European Medicines Agency
Evaluation of Medicines for Human Use

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

The Committee for Medicinal Products for Human Use (CHMP) held its April plenary meeting on 20-23 April 2009.

CENTRALISED PROCEDURE

Initial applications for marketing authorisation

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

New medicinal products

- **Instanyl** (fentanyl citrate), from Nycomed Danmark ApS, indicated as a nasal spray for the treatment of breakthrough pain in cancer patients who receive chronic opioid treatment for the management of their background pain. EMEA review began on 2 December 2007, with an active review time of 205 days.
- **Iressa** (gefitinib), from AstraZeneca AB, indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with activating mutations of EGFR-TK. EMEA review began on 28 May 2008, with an active review time of 210 days.
- **Nymusa** (caffeine citrate), from Chiesi Farmaceutici SpA, indicated for the treatment of primary apnoea in premature newborns. EMEA review began on 28 May 2008, with an active review time of 204 days. Nymusa is the **54th orphan medicine** to receive a positive opinion from the CHMP.
- **Victoza** (liraglutide), from Novo Nordisk A/S, indicated for the treatment of type-2 diabetes mellitus. EMEA review began on 25 June 2008, with an active review time of 204 days.

Generic medicinal products

- **Repaglinide Teva** (repaglinide), from Teva Pharma B.V., indicated for the treatment of type-2 diabetes mellitus. The reference medicine for Repaglinide Teva is NovoNorm, which is already authorised in the European Union in the indication applied for. EMEA review began on 24 September 2008, with an active review time of 177 days.
- **Ribavirin Teva Pharma BV** (ribavirin), from Teva Pharma B.V., indicated for the treatment of chronic hepatitis C. The reference medicine for Ribavirin Teva Pharma BV is Rebetol, which is already authorised in the European Union in the indication applied for. EMEA review began on 24 September 2008, with an active review time of 177 days.

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.

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

The EMEA has been formally requested by Gilead Sciences International Ltd to re-examine the negative opinion adopted during the CHMP meeting on 16–19 March 2009 on **Cayston** (aztreonam lysine), intended for use in the management of adult cystic fibrosis patients with chronic airway infection caused by *Pseudomonas aeruginosa* bacteria, to improve their pulmonary function and respiratory symptoms.

Withdrawals

The EMEA has been formally notified by Teva Pharma B.V. of its decision to withdraw its application for a centralised marketing authorisation for **Clopidogrel Teva Pharma** (clopidogrel hydrobromide) 75 mg film-coated tablets. Clopidogrel Teva Pharma was developed as a generic medicine to be used for the prevention of atherothrombotic events in patients who have myocardial infarction, ischaemic stroke or established peripheral arterial disease. The reference medicine for Clopidogrel Teva Pharma is Plavix (clopidogrel hydrogensuphate), which has been authorised in the European Union since July 1998. A separate press release document with more information is available and a question-and-answer document will be available after the May 2009 CHMP plenary meeting.

The question-and-answer document on the withdrawal of application for **Ixempra** (ixebepilone), which was originally announced in the March CHMP monthly report, is now available on the EMEA website.

Post-authorisation procedures

Extensions of indication and other recommendations

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

- **Aptivus (**tipranavir), from Boehringer Ingelheim, to extend the indication to the treatment of human immunodeficiency virus (HIV-1) infection in highly pre-treated adolescents with virus resistant to multiple protease inhibitors above the age of 12 years, and also to extend the indication in highly pre-treated children aged 2 to 12 years. The latter indication comes with a new oral solution formulation. Aptivus is currently indicated for combination antiretroviral treatment of HIV-1 infection in highly pre-treated adult patients with virus resistant to multiple protease inhibitors.
- **Prezista (**darunavir), from Tibotec, to extend the indication to include the treatment of human immunodeficiency virus (HIV-1) infection in treatment-experienced children and adolescents above the age of 6. This indication also comes with the new strengths 75mg and 150mg film-coated tablets. Prezista is currently indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in treatment-experienced adult patients.
- **Janumet**, **Efficib** and **Velmetia** (sitagliptin phosphate monohydrate / metformin hydrochloride), and **Januvia**, **Tesavel** and **Xelevia** (sitagliptin), from Merck Sharp & Dohme Ltd, to extend the indication of these medicines to use in combination with a PPARγ agonist and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. Janumet, Efficib and Velmetia are currently authorised for the treatment of type-2 diabetes mellitus, as an adjunct to diet and exercise, to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of metformin. Additionally, they are also indicated as triple combination with a sulphonylurea in patients inadequately controlled on their maximal tolerated dose of metformin and sulphonylurea. Januvia, Tesavel and Xelevia are currently authorised for the treatment of type-2 diabetes mellitus, in combination with metformin, in combination with a sulphonylurea, in combination with a PPARγ agonist or in triple combination with a sulphonylurea and metformin, as an adjunct to diet and exercise, to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of the previously mentioned agents.
- **Aclasta** (zoledronic acid) from Novartis, to extend the indication to include treatment of osteoporosis associated with long-term systemic glucocorticoid therapy in post-menopausal women and in men at increased risk of fracture. Aclasta is currently indicated in the treatment of osteoporosis
  - in post-menopausal women

- in men

at increased risk of fracture, including those with a recent low-trauma hip fracture.
Aclasta is also currently indicated in treatment of Paget's disease of the bone.

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.

The Committee adopted a **negative opinion**, recommending the refusal of an extension of the indication to the treatment of fibromyalgia in adults experiencing moderate to severe pain, for **Lyrica** (pregabalin), from Pfizer Ltd. Lyrica is currently authorised for the treatment of neuropathic pain, epilepsy and generalised anxiety disorder in adults. A question-and-answer document with more information on the negative opinion can be found here

Addition of warning

The CHMP adopted an amendment to update sections 4.4 and 4.5 of the Summary of Product Characteristics (SPC) for **Doribax** (doripenem) from Janssen-Cilag International NV, with information on the interaction between Doribax and valproic acid as a result of a drug-drug interaction study in healthy human volunteers. The results of this clinical study showed that co-administration of doripenem and valproic acid significantly reduces serum valproic acid levels below the therapeutic range. The lowered valproic acid levels can then lead to inadequate seizure control. The Package Leaflet has been updated accordingly. The interaction is believed to be a class effect for carbapenems. Therefore, the CHMP proposed the initiation of a class review on the interaction between carbapenems and valproate and agreed to make a request to the PhVWP, asking them to consider this issue.

Other information

The CHMP adopted several amendments to update sections 4.4 and 4.8 of the SPC for **Tarceva** (erlotinib) from Roche Registration Ltd, with information concerning the risk of the association of Tarceva with gastrointestinal perforation, as well as very rare cases suggestive of Stevens-Johnson syndrome and very rare cases of corneal perforation or ulceration. The CHMP agreed on the text for a Direct Healthcare Professional Communication (DHPC) to be distributed by the marketing authorisation holder (MAH) to inform healthcare professionals that patients receiving Tarceva are at increased risk of developing gastrointestinal perforations. In addition, patients receiving concomitant anti-angiogenic agents, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) or taxane-based chemotherapy, or who have a prior history of peptic ulceration or diverticular disease are at increased risk. Tarceva should be permanently discontinued in patients who develop gastrointestinal perforation. Finally bullous, blistering and exfoliative skin conditions including very rare cases (less than 1 per 10,000 patients) suggestive of Stevens-Johnson syndrome/toxic epidermal necrolysis have been reported. The product information was revised accordingly.

The CHMP introduced new warnings in the product information of **Enbrel** (etanercept) from Wyeth Europa Ltd to include information on the occurrence of non-melanoma skin cancer, which may be causally related to etanercept therapy and recommending that Enbrel not be used in patients for the treatment of alcoholic hepatitis. This followed a review of data from a pooled analysis of clinical trials, findings from published epidemiological studies and information from the MAH's pharmacovigilance database.

The MAH, Roche Registration Ltd, agreed with the CHMP on a DHPC informing healthcare professionals that cases of pure red cell aplasia (PRCA) have been reported in patients treated with **CellCept** (mycophenolate mofetil). Physicians should consider dose reduction or discontinuation of CellCept in patients who develop PRCA. Furthermore, the CHMP agreed to update sections 4.4 and 4.8 of the SPC with further information and recommendations on PRCA. The MAHs of the generic products of CellCept will be requested to update their product information accordingly.

Abacavir and the risk of heart attack

Finalising a review of recent data on the risk of heart attack (myocardial infarction) associated with the use of abacavir in HIV-infected patients, the CHMP concluded that there is insufficient evidence to recommend changes to the therapeutic management of patients. This followed the Committee's review of findings from the D:A:D study in April 2008, which concluded that further data were needed to determine this risk.
Data from observational studies that had become available since April 2008, including the French Hospital Database on HIV, continued to show a possible link between myocardial infarction and the use of abacavir. Data from clinical trials showed low numbers of myocardial infarction and could not exclude a small increase in risk.
However, the CHMP concluded that there were inconsistencies between the different studies' findings, and that a causal relationship between treatment with abacavir and the risk of myocardial infarction could neither be confirmed nor refuted. To date, there is no established biological mechanism that could explain a potential increase in risk.
Nevertheless, when prescribing abacavir-containing medicines, prescribers should take action to minimise modifiable risk factors, such as smoking, high blood pressure and high blood-fat levels. The product information for abacavir-containing medicines will be updated to reflect this information.
Abacavir is a nucleoside reverse transcriptase inhibitor (NRTI) indicated in antiretroviral combination therapy for the treatment of HIV infection. In the European Union, it is available as Ziagen, in combination with lamivudine as Kivexa, and in combination with lamivudine and zidovudine as Trizivir.

The press release 'Further data needed to determine risk of heart attack with abacavir', from April 2008, is available here.

OTHER INFORMATION ON THE CENTRALISED PROCEDURE

Lists of Questions

The Committee adopted twelve Lists of Questions on initial applications (including four under the mandatory scope and eight under the optional scope).

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 March 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 March 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

Referral procedures concluded

The CHMP concluded two referral procedures under Article 29 of Directive 2001/83/EC, as amended. 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 medicinal products concerned are:

- **Ciclosporin IDL and associated names** (ciclosporin), 25mg, 50mg and 100mg capsules, from International Drug Licensing, used as an immunosuppressant drug. The procedure was initiated as a result of disagreements between some Member States regarding the bioequivalence of this medicine with the reference medicine. The CHMP concluded that the data and the justification presented were not adequate to confirm the bioequivalence. The CHMP recommended by majority the refusal of the marketing authorisation in the concerned Member States, and the suspension of the marketing authorisation for Ciclosporin IDL in the Member States where the medicine is currently authorised.
- **Prokanazol and associated names** (itraconazole), 100 mg hard capsules, from PRO.MED.CS Praha a.s., intended for the treatment of certain fungal infections. The procedure was initiated because of concerns by some Member States over bioequivalence of the medicine with the reference medicine. The CHMP concluded by consensus that bioequivalence with the reference medicine has not been demonstrated. The CHMP recommended the refusal of the marketing authorisations in the concerned Member States, and the suspension of the marketing authorisation in the Member States where the product is currently authorised.

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

Referral procedures started

The CHMP started a referral procedure under Article **31** of Regulation (EC) 83/2001, as amended for **valproate-containing medicines**, on the request of the Netherlands, because of concerns related to the efficacy of these medicines when used in the treatment of manic episodes in patients with bipolar disorder

The CHMP started a referral procedure under Article 29 of Directive 2001/83/EC, as amended for **WinRho SDF** (Human anti-D immunoglobulin), 1500U and 5000U powder for solution for injection/infusion from Cangene Europe Ltd, used to increase patients' platelet counts. The procedure was initiated because of disagreements regarding safety and efficacy.

The CHMP started a referral procedure under Article 30 of Directive 2001/83/EC as amended for **Fortum and associated names** (ceftazidime), from GSK group of companies and associated companies, used as an antibiotic. This type of procedure was initiated with a view to harmonising product information for medicinal products authorised at Member State level.

MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES - HUMAN

The CHMP noted the report from the 39th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 20-21 April 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 March and 1 April 2009. For further details, please see **Annex 6**.

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

UPCOMING MEETINGS FOLLOWING THE APRIL 2009 CHMP PLENARY MEETING

- The 55th meeting of the CHMP will be held at the EMEA on 26-29 May 2009.
- The next Name Review Group meeting will be held at the EMEA on 12 May 2009.
- The 40th CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the EMEA on 26-27 May 2009.

ORGANISATIONAL MATTERS

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

- Discussion regarding advice from the European Commission on the status of medicinal products subject to prescription or not, providing further clarification on the applicability of non-prescription status.
- A report on patients', consumers' and healthcare professionals' expectations in term of information on benefits and risks of medicines based on a recent survey carried out with the Patients' and Consumers' Working Party and the Healthcare Professionals' working group. It relates to information on benefits and risks presented in the Summary of Product Characteristics, Package Leaflet, Public Assessment report and safety announcements. Further developments on this topic are expected in the near future.
- Discussion on the experience obtained following recent suspensions and withdrawals of marketing authorisations for centrally authorised products.
- Discussion on the current EMEA handling of conflicts of interest of Committee members and experts in the light of 2006-2008 experience.
- Update regarding the business pipeline activity and forecast of MAAs through the Centralised Procedure.
- A presentation regarding the report on nanomedicine activities for 2009-2010. The Committee agreed to set up a temporary ad-hoc expert group to work in this field.
- The revision of the Letter of Undertaking template and a new template for the cover letter for the MAH when submitting post-authorisation measure-related data. The documents will be published shortly on the EMEA website.
- The appointment of Dr Gopalan Narayanan as an additional member to the SAWP. Dr Gopalan Narayanan is also a member of the Committee for Advanced Therapies (CAT).

PROCEDURAL ANNOUNCEMENT

Update of User guide regarding generation of PDF versions of the Product Information

The "User guide on how to generate PDF versions of the Product Information" (http://www.emea.europa.eu/htms/human/qrd/docs/52402007en.pdf) has been updated to implement major changes to the “File naming convention to be used for the generated PDF files” (p8). These changes were introduced to comply with the ICH eCTD file naming convention. Applicants should use the new file naming convention when submitting PDF versions of the Product Information.

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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 APRIL 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	4	2	0	16	2	1	3	28	798
Positive opinions	5	9	0	5	3	1	1	24	517
Negative opinions[1]	1	0	0	0	2	0	1	4	25
Withdrawals prior to opinion	0	0	0	1	1	2	1	5	144
Marketing authorisation granted by the Commission	9	2	0	2	8	1	4	26	511

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	2009	1995 onwards
Compassionate use applications	0	0
Art. 58 applications	0	4
Consultation for medical devices[2]	1	6
PMF (Click here for a list of PMF certifications)	0	13
VAMF	0	0

[1] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[2] 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 APRIL 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 APRIL 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)	345	6714
Type II Variations (positive opinions)	355	4898
Type II Variations (negative opinions)	1	17
Annex II Applications (positive opinions)	29	212
Annual Re-assessments (positive opinions)	7	-
Opinions for renewals of conditional MA's (positive opinions)	1	7
5-year Renewals (positive opinions)	29	-

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
3 Extension of indication	2 Positive opinions 1 Negative opinion
47 SPC changes	47 Positive opinions
44 Quality changes	44 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Yondelis (ecteinascidin) PharmaMar S.A	Positive Opinion adopted	The marketing authorisation remains under exceptional circumstances.
Naglazyme (galsulfase) BioMarin Pharmaceutical Inc	Positive Opinion adopted	The marketing authorisation remains under exceptional circumstances.
Prialt (ziconotide) Eisai Ltd	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**
N/A	**N/A**	**N/A**

Opinions for 5-Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Arava (leflunomide) sanofi-aventis Deutschland GmbH	Positive Opinion adopted	Unlimited validity
Ariclaim (duloxetine) Eli Lilly Nederland B.V	Positive Opinion adopted	Unlimited validity
Cymbalta (duloxetine hydrochloride) Eli Lilly Nederland B.V	Positive Opinion adopted	Unlimited validity
Xeristar (duloxetine hydrochloride) Boehringer Ingelheim International GmbH	Positive Opinion adopted	Unlimited validity
Erbitux (cetuximab) Merck KGaA	Positive Opinion adopted	Unlimited validity
Paxene (paclitaxel) Norton Healthcare Ltd	Positive Opinion adopted	Unlimited validity
Remicade (infliximab) Centocor BV	Positive Opinion adopted	Unlimited validity
Yentreve (duloxetine hydrochloride) Eli Lilly Nederland B.	Positive Opinion adopted	Unlimited validity
Integrilin (eptifibatide) Glaxo Group Limited	Positive Opinion adopted	Unlimited validity
Angiox (bivalirudin) The Medicines Company UK	Positive Opinion adopted	Recommending additional renewal

ANNEX 3 TO CHMP MONTHLY REPORT APRIL 2009

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

Invented Name	CONBRIZA
INN	bazedoxifene
Marketing Authorisation Holder	Wyeth Europa Ltd
Proposed ATC code	G03XC02
Indication	CONBRIZA is indicated for the treatment of postmenopausal osteoporosis in women at increased risk of fracture. A significant reduction in the incidence of vertebral fractures has been demonstrated; efficacy on hip fractures has not been established. When determining the choice of CONBRIZA or other therapies, including oestrogens, for an individual postmenopausal woman, consideration should be given to menopausal symptoms, effects on uterine and breast tissues, and cardiovascular risks and benefits.
CHMP Opinion date	19.02.2009
Marketing Authorisation Date	17.04.2009

Invented Name	IXIARO
INN	Japanese encephalitis vaccine (inactivated, adsorbed)
Marketing Authorisation Holder	Intercell AG
Proposed ATC code	J07BA02
Indication	IXIARO is indicated for active immunization against Japanese encephalitis for adults. IXIARO should be considered for use in individuals at risk of exposure through travel or in the course of their occupation
CHMP Opinion date	18.12.2008
Marketing Authorisation Date	31.03.2009

Invented Name	Removab
INN	catumaxomab
Marketing Authorisation Holder	Fresenius Biotech GmbH
Proposed ATC code	L01XC09
Indication	Removab is indicated for the intraperitoneal treatment of malignant ascites in patients with EpCAM-positive carcinomas where standard therapy is not available or no longer feasible.
CHMP Opinion date	19.02.2009
Marketing Authorisation Date	20.04.2009

Invented Name	Synflorix
INN	Pneumococcal polysaccharide conjugate vaccine (adsorbed)
Marketing Authorisation Holder	GlaxoSmithKline Biologicals S.A
Proposed ATC code	J07AL52
Indication	Active immunisation against invasive disease and acute otitis media caused by *Streptococcus pneumoniae* in infants and children from 6 weeks up to 2 years of age. See sections 4.4 and 5.1 for information on protection against specific pneumococcal serotypes. The use of Synflorix should be determined on the basis of official recommendations taking into consideration the impact of invasive disease in different age groups as well as the variability of serotype epidemiology in different geographical areas.
CHMP Opinion date	22.01.2009
Marketing Authorisation Date	30.03.2009

Invented Name	Exalief
INN	eslicarbazepine
Marketing Authorisation Holder	BIAL - Portela & Ca, S.A
Proposed ATC code	N03AF04
Indication	Exalief is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation.
CHMP Opinion date	19.02.2009
Marketing Authorisation Date	21.04.2009

Invented Name	Zebinix
INN	eslicarbazepine
Marketing Authorisation Holder	BIAL - Portela & Ca, S.A
Proposed ATC code	N03AF04
Indication	Zebinix is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation.
CHMP Opinion date	19.02.2009
Marketing Authorisation Date	21.04.2009

Invented Name	Ribavirin Teva
INN	Ribavirin
Marketing Authorisation Holder	Teva Pharma B.V
Proposed ATC code	J05A B04
Indication	Ribavirin Teva is indicated for the treatment of chronic hepatitis C and must only be used as part of a combination regimen with peginterferon alfa-2b (adults) or interferon alfa-2b (adults, children (3-years of age or older), and adolescents). Ribavirin monotherapy must not be used. There is no safety or efficacy information on the use of Ribavirin with other forms of interferon (i.e., not alfa-2b), or on the use of Ribavirin with peginterferon alfa-2b in children or adolescents. Please refer also to the peginterferon alfa-2b or interferon alfa-2b Summary of Product Characteristics (SPC) for prescribing information particular to that product. Naïve patients *Adult patients:* Ribavirin Teva is indicated, in combination with interferon alfa-2b, for the treatment of adult patients with chronic hepatitis C, not previously treated, without liver decompensation, with elevated alanine aminotransferase (ALT), who are positive for serum HCV-RNA (see section 4.4). Additionally, Ribavirin Teva is indicated, in combination with peginterferon alfa-2b, for the treatment of adult patients with chronic hepatitis C, not previously treated, without liver decompensation, with elevated alanine aminotransferase (ALT), who are positive for serum HCV-RNA, including patients with clinically stable HIV co-infection (see section 4.4). *Children and adolescents*: Ribavirin Teva is intended for use, in a combination regimen with interferon alfa2b, for the treatment of children and adolescents 3 years of age and older, who have chronic hepatitis C, not previously treated, without liver decompensation, and who are positive for serum HCV-RNA. The decision to treat should be made on a case by case basis, taking into account any evidence of disease progression such as hepatic inflammation and fibrosis, as well as prognostic factors for response, HCV genotype and viral load. The expected benefit of treatment should be weighed against the safety findings observed for paediatric subjects in the clinical trials (see sections 4.4, 4.8 and 5.1). Previous treatment failure patients *Adult patients:* Ribavirin Teva is indicated, in combination with interferon alfa-2b, for the treatment of adult patients with chronic hepatitis C who have previously responded (with normalisation of ALT at the end of treatment) to interferon alpha monotherapy but who have subsequently relapsed. Additionally, Ribavirin Teva is indicated, in combination with peginterferon alfa-2b, for the treatment of adult patients with chronic hepatitis C who have failed previous treatment with interferon alpha (pegylated or nonpegylated) and ribavirin combination therapy or interferon alpha monotherapy (see section 5.1).
CHMP Opinion date	22.01.2009
Marketing Authorisation Date	31.03.2009

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

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
Ethyl eicosopentaenoate	Amarin Neuroscience Ltd. UK	EU/3/00/013	treatment of Huntington's disease
Pazopanib hydrochloride	Glaxo Group Limited UK	EU/3/06/382	treatment of renal cell carcinoma

ANNEX 5 TO CHMP MONTHLY REPORT APRIL 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									77	88
Justification for retention of invented name *	5	1	3	1									8	2

*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									199	105
Criterion - Safety concerns														
Similarity with other Invented name	100	56	67	36									167	92
Conveys misleading therapeutic/pharmaceutical connotations	6	0	1	1									7	1
Misleading with respect to composition	0	0	3	0									3	0
Criterion - INN concerns														
Similarity with INN	2	3	1	1									3	4
Inclusion of INN stem	3	0	0	1									3	1
Criterion - Other public health concerns														
Unacceptable qualifiers	4	1	0	1									4	2
Conveys a promotional message	1	0	5	0									6	0
Appears offensive or has a bad connotation	1	1	0	0									1	1
Similarity between name of individual active substance and fixed combinations and/or between fixed combinations	3	4	2	0									5	4
Similarity between name of prodrug and related active substance	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 APRIL 2009

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

	1995 - 2008	2009	Overall Total
Scientific Advice	887	**65**	952
Follow-up to Scientific Advice	171	**14**	185
Protocol Assistance	198	**11**	209
Follow-up to Protocol Assistance	90	**4**	94
	1346	**94**	1440

OUTCOME OF THE APRIL 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				
Chemical	Treatment of type 2 diabetes mellitus	X					X	X	
Biological	Treatment of type 1 diabetes mellitus	X					X	X	
Chemical	Treatment of Chronic Idiopathic Myelofibrosis.				X	X			
Chemical	Treatment of malignant pleural mesothelioma	X					X	X	
Chemical	Treatment of acute lymphoblastic leukaemia				X		X		
Chemical	Treatment of acute lymphoblastic leukaemia				X		X		
Chemical	Treatment of breast cancer.			X				X	
Biological	Medical Device Qualification			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 metastatic melanoma	X						X	
Chemical	Treatment of bladder cancer	X				X	X	X	
Chemical	Treatment of gastro-entero-pancreatic neuroendocrine tumours		X				X	X	X
Biological	Treatment of anaemia in Chronic Kidney Disease	X					X		
Chemical	Treatment of hypertension	X					X	X	
Chemical	Treatment of onychomycosis	X				X	X	X	
Chemical	Treatment of pneumoniae and acute bacterial exacerbations of chronic obstructive pulmonary disease	X						X	
Biological	Prevention of invasive disease in infants caused by Group B streptococci	X					X	X	
Biological	Immunization against influenza virus strains			X				X	
Chemical	Treatment of chronic hepatitis C			X			X	X	
Biological	Treatment of metachromatic leukodystrophy		X				X	X	
Chemical	Treatment of iron overload due to hereditary hemochromatosis		X					X	X
Biological	Smoking cessation and prevention of relapse in ex-smokers			X			X	X	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 10 Scientific Advice letters, 3 Protocol Assistance letters, 5 Follow-up Scientific Advice and 3 Follow-up Protocol Assistance letters were adopted at the 20-23 April 2009 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 35 new Requests for which the procedure started at the SAWP meeting held on 30 March – 1 April 2009. The new requests are divided as follows: 24 Initial Scientific Advice, 5 Follow-up Scientific Advice, 4 Initial Protocol Assistance and 2 Follow-up Protocol Assistance.

ANNEX 7 TO CHMP MONTHLY REPORT APRIL 2009

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

BIOLOGICS WORKING PARTY (BWP)

Reference number	Document	Status[3]
EMEA/CHMP/BWP/ 133895/2009/Rev 1	Ad-hoc Influenza Working party: EU Strain selection for the influenza vaccines for the season 2009/2010 Revised EU recommendation for the seasonal influenza vaccine composition for the season 2009/2010	Adopted
EMEA/CHMP/BWP/ 452081/2007 EMEA/CHMP/BWP/ 513210/2008	Guideline on the Replacement of Rabbit Pyrogen testing by an Alternative Test for Plasma-derived Medicinal Product Overview of comments	Adopted

BIOSIMILAR WORKING PARTY (BMWP)

Reference number	Document	Status[3]
EMEA/CHMP/BMWP/ 102046/2006	Reflection paper on Non-clinical and Clinical Development of Similar Medicinal Products containing Recombinant Interferon Alfa	Adopted

PHARMACOGENOMICS WORKING PARTY (PgWP)

Reference number	Document	Status[3]
EMEA/CHMP/PGxWP/ 63270/2009	Concept Paper on the Development of a Guideline on the Use of Pharmacogenomic Methodologies in the Pharmacokinetic Evaluation of Medicinal Products	Adopted for 2-month public consultation

EFFICACY WORKING PARTY (EWP)

Reference number	Document	Status[3]
CPMP/EWP/4891/03 EMEA/537007/2008	Guideline on the Clinical Investigation of Medicinal Products for the Treatment of Ankylosing Spondylitis Overview of comments received	Adopted
EMEA/CHMP/EWP/ 30039/2008 EMEA/144962/2009	Guideline on the Clinical Evaluation of Direct Acting Antiviral Agents Intended for Treatment of Chronic Hepatitis C Overview of comments received	Adopted
CPMP/EWP/784/97 Rev. 1	Guideline on Clinical Investigation of Medicinal Products used in the Treatment of Osteoarthritis	Adopted for 6-month public consultation
CPMP/EWP/1776/99 Rev. 1	Guideline on Missing Data in confirmatory trials	Adopted for 6-month public consultation