EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Monthly Report

Committee for Medicinal Products for Human Use (CHMP)

14-17 December 2009

CENTRALISED PROCEDURE

Initial applications for marketing authorisation

The CHMP adopted seven positive opinions by consensus on initial marketing authorisation applications.

New medicinal products

- **DuoCover** (Clopidogrel/acetylsalicylic acid), from Bristol-Myers Squibb Pharma EEIG, and **DuoPlavin** (Clopidogrel/acetylsalicylic acid), from Sanofi Pharma Bristol-Myers Squibb SNC; both are fixed combination medicinal products intended for the prevention of atherothrombotic events. The review for DuoCover and DuoPlavin began on 25 March 2009 with an active review time of 172 days.
- **ImmunoGam** (human hepatitis B immunoglobulin), from Cangene Europe Ltd, intended for the immunoprophylaxis against Hepatitis B. The review for ImmunoGam began on 20 August 2008 with an active review time of 205 days.
- **Menveo** (MenACWY), from Novartis Vaccines and Diagnostics S.r.l., intended for the active immunisation of adolescents (from 11 years of age) and adults at risk of exposure to *Neisseria meningitidis* groups A, C, W-135 and Y, to prevent invasive disease. The review for Menveo began on 19 November 2008 with an active review time of 205 days.
- **Prolia** (denosumab), from Amgen Europe B.V., intended for the treatment of osteoporosis in postmenopausal women at increased risk of fractures and for the treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. The review for Prolia began on 28 January 2009 with an active review time of 212 days.

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7051
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

- **Revolade** (eltrombopag olamine), from GlaxoSmithKline Trading Services Ltd, intended for the treatment of chronic immune (idiopathic) thrombocytopenic purpura (ITP). The review of Revolade began on 24 December 2008 with an active review time of 201 days.
- **Tepadina** (thiotepa), from ADIENNE S.r.l., intended for the conditioning treatment prior to conventional haematopoietic progenitor cell transplantation. The review for Tepadina began on 23 July 2008 with an active review time of 206 days.

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

Negative opinion

The Committee adopted a negative opinion by consensus, denying a marketing authorisation for the following medicine:

- **Cerepro** (sitimagene ceradenovec - adenoviral vector-mediated Herpes Simplex Virus-thymidine kinase gene used with subsequent administration of ganciclovir), from Ark Therapeutics Ltd. Cerepro is a gene therapy medicinal product, intended for the treatment of high-grade glioma (a type of brain tumour).

  Because Cerepro is an advanced therapy medicinal product, it was assessed by the Committee for Advanced Therapies (CAT). Taking into account the assessment performed by the CAT, the CHMP concluded that the benefits of Cerepro did not outweigh its risks and recommended that it be refused marketing authorisation.

More information about Cerepro is available in a question-and-answer document.

Generic medicinal products

The Committee adopted three positive opinions by consensus for generic medicines:

- **Temozolomide Hexal** (temozolomide), from Hexal AG, **Temozolomide Sandoz** (temozolomide), from Sandoz Pharmaceuticals GmbH and **Temozolomide Hospira** (temozolomide), from Hospira UK Ltd, generics of Temodal, which is authorised in the EU for the treatment of glioblastoma and malignant glioma.

Summaries of opinion for these medicinal products are available 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 opinions for 'informed consent' applications adopted

The Committee adopted two positive opinions by consensus for marketing authorisations that were submitted as 'informed consent' applications. This type of application requires that reference is made to an authorised medicinal product and that the marketing authorisation holder of the reference product has given consent to the use of their dossier in the application procedure. The medicines concerned are:

- **Ristaben** (sitagliptin), from Merck Sharp & Dohme Ltd, intended for the treatment of type 2 diabetes mellitus. The reference medicine for Ristaben is Januvia.
- **Ristfor** (sitagliptin / metformin hydrochloride), from Merck Sharp & Dohme Ltd, intended for the treatment of type 2 diabetes mellitus. The reference medicine for Ristfor is Janumet.

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

Post-authorisation procedures

Extensions of indications and other recommendations

The Committee gave two positive opinions by consensus for applications for extension of indication, adding a new treatment option, for the following medicines:

- **Herceptin** (trastuzumab), from Roche Registration Ltd, to extend the indication to include the treatment of patients with HER2 positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction who have not received prior anti-cancer treatment for their metastatic disease in combination with capecitabine or 5-fluorouracil and cisplatin. Herceptin is currently authorised as mono-therapy or in combination with other medicines for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2. It is also authorised for the treatment of patients with HER2-positive early breast cancer following surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy.
- **Orencia** (abatacept), from Bristol-Myers Squibb Pharma EEIG, to extend the indication to include treatment of moderate to severe active polyarticular juvenile idiopathic arthritis in paediatric patients from 6 years of age who have had an insufficient response to other disease-modifying anti-arthritic drugs including at least one tumour necrosis factor inhibitor. Orencia is currently authorised as combination therapy for the treatment of moderate to severe active rheumatoid arthritis in adult patients.

Summaries of opinion for these extensions of indication are available here.

Further information will be included in the EPARs once the European Commission has granted final approval.

Withdrawals

The European Medicines Agency has been formally notified by Axxonis Pharma AG of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Nenad** (lisuride), 2.5 and 5.0 microgram/h transdermal patch. Nenad was expected to be used in adults with moderate-to-severe idiopathic restless legs syndrome. 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 Amarin Neuroscience Ltd of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Ethyl Eicosapent** (ethyl eicosapent), 500 mg soft gelatine capsules. Ethyl Eicosapent was expected to be used for the long-term stabilisation of symptoms in patients with Huntington's disease, a hereditary neurological disorder of the central nervous system that causes progressive degeneration of cells in the brain. 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 Bayer Schering Pharma of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Recothrom** (thrombin alfa) 1,000 IU/ml. Recothrom was expected to be used as supportive treatment in surgery to improve haemostasis where standard surgical techniques are insufficient. 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 Antigenics Therapeutics Limited of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Oncophage** (vitespen), 20 µg solution for infusion. Oncophage was expected to be used as an adjuvant treatment for localised renal cell carcinoma (RCC) patients at increased risk of recurrence with the following features: primary tumour stage T1b or T2 with high grade (3 or 4) histology with no nodal involvement. 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 Otsuka Pharmaceutical Europe Ltd in November of its decision to withdraw its application for an extension of indication for the centrally authorised medicine **Abilify** (aripiprazole) tablets, orodispersible tablets and oral solution. Abilify was expected to be used in the treatment of major depressive episodes, as adjunctive therapy, in patients who have had an inadequate response to previous treatment with antidepressants. An additional question-and-answer document with more information is now available.

Additional safety information

Wyeth Europa Ltd, Marketing Authorisation Holder for **Rapamune** (sirolimus) agreed with the CHMP on a Direct Healthcare Professional Communication informing healthcare professionals that adjustments to the targeted therapeutic dose range of sirolimus must only be made with a detailed knowledge of the specific assay used to measure the drug concentration in the patient. Currently, Rapamune whole-blood concentrations are measured using either the reference assay high performance liquid chromatography (HPLC), or an immunoassay. Switching between different immunoassays, or between an immunoassay and HPLC in a single patient, can lead to clinically significant differences in results and, therefore, incorrect dose adjustments. This, in turn, may have potential adverse consequences, such as allograft rejection if drug exposure is too low or toxic side effects if exposure is too high. Prescribers are therefore encouraged to regularly contact their laboratory and ascertain whether the assay used recently has been changed, and whether there have been any changes to the laboratory's reference range. Furthermore the CHMP agreed, on the basis of these findings, to update section 4.2 of the Summary of Product Characteristics.

Supply shortage of Fabrazyme

In the course of routine quality control, Genzyme has detected foreign particles in **Fabrazyme** (agalsidase beta) vials filled at the manufacturing site. Genzyme has also received reports of foreign particles identified in some of the product vials. Based on these observations, Genzyme temporarily halted the fill-finish activities at the manufacturing site to allow for implementation of corrective actions. As a consequence of this temporary shutdown and a lower than expected yield, Fabrazyme inventories will remain low for a longer time period than communicated previously. The temporary treatment recommendations, as outlined in September 2009, will therefore remain in place until the end of March 2010.

New paediatric indication for Diovan

The CHMP recommended a line extension for Diovan (valsartan), from Novartis Pharma AG, to add an oral solution, a pharmaceutical formulation suitable for the paediatric population. The paediatric formulation has been developed for the treatment of children and adolescents between 6 and 18 years with hypertension. The CHMP also recommended that this indication be approved for the currently available presentations of Diovan (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 Diovan 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 obtain approval for the new formulation and indication in all EU Member States where the medicine is authorised.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted four Lists of Questions on initial applications (under the optional scope), two Lists of Questions on "line extension" applications (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003) and three Lists of Questions based on Article 29 in accordance with the Paediatric Commission Regulation (EC) No. EC 1901/2006.

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 November 2009 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 November 2009 CHMP plenary meeting are provided in **Annex 4**.

Name Review Group (NRG)

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

REFERRAL PROCEDURES

Harmonisation referrals concluded

The Committee recommended harmonisation of the prescribing information for **Protium** and associated names (pantoprazole) from Nycomed. 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 valproate concluded

The Committee completed a review of the safety and efficacy of **valproate** in the treatment of manic episodes in bipolar disorder, concluding that the benefits of valproate in this condition outweigh its risks, and that marketing authorisations for all solid formulations (e.g. tablets, capsules or granules) of medicines containing valproate throughout the EU should be amended to include the treatment of manic episodes in bipolar disorders when lithium is contraindicated or not tolerated.

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

Referrals procedures started

The Committee started a referral procedure under Article 29 of Directive 2001/83/EC, as amended for **Prevora** (Chlorhexidine Diacetate), 100 mg/ml dental Solution from CHX Technologies Europe Limited, indicated/used for the prevention of root caries in adult patients at high-risk of dental caries. The procedure was initiated because of disagreements regarding the efficacy of the product. This type of procedure is initiated by one or more Member States in cases where an agreement cannot be reached in the context of the mutual recognition procedure or the decentralised procedure.

The Committee started two referral procedures under Article 30 of Directive 2001/83/EC as amended. The medicinal products concerned are:

- **Vascace Plus** and associated names (cilazapril hydroclortiazide), from Roche Products Ltd group of companies and associated companies, used in the treatment of hypertension in patients not responding satisfactorily to each component administered alone.
- **Lipitor** and associated names (atorvastatin), from Pfizer group of companies, used in the treatment of hypercholesterolaemia.

Re-examination procedures started under Article 32(4) of the Directive 2001/83/EC, as amended

The EMEA has been formally notified by GE Healthcare (Marketing Authorisation Holder for **Omniscan** (gadodiamide)) to re-examine the positive opinion adopted during the CHMP meeting on 16–19 November 2009 recommending changes to the Summary of Products Characteristics and Patient Leaflet following a review of **gadolinium-containing contrast agents** under Article 31 of the Directive 2001/83/EC as amended. The MAH did not agree with the adopted changes. Gadolinium-containing contrast agents are used in patients undergoing magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA) scans.

Update on the review of sibutramine

The Committee is reviewing data from the Sibutramine Cardiovascular OUTcomes (SCOUT) trial that indicate an increased risk of serious cardiovascular events, such as stroke or heart attack, with medicines containing **sibutramine**. These weight-loss medicines are used to treat obese patients and overweight patients who also have other risk factors such as type-2 diabetes or dyslipidaemia (abnormal levels of fat in the blood).

More information about the ongoing review of sibutramine is available in a separate press release document.

Review of topical formulations of Ketoprofen started

The Committee started a safety review of topical formulations of **ketoprofen**, an anti-inflammatory treatment, because of concerns over serious photosensitivity reactions. The review was triggered by France under Article 107 of Directive 2001/83/EC as amended. As part of this procedure the CHMP will assess the benefit-risk balance of these medicines and make a recommendation whether their marketing authorisations should be maintained, changed, suspended or revoked.

Recommendation for withdrawal of Benfluorex

The European Medicines Agency has recommended the withdrawal of all medicines containing benfluorex in the European Union, because their risks, particularly the risk of heart valve disease, are greater than their benefits. The review was carried out under Article 107 of Directive 2001/83/EC as amended.

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

MUTUAL-RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 46th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 14-15 December 2009. 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 30 November / 1 – 2 December 2009. For further details, please see
Annex 6.

Documents prepared by the CHMP Working Parties adopted during the December 2009 CHMP meeting are listed in **Annex 7**.

UPCOMING MEETINGS FOLLOWING THE DECEMBER 2009 CHMP PLENARY MEETING

- The 62nd meeting of the CHMP will be held at the Agency on 18-21 January 2010.
- The next Name Review Group meeting will be held at the Agency on 26 January 2010.
- The 47th CMD(h) will be held at the Agency on 18-19 January 2010.

ORGANISATIONAL MATTERS

The main topics addressed during the December 2009 CHMP meeting related to:

- The election of Pr Seitz as Chair of the Blood Product Working Party and Dr Ljungberg as Vice Chair.
- Update on activities regarding the CHMP/EMA Benefit/Risk methodology project. A report was given to the Committee on description of the current practice of benefit-risk assessment for centralised procedure products in the EU regulatory network.
- The monitoring of the use of recently adopted templates namely the CHMP Assessment Report templates on Benefit/Risk will start in January 2010.
- The creation of an Agency task force regarding the High Level Pharmaceutical Forum recommendations about European Public Assessment Report's (EPAR) contribution to relative effectiveness assessment. The Agency has started a dialogue with the EUnetHTA Collaboration in order to address one of the recommendations of the High Level Pharmaceutical Forum, namely, that the European Medicines Agency should continue their efforts to consider how the EPAR can further contribute to relative effectiveness assessments. It is expected that 1-2 workshops will take place in 2010 to progress this issue.
- The nomination of Dr Leufkens as CHMP representative on the ENCePP Steering Group.
- The announcement of a workshop on Radiopharmaceuticals labelled with Radionuclides produced in Reactors to be held on 4th-5th February 2010.

Noël Wathion

Head of Unit

Patient Health Protection, Tel. (+44-20) 74 18 85 92

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

PROCEDURAL ANNOUNCEMENT

From **January 2010**, Applicants should use the new **Pre-submission request form** that will shortly be released on the Agency's website with any additional supportive documentation required for:

- Intent to submit ATMP classification request
- ATMP Classification Request
- Eligibility for EMEA Procedure (ITF)
- Intent to Submit ATMP Certification Request
- ATMP Certification Request
- Eligibility to Centralised Procedure
- Intent to Submit a MA Application
- Pre-submission Meeting Request (MAA)
- Accelerated Assessment (MAA) Request

With regard to ongoing pre-submission requests, this form should also be used for

- Notification of Change (administrative request, e.g. change of Applicant and contact details)
- Withdrawal of Pre-Submission Request

This form should always be submitted **electronically** to h-cig2@ema.europa.eu except in the following cases:

Requests for Eligibility to the Centralised Procedure, where the pre-submission form should be sent to CPeligibility@ema.europa.eu, together with the relevant additional justification (Annex 1 SPC and Annex 2 Justification for eligibility), as separate Word documents.

Intent to Submit an ATMP classification and ATMP classification request, where the pre-submission form should be sent to AdvancedTherapies@ema.europa.eu. For the ATMP classification request, the 'ATMP classification briefing information' should be included as a separate Word document.

Temporary derogations to certain eligibility criteria for whole blood and blood components donors in the context of a risk of shortage caused by the Influenza A(H1N1) pandemic.

The European Commission Directive 2009/135/EC allows Member States confronted with a serious risk or actual shortage in the supply of blood and blood components directly due to the A(H1N1) Influenza pandemic, to apply temporary derogations to certain eligibility criteria for donors.

(**http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:288:0007:0009:EN:PDF**).

The EMEA considers that implementation of the above mentioned directive does not require the submission of a variation to update the PMF, where only a confirmation of compliance with the selection/exclusion criteria for blood/plasma donors in Directive 2001/83/EC, Directive 2002/98, Directive 2004/33/EC and the requirements of the European Pharmacopoeia Monographs (see Guideline on the Scientific data requirements for a plasma master file PMF- EMEA/CHMP/BWP/3794/03 current version) is included in the PMF.

For any additional queries regarding PMF dossiers, please contact Silvia Domingo Roige at the Agency.

ANNEX 1 TO CHMP MONTHLY REPORT DECEMBER 2009

PRE-AUTHORISATION: MARKETING AUTHORISATION APPLICATIONS

Activity	2009								1995 onwards
	Optional Scope				Mandatory scope			Total	Overall total
	NAS	Significant innovation	Interest of Patients	Generics	Biotech	Indications	Orphans		
Applications for MA submitted	25	5	0	38	10	4	10	92	890
Positive opinions	24	11	0	52	14[1]	6	8	115	607
Negative opinions[2]	0	3	0	0	3	0	2	8	29
Withdrawals prior to opinion	5	0	0	1	4	2	5	17	156
Marketing authorisation granted by the Commission	22	11	0	42	13	4	10	102	687

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	2009	1995 onwards
Compassionate use applications	0	0
Art. 58 applications	0	4
Consultation for medical devices[3]	1	6
PMF (Click here for a list of PMF certifications)	2	15
VAMF	0	0

[1] Figure being corrected due to inaccuracy in the monthly report previously published.
[2] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[3] Consultation in accordance with Council Directive 93/42/EEC concerning medical devices as amended by Directive 2000/70/EC as regards medical devices incorporating stable derivates of human blood or plasma and Directive 2001/104/EC

OUTCOME OF THE DECEMBER 2009 CHMP MEETING IN RELATION TO ACCELERATED ASSESSMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Chemical	Treatment of relapsing multiple sclerosis		X

ANNEX 2 TO CHMP MONTHLY REPORT DECEMBER 2009

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

Activity	2009	Overall total 1995 onwards
Type I Variations (positive notifications)	1239	7609
Type II Variations (positive opinions)	1109	5652
Type II Variations (negative opinions)	4	20
Annex II Applications (positive opinions)	49	232
Annual Re-assessments (positive opinions)	15	-
Opinions for renewals of conditional MA's (positive opinions)	4	10
5-year Renewals (positive opinions)	58	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
3 Extension of indication	3 Positive opinions
54 SPC changes	53 Positive opinions 1 Withdrawal prior to opinion
50 Quality changes	47 Positive opinions 1 Negative opinion 2 Withdrawals prior to opinion

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Evoltra (clofarabine), Genzyme B.V.	Positive Opinion adopted	The marketing authorisation remains under exceptional circumstances
Replagal (agalsidase alfa), TKT Europe-5S AB	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**
Vectibix (panitumumab), Amgen Europe B.V.	Positive Opinion adopted	N/A

Opinions for 5-Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
IntronA (interferon alfa-2b), SP Europe	Positive Opinion adopted	Unlimited validity
Aloxi (palonosetron hydrochloride), Helsinn Birex Pharmaceuticals Ltd.	Positive Opinion adopted	Unlimited validity

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

Invented Name	**Multaq**
INN	dronedarone
Marketing Authorisation Holder	sanofi-aventis
Proposed ATC code	not yet assigned
Indication	MULTAQ is indicated in adult clinically stable patients with a history of, or current non-permanent atrial fibrillation (AF) to prevent recurrence of AF or to lower ventricular rate
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	26.11.2009

Invented Name	**Irbesartan / Hydrochlorothiazide Teva**
INN	irbesartan / hydrochlorothiazide
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	C09D A04
Indication	Treatment of essential hypertension
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	26.11.2009

Invented Name	**Sildenafil Teva**
INN	sildenafil
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	G04B E03
Indication	Treatment of men with erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	30.11.2009

Invented Name	**Zutectra**
INN	human hepatitis B immunoglobulin
Marketing Authorisation Holder	Biotest Pharma GmbH
Proposed ATC code	J06BB04
Indication	Prevention of hepatitis B virus (HBV) re-infection in HBV-DNA negative patients ≥ 6 months after liver transplantation for hepatitis B induced liver failure
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	30.11.2009

Invented Name	**Onbrez Breezhaler**
INN	indacaterol
Marketing Authorisation Holder	Novartis Europharm Limited
Proposed ATC code	not yet assigned
Indication	Maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD).
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	30.11.2009

Invented Name	**Nevirapine Teva**
INN	nevirapine
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	J05AG01
Indication	In combination with other anti-retroviral medicinal products for the treatment of HIV-1 infected adults, adolescents, and children of any age
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	30.11.2009

Invented Name	**Oslif Breezhaler**
INN	indacaterol
Marketing Authorisation Holder	Novartis Europharm Limited
Proposed ATC code	not yet assigned
Indication	Maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD).
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	30.11.2009

Invented Name	**Hirobriz Breezhaler**
INN	indacaterol
Marketing Authorisation Holder	Novartis Europharm Limited
Proposed ATC code	not yet assigned
Indication	Maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD).
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	30.11.2009

Invented Name	**Olanzapine Glenmark**
INN	olanzapine
Marketing Authorisation Holder	Glenmark Generics (Europe) Limited
Proposed ATC code	N05A H03
Indication	Olanzapine is indicated for the treatment of schizophrenia. Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response. Olanzapine is indicated for the treatment of moderate to severe manic episode. In patients whose manic episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	03.12.2009

Invented Name	**Olanzapine Glenmark Europe**
INN	olanzapine
Marketing Authorisation Holder	Glenmark Generics (Europe) Limited
Proposed ATC code	N05A H03
Indication	Olanzapine is indicated for the treatment of schizophrenia. Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response. Olanzapine is indicated for the treatment of moderate to severe manic episode. In patients whose manic episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	03.12.2009

Invented Name	**Prevenar 13**
INN	Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)
Marketing Authorisation Holder	Wyeth Lederle Vaccines S.A.
Proposed ATC code	J07AL02
Indication	Active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae* in infants and children from 6 weeks to 5 years of age.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	09.12.2009

Invented Name	**Olazax Disperzi**
INN	olanzapine
Marketing Authorisation Holder	Glenmark Pharmaceuticals s.r.o
Proposed ATC code	N05A H03
Indication	*Adults* Olanzapine is indicated for the treatment of schizophrenia. Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response. Olanzapine is indicated for the treatment of moderate to severe manic episode. In patients whose manic episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	10.12.2009

Invented Name	**Sildenafil Actavis**
INN	sildenafil
Marketing Authorisation Holder	Actavis Group PTC ehf.
Proposed ATC code	G04B E03
Indication	Treatment of men with erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	10.12.2009

Invented Name	**Lamivudine Teva Pharma B.V.**
INN	lamivudine
Marketing Authorisation Holder	TEVA Pharma B.V.
Proposed ATC code	J05AF05
Indication	Part of antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults and children.
CHMP Opinion date	24.09.2009

Marketing Authorisation Date	10.12.2009

Invented Name	**Olazax**
INN	olanzapine
Marketing Authorisation Holder	Glenmark Pharmaceuticals s.r.o
Proposed ATC code	N05A H03
Indication	*Adults* Olanzapine is indicated for the treatment of schizophrenia. Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response. Olanzapine is indicated for the treatment of moderate to severe manic episode. In patients whose manic episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	11.12.2009

Invented Name	**Rivastigmine 1 A Pharma**
INN	rivastigmine
Marketing Authorisation Holder	1 A Pharma GmbH
Proposed ATC code	N06DA03
Indication	Symptomatic treatment of mild to moderately severe Alzheimer's dementia. Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	11.12.2009

Invented Name	**Rivastigmine HEXAL**
INN	rivastigmine
Marketing Authorisation Holder	HEXAL AG
Proposed ATC code	N06DA03
Indication	Symptomatic treatment of mild to moderately severe Alzheimer's dementia. Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease.

CHMP Opinion date	24.09.2009
Marketing Authorisation Date	11.12.2009

Invented Name	**Rivastigmine Sandoz**
INN	rivastigmine
Marketing Authorisation Holder	Sandoz Pharmaceuticals GmbH
Proposed ATC code	N06DA03
Indication	Symptomatic treatment of mild to moderately severe Alzheimer's dementia. Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease.
CHMP Opinion date	24.09.2009
Marketing Authorisation Date	11.12.2009

Invented Name	**Sildenafil ratiopharm**
INN	sildenafil
Marketing Authorisation Holder	ratiopharm GmbH
Proposed ATC code	G04B E03
Indication	Treatment of men with erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance.
CHMP Opinion date	22.10.2009
Marketing Authorisation Date	23.12.2009

Invented Name	**ZENAS**
INN	amifampridine
Marketing Authorisation Holder	EUSA Pharma SAS
Proposed ATC code	N07XX05
Indication	Symptomatic treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.
CHMP Opinion date	22.10.2009
Marketing Authorisation Date	23.12.2009

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION: UPDATE SINCE THE NOVEMBER 2009 CHMP MEETING

Active substance	Sponsor/applicant	EU Designation Number and Date of Orphan Designation	Designated Orphan Indication
Mannitolum	Pharmaxis Pharmaceuticals Ltd	EU/3/05/325	Treatment of cystic fibrosis
Cholic acid	Laboratoires CTRS	EU/3/02/127	Treatment of inborn errors of primary bile acid synthesis
Tegafur/gimeracil/oteracil potassium	Taiho Pharma Europe Ltd	EU/3/07/515	Treatment of gastric cancer
Homoharringtonine (Omacetaxine Mepesuccinate)	ChemGenex Europe S.A.S	EU/3/04/224	Treatment of chronic myeloid leukaemia

ANNEX 5 TO CHMP MONTHLY REPORT DECEMBER 2009
INVENTED NAME REVIEW GROUP (NRG)

	NRG meeting; 27 Jan 2009		NRG meeting; 17 Mar 2009		NRG meeting; 12 May 2009		NRG meeting; 28 Jul 2009		NRG meeting; 15 Sep 2009		NRG meeting; 24 Nov 2009		2009	
	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected
Proposed invented names	1. 47	52	2. 30	3. 36	27	28	43	47	39	38	4. 53	43	5. 239	244
Justification for retention of invented name *	6. 5	7. 1	8. 3	9. 1	2	1	10. 2	11. 6	2	1	12. 1	13. 8	14. 15	15. 18

*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.

	NRG meeting; 27 January 2009		NRG meeting; 17 March 2009		NRG meeting; 12 May 2009		NRG meeting; 28 July 2009		NRG meeting; 15 September 2009		NRG meeting; 24 November 2009		2009	
Objections	Accepted	Rejected	Accepte	Rejecte	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected	Accepted	Rejected
Total number of objections raised	120	65	79	40	56	46	75	45	63	45	87	49	480	290
Criterion - Safety concerns														
Similarity with other Invented name	100	56	67	36	51	39	68	39	56	32	65	29	407	231
Conveys misleading therapeutic/pharmaceutical connotations	6	0	1	1	0	0	0	1	0	0	3	7	10	9
Misleading with respect to composition	0	0	3	0	0	2	0	2	0	1	3	2	6	7
Criterion - INN concerns														
Similarity with INN	2	3	1	1	1	4	2	2	2	2	5	0	13	12
Inclusion of INN stem	3	0	0	1	0	1	1	0	0	0	3	2	7	4
Criterion - Other public health concerns														
Unacceptable qualifiers	4	1	0	1	0	0	1	0	3	4	2	0	10	6
Conveys a promotional message	1	0	5	0	0	0	3	1	0	4	0	5	9	10
Appears offensive or has a bad connotation	1	1	0	0	1	0	0	0	1	0	1	1	4	2
Similarity between name of individual active substance and fixed combinations and/or between fixed combinations	3	4	2	0	3	0	0	0	1	2	5	3	14	9
Similarity between name of prodrug and related active substance	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

ANNEX 6 TO CHMP MONTHLY REPORT DECEMBER 2009

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

	1995 - 2008	2009	Overall Total
Scientific Advice	887	**247**	**1134**
Follow-up to Scientific Advice	171	**61**	**232**
Protocol Assistance	198	**47**	**245**
Follow-up to Protocol Assistance	90	**19**	**109**
	1346	**374**	**1720**

OUTCOME OF THE DECEMBER 2009
CHMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Final Scientific Advice Procedures

Substance	**Intended indications(s)**	**Type of Request[4]**				**Topic**			
		New		**Follow -up**		**Pharma ceutical**	**Pre-clinical**	**Clinical**	**Significant Benefit**
		SA	**PA**	**SA**	**PA**				
Chemical	Treatment of Type 2 Diabetes			x				x	
Chemical	Treatment of Irritable Bowel Syndrome.	x				x	x	x	
Chemical	Treatment of infantile colic			x			x		
Chemical	Treatment of opioid induced constipation	x						x	
Chemical	Treatment of Type 2 diabetes mellitus	x						x	
Chemical	Treatment of hyperphosphat-aemia	x					x		
Chemical	Treatment of multiple myeloma				x			x	

[4] Information missing in the monthly report previously published has been included.

Substance	Intended indications(s)	Type of Request[4]				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of acute lymphoblastic leukaemia		x					x	
Chemical	Treatment of Philadelphia Chromosome Positive Chronic Myeloid Leukaemia	x				x		x	
Biological	Treatment of neutropenia			x				x	
Biological	Intended of neutropenia	x				x	x	x	
Chemical	Treatment of peritoneal carcinomatosis	x					x	x	
Biological	Treatment of Rheumatoid arthritis, Adult Crohn's disease, Paediatric Crohn's disease, Ulcerative colitis, Ankylosing spondylitis, Psoriatic arthritis and Psoriasis			x		x	x		
Biological	Treatment Rheumatoid arthritis, Adult Crohn's disease, Paediatric Crohn's disease, Ulcerative colitis, Ankylosing spondylitis, Psoriatic arthritis and Psoriasis	x						x	

Substance	Intended indications(s)	Type of Request[4]				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of metastatic castration-resistant prostate cancer	x				x	x	x	
Biological	Treatment of ovarian cancer	x						x	
Biological	Treatment of non- Hodgkin's lymphoma			x				x	
Biological	Treatment of non- Hodgkin's lymphoma	x					x		
Biological	Treatment of thrombotic thrombocytopenic purpura		x			x	x	x	x
Chemical	Treatment of non-ST acute coronary syndrome	x						x	
Chemical	Treatment of solar urticaria		x					x	
Biological	Treatment of chronic idiopathic urticaria	x					x	x	
Biological	Treatment of *C. difficile* infection	x					x	x	
Chemical	Treatment of chronic hepatitis C	x					x	x	
Chemical	Treatment of vaginal atrophy	x					x	x	
Biological	Treatment of multiple sclerosis			x			x		
Chemical	Treatment of insomnia	x						x	
Chemical	Treatment of Amyotrophic Lateral Sclerosis		x			x	x	x	x
Biological	Treatment of Alzheimer's disease	x				x	x	x	

Substance	Intended indications(s)	Type of Request[4]				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	Treatment of mild, moderate and severe asthma and chronic obstructive pulmonary disease	x				x			
Biological	Treatment of Acute Lung Injury / Acute Respiratory Distress Syndrome		x			x	x	x	
Other innovative	Treatment of cystic fibrosis		x				x		
Chemical	Treatment of chronic obstructive pulmonary disease	x					x	x	
Chemical	Treatment of inner ear tinnitus	x					x	x	
Chemical	Prevention and treatment of postoperative pain and inflammation associated with cataract surgery	x				x	x	x	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 22 Scientific Advice letters, 6 Protocol Assistance letters, 6 Follow-up Scientific Advice and 1 Follow-up Protocol Assistance letters were adopted at the 14-17 December 2009 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 32 new Requests for which the procedure started at the SAWP meeting held on 30 November - 02 December 2009. The new requests are divided as follows: 14 Initial Scientific Advice, 9 Follow-up Scientific Advice, 6 Initial Protocol Assistance and 3 Follow-up Protocol Assistance.

ANNEX 7 TO CHMP MONTHLY REPORT DECEMBER 2009

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE DECEMBER 2009 CHMP MEETING

GENE THERAPY WORKING PARTY (GTWP)

Reference number	Document	Status[5]
EMEA/CHMP/GTWP/ BWP/234523/2009	Concept paper on the revision of the Note for Guidance on the Quality, Pre-Clinical and Clinical aspects of Gene Transfer Medicinal Products	Adopted for 3-month public consultation
EMEA/CHMP/GTWP/ 212377/2009	Question-and-Answer document on Gene Therapy topics	Adopted
EMEA/CHMP/CPWP/ 420173/2009	GTWP Work Programme for 2010	Adopted

WORKING PARTY ON CELL-BASED PRODUCTS (CPWP)

Reference number	Document	Status[5]
EMA/CHMP/CPWP/ 708420/2009	Concept Paper on the Risk-based Approach (jointly with GTWP) as adopted by CAT	Adopted for 3-month public consultation

QUALITY WORKING PARTY (QWP)

Reference number	Document	Status[5]
EMA/CHMP/CVMP/ QWP/809114/2009	Concept paper for the revision of the Guideline on Process Validation	Adopted for 3-month public consultation subject to final adoption by CVMP
EMA/CHMP/QWP/811 210/2009 Rev 1	Draft revised Guideline on Real Time Release Testing (former Parametric Release)	Adopted for 6-month public consultation
EMA/CHMP/QWP/ 292235/2009	Discussion paper on Harmonisation of Policies for High Risk Impurities	Adopted

[5] 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").

SAFETY WORKING PARTY (EWP)

Reference number	Document	Status[5]
EMEA/CHMP/SWP/ 413709/2009 Rev 1	Revised SWP Workplan 2010-2011	Adopted
EMEA/CHMP/SWP/ 431994/2007 Rev 2	Revised Question & Answer document on the CHMP Guideline on the Limits of Genotoxic Impurities	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[5]
EMEA/CHMP/EWP/ 342691/2009	Guideline on the Evaluation of Drugs for the Treatment of Gastroesophageal Reflux Disease	Adopted for 6-month public consultation
EMEA/CHMP/EWP/ 248088/2009 Rev 1	Revised EWP Work Plan 2010	Adopted