28th January 2010
EMA/CHMP/35712/2010

Monthly Report

Committee for Medicinal Products for Human Use (CHMP)

18-21 January 2010

The CHMP welcomed Dr Mark Ainsworth as the new CHMP Alternate from Denmark, replacing Dr Jens Ersbøll in this role.

CENTRALISED PROCEDURE

4th pandemic vaccine recommended for approval

The Agency's Committee for Medicinal Products for Human Use (CHMP) recommended the granting of a conditional marketing authorisation by consensus for a fourth pandemic vaccine, **Arepanrix** (split virion, inactivated, AS03 adjuvanted influenza H1N1 pandemic vaccine), from GlaxoSmithKline Biologicals, intended for the prophylaxis of influenza in an officially declared pandemic situation. This recommendation was made using an emergency procedure which fast-tracks evaluation of new vaccines developed during a pandemic.

More information on pandemic medicines is available in a separate press release

Initial applications for marketing authorisation

The CHMP adopted a positive opinion by consensus on an initial marketing authorisation application recommending the granting of a conditional marketing authorisation.

New medicinal products

- **Arzerra** (ofatumumab), from Glaxo Group Ltd, intended for the treatment of patients with chronic lymphocytic leukaemia who are refractory to fludarabine and alemtuzumab. The review for Arzerra began on 25 February 2009 with an active review time of 188 days. Arzerra is the 62nd orphan medicinal product to receive a positive opinion by the CHMP.

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A marketing authorisation under conditional approval means that further evidence on the medicinal product is awaited. In the case of Arzerra this relates to clinical data on the long term use of Arzerra in the double (fludarabine and alemtuzumab) refractory population and comparative clinical data on the use of Arzerra in the fludarabine-refractory, bulky lymphadenopathy population (patients ineligible for alemtuzumab). The European Medicines Agency will review new information within one year and update the product information as necessary.

Generic medicinal products

The Committee adopted a positive opinion by consensus for the following generic medicine:

- **Ribavirin BioPartners** (ribavirin), from BioPartners GmbH, a generic of Rebetol, which is authorised in the European Union for the treatment of hepatitis C as part of a combination treatment with peginterferon alfa-2b or interferon alfa-2b.

Summaries of opinion for 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.

Positive opinion for the first 'compassionate use' application adopted

The Committee adopted the first positive opinion on compassionate use under the European rules on compassionate use. This application related to **Tamiflu IV**, a new intravenous formulation of oseltamivir, from F. Hoffmann-La Roche Ltd, to treat critically ill patients having a life-threatening condition due to pandemic or seasonal influenza.

A separate press release with more information about the compassionate use procedure is available here.

Post-authorisation procedures

Withdrawals

The European Medicines Agency has been formally notified by Wyeth Consumer Healthcare of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Ibuprofen/Diphenhydramine Hydrochloride Wyeth** 200 mg/25 mg soft capsules. This medicine was intended to be used for the short-term treatment of mild to moderate pain in adults who experience sleeplessness as a result of the pain. A separate press release document and a question-and-answer document with more information are available.

The European Medicines Agency has been formally notified by Janssen-Cilag International NV of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Comfyde** (carisbamate), 100 mg, 200 mg, 400 mg and 600 mg, film-coated tablets. This medicine was intended to be used for adjunctive treatment of partial onset seizures with or without secondary generalisation in patients aged 16 years or older. A separate press release document and a question-and-answer document with more information are available.

The European Medicines has been formally notified by Sanofi Aventis in December 2009 of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Sliwens** (eplivanserin), 5 mg, film-coated tablets. Sliwens was intended to be used for the treatment of chronic insomnia. An additional question-and-answer document is now available.

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

The European Medicines Agency has been formally requested by Ark Therapeutics Ltd 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). The Committee for Advanced Therapies (CAT) will be responsible for preparation of the draft opinion on this re-examination procedure according to Article 8(1) of Regulation (EC) No. 1394/2007 which will then be transmitted to the CHMP for final adoption.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

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

Detailed information on the centralised procedure

From January 2010 onwards, the 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 (the relevant link will be set up shortly following the publication of this report and will be advertised in the February CHMP monthly report). 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 December 2009 is provided in **Annex 2.**

REFERRAL PROCEDURES

Review of Tysabri concluded

Finalising a review of **Tysabri** (natalizumab), from Elan Pharma International Ltd, and the risk of progressive multifocal leukoencephalopathy (PML), a rare brain infection caused by the JC virus, the Committee concluded that the benefits of this medicine continue to outweigh its risks for patients with highly active relapsing-remitting multiple sclerosis, but recommended further measures to manage the risk of PML. The review was carried out under Article 20 of Regulation (EC) No 726/2004.

More information about this review is available in a separate press release and a question-and-answer document.

Review of sibutramine concluded

The Committee completed a review of the safety and efficacy of **sibutramine**-containing medicines, recommending the suspension of the marketing authorisation for these medicines because their benefits as a weight-loss aid did not outweigh their cardiovascular risks. The review was initiated by Germany and carried out under Article 107(2) of Directive 2001/83/EC as amended.

More information about the review is available in a separate press release and a question-and-answer document.

Harmonisation referrals concluded

The Committee recommended harmonisation of the prescribing information for **Losec** and associated names (omeprazole) from AstraZeneca group of companies and associated companies. The medicine is authorised to treat diseases where the stomach produces too much acid. The review was initiated because of differences in the Summaries of Product Characteristics (SPCs), labelling and package leaflets in the countries where the product is marketed. The review was carried out under Article 30 of Directive 2001/83/EC as amended.

A question-and-answer document with more information about this referral can be found here.

Review of bufexamac started

The Committee started a safety review of **bufexamac** containing topical medicinal products, because of concerns over allergic contact reactions. Bufexamac is a non-steroidal anti-inflammatory drug (NSAID) used to treat dermatological and proctological diseases. The review was triggered by Germany under Article 107(2) of Directive 2001/83/EC. As part of this procedure the CHMP will assess the impact of these concerns on the benefit-risk balance of these medicines and make a recommendation whether their marketing authorisations should be maintained, changed, suspended or revoked.

MUTUAL-RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 47th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 18-19 January 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 5-7 January 2010. For further details, please see **Annex 3**.

Documents prepared by the CHMP Working Parties adopted during the January 2010 CHMP meeting are listed in **Annex 4**.

UPCOMING MEETINGS FOLLOWING THE DECEMBER 2009 CHMP PLENARY MEETING

- The 63rd meeting of the CHMP will be held at the Agency on 15-18 February 2010.
- The next Name Review Group meeting will be held at the Agency on 26 January 2010.
- The 48th CMD(h) will be held at the Agency on 15-16 February 2010.
- The workshop on Radiopharmaceuticals labelled with Radionuclides produced in Reactors will be held at the Agency on 4th-5th February 2010.

ORGANISATIONAL MATTERS

There were no topics addressed during the January 2010 CHMP meeting related to organisational matters.

PROCEDURAL ANNOUNCEMENT

Modifications of CHMP Monthly Report Annexes

From January 2010 onwards, the 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 (the relevant link will be set up shortly following the publication of this report and will be advertised in the February CHMP monthly report). The remaining annexes regarding outcomes of annual re-assessments, renewals, accelerated assessments, list of medicinal products for which marketing authorisations have been granted by the European Commission, orphan drug designations outcome, overview of scientific advice and Working Parties outputs will remain as is.

Implementation of Variations Regulation (EC) No 1234/2008

Further to the implementation of Variation Regulation (EC) No 1234/2008, please be informed that the documents bellow can be found in a dedicated section on the new Variation Regulation on the Agency's website, under Regulatory and procedural guidance, Post-marketing Authorisation:

- Final procedural and classification guidelines adopted by the Commission on 21 December 2009; the guidelines apply from 1 January 2010

http://ec.europa.eu/enterprise/sectors/pharmaceuticals/files/betterreg/pharmacos/procedural_guideline_adopted.pdf

http://ec.europa.eu/enterprise/sectors/pharmaceuticals/files/betterreg/pharmacos/classification_guideline_adopted.pdf

- Final variation application form and explanatory notes on the application form

http://ec.europa.eu/enterprise/sectors/pharmaceuticals/files/eudralex/vol-2/upd/variation_form_2009-12.pdf

http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/procedural_guidance/Variations/CMDh-133-2010-Rev0.pdf

- eCTD Variations question-and-answer document

http://esubmission.ema.europa.eu/doc/QA%20eCTD%20variations%20vers%205%20(Jan%2010)%20-%20clean%20version.doc

- Post-authorisation procedural advice on the new variation regulation

http://www.ema.europa.eu/pdfs/human/regaffair/4040410en.pdf

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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

Opinion for renewals of conditional MA's		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Increlex (Mecasermin), Tercica Inc (US),	**Positive Opinion adopted**	The marketing authorisation remains under exceptional circumstances.
Ventavis (iloprost), Bayer Schering	**Positive Opinion adopted**	The marketing authorisation remains under exceptional circumstances.

Opinion for renewals of conditional MA's		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Tyverb (lapatinib), Glaxo Group Ltd.	**Positive Opinion adopted**	N/A

Opinions for 5-Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Aclasta (zoledronic acid), Novartis Europharm Ltd	**Positive Opinion adopted**	Unlimited validity

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE DECEMBER 2009 CHMP MONTHLY REPORT

Invented Name	Scintimun
INN	besilesomab
Marketing Authorisation Holder	CIS bio international
Proposed ATC code	V09HA03
Indication	Scintigraphic imaging, in conjunction with other appropriate imaging modalities, for determining the location of inflammation/infection in peripheral bone in adults with suspected osteomyelitis.
CHMP Opinion date	22.10.2009
Marketing Authorisation Date	11.01.2010

ANNEX 3 TO CHMP MONTHLY REPORT JANUARY 2010

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

	1995 - 2009	2010	Overall Total
Scientific Advice	1134	**14**	**1148**
Follow-up to Scientific Advice	232	**11**	**243**
Protocol Assistance	245	**7**	**252**
Follow-up to Protocol Assistance	109	**4**	**113**
	1720	**36**	**1756**

OUTCOME OF THE JANUARY 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 type 2 diabetes.			x				x	
Chemical	Treatment of acute myeloid leukemia.				x			x	
Chemical	Treatment of soft tissue sarcomas.		x					x	x
Chemical	Treatment of acute myeloid leukaemia.		x			x			
Chemical	Treatment of Wegener's granulomatosis.				x			x	
Chemical	Treatment of castrate-resistant prostate cancer.	x						x	
Chemical	Treatment of cutaneous T-cell lymphoma.		x			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	Treatment of urinary bladder carcinoma.	x					x	x	
Chemical	Treatment of breast cancer.	x						x	
Biological	Treatment and prophylaxis of bleeding in haemophilia B.				x	x			
Biological	Prevention of bleeding in patients with Congenital FXIII A-subunit deficiency.		x			x		x	
Biological	Treatment of hemolytic uremic syndrome.		x					x	
Biological	Treatment and prophylaxis of bleeding in haemophilia A.	x				x		x	
Advanced therapy	Treatment of acute myocardial infarction and chronic heart failure.	x				x	x	x	
Biological	Treatment of acute decompensated congestive heart failure.			x				x	
Biological	Treatment of diabetic foot ulcer.	x				x	x	x	
Biological	Prevention against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis, and invasive diseases cause by H.influenzae Type b and Meningococcal serogroup C infections.	x					x	x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Prevention of herpes zoster and post-herpetic neuralgia.			x				x	
Biological	Active immunization against influenza virus.			x				x	
Chemical	Treatment of cytomegalovirus infection or disease.	x					x	x	
Other innovative	Treatment of S. aureus infections of the lung.	x				x	x	x	
Chemical	Reversal of neuromuscular blockade induced by rocuronium or vecuronium.			x			x	x	
Advanced therapy	Repair of single symptomatic cartilage defects of the femoral condyle of the knee.			x				x	
Chemical	Treatment of partial onset seizures.	x						x	
Chemical	Treatment of Parkinson's Disease.			x				x	
Chemical	Treatment of cancer pain and pain in patients requiring opioid therapy.			x				x	
Chemical	Treatment of excessive daytime sleepiness in Parkinson's disease.			x				x	
Chemical	Treatment of excessive daytime sleepiness.				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	Treatment of excessive daytime sleepiness in Narcolepsy.		x				x		
Chemical	Treatment of bronchial asthma.	x						x	
Other innovative	Treatment of asthma.	x					x	x	
Chemical	Treatment of asthma.	x						x	
Advanced therapy	Treatment of total bilateral and unilateral limbal stem cell deficiency.			x		x	x	x	
Biological	Treatment of focal vitreomacular adhesion.	x				x			
Biological	Treatment of atypical hemolytic uremic syndrome.		x				x	x	
Chemical	Intended for the use during magnetic resonance cholangiopancreatography for detection of pancreatic abnormalities in acute or acute recurrent pancreatitis.	x				x		x	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 14 Scientific Advice letters, 7 Protocol Assistance letters, 11 Follow-up Scientific Advice and 4 Follow-up Protocol Assistance letters were adopted at the 18 - 21 January 2010 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 33 new Requests for which the procedure started at the SAWP meeting held on 05 - 07 January 2010. The new requests are divided as follows: 23 Initial Scientific Advice, 7 Follow-up Scientific Advice, 3 Initial Protocol Assistance and 0 Follow-up Protocol Assistance.

ANNEX 4 TO CHMP MONTHLY REPORT JANUARY 2010

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

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[1]
CPMP/EWP/566/98 Rev.2	Guideline on Clinical Investigation of Medicinal Products in the Treatment of Epileptic Disorders	Adopted
EMEA/CHMP/EWP/ 14377/2008	Addendum to the Note for Guidance on Evaluation of Medicinal Products Indicated for the Treatment of Bacterial Infections to Specifically Address the Clinical Development of New Agents to Treat Disease Due to Mycobacterium Tuberculosis	Adopted
CPMP/EWP/QWP/1401/ 98 Rev.1	Guideline on the Investigation of Bioequivalence • Overview of comments received (EMA/CHMP/EWP/26817/2010)	Adopted
CPMP/EWP/784/97 Rev.1	Guideline on Clinical Investigation of Medicinal Products used in the Treatment of Osteoarthritis • Overview of comments received (EMA/818496/2009)	Adopted
EMA/CHMP/EWP/ 604040/2009	Concept Paper on the need for Revision of the Points to consider on the Clinical Investigation of Medicinal Products other than NSAIDs in Rheumatoid Arthritis CPMP/EWP/556/95	3-month public consultation
CPMP/EWP/1080/2000 Rev.1	Guideline on Clinical Investigation of Medicinal Products in the Treatment of Diabetes Mellitus	6-month public consultation
EMA/182470/2009	Overview of comments received on draft Guideline on Clinical Evaluation of Diagnostic Agents Rev.1	Adopted
EMA/CHMP/EWP/ 15912/2010	Concept Paper on the need for an addendum on the Clinical investigation of Medicinal Products intended for treatment of Glucocorticoid-induced Osteoporosis	3-month public consultation

[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").