European Medicines Agency
Evaluation of Medicines for Human Use

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SEPTEMBER 2009 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its September plenary meeting on 21-24 September 2009.

The CHMP welcomed Dr Martina Weise as the new CHMP Alternate from Germany, replacing Dr.Broich in this role.

The CHMP also noted that this was the last meeting for Prof Ingemar Persson and thanked him for his efforts and contributions during his time on the Committee. Prof. Persson was elected in 2004 as a co-opted member in Pharmacovigilance, with expertise in epidemiology and risk management, and re-elected in this position in 2007.

CENTRALISED PROCEDURE

Two vaccines against influenza pandemic (H1N1) 2009 recommended for authorisation
The European Medicines Agency has recommended that two pandemic vaccines against influenza A(H1N1)v ('swine flu') be granted marketing authorisation. The vaccines concerned are:

- **Focetria** from Novartis Vaccines and Diagnostics S.r.l.;
- **Pandemrix** from GlaxoSmithKline Biologicals S.A.

More information is available in a separate press release and a question-and-answer document published on the Agency's website.

Initial applications for marketing authorisation

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

New medicinal products

- **Multaq** (dronedarone hydrochloride), from Sanovi-Aventis, intended for 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. The review of Multaq began on 23 July 2008, with an active review time of 183 days.
- **Onbrez Breezhaler**, **Hirobriz Breezhaler** and **Oslif Breezhaler** (indacaterol maleate), all from Novartis Europharm Ltd, intended for the maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD). The review of Onbrez Breezhaler began on 28 January 2009, with an active review time of 178 days. The review of Hirobriz Breezhaler and Oslif Breezhaler began on 26 July 2009 with an active review time of 60 days.
- **Prevenar 13** (pneumococcal polysaccharide conjugated vaccine, 13-valent adsorbed), from Wyeth Lederle Vaccines S.A., intended for the prevention of invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae.* The review of Prevenar 13 began on 24 December 2008 with an active review time of 204 days.

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- **Zutectra** (human hepatitis B immunoglobulin), from Biotest Pharma GmbH, intended for the prevention of Hepatitis B virus re-infection in HBV-DNA negative patients ≥ 6 months after liver transplantation for Hepatitis B-induced liver failure. The review of Zutectra began on 19 November 2008, with an active review time of 204 days.

Positive opinions for 'informed consent' duplicate applications

The Committee adopted three positive opinions by consensus for duplicate applications, for which 'informed consent' applications were submitted:

- **Rivastigmine 1 A Pharma** (rivastigmine) from 1 A Pharma GmbH;
- **Rivastigmine HEXAL** (rivastigmine) from Hexal AG;
- **Rivastigmine Sandoz** (rivastigmine) from Sandoz Pharmaceuticals GmbH.

The products are intended for the symptomatic treatment of mild to moderately severe Alzheimer's dementia and for the treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease.

When submitting 'informed consent' duplicate applications, applicants can make reference to a medicine that is already authorised in the European Union (EU), provided that they have obtained consent from the marketing authorisation holder of the reference medicine to do so.

Generic medicinal products

The Committee adopted nine positive opinions by consensus for the following generic medicines, for which a reference medicine is already authorised in the EU. The medicines concerned are:

- **Irbesartan Hydrochlorothiazide Teva** (irbesartan hydrochlorothiazide), from Teva Pharma B.V., a generic of CoAprovel, indicated for the treatment of hypertension;
- **Lamivudine Teva Pharma B.V.** (lamivudine), from Teva Pharma B.V., a generic of Epivir, indicated as part of antiretroviral combination therapy for the treatment of human immunodeficiency virus (HIV)-infected adults and children;
- **Olanzapine Glenmark Europe**, **Olanzapine Glenmark** (olanzapine), from Glenmark Generics (Europe) Ltd, and **Olazax Desperzi** and **Olazax** (olanzapine), from Glenmark Phamaceuticals s.r.o., all generics of Zyprexa, indicated for the treatment of schizophrenia and moderate to severe manic episodes;
- **Sildenafil Actavis** (sildenafil citrate), from Actavis Group PTC and **Sildenafil Teva** (sildenafil citrate) from Teva Pharma B. V., both generics of Viagra, intended to treat erectile dysfunction;
- **Nevirapine Teva** (nevirapine), from Teva Pharma B.V., a generic of Viramune, indicated for treatment of HIV-1-infected adults, adolescents, and children of any age.

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.

Post-authorisation procedures

Extension of indication for Tamiflu for use in children less than six months of age

The Committee has recommended an extension of indication for **Tamiflu** (oseltamivir), from Roche Registration Ltd., to include treatment of children less than six months of age during pandemic influenza and post-exposure prophylaxis for children less than one year of age. Tamiflu is currently indicated for the treatment of influenza in patients one year of age and older who present with symptoms typical of

influenza, when influenza virus is circulating in the community. It is also indicated for the treatment of children 6 to 12 months of age during a pandemic influenza outbreak.

In parallel, the Committee has approved instructions on how to prepare home and pharmacy extemporaneous formulations from Tamiflu 30, 45 and 75mg capsules and dosing recommendations from these extemporaneous formulations for children under one year of age.

Additional information including the recommended updated product information in English will be published shortly.

Extensions of indication and other recommendations

The Committee gave twelve positive opinions by consensus for applications for extensions of indication, adding new treatment options, for the following medicines:

- **Januvia, Tesvel** and **Xelevia** (sitagliptin), from Merck Sharp & Dohme Ltd, and **Janumet, Efficib** and **Velmetia** (sitagliptin phosphate monohydrate / metformin hydrochloride), to extend the indication of these medicines to include combination therapy with insulin (with or without metformin). These medicines are currently authorised for the treatment of type-2 diabetes mellitus, as an adjunct to diet and exercise, in monotherapy, in dual combination with metformin or a sulphonylurea or a PPARγ agonist, in triple combination with metformin and sulphonylurea or with a PPARγ agonist and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control;
- **Corlentor** and **Procoralan** (ivabradine), both from Les Laboratoires Servier, to extend the indication to use the medicines in combination with beta-blockers in patients who are inadequately controlled with an optimal beta-blocker dose and whose heart rate is greater than 60 beats per minute (bpm). Corlentor and Procoralan are currently indicated for the symptomatic treatment of chronic stable angina pectoris in coronary-artery-disease patients with normal sinus rhythm, in patients unable to tolerate or with a contra-indication to the use of beta-blockers, or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is greater than 60 bpm;
- **Yondelis** (trabectedin), from Pharma Mar S.A., to extend the indication to use the medicine in combination with pegylated liposomal doxorubicin (PLD) for the treatment of patients with relapsed platinum-sensitive ovarian cancer. Yondelis is currently indicated for the treatment of patients with advanced soft tissue sarcoma, after failure of anthracyclines and ifosfamide, or who are unsuited to receive these agents;
- **PegIntron** and **ViraferonPeg** (peginterferon alfa-2b), from Schering-Plough Europe, to extend the therapeutic indication of combination therapy with ribavirin to include treatment of the paediatric population and to include the treatment of adult patients with compensated cirrhosis. PegIntron and ViraferonPeg are currently indicated for the treatment of adult patients with chronic hepatitis C who have elevated transaminases without liver decompensation and who are positive for serum HCV-RNA or anti-HCV, including naïve patients with clinically stable HIV co-infection. It is also indicated for the treatment of hepatitis C in adult patients who have failed previous treatment with interferon alpha (pegylated or non-pegylated) in combination therapy with ribavirin.

  The same extension of indication applies to **Rebetol** (ribavirin) used in combination with peginterferon alfa-2b from Schering-Plough Europe.

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.

Annual re-assessment

The CHMP reviewed the data submitted by the marketing authorisation holder in the framework of the sixth annual reassessment procedure and concluded that the benefit/risk profile for **Xigris** (drotrecogin alfa (activated)) remained unchanged.
Xigris is indicated for the treatment of adult patients with severe sepsis with multiple organ failure when added to best standard care. The use of Xigris should be considered mainly in situations when therapy can be started within 24 hours after the onset of organ failure.

Since there is still a specific obligation that remains to be fulfilled, the marketing authorisation for Xigris will remain under exceptional circumstances.
In addition, the CHMP recommended the update of Xigris's Product Information as follows:
- Update of section 4.3 of the Summary of Product Characteristics (SmPC) to include a contra-indication for children below 18 years of age as a precautionary measure;
- Update of section 4.4 of the SmPC to include that 'no further study has confirmed the efficacy results of the single pivotal trial' since the results of ADDRESS and RESOLVE trials did not confirm the results of the initial PROWESS trial;
- Update of section 5.1 of the SmPC to mention the fact that the ADDRESS trial did not confirm the efficacy results of the PROWESS study.

Withdrawals

The European Medicines Agency has been formally notified by CTI Life Sciences Ltd. of its decision to withdraw its application for a centralised marketing authorisation for **Opaxio** (paclitaxel poliglumex) 269 mg powder for concentrate for solution for infusion. Opaxio was expected to be used for first line monotherapy treatment of PS2 patients with advance Non Small Cell Lung Cancer. A separate press release document with more information is available. An additional question-and-answer document will be available following the October CHMP meeting.

The Agency was formally notified by Targanta Netherlands B.V. at the end of August 2009 of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Ramvocid** (oritavancin), 100 mg powder for solution for infusion. Ramvocid was expected to be used for the treatment of complicated skin and soft tissue infections. A separate press release and a question-and-answer document with more information are available.

The EMEA was formally notified by GlaxoSmithKline Research & Development Limited at the end of July 2009 of its decision to withdraw the application for a centralised marketing authorisation for **Bosatria** (mepolizumab), powder for solution for infusion, 250 mg/vial. A separate press release document with more information is available. An additional question-and-answer document will be available shortly.

Updated safety information

Following the Pharmacovigilance Working Party's (PhVWP's) conclusions on the risk of venous thromboembolism (VTE) associated with antipsychotics, the CHMP recommended updating the product information for **Abilify** (aripiprazole), from Otsuka Pharmaceutical Europe Ltd, and **Invega** (paliperidone), from Janssen-Cilag International NV to reflect the fact that cases of VTE (including cases of pulmonary embolism and deep vein thrombosis) have been reported with antipsychotic drugs and, since patients treated with antipsychotics often present with acquired risk factors for VTE, that all possible risk factors for VTE should be identified before and during treatment with these medicines and preventive measures undertaken.

The CHMP adopted an amendment to section 4.4 of the SPC for **Adrovance/Fosavance** (alendronate sodium / colecalciferol), recommending that prescribers should consider the benefits and potential risks of alendronate on an individual patient basis in patients with known Barrett's oesophagus,

The MAH (Janssen-Cilag International NV) for **Intelence** (etravirine) agreed with the CHMP on a Direct Healthcare Professional Communication, informing of recent cases of severe hypersensitivity syndromes, including drug rash with eosinophilia and systemic symptoms (DRESS) and TEN (toxic epidermal necrolysis), sometimes fatal, reported with the use of Intelence. Healthcare Professionals are advised to discontinue use of Intelence immediately if severe rash or hypersensitivity reaction is suspected. The Product Information has been updated accordingly.

Section 4.4 "Special warnings and precautions for use" of the SPC for **RotaTeq** was updated to reflect post-marketing cases of gastroenteritis associated with vaccine virus, in infants with severe combined immunodeficiency (SCID).

The CHMP adopted an amendment to section 4.3 of the SPC for **Norvir** (ritonavir), to add a contraindication on concomitant use of sildenafil with ritonavir in pulmonary arterial hypertension patients.

The CHMP adopted an amendment to section 4.4 of the SPC for **Noxafil** (posaconazole), recommending that the product should be used with caution in hepatic impaired patients due to limited clinical experience and the possibility that posaconazole plasma levels may be higher in these patients.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted seven Lists of Questions on initial applications (all of them under the optional scope) and one List of Questions on a "line extension" application (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003). In addition, the Committee adopted two Lists of Questions on Article 29 for paediatric indication applications (in accordance with (EC) No. 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 July 2009 is provided in **Annex 3.**

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 4**.

REFERRAL PROCEDURES

Referral procedures concluded

The Committee concluded a review of issues related to the risk of osteonecrosis of the jaw associated with the use of **bisphosphonates** under Article 5(3) of Regulation (EC) No 726/2004[1].
The CHMP was asked to give a scientific opinion on:

- the criteria that define osteonecrosis of the jaw related to bisphosphonates;
- how bisphosphonates may cause osteonecrosis of the jaw
- whether the risk of osteonecrosis of the jaw is greater with some bisphosphonates or for some groups of patients
- the measures that could be taken to minimise this risk.

The CHMP concluded that there is an increased risk of osteonecrosis of the jaw in patients using these medicines. However, further studies should be carried out to better identify the factors that increase the risk and the measures needed to minimise it.

More information on the review, including recommendations for patients, dentists and prescribers can be found in a separate question-and-answer document. An opinion will be available shortly.

[1] Article 5(3) of Regulation (EC) 726/2004, opinion on any scientific matter concerning the evaluation of medicinal products for human use.

Referral procedures started

The CHMP started three referral procedures under Article 30 of Directive 2001/83/EC as amended. This type of procedure is initiated with a view to harmonising product information for medicinal products authorised at Member State level. The medicinal products concerned are:

- **Vascace and associated names** (cilazapril), from Roche group of companies and associated companies, indicated in the treatment of essential hypertension and used in heart failure;
- **Escitalopram containing medicinal products** (escitalopram oxalate), from Alfred E. Tiefenbacher GmbH group of companies and associated companies, indicated in the treatment of major depressive disorder episodes;
- **Escitalopram Arrow 5 mg/10 mg/20 mg** (escitalopram oxalate), from Arrow Generics Ltd group of companies and associated companies, indicated in the treatment of major depressive disorder episodes.

The CHMP started two referral procedures under Article 107 of Directive 2001/83/EC as amended. This type of procedure is initiated when a Member State is considering the suspension or revocation of the marketing authorisation for a medicinal product authorised in its territory as a result of the emergence of new pharmacovigilance data:

- **Propacetamol** (injectable), approved only in France for the symptomatic treatment of pain and fever further to the decision to withdraw the product from the market, due to the risk of serious hypersensitivity reactions, cases of thrombosis and administration site reactions.
- **Antiadiposo** (iodocasein/thiamine), approved only in Italy for treatment of obesity further to the decision to suspend the product from the market due to cases of hyperthyroidism and thyrotoxicosis.

Withdrawal

The CHMP has been formally notified by Cangene Europe Ltd of its decision to withdraw its MRP licenses and applications for the medicinal product **WinRho SDF** from the concerned Member States, due to the company's marketing strategy. In April 2009, the CHMP initiated a referral procedure under Article 29 of Directive 2001/83/EC, as amended for WinRho SDF (Human anti-D immunoglobulin), powder for solution for injection/infusion because of disagreements regarding safety and efficacy.

MUTUAL-RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 43rd CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 21-23 September 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 1-3 September 2009. For further details, please see **Annex 5**.

Documents prepared by the CHMP Working Parties adopted during the September 2009 CHMP meeting are listed in **Annex 6**.

UPCOMING MEETINGS FOLLOWING THE SEPTEMBER 2009 CHMP PLENARY MEETING

- The 59th meeting of the CHMP will be held at the Agency on 19-22 October 2009.
- The next Name Review Group meeting will be held at the Agency on 24 November 2009.
- The 44th CMD(h) will be held at the Agency on 19-20 October 2009.

ORGANISATIONAL MATTERS

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

- the adoption of a revision of the procedural advice for appointment of (Co)-Rapporteurs, to take advanced-therapy medicinal products into consideration (EMEA/124066/2005 Rev 1);
- amendment of existing CHMP templates and guidance documents (last updated in 2006) as well as creation of new templates used by Rapporteurs for the assessment of new drug applications in the centralised procedure. This update is based on discussions of the benefit-risk assessment communication, new paediatric legislation and other scientific requirements. These revised/new templates will be made available on the EMEA website in October 2009 and will come into use by the end of the year.
- preliminary recommendations based on Member-State experiences regarding best practices for handling risk management plans. It is foreseen that the guidance for CHMP members will be updated together with a revision of the guideline on risk management systems due in 2010;
- information regarding the agenda of the CHMP informal meeting to be held on 1-2 October 2009 in Stockholm under the Swedish presidency. Part of the meeting will be a joint meeting with various Committees such as the Committee for Advanced Therapies (CAT), Paediatric Committee (PDCO) and Committee for Orphan Medicinal Products (COMP) participating;
- the publication of the Joint Technical Report from the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency: 'The bacterial challenge - time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and development of new antibacterial agents.'

PROCEDURAL ANNOUNCEMENT

Summary of Product Characteristics (SmPC) revision

The revision 2 of the guidance document on Summary of Product Characteristics (SmPC) was published in Notice to Applicants, Volume 2C, on 21 September 2009. It will apply as from 1 May 2010, but submissions in accordance with the updated guidance will also be possible prior to that date.
The document can be found here.

Centralised procedure (CP) product-related e-mails – New requirements for applicants, marketing authorisation holders (MAHs) and National Competent Authorities (NCAs)

As of 15th of October, all Active CP product-related e-mails and Eudralink messages sent to an EMEA addressee should also be sent in "**Cc.**" to the corresponding product e-mail address.
Please take note that e-mail addresses and related guidance will be provided to relevant parties.
For further information, please liaise directly with the relevant EMEA Product Team Leader (PTL).

Important note: this product e-mail address should only be used in the "**Cc**" field. Failure to do so will result in an automatic error message informing the sender that delivery has failed.

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

ANNEX 1 TO CHMP MONTHLY REPORT SEPTEMBER 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	18	4	0	37	7	2	5	73	871
Positive opinions	19	10	0	44	11	3	5	92	585
Negative opinions[2]	0	2	0	0	2	0	1	5	26
Withdrawals prior to opinion	3	0	0	1	3	2	2	11	150
Marketing authorisation granted by the Commission	13	10	0	21	8	3	8	63	548

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)	1	14
VAMF	0	0

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

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

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Chemical	N/A	N/A	N/A
Biological	N/A	N/A	N/A

ANNEX 2 TO CHMP MONTHLY REPORT SEPTEMBER 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)	876	72458
Type II Variations (positive opinions)	838	5381
Type II Variations (negative opinions)	2	18
Annex II Applications (positive opinions)	44	227
Annual Re-assessments (positive opinions)	14	-
Opinions for renewals of conditional MA's (positive opinions)	3	9
5-year Renewals (positive opinions)	48	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
19 Extension of indication	19 Positive opinions
69 SPC changes	69 Positive opinions
69 Quality changes	69 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Atriance (nelarabine), Glaxo Group Limited	Positive Opinion	The marketing authorisation remains under exceptional circumstances.
Velcade (bortezomib), Janssen-Cilag International NV	Positive Opinion	The marketing authorisation remains under exceptional circumstances.
Aldurazyme (laronidase), Genzyme Europe B.V	Positive Opinion	The marketing authorisation remains under exceptional circumstances
Xigris (drotrecogin alfa (activated)), Eli Lilly Nederland B.V.	Positive Opinion	The marketing authorisation's exceptional circumstances are being lifted

Opinion for renewals of conditional MA's		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Diacomit (stiripentol), Laboratoires Biocodex	Positive Opinion adopted	N/A

Opinions for 5-Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Fendrix (hepatitis b (rdna) vaccine (adjuvanted, adsorbed)), GlaxoSmithKline Biologicals S.A	Positive Opinion adopted	Recommending additional renewal
Kivexa (abacavir / lamivudine), Glaxo Group Ltd.	Positive Opinion adopted	Recommending additional renewal
Enbrel (etanercept), Wyeth Europa Ltd	Positive Opinion adopted	Unlimited validity
Renagel (sevelamer), Genzyme Europe B.V.	Positive Opinion adopted	Unlimited validity

ANNEX 3 TO CHMP MONTHLY REPORT SEPTEMBER 2009

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

Invented Name	Samsca
INN	tolvaptan
Marketing Authorisation Holder	Otsuka Pharmaceutical Europe Ltd.
Proposed ATC code	C03XA01
Indication	Treatment of adult patients with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH).
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	03.08.2009

Invented Name	Javlor
INN	vinflunine ditartrate
Marketing Authorisation Holder	Pierre Fabre Médicament
Proposed ATC code	L01CA05
Indication	Treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Cayston
INN	aztreonam
Marketing Authorisation Holder	Gilead Sciences International Ltd.
Proposed ATC code	J01DF01
Indication	Cayston is indicated for the suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis (CF) aged 18 years and older.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Mozobil
INN	plerixafor
Marketing Authorisation Holder	Genzyme Europe B.V.
Proposed ATC code	L03AX16
Indication	Mozobil is indicated in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma whose cells mobilise poorly.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	31.07.2009

Invented Name	Topotecan Actavis
INN	topotecan
Marketing Authorisation Holder	Actavis Group PTC ehf
Proposed ATC code	L01XX17
Indication	Topotecan monotherapy is indicated for the treatment of patients with relapsed small cell lung cancer [SCLC] for whom re-treatment with the first-line regimen is not considered appropriate. Topotecan in combination with cisplatin is indicated for patients with carcinoma of the cervix recurrent after radiotherapy and for patients with Stage IVB disease. Patients with prior exposure to cisplatin require a sustained treatment free interval to justify treatment with the combination.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	24.07.2009

Invented Name	Afinitor
INN	everolimus
Marketing Authorisation Holder	Novartis Europharm Ltd.
Proposed ATC code	L01XE10
Indication	Afinitor is indicated for the treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	03.08.2009

Invented Name	Clopidogrel Teva
INN	clopidogrel
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. • Patients suffering from acute coronary syndrome: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA). - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Clopidogrel 1A Pharma
INN	clopidogrel
Marketing Authorisation Holder	Acino Pharma GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. • Patients suffering from acute coronary syndrome: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA). - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Grepid
INN	clopidogrel
Marketing Authorisation Holder	Pharmathen S.A.
Proposed ATC code	B01AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	28.07.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Topotecan Teva
INN	topotecan
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	L01XX17
Indication	Topotecan monotherapy is indicated for the treatment of: • patients with metastatic carcinoma of the ovary after failure of first line or subsequent therapy. • patients with relapsed small cell lung cancer [SCLC] for whom re-treatment with the first-line regimen is not considered appropriate (see section 5.1). Topotecan in combination with cisplatin is indicated for patients with carcinoma of the cervix recurrent after radiotherapy and for patients with Stage IVB disease. Patients with prior exposure to cisplatin require a sustained treatment free interval to justify treatment with the combination.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Vizarsin
INN	sildenafil
Marketing Authorisation Holder	KRKA, d.d., Novo mesto
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. In order for Vizarsin to be effective, sexual stimulation is required.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Clopidogrel Dura
INN	clopidogrel
Marketing Authorisation Holder	Mylan dura GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Clopidogrel HCS
INN	clopidogrel
Marketing Authorisation Holder	HCS bvba
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Clopidogrel Mylan
INN	clopidogrel
Marketing Authorisation Holder	Mylan S.A.S.
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Zopya
INN	clopidogrel
Marketing Authorisation Holder	Norpharm Regulatory Services Ltd
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Zylagren
INN	clopidogrel
Marketing Authorisation Holder	KRKA, d.d., Novo mesto
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Clopidogrel Hexal
INN	clopidogrel
Marketing Authorisation Holder	Acino Pharma GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. • Patients suffering from acute coronary syndrome: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA). - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Clopidogrel Ratiopharm
INN	clopidogrel
Marketing Authorisation Holder	Acino Pharma GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. • Patients suffering from acute coronary syndrome: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA). - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Clopidogrel Acino
INN	clopidogrel
Marketing Authorisation Holder	Acino Pharma GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. • Patients suffering from acute coronary syndrome: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA). - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.
CHMP Opinion date	29.05.2009
Marketing Authorisation Date	28.07.2009

Invented Name	Clopidogrel Sandoz
INN	clopidogrel
Marketing Authorisation Holder	Acino Pharma GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

Invented Name	Clopidogrel Acino Pharma GmbH
INN	clopidogrel
Marketing Authorisation Holder	Acino Pharma GmbH
Proposed ATC code	BO1AC04
Indication	Clopidogrel is indicated in adults for the prevention of atherothrombotic events in: • Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
CHMP Opinion date	25.06.2009
Marketing Authorisation Date	21.09.2009

ANNEX 4 TO CHMP MONTHLY REPORT SEPTEMBER 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	47	52	30	36	27	28	43	47	39	38			186	201
Justification for retention of invented name *	5	1	3	1	2	1	2	6	2	1			14	10

*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			393	241
Criterion - Safety concerns														
Similarity with other Invented name	100	56	67	36	51	39	68	39	56	32			342	202
Conveys misleading therapeutic/pharmaceutical connotations	6	0	1	1	0	0	0	1	0	0			7	2
Misleading with respect to composition	0	0	3	0	0	2	0	2	0	1			3	5
Criterion - INN concerns														
Similarity with INN	2	3	1	1	1	4	2	2	2	2			8	12
Inclusion of INN stem	3	0	0	1	0	1	1	0	0	0			4	2
Criterion - Other public health concerns														
Unacceptable qualifiers	4	1	0	1	0	0	1	0	3	4			8	6
Conveys a promotional message	1	0	5	0	0	0	3	1	0	4			9	5
Appears offensive or has a bad connotation	1	1	0	0	1	0	0	0	1	0			3	1
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			9	6
Similarity between name of prodrug and related active substance	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 5 TO CHMP MONTHLY REPORT SEPTEMBER 2009

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

	1995 - 2008	2009	Overall Total
Scientific Advice	887	**174**	**1061**
Follow-up to Scientific Advice	171	**35**	**206**
Protocol Assistance	198	**31**	**229**
Follow-up to Protocol Assistance	90	**12**	**102**
	1346	**252**	**1598**

OUTCOME OF THE SEPTEMBER 2009 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				
Biological	Treatment of Fabry Disease.			x				x	
Chemical	Treatment of constipation-predominant Irritable Bowel Syndrome.			x				x	
Chemical	Treatment to improve glycaemic control.	x					x	x	
Chemical	Treatment of Hepatocellular Carcinoma.		x				x	x	
Biological	Treatment of Rheumatoid Arthritis.			x				x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharma ceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Advanced Therapy	Prevention of acute graft vs host disease and acceleration of immune reconstitution following allogeneic stem cell transplantation.				x	x	x		
Chemical	Treatment of Secondary Acute Myeloid Leukaemia.		x					x	x
Biological	Treatment of peritoneal carcinomatosis due to gastric cancer.		x				x	x	x
Chemical	Treatment of Acute Myeloid Leukaemia.		x					x	
Chemical	Treatment of several solid tumours	x					x	x	
Biological	Treatment of inflammatory diseases.	x				x	x		
Chemical	Treatment of melanoma.	x						x	
Biological	Treatment of colorectal carcinoma.	x					x	x	
Chemical	Treatment of non small cell lung cancer.	x					x	x	
Chemical	Treatment of melanoma.	x				x			
Biological	Treatment of non muscle-invasive transitional cell carcinoma of the bladder.	x						x	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Treatment of neutropenia.	x						x	
Chemical	Prevention of stroke/systemic embolic events.	x						x	
Biological	Treatment of acute haemorrhages.	x				x	x	x	
Biological	Tissue sealing and suture support in surgical procedures.	x					x	x	
Biological	Treatment in surgery for improvement of haemostasis ad suture support.	x				x	x	x	
Chemical	Treatment of chronic heart failure.			x				x	
Chemical	Treatment of acute coronary syndrome.	x					x	x	
Chemical	Treatment of pneumonia.	x					x	x	
Chemical	Treatment of chronic hepatitis C infection.	x					x	x	
Chemical	Treatment of chronic pulmonary infection due to pseudomonas aeruginosa in cystic fibrosis.		x				x	x	x
Biological	Prevention of herpes zoster and post-herpetic neuralgia.			x				x	
Chemical	Hormonal contraception.	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 localised postoperative pain.			x		x	x	x	
Chemical	Treatment of insomnia.	x					x	x	
Chemical	Treatment of Alzheimer Disease.	x						x	
Chemical	Treatment of schizophrenia.	x						x	
Chemical	Treatment of asthma and chronic obstructive pulmonary diseases.	x				x		x	
Chemical/ Biological	Treatment of sinusitis.	x						x	
Other innovative	Treatment of dry eye.			x			x		
Other innovative	Treatment of dry eye.	x				x			
Biological	Treatment of osteoporosis.	x				x	x	x	
Advanced Therapy	Treatment of chondral defects up to 10 cm².			x				x	
Chemical	Characterization of lymph nodes visualised with magnetic resonance imaging.			x				x	
Chemical	Treatment of Gaucher disease type 1.		x					x	x
Biological	Treatment of birch pollen allergic rhinitis and/or conjunctivitis.	x				x			

SA: Scientific Advice

PA: Protocol Assistance

The above-mentioned 25 Scientific Advice letters, 6 Protocol Assistance letters, 9 Follow-up Scientific Advice and 1 Follow-up Protocol Assistance letters were adopted at the 21-24 September 2009 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 39 new Requests for which the procedure started at the SAWP meeting held on 1-4 September 2009. The new requests are divided as follows: 26 Initial Scientific Advice, 7 Follow-up Scientific Advice, 2 Initial Protocol Assistance and 4 Follow-up Protocol Assistance.

ANNEX 6 TO CHMP MONTHLY REPORT SEPTEMBER 2009

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

QUALITY WORKING PARTY (QWP)

Reference number	Document	Status[4]
EMEA/CHMP/CVMP/362268/2009	Concept paper for the Revision of the Guideline on Radiopharmaceuticals based on Monoclonal Antibodies	Adopted for 3 month public consultation

SAFETY WORKING PARTY (SWP)

Reference number	Document	Status[4]
EMEA/545447/2009	Overview of Comments received on the Guideline on Risk Assessment of Medicinal Products on Human Reproductive and Developmental Toxicities: from Data to Labelling	Adopted
EMEA/CHMP/SWP/413709/2009	SWP Work Plan 2010-2011	Adopted

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[4]
EMEA/CHMP/EWP/248088/2009	Draft EWP Work Plan 2010	Adopted
EMEA/CHMP/EWP/484366/2009	Concept Paper on the Need for Revision of Note for Guidance on Clinical Investigation of Medicinal Products in the Treatment of Depression with regards to Treatment Resistant Depression	Adopted for 3 month public consultation

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