, already authorised in the European Union, in the indication applied for. The review for Nivestim began on 25 March 2009 with an active review time of 210 days.

The summary of opinion for this medicine, including the full indication, can be found here.

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Generic medicinal products

The Committee adopted four positive opinions by consensus for the following generic medicines:

- **Olanzapine Apotex** (olanzapine), from Apotex Europe BV, a generic of Zyprexa, which is authorised in the European Union for the treatment of schizophrenia.
- **Ribavirin Three Rivers** (ribavirin), from Three Rivers Global Pharma Ltd, a generic of Rebetol, which is authorised in the European Union for the treatment of chronic hepatitis C.
- **Tolura** (telmisartan), from Krka, d.d., Novo mesto, a generic of Micardis, which is authorised in the European Union for the treatment of hypertension.
- **Topotecan Hospira** (topotecan), from Hospira UK Ltd, a generic of Hycamtin, which is authorised in the European Union for the treatment of carcinoma of the ovary and cervix and of small cell lung cancer.

Summaries of opinion for all above mentioned medicines, including their full indication, can be found here.

Further information will be included in the European Public Assessment Reports (EPARs) once the European Commission has granted final approval for the above mentioned positive opinions.

Withdrawals

The European Medicines Agency has been formally requested by Ark Therapeutics Ltd of their intention to withdraw their request to re-examine the negative opinion adopted during the CHMP meeting on 14-17 December 2009 on **Cerepro** (sitimagene ceradenovec - adenoviral vector-mediated Herpes Simplex Virus-thymidine kinase gene used with subsequent administration of ganciclovir) intended for the treatment of high-grade glioma (a type of brain tumour). A separate press release with more information is available.

The European Medicines Agency has been formally notified by Mylan S.A.S. of its decision to withdraw the application for a centralized marketing authorisation for the medicinal product **Docetaxel Mylan** (docetaxel), 10mg/ml powder and solvent for solution for infusion. The medicine was developed as a generic medicine for breast cancer, prostate cancer, gastric adenocarcinoma and head and neck cancer. A separate press release with more information is available.

The European Medicines Agency was formally notified by United Therapeutics Europe Ltd in February 2010 of its decision to withdraw the application for a centralised marketing authorisation for the medicine **Tyvaso** (treprostinil sodium) 0.6 mg/ml nebuliser solution. This medicine was intended for use as adjuvant therapy in patients with pulmonary arterial hypertension who were also receiving either an endothelin receptor antagonist or a phosphodiesterase-5 inhibitor. A question-and-answer document is now available.

On 25 February 2010, ratiopharm GmbH officially notified the European Medicines Agency of it's decision to withdraw the application for a marketing authorisation for **Ratioepo**, for the treatment of symptomatic anaemia in adults with chronic renal failure or non-myeloid cancer. A question-and-answer document with more information is now available.

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

The European Medicines Agency has been formally requested by Janssen-Cilag International NV to re-examine the negative opinion adopted during the CHMP meeting held on 15-18 February 2010 for **Zeftera** (ceftobiprole medocaril) an antibiotic, intended for the treatment of patients with complicated skin and soft tissue infections.

Post-authorisation procedures

Extensions of indications and other recommendations

The CHMP adopted one positive opinion by majority for an application for an extension of indication of the therapeutic indication, adding a new treatment option for the following previously approved medicine:

- **Tarceva** (erlotinib), from Roche Registration Ltd. The Committee recommended extending the therapeutic indication to include maintenance treatment in patients with locally advanced or metastatic non-small cell lung cancer with stable disease after four cycles of standard platinum-based first-line chemotherapy.

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

Restriction of indication for Kepivance adopted

The Committee recommended to restrict the therapeutic indication of **Kepivance** (palifermin), from Biovitrum AB (publ), to patients with haematological malignancies receiving myeloablative radiochemotherapy associated with a high incidence of severe mucositis and requiring autologous haemopoietic stem cell support, further to the results of a clinical study.

The summary of opinion for this medicine, including the full indication, can be found here.

Additional safety information

The CHMP adopted amendments to sections 4.4 of the Summary of Product Characteristics (SPC) of **Enbrel** (etanercept) from Wyeth Europa Ltd. Section 4.4 of the SPC was amended with information regarding reports of hypoglycaemia following initiation of Enbrel in patients receiving medication for diabetes. The Package leaflet is updated accordingly. This variation application was submitted further to spontaneous reports of hypoglycaemia following initiation of etanercept therapy in patients receiving medication for diabetes, necessitating a reduction in anti-diabetic medication in some of these patients. This is supported by further evidence from the medical literature which suggested that impaired glucose tolerance had improved in some patients treated with tumour necrosis factor inhibitors including etanercept.

Further to a CHMP request related to the results of study AC-052-211, an exploratory safety study conducted in patients with chronic obstructive pulmonary disease (COPD), the Committee adopted amendments to section 4.4 of the SPC of **Tracleer** (bosentan) from Actelion Registration Ltd. Tracleer is not indicated in patients with pulmonary hypertension secondary to COPD, however a warning statement was introduced as follows "*Safety and tolerability of bosentan was investigated in an exploratory, uncontrolled 12-week study in 11 patients with pulmonary hypertension secondary to severe COPD (stage III of Gold classification). An increase in minute ventilation and a decrease in oxygen saturation were observed and the most frequent adverse event was dyspnea, which resolved with discontinuation of bosentan".*

The CHMP adopted several amendments to sections 4.4 and 4.8 of the SPC of **Velcade** (bortezomib) from Janssen-Cilag International N.V. Section 4.4 of the SPC was amended to include a warning on reversible posterior leukoencephalopathy syndrome. Section 4.8 of the SPC was amended to add the adverse drug reactions posterior leukoencephalopathy syndrome, acute febrile neutrophilic dermatosis and leukocytoclastic vasculitis. This variation application was submitted further to the conduct of cumulative safety reviews requested by the CHMP.

Following two post-marketing reports of fatal infusion reactions occurring within 24 hours of administration of panitumumab, the CHMP adopted several amendments to sections 4.3, 4.4 and 4.8 of the SPC of **Vectibix** (panitumumab) from Amgen Europe BV. The contraindication of the use of Vectibix in cases of hypersensitivity was amended, so that Vectibix is contraindicated in patients with a history of severe or life-threatening hypersensitivity reactions to the active substance or to any of the excipients. The warnings on infusion-related and other hypersensitivity reactions were updated with information on the two reports of fatal infusion reactions and also regarding the management of such reactions. Clinical manifestations of hypersensitivity reactions, including (but not limited to) angioedema and anaphylactic reaction, were added to section 4.8 of the SPC. The Package Leaflet was amended accordingly.

The CHMP adopted several amendments to sections 4.4 and 4.5 of the SPC of **Plavix** (clopidogrel) from Sanofi Pharma Bristol-Myers Squibb SNC. Section 4.4 of the SPC was amended to delete the class warning for all Proton Pump Inhibitors. The SPC was also updated to introduce a warning in section 4.5 stating that only the concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged. In addition a description of the results of the two recent studies that show the interaction between clopidogrel and omeprazole has been added to this section in the product information. A public statement with more information is also available.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted eight Lists of Questions on initial applications (including four under the mandatory scope, and four under the optional scope) as per Regulation (EC) No. 726/2004.

Detailed information on the centralised procedure

Monthly figures related to the centralised procedure activities are published independently on the Agency's website within two weeks following the end of the CHMP meeting and can be found here. The overview of opinions for annual re-assessments and renewals is provided in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CHMP plenary meeting in February 2010 is provided in **Annex 2.**

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 February 2010 CHMP plenary meeting are provided in **Annex 3**.

REFERRAL PROCEDURES

Arbitration on Levact concluded

The Committee completed an arbitration procedure initiated because of disagreement among EU Member States regarding the authorisation of **Levact** powder for concentrate for solution for infusion (bendamustine hydrochloride) and associated names, from Astellas Pharma GmbH. These medicines are indicated for the treatment of chronic lymphocytic leukaemia in patients for whom treatment with fludarabine is not appropriate, of non-Hodgkin's lymphoma in patients who have had a relapse following treatment containing rituximab, and of multiple myeloma in combination with prednisone for patients older than 65 years who are not eligible for autologous stem cell transplantation and cannot be treated with thalidomide or bortezomib. This procedure was initiated because of concerns regarding the efficacy of the medicinal product in non-Hodgkin's lymphoma and in multiple myeloma. The Committee concluded that the benefit-risk profile of these medicines was positive in non-Hodgkin's lymphoma and in multiple myeloma and recommended that marketing authorisations should be granted in all indications applied for.

Question-and-answer documents with more information about these referrals can be found here.

Harmonisation referrals on candesartan concluded

The Committee recommended harmonisation of the prescribing information for **Atacand** (candesartan cilexetil) and associated names, from AstraZeneca and associated companies. These medicines are authorised to treat patients with essential hypertension and patients with heart failure and impaired left ventricular systolic function. The review was initiated because of differences in the Summaries of Product Characteristics, labelling and package leaflets in the countries where these products are marketed.

A question-and-answer document with more information about these referrals can be found here.

Review of Antifibrinolytics started

The Committee has started an assessment of the benefits and risks of **antifibrinolytics** containing **aprotinin, aminocaproic acid** and **tranexamic acid**. Antifibrinolytics are used to prevent the loss of blood or reduce the number of transfusions needed during surgery.

This follows an earlier review of aprotinin-containing medicines, which led to the suspension of their marketing authorisations on 15 February 2008 due to concerns over an increased risk of mortality observed in a clinical study. Germany has now requested a review under Article 31 of Directive 2001/83/EC to compare the benefits and risks of the above mentioned antifibrinolytics. The CHMP is asked to make a recommendation on whether the suspension of the marketing authorisations of aprotinin-containing medicinal products should be maintained or lifted, or whether their marketing authorisations should be revoked. The Committee will also make a recommendation on whether the marketing authorisations of aminocaproic acid and tranexamic acid containing medicinal products should be maintained, changed, suspended or revoked.

Re-examination procedure on gadolinium containing contrast agents concluded

The Committee concluded a re-examination of **gadolinium-containing contrast agents**, confirming its previous opinion and the set of recommendations aimed at minimising the risk of nephrogenic systemic fibrosis (NSF) associated with the use of these agents.

Gadolinium-containing contrast agents are used in patients undergoing magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA) scans. The CHMP reviewed these agents because of the association between the use of gadolinium-containing contrast agents and NSF, a rare, serious and sometimes life-threatening condition that is characterised by the formation of connective tissues in the skin, joints, muscles and internal organs, in patients with severe kidney problems.

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

The CHMP has been formally requested by a group of Marketing Authorisation Holders to re-examine the opinion, adopted during the CHMP meeting on 14-17 December 2009, on a referral procedure under Article 31 of Directive 2001/83/EC1, as amended, for **valproic acid/valproate containing medicinal products**, recommending the variation of the Marketing Authorisations. Valproic acid/valproate-containing medicinal products are indicated amongst other indications for the treatment of manic episode in bipolar disorder.

New paediatric indication for Sortis

The CHMP recommended a line extension for **Sortis and associated names** (atorvastatin calcium), from Pfizer Ltd, to add chewable tablets, a pharmaceutical formulation suitable for the paediatric population. The paediatric formulation has been developed for the treatment of hypercholesterolaemia in adolescents and children aged 10 years or older. The CHMP also recommended that this indication be approved for the currently available presentations of Sortis and associated names (film-coated tablets).

The Committee's recommendation was made on the basis of data generated in accordance with an agreed paediatric investigation plan (PIP).

The changes to the marketing authorisation for Sortis and associates names were recommended under Article 29 of Regulation 1901/2006, the Paediatric Regulation. This allows companies to submit to the European Medicines Agency an application for a new indication, a new pharmaceutical form or a new route of administration for medicines that are already authorised at the level of the Member States. Once the CHMP opinion has been transformed into a decision by the European Commission, the company will be able to market Sortis and associated names with the new formulation and indication in all EU Member States where the medicine is authorised.

Withdrawal of Applications

In February 2010 the CHMP was formally notified by Bayer B.V. of its decision to withdraw its MRP variation applications from the concerned Member States for the medicinal products

- **YAZ 24+4** (ethinylestradiol/dospirenone) and associated names (film-coated tablets) and
- **Ethinylestradiol/Drospirenon 24+4** (ethinylestradiol/drospirenone) and associated names (film-coated tablets)

indicated for female contraception. In July 2009, the CHMP had initiated referral procedures under Article 6 (12) of Regulation (EC) No 1084/2003 due to disagreements on the inclusion of study results on Premenstrual Dysphoric Disorder (PMDD) in the Product Information.

MUTUAL-RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 49th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 15-16 March 2010. 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 22-24 February 2010. For further details, please see **Annex 4**.

Documents prepared by the CHMP Working Parties adopted during the March 2010 CHMP meeting are listed in **Annex 5**.

UPCOMING MEETINGS FOLLOWING THE MARCH 2010 CHMP PLENARY MEETING

- The 65th meeting of the CHMP will be held at the Agency on 19-22 April 2010.
- The most recent Name Review Group meeting was held at the Agency on 23 March 2010.
- The 50th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the Agency on 19-20 April 2010.
- A workshop on Nanomedicines will be held at the Agency on 26-27 April 2010.

ORGANISATIONAL MATTERS

The main topics addressed during the March 2010 CHMP meeting related to:

- The most recent implementation plans regarding the revised SmPC guideline. Within such context, a EudraSmPC webpage for use by National Competent Authorities and the Agency will be launched on 22nd March 2010. The website provides information to facilitate the review of SmPCs and offers the possibility to seek advice from the SmPC advisory group, the mandate of which was adopted by the Committee. It is foreseen that the webpage will be made public after one year of experience.
- Proposals to amend the procedural advice paper on Rapporteurs' appointment to reflect special requirements for non-prescription medicinal products. The Committee agreed to the proposed revision, mainly related to the fact that experience in non-prescription dossier assessments / changes in legal status / communication with patients will be expected within the teams of (Co)Rapporteurs appointed for non-prescription medicinal products to be assessed via the centralised procedure. In addition, for situations where a change in legal status is foreseen, a peer reviewer with the above mentioned experience will be appointed. The revised paper will be published shortly.
- Follow-up discussion on the draft Reflection Paper on the acceptability of clinical trials conducted in third countries for marketing authorisation applications to be submitted in EU. This paper will be

released for public consultation at the end of April 2010 and a workshop is planned for 6-7 September 2010.

- Follow-up discussion on the development of a policy regarding the cessation of placing on the market of centrally authorised products for human use. (see procedural announcement February 2010 CHMP report).
- Discussions on communications on emerging safety related issues for medicines for human use evaluated by the European Medicines Agency. Experience since 2008 has now been presented in a policy document for publication at a later stage.

PROCEDURAL ANNOUNCEMENT

Submission deadline of variations according to Article 18 of Commission Regulation (EC) No 1234/2008

The CHMP informs all Marketing Authorisation holders of centrally approved seasonal influenza vaccines that the deadline for submission to the European Medicines Agency of the annual strain change variation is 14th June 2010.

Adjusted fees for application to the EMEA to come into effect on 1st April 2009

Applicants are reminded that the European Commission is in the process of adopting a regulation adjusting the fees payable to the EMEA in line with inflation and amending Council Regulation (EC) No 297/95. It is expected that the adopted Commission Regulation will be published shortly.

Details of the revised fees will be published shortly thereafter, in the section Guidelines on fees payable to EMEA

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

ANNEX 1 TO CHMP MONTHLY REPORT MARCH 2010

Opinions for annual re-assessment applications		
Name of medicinal product (INN) MAH	**Outcome**	**Comments**
Onsenal (celecoxib), Pfizer Limited	Positive Opinion	Marketing authorisation remains under exceptional circumstances.
Zavesca (miglustat), Actelion Ltd	Positive Opinion	Marketing authorisation remains 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**
Avandia (rosiglitazone), Smithkline Beecham Ltd	Positive Opinion	Recommending additional Renewal

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ANNEX 2 TO CHMP MONTHLY REPORT MARCH 2010

Medicinal products granted a community marketing authorisation under the centralised procedure since the February 2010 CHMP monthly report

Invented name	**Revolade**
INN	eltrombopag
Marketing Authorisation Holder	GlaxoSmithKline Trading Services Limited
Proposed ATC code	B02BX 05
Indication	Adult chronic immune (idiopathic) thrombocytopenic purpura (ITP) splenectomised patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). Second line treatment for adult non-splenectomised patients where surgery is contraindicated.
CHMP Opinion date	17/12/2009
Marketing Authorisation Date	11/03/2010

Invented name	**Temozolomide Hospira**
INN	temozolomide
Marketing Authorisation Holder	Hospira UK Ltd
Proposed ATC code	L01A X03
Indication	Treatment of: - Adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment. - children from the age of three years, adolescents and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy.
CHMP Opinion date	17/12/2009
Marketing Authorisation Date	15/03/2010

Invented name	Temozolomide HEXAL
INN	temozolomide
Marketing Authorisation Holder	HEXAL AG
Proposed ATC code	L01A X03
Indication	treatment of: - adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment, - children from the age of three years, adolescents and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma showing recurrence or progression after standard therapy.
CHMP Opinion date	17/12/2009
Marketing Authorisation Date	15/03/2010

Invented name	Temozolomide SANDOZ
Common Name	temozolomide
Marketing Authorisation Holder	Sandoz Pharmaceuticals GmbH
Proposed ATC code	L01A X03
Indication	treatment of: - adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment, - children from the age of three years, adolescents and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy.
CHMP Opinion date	17/12/2009
Marketing Authorisation Date	15/03/2010

Invented name	DuoPlavin
Common Name	clopidogrel (as hydrogen sulphate) and acetylsalicylic acid.
Marketing Authorisation Holder	Sanofi Pharma Bristol-Meyers Squibb SNC
Proposed ATC code	B01AC30
Indication	Prevention of atherothrombotic events in adult patients already taking both clopidogrel and acetylsalicylic acid (ASA). DuoPlavin is a fixed dose combination medicinal product for continuation of therapy in: - 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 - ST segment elevation acute myocardial infarction in medically treated patients eligible for thrombolytic therapy
CHMP Opinion date	17/12/2009

Invented name	DuoPlavin
Marketing Authorisation Date	15/03/2010

Invented name	Ristaben
Common Name	sitagliptin
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	A10BH01
Indication	For patients with type 2 diabetes mellitus, Ristaben is indicated to improve glycaemic control: as **monotherapy** **-** in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. as **dual oral therapy** in combination with - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a PPARg agonist (i.e. a thiazolidinedione) when use of a PPARg agonist is appropriate and when diet and exercise plus the PPARg agonist alone do not provide adequate glycaemic control. as **triple oral therapy** in combination with - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARg agonist and metformin when use of a PPARg agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. Ristaben is also indicated as add on to insulin (with or without metformin) when diet and exercise plus stable dosage of insulin do not provide adequate glycaemic control.
CHMP Opinion date	17/12/2009
Marketing Authorisation Date	15/03/2010

Invented name	Ristfor
Common Name	sitagliptin (as phosphate monohydrate) and metformin hydrochloride.
Marketing Authorisation Holder	Merck Sharp & Dohme Ltd
Proposed ATC code	A10BD07

Invented name	Ristfor
Indication	For patients with type 2 diabetes mellitus: Ristfor 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. Ristfor is 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. Ristfor is indicated as triple combination therapy with a PPARg agonist (i.e., a thiazolidinedione) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a PPARg agonist. Ristfor is also indicated as add on to insulin (i.e., triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in patients when stable dosage of insulin and metformin alone do not provide adequate glycaemic control.
CHMP Opinion date	17/12/2009
Marketing Authorisation Date	15/03/2010

ANNEX 3 TO CHMP MONTHLY REPORT MARCH 2010

Overview of designated orphan medicinal products that have been the subject of a centralised application for marketing authorisation:

UPDATE SINCE THE FEBRUARY 2010 CHMP MEETING

Active substance	Sponsor/applicant	EU designation number & Date of orphan designation	Designated orphan indication
Cyclo {{(E,Z)-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)nona-6,8-dienoyl}-L-2-aminobutyryl-Nmthyl-glycyl-Nmethyl-L-leucyl-L-valyl-Nmethyl-L-leucyl-L-alanyl-Dalanyl-N-methyl-L-leucyl-Nmethyl-L-leucyl-N-methyl-Lvalyl}	Lux Biosciences GmbH	EU/3/07/472	Treatment of chronic non-infectious uveitis

Annex 4 to CHMP monthly report March 2010

Pre-authorisation: scientific advice and protocol assistance emea centralised procedures

	1995 - 2009	2010	Overall total
Scientific Advice	1134	52	**1186**
Follow-up to Scientific Advice	232	26	**258**
Protocol Assistance	245	15	**260**
Follow-up to Protocol Assistance	109	5	**114**
	1720	**98**	**1818**

Outcome of the March 2010 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 Ulcerative Colitis.		*x*				*x*	*x*	
Advanced Therapy	Treatment of patients with urea cycle disorders.		*x*					*x*	
Biological	Management of weight.			*x*				*x*	
Chemical/ Biological	Treatment of type 2 diabetes.	*x*				*x*	*x*	*x*	
Chemical	Treatment of type 2 diabetes.								
Advanced Therapy	Treatment of resectable colon cancer.	*x*				*x*		*x*	
Biological	Treatment of patients with relapsed or refractory follicular B cell NHL.			*x*				*x*	
Chemical	Treatment of multiple myeloma.	*x*						*x*	
Biological	Treatment of non-small cell lung cancer.	*x*					*x*	*x*	
Biological	Treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukaemia and	*x*				*x*	*x*		

		Type of request				Topic			
	rheumatoid arthritis.								
Biological/Advanced Therapy	Prophylaxis of transplant rejection in adult kidney or liver allograft recipients and treatment of allograft rejection resistant other immunosuppressants.			*x*				*x*	
Biological	Treatment of rheumatoid arthritis.			*x*		*x*	*x*		
Chemical	Generic clopidogrel intended for the same indications as the reference product.	*x*						*x*	
Biological	Treatment and prophylaxis of bleeding in patients with haemophilia B.	*x*				*x*	*x*	*x*	
Biological	Prophylaxis and treatment of bleeding episodes in patients with haemophilia A.	*x*				*x*	*x*	*x*	
Biological	Treatment of haemophilia B.	*x*				*x*		*x*	
Chemical	Maintenance of sinus rhythm in patients with non-permanent atrial fibrillation.	*x*					*x*	*x*	
Chemical/Other innovative	Reduction in the frequency of acute exacerbations in COPD patients chronically colonized with respiratory pathogens.	*x*					*x*	*x*	
Biological	Prevention of serious lower respiratory tract RSV infections.	*x*				*x*	*x*	*x*	
Biological	Active immunization against invasive disease, pneumonia and otitis media caused by S. pneumoniae in infants and children.	*x*				*x*		*x*	
Chemical	Treatment of chronic low back pain.			*x*				*x*	
Advanced	Repair of symptomatic,			*x*		*x*	*x*		

		Type of request				Topic			
Therapy	articular cartilage defects of the femoral condyle.								
Chemical	Treatment of chronic pain.	*x*				*x*	*x*		
Chemical	Treatment of Major Depressive Disorder.	*x*						*x*	
Chemical	Treatment of Generalized Anxiety Disorder.	*x*						*x*	
Chemical	Treatment of idiopathic Restless Legs Syndrome in children age 6 - 17 years.	*x*					*x*	*x*	
Advanced Therapy	Treatment of congenital alpha-1 antitrypsin deficiency.		*x*			*x*	*x*	*x*	
Biological	Treatment of birch pollen allergic rhinitis and/or conjunctivitis.			*x*			*x*	*x*	

SA: scientific advice

PA: protocol assistance

The above-mentioned 18 Scientific Advice letters, 3 Protocol Assistance letters, 7 Follow-up Scientific Advice and 0 Follow-up Protocol Assistance letters were adopted at the 15 - 18 March 2010 CHMP meeting

New requests for scientific advice procedures

The Committee accepted 35 new Requests for which the procedure started at the SAWP meeting held on 22 - 24 February 2010. The new requests are divided as follows: 20 Initial Scientific Advice, 7 Follow-up Scientific Advice, 4 Initial Protocol Assistance and 4 Follow-up Protocol Assistance.

ANNEX 5 TO CHMP MONTHLY REPORT MARCH 2010

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE MARCH 2010 CHMP MEETING

BIOLOGICS WORKING PARTY

Reference number	Document	Status [1]
EMA/CHMP/BWP/107653/2010	EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2010/2011	Adopted

BLOOD PRODUCT WORKING PARTY

Reference number	Document	Status [1]
EMA/CHMP/BPWP/94033/2007 Rev.2	Guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg) (CPMP/BPWG/388/95 rev.2)	Adopted for 1-month public consultation

WORKING PARTY ON SIMILAR BIOLOGICALS MEDICINAL PRODUCTS

Reference number	Document	Status [1]
EMA/CHMP/BMWP/86572/2010	Concept Paper on Similar Biological Products containing Recombinant Interferon beta	Adopted for 3-month public consultation
EMA/CHMP/BMWP/94899/2010	Concept Paper on Similar Biological Medicinal Products containing Recombinant Follicle Stimulation Hormone	Adopted for 3-month public consultation
EMEA/CHMP/BMWP/301636/2008	Guideline on Non-Clinical and Clinical Development of Similar Biological Medicinal Products containing Recombinant Erythropoietins EMEA/CHMP/BMWP/94526/2005 Rev.1	Adopted for 6 month public consultation

WORKING PARTY ON CELL BASED PRODUCTS

Reference number	Document	Status [1]
EMA/CHMP/CPWP/571134/2009	Draft Reflection paper on Stem Cell-Based Medicinal Products	Adopted
EMEA/CAT/CPWP/288934/2009	Reflection Paper on *In-Vitro* Cultured Chondrocyte containing Products for Cartilage Repair of the Knee	Adopted

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

SAFETY WORKING PARTY

Reference number	Document	Status [1]
CPMP/SWP/1042/99. Rev 1 • EMA/402716/2008	Guideline on Repeated Dose Toxicity Overview of comments received	Adopted