EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 March 2011
EMA/CHMP/224689/2011

Monthly Report

Committee for Medicinal Products for Human Use (CHMP)

14 – 17 March 2011

Centralised procedure

Initial applications for marketing authorisation

New medicinal products

The Committee adopted four positive opinions by consensus recommending the granting of marketing authorisations for the following new medicines:

- **Eliquis** (apixaban), from Bristol-Myers Squibb/Pfizer EEIG, intended for the prevention of venous thromboembolic events in adult patients who have undergone elective hip or knee replacement surgery. The review for Eliquis began on 24 March 2010 with an active review time of 210 days.
- **Yellox** (bromfenac), from Croma-Pharma GmbH, intended for the treatment of postoperative ocular inflammation following cataract extraction in adults. The review for Yellox began on 22 July 2009 with an active review time of 210 days.
- **Zoely** and **IOA** (nomegestrol acetate/estradiol), from Merck Serono Europe Ltd and N.V. Organon, intended for oral contraception. The review for Zoely began on 19 August 2009 with an active review time of 210 days. The review for IOA began on 23 December 2009 with an active review time of 210 days.

The Committee gave also a positive opinion by consensus for **Cinryze** (C1 inhibitor, human), an orphan medicine from ViroPharma SPRL, intended for the treatment and prevention of angioedema attacks in patients with C1 inhibitor deficiency. The review for Cinryze began on 24 March 2010 with an active review time of 201 days.

However, the CHMP noted that ViroPharma is considered the same applicant as Sanquin, which holds marketing authorisations in some European Union (EU) Member States for a medicine with the same

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composition and pharmaceutical form and overlapping indications with Cinryze. This may preclude the granting of a marketing authorisation for Cinryze.

The summaries of opinion for all medicines, including their full therapeutic indications, can be found here.

Post-authorisation procedures

Positive opinions for extensions of therapeutic indications adopted

The Committee adopted four positive opinions by consensus for applications for extensions of therapeutic indications, adding new treatment options for medicines that are already authorised in the EU, for:

- **Herceptin** (trastuzumab), from Roche Registration Ltd, to include treatment of patients with HER2-positive early breast cancer in combination with adjuvant chemotherapy consisting of paclitaxel or docetaxel following adjuvant chemotherapy with doxorubicin and cyclophosphamide, or consisting of docetaxel and carboplatin.
- **Lucentis** (ranibizumab), from Novartis Europharm Ltd, to include treatment of visual impairment due to macular oedema secondary to retinal vein occlusion.
- **Remicade** (infliximab), from Janssen Biologics B.V., to extend the approved indication for severe Crohn's disease to patients with moderately to severely active disease.
- **Revatio** (sildenafil), an orphan medicine from Pfizer Ltd, to include paediatric patients aged one to 17 years with pulmonary arterial hypertension.

The summaries of opinions for the mentioned medicines, including their full therapeutic indications, can be found here.

Negative opinion for extension of therapeutic indications adopted

The Committee adopted a negative opinion by majority for **Vectibix** (panitumumab), from Amgen Europe B.V., recommending that the current indication should not be extended to include the use of panitumumab in combination with chemotherapy in patients with wild-type *KRAS* metastatic carcinoma of the colon or rectum.

More information about the reasons for this negative opinion is available in a separate question-and-answer document which can be found here.

Additional safety information

The CHMP adopted a positive opinion by consensus recommending a variation to the terms of the marketing authorisation for the medicinal product **Telzir** (fosamprenavir) from ViiV Healthcare UK Limited to include contraindications with regard to co-administration with alfuzosin and co-administration with sildenafil used in the treatment of pulmonary arterial hypertension, due to pharmacokinetic interactions. In addition, a warning regarding co-administration with PDE5 inhibitors used in the treatment of erectile dysfunction has been included in the product information.

The Committee recommended by consensus an update to the contraindications of **Xyrem** (sodium oxybate), from UCB Pharma Ltd, following review of safety information obtained during the studies conducted in fibromyalgia patients. The new contraindication is for patients with major depression. In this update, the Committee considered that the benefit-risk balance of Xyrem in fibromyalgia patients

was negative. The Committee also recommended update of other sections of the Summary of Product Characteristics (SmPC) as a result of this variation. These included an update in the warnings related to respiratory depression, abuse potential and dependence recommending close monitoring of patients with a BMI ≥40 kg/m2 because of higher risk of sleep apnoea and that prior to treatment, physicians should evaluate patients for a history of or susceptibility to drug abuse. Patients should be routinely monitored and in the case of suspected abuse, treatment with sodium oxybate should be discontinued. The warning related to neuropsychiatric events was also updated to include anxiety as possible events. Xyrem is currently authorised for the treatment of narcolepsy with catalepsy in adult patients.

The summary of opinion for the mentioned medicine can be found here.

The CHMP recommended by consensus to update section 4.8 of the SmPC of **Efient** (prasugrel) from Eli Lilly Nederland B.V. to include hypersensitivity including angioedema, thrombotic thrombocytopaenic purpura and thrombocytopaenia. Section 4.4 of the SmPC was updated additionally to include a warning of hypersensitivity reactions including angioedema reported in patients receiving prasugrel, including in patients with a history of hypersensitivity reaction to clopidogrel. Therefore, monitoring for signs of hypersensitivity in patients with a known allergy to thienopyridines is advised. The Committee agreed on a Direct Healthcare Professional Communication (DHPC).

The CHMP adopted by consensus an update of sections 4.2, 4.4 and 5.2 of the SmPC of **Votrient** (pazopanib) from Glaxo Group Ltd to include information regarding dosing recommendations and warnings for patients with mild hepatic impairment further to the assessment of new pharmacokinetic data available in this patient population. The new recommendations inform prescribers that patients with mild abnormalities in liver parameters (defined as either normal bilirubin and any degree of alanine aminotransferase (ALT) elevation or as an elevation of bilirubin (> 35 % direct) up to 1.5 x upper limited of normal (ULN) regardless of the ALT value) should be treated initially with 800 mg pazopanib once daily.

The CHMP further adopted a positive opinion by consensus recommending amendments to the product information (PI) for **Vimpat** (lacosamide) from UCB Pharma SA. Information regarding second-degree or higher atrioventricular block, atrial fibrillation and atrial flutter has been added to section 4.4 of the SmPC. Section 4.8 has been updated with addition of the post marketing events of suicide attempt, suicidal ideation, atrial fibrillation, atrial flutter, aggression, agitation, insomnia, psychotic disorder, angioedema and urticaria.

Other information on the centralised procedure

Possible supply shortage of Thyrogen

The Committee has been informed by Genzyme Europe B.V., the marketing authorisation holder for **Thyrogen** (thyrotropin alfa), that due to a manufacturing issue there will be a supply shortage of this medicine until July 2011. Genzyme will only be able to supply Thyrogen to meet approximately 45% of EU demand through to July 2011.

Thyrogen is authorised for the diagnosis and treatment of thyroid tissue remnants post thyroidectomy in patients with thyroid cancer.

The Committee has endorsed a DHPC informing healthcare professionals of the following recommendations:

During the shortage, Thyrogen use should be restricted to those patients who are not able to tolerate thyroid hormone withdrawal, or in whom thyroid hormone withdrawal would not be effective.

Where possible, Thyrogen use for other patients should be delayed until supply of Thyrogen improves. If such delay is not acceptable, the treating physician and patient should consider alternative treatment options.

These are only interim recommendations during the shortage and do not change the currently approved product information for Thyrogen.

Lists of Questions

The Committee adopted thirteen Lists of Questions on initial applications (including two under the mandatory scope and eleven under the optional scope as per Regulation (EC) No. 726/2004), together with two Lists of Questions on "line extension" applications (in accordance with Annex I of Commission Regulation (EC) No. 1234/2008).

Detailed information on the centralised procedure

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

Applications for marketing authorisation for orphan medicinal products

Details of those orphan medicinal products that have been subject of a centralised application for marketing authorisation since the February 2011 CHMP plenary meeting are provided in **Annex 3**.

Referral procedures

Review of pioglitazone-containing medicines started

The Committee has begun looking at the benefit-risk balance of the antidiabetic **pioglitazone-containing medicines**[1], from Takeda Global Research and Development Centre (Europe) Ltd, to further explore the signal of a possible increased risk of bladder cancer with pioglitazone.

The risk of bladder cancer in association with pioglitazone has been under close review by the Committee since the granting of the first marketing authorisation in 2000. Takeda is conducting a number of post-authorisation studies, including a ten-year epidemiological study aimed at identifying incident malignancies associated with pioglitazone treatment in a cohort of diabetic patients.

The three interim study reports have so far not confirmed a clear association between the use of pioglitazone and the occurrence of bladder cancer.

However, prompted by an increased number of spontaneous reports of bladder cancer, the Committee considered that the accumulated evidence provided also by preclinical studies, epidemiological data and the PROactive trial (a placebo controlled clinical trial) taken in its totality, represents a clinically relevant signal which requires further evaluation.

[1] The review of the centrally authorised pioglitazone-containing medicines Actos, Glustin, Competact, Glubrava and Tandemact and the occurrence of bladder cancer is being conducted in the context of a formal review, initiated at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004, on 16 March 2011.

The Committee will now review all available data thoroughly, including published data, non-clinical and clinical data, post-marketing reports and pharmacoepidemiological studies, and will assess their impact on the balance of risks and benefits of these medicines.

Review of Revlimid started

The Committee has begun looking at the benefit-risk balance of the orphan medicine **Revlimid**[2] (lenalidomide), from Celgene Europe Ltd, following reports indicating that lenalidomide may be associated with an increased risk of second primary malignancies.

Revlimid is authorised in the EU for use in combination with dexamethasone for the treatment of multiple myeloma in patients who have received at least one prior therapy.

This review follows observation of a higher incidence of second primary malignancies in patients treated with lenalidomide in clinical studies conducted outside of the authorised indication.

The Committee will now review all available data thoroughly, including published data, non-clinical and clinical data and post-marketing reports, and will assess their impact on the balance of risks and benefits of this medicine in its authorised indication.

While the review is ongoing, the Committee is not recommending a delay, modification or restriction in the use of lenalidomide for patients treated according to the authorised indication.

Trials currently under way using lenalidomide as an experimental drug are under periodic safety monitoring, and the current review does not affect enrolment/participation of patients in these trials.

Review of Vivaglobin and associated names started

The Committee has begun a review of **Vivaglobin**[3] and associated names (human normal immunoglobin for subcutaneous use), from CSL Behring, following reports indicating that Vivaglobin may be associated with thromboembolic events.

Vivaglobin is a solution for subcutaneous injection that contains the active substance human normal immunoglobulin. It is used to treat primary immunodeficiency syndromes and as replacement therapy for patients with secondary hypogammaglobulinaemia and recurrent infections due to myeloma or chronic lymphatic leukaemia.

Although thromboembolic events are known to occur with intravenous immunoglobulin medicines, they have not previously been linked with subcutaneous immunoglobulins.

The Committee will now review all available data on the manufacturing process of Vivaglobin thoroughly and will assess their impact on the balance of the risks and benefits of the medicine. The review will include the assessment of the root cause of the thromboembolic potential of the medicine

[2] The review of Revlimid and the occurrence of second primary malignancies is being conducted in the context of a formal review, initiated at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004, on 9 March 2011. The review covers the benefit/risk of Revlimid in the authorised indications.
On 30 May 2008, Celgene Europe Ltd notified the Committee that it wished to withdraw its application for a marketing authorisation for lenalidomide, for the treatment of anaemia due to myelodysplastic syndromes. The Committee had given a negative opinion and did not recommend a marketing authorisation for lenalidomide for this indication. The Committee had concerns over the way the pivotal study was carried out. In particular, because the study did not compare the medicine to any other treatment, it was difficult to determine if treatment with lenalidomide increased the risk of progression to acute myeloid leukaemia. More information about this procedure is available on the Agency's website.

[3] The review of Vivaglobin and associated names is being conducted in the context of a formal review, initiated by Germany on 17 March 2011, under Article 36 of Directive 2001/83/EC, as amended. The Committee will make recommendations on whether the marketing authorisations for Vivaglobin should be maintained, changed, suspended or revoked. Vivaglobin and associated names are authorised via the mutual recognition procedure in 20 EU Member States and are marketed by CSL Behring.

and the possible switch to an alternative manufacturing process with appropriate controls to effectively reduce the thromboembolic contaminants in the product.

Review of Novosis Goserelin, Goserelin cell pharm, Novimp and associated names started

The Committee has begun looking at the results of a good clinical practice (GCP) inspection indicating that the clinical studies performed as part of the marketing authorisation applications for **Novosis Goserelin, Goserelin cell pharm, Novimp** and associated names (goserelin)[4], have not been GCP compliant.

Goserelin is used to treat patients with advanced prostate cancer where an endocrine treatment is indicated.

In the light of the GCP results, the marketing authorisations of these medicines have been suspended in the concerned Member States and the medicines have been recalled in Germany and the United Kingdom, the only Members States where these medicines are currently being marketed.

The Committee will now review all available data on the clinical studies performed with these medicines thoroughly and will assess their impact on the quality and reliability of the documentation submitted in support of the marketing authorisation.

Review of Priligy film-coated tablets started

The Committee started a referral procedure[5] for **Priligy** (dapoxetine hydrochloride) 30 mg and 60 mg film-coated tablets, from Janssen Cilag group of companies. The procedure was initiated because of disagreements regarding the benefit-risk ratio for the 60 mg dose.

Arbitration concluded

The Committee completed an arbitration procedure[6] initiated because of disagreement among EU Member States regarding the authorisation of the generic medicine **Canazole** (Clotrimazole Cream 1%), from Pinewood Laboratories Ltd. This medicine is an anti-fungal intended for the treatment of skin infections caused by fungi, such as thrush, ringworm or athlete's foot.

This procedure was initiated because of concerns that therapeutic equivalence of this medicine to the reference product Canesten had not been shown and would need to be proven through a therapeutic equivalence study or other validated model. The Committee concluded that the data provided by the company was neither robust nor extensive enough to warrant waiving a clinical study, or other validated model, to show therapeutic equivalence and that it was therefore not possible to establish a positive benefit-risk balance. The Committee recommended that a marketing authorisation should not be granted in the concerned Member State, the United Kingdom, and that the marketing authorisation in Ireland should be suspended, until further studies have been performed.

A question-and-answer document with more information about this arbitration procedure is available on the Agency's website.

[4] The review of Novosis Goserelin, Goserelin cell pharm, Novimp and associated names is being conducted in the context of a formal review, initiated by Germany on 16 March 2011, under Article 36 of Directive 2001/83/EC, as amended. The Committee will make recommendations on whether the marketing authorisations for these medicines should be maintained, changed, suspended or revoked. Novosis Goserelin, Goserelin cell pharm, Novimp and associated names are authorised via the decentralised procedure and are marketed by Acino AG and Cell Pharm GmbH in the Reference Member State.
[5] The review of Priligy 30 mg and 60 mg film-coated tablets is being conducted in the context of a formal review, initiated by Sweden under Article 29(4) of Directive 2001/83/EC, as amended.
[6] The arbitration procedure for Canazole was conducted under Article 29(4) of Directive 2001/83/EC.

Harmonisation procedure concluded

The Committee recommended the harmonisation[7] of the prescribing information for **Arimidex** (anastrozole), from AstraZeneca. This medicine is used to treat breast cancer in post-menopausal women.

This review was initiated because of differences in the summaries of product characteristics, labelling and package leaflets in the countries where this product is marketed.

A question-and-answer document with more information about this referral is available on the Agency's website.

Mutual-recognition and decentralised procedures - Human

The CHMP noted the report from the 60th CMDh (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 14 - 16 March 2011. For further details, please see the relevant press release on the CMDh 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 2 - 4 March 2011. For further details, please see **Annex 4**.

Documents adopted during the March 2011 CHMP meeting are listed in **Annex 5**.

Upcoming meetings following the March 2011 CHMP plenary meeting

- The 76th meeting of the CHMP will be held at the Agency on 11-14 April 2011.
- The next Name Review Group meeting will be held at the Agency on 24 May 2011.
- The 61th CMDh (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the Agency on 11-13 April 2011.

Organisational matters

The main topics addressed during the March 2011 CHMP meeting related to:

- The appointment of Dr Concepcion Prieto Yerro as the new Spanish Member replacing Dr Gonzalo Calvo Rojas and of Dr Arantxa Sancho-Lopez as the new Spanish Alternate. Furthermore Dr Reynir Arngrimsson was appointed as the new Icelandic Alternate and Dr Lyubina Todorova as the new Bulgarian Alternate. Dr Dana Gabriela Marin who was appointed as the new Romanian alternate in January 2011, will also take on the role of CHMP representative in PDCO.
- The appointment of Dr Ian Hudson as chairperson of the Guideline Consistency Group.
- The presentation of the implementation of the revised policy for handling of Conflicts of Interest of Scientific Committee Members and Experts - timelines and implications for implementation and presentation of new e-DoI (e-Declaration of Interest) form.
- General discussion on companies' requests to Working Parties - the procedure on how to deal with requests from companies to EMA Working Parties was discussed.

[7] The harmonisation procedure for Arimidex was conducted under Article 30 of Directive 2001/83/EC.

Procedural Announcement

Type IA Pre-Notification Checklist

In the year since Commission Regulation 1234/2008 (variation regulation) entered into force, the European Medicines Agency (Agency) received and processed nearly 2000 Type IA variation notifications. The number submitted has grown throughout the year, and we expect to exceed this figure in 2011.

A significant number of the Type IA notifications received so far, however, have been incomplete or have contained errors. To continue to ensure the efficient operation of the Agency's core business (see press release), it is important that all Type IA variation notifications are submitted correctly. For this purpose, additional help to MAHs in the form of a Pre-Notification Checklist is provided on the EMA website. As well as ensuring full compliance with legal obligations, this will greatly assist the Agency with timely and efficient processing.

Sending of Type IA Acknowledgments of Receipt and Type IB Notifications in Electronic Format Only

Consistent with the switch in December 2010 from sending CHMP opinions in paper format to electronic format only, the European Medicines Agency will, from 1 April 2011, send the signed Type IA Acknowledgments of Receipt and Type IB notifications and accompanying documentation to the Marketing Authorisation Holder in electronic (PDF) format only. Transmission will occur using a secure mail distribution platform (Eudralink) and documents will be the replica of the electronic copy sent simultaneously to the European Commission and of the electronic copy retained at the Agency, marked as un-modifiable according to the Agency's Records Management Policy.

As no paper version will follow by postal mail/courier, the Marketing Authorisation Holder should acknowledge download of the package and safe receipt of the message received by Eudralink.

Requests for New EU Sub-numbers for Type IA Notifications

Further to the experience gained with the operation of the new Variations Regulation, Marketing Authorisation Holders are hereby informed that as of 1st April 2011 new EU sub-numbers for type IA variations concerning an additional presentation (e.g. new pack size) should be requested from the European Medicines Agency, similarly to the procedure already in place for obtaining new EU sub-numbers for Type IB variations.
For further information, please refer to the revised question and answer 10 of the Post-authorisation procedural advice - human medicinal products, Type IA variations, available on the EMA website.

Adjusted fees for application to the EMA to come into effect on 1st April 2011

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

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

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Annex 1 to CHMP Monthly Report March 2011

Opinions for annual re-assessment applications		
Name of medicinal product (INN) MAH	**Outcome**	**Comments**
Increlex (mecasermin), Ipsen Pharma	Positive Opinion	Marketing Authorisation remains under exceptional circumstances
Zavesca (Miglustat), Actelion Registration Ltd.	Positive Opinion	Marketing Authorisation remains under exceptional circumstances

Opinion for renewals of conditional Marketing Authorisation		
Name of medicinal product (INN) MAH	**Outcome**	**Comments**
Humenza (Pandemic Influenza Vaccine (H1N1) (Split Virion, Inactivated, Adjuvanted)), Sanofi Pasteur S.A.	Positive Opinion	Marketing Authorisation remains under conditional approval

Opinions for 5-Year Renewal applications		
Name of medicinal product (INN) MAH	**Outcome**	**Comments**
Champix (Varenicline Tartrate), Pfizer Ltd.	Positive Opinion	Recommending additional renewal
Competact (Pioglitazone / Metformin), Takeda Global Research and Development Centre (Europe) Ltd.	Positive Opinion	Recommending additional renewal
Glubrava (Pioglitazone / Metformin Hydrochloride), Takeda Global Research and Development Centre (Europe) Ltd.	Positive Opinion	Recommending additional renewal
Baraclude (Entecavir), Bristol-Myers Squibb Pharma EEIG	Positive Opinion	Unlimited validity
Ketek (telithromycin), Aventis Pharma S.A.	Positive Opinion	Unlimited validity

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M-M-RVAXPRO (measles, mumps and rubella vaccine (live)), Sanofi Pasteur MSD	Positive Opinion	Unlimited validity
MabCampath (Alemtuzumab), Genzyme Europe B.V.,	Positive Opinion	Unlimited validity
RotaTeq (Rotavirus Vaccine, Live, Oral), Sanofi Pasteur MSD, SNC	Positive Opinion	Unlimited validity
DepoCyte (Cytarabine), Pacira Ltd.	Positive Opinion	Unlimited validity

Accelerated Assessment Procedures			
Substance	**Intended Indication(s)**	**Accelerated Assessment Requests**	
		Accepted	Rejected
N/A			

Annex 2 to CHMP Monthly Report March 2011

Medicinal products granted a community marketing authorisation under the centralised procedure since the February 2011 CHMP Monthly Report

Invented name	**Pumarix**
INN	Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)
Marketing Authorisation Holder	GlaxoSmithKline Biologicals s.a.
Proposed ATC code	J07BB02
Indication	Prophylaxis of influenza in an officially declared pandemic situation.
CHMP Opinion date	18/11/2010
Marketing Authorisation Date	04/03/2011

Invented name	**Repso**
INN	leflunomide
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	L04AA13
Indication	Treatment of adult patients with: • active rheumatoid arthritis as a "disease-modifying antirheumatic drug" (DMARD), • active psoriatic arthritis.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	14/03/2011

Invented name	**Lamivudine/Zidovudine Teva**
INN	Lamivudine and Zidovudine
Marketing Authorisation Holder	TEVA Pharma B.V
Proposed ATC code	J05AR01
Indication	Indicated in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection.
CHMP Opinion date	18/11/2010
Marketing Authorisation Date	28/02/2011

Invented name	**Teysuno**
INN	tegafur, gimeracil and oteracil
Marketing Authorisation Holder	Taiho Pharma Europe, Limited
Proposed ATC code	L01BC53
Indication	Treatment of advanced gastric cancer when given in combination with cisplatin.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	14/03/2011

Invented name	**Xiapex**
INN	collagenase *clostridium histolyticum*
Marketing Authorisation Holder	Pfizer Limited
Proposed ATC code	M09AB02
Indication	Treatment of Dupuytren's contracture in adult patients with a palpable cord.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	28/02/2011

Invented name	**Entacapone Teva**
INN	entacapone
Marketing Authorisation Holder	Teva Pharma B.V.
Proposed ATC code	N04BX02
Indication	As an adjunct to standard preparations of levodopa/benserazide or levodopa/carbidopa for use in adult patients with Parkinson's disease and end-of-dose motor fluctuations, who cannot be stabilised on those combinations.
CHMP Opinion date	18/11/2010
Marketing Authorisation Date	18/02/2011

Invented name	**Xeplion**
INN	paliperidone
Marketing Authorisation Holder	Janssen-Cilag International NV
Proposed ATC code	N05AX13
Indication	Treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. In selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, XEPLION may

Invented name	**Xeplion**
	be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	04/03/2011

Invented name	**Esbriet**
INN	pirfenidone
Marketing Authorisation Holder	InterMune Europe Ltd
Proposed ATC code	L04AX05
Indication	Treatment of mild to moderate Idiopathic Pulmonary Fibrosis (IPF).
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	28/02/2011

Invented name	**Ifirmacombi**
INN	irbesartan and hydrochlorothiazide
Marketing Authorisation Holder	KRKA, d.d., Novo mesto
Proposed ATC code	C09DA04
Indication	Treatment of essential hypertension.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	04/03/2011

Invented name	**Daliresp**
INN	roflumilast
Marketing Authorisation Holder	Nycomed GmbH
Proposed ATC code	R03DX07
Indication	Maintenance treatment of severe chronic obstructive pulmonary disease (COPD) (FEV1 post-bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations as add on to bronchodilator treatment.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	28/02/2011

Invented name	**Libertek**
INN	roflumilast
Marketing Authorisation Holder	Nycomed GmbH
Proposed ATC code	R03DX07
Indication	Maintenance treatment of severe chronic obstructive pulmonary disease (COPD) (FEV1 post-bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations as add on to bronchodilator treatment.
CHMP Opinion date	16/12/2010
Marketing Authorisation Date	28/02/2011

Annex 3 to CHMP Monthly Report March 2011

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

Update since the February 2011 CHMP meeting

Active substance	Invented name	Sponsor/applicant	EU designation number & Date of orphan designation	Designated orphan indication
Romidepsin (INN) (E)-(1S,4S,10S,21R)-7-[(Z)-ethylidene]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone	TBC	Celgene Europe Limited	EU/3/05/328	Treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic/disseminated)

Annex 4 to CHMP Monthly Report March 2011

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

	1995 - 2010	2011	Overall total
Scientific Advice	1368	56	1424
Follow-up to Scientific Advice	320	14	334
Protocol Assistance	297	17	314
Follow-up to Protocol Assistance	133	6	139
	2118	**93**	**2211**

FDA Parallel Scientific Advice	2006 - 2010	2011	Overall total
Completed	9	1	10
Ongoing	0	4	4
Foreseen	0	3	3
	9	**8**	**17**

Outcome of the March 2011 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 Clostridium difficile infection.	*x*					*x*	*x*	
Biological	Treatment of type 2 diabetes.			*x*				*x*	
Biological	Treatment of type 2 diabetes.	*x*					*x*		
Advanced therapy	Treatment of complex anal fistula.		*x*				*x*	*x*	
Chemical	Treatment of type-2 diabetes mellitus.	*x*						*x*	
Chemical	Treatment of gastro-entero-pancreatic neuroendocrine tumours.				*x*	*x*	*x*	*x*	
Chemical	Treatment of head and neck squamous cell carcinoma.	*x*						*x*	
Chemical	Treatment of systemic lupus erythematosus.	*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 chondrosarcoma.	x					x	x	
Other innovative	Treatment of graft-versus-host disease.				x			x	
Chemical	Treatment of ovarian cancer.		x				x		
Chemical	Treatment of head and neck squamous cell carcinoma.			x				x	
Chemical	Treatment of Chronic myeloid leukemia.		x			x			
Biological	Treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukaemia and rheumatoid arthritis.	x				x	x	x	
Biological	Treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukaemia and rheumatoid arthritis.			x			x	x	
Biological	Treatment of non-Hodgkin's lymphoma, and rheumatoid arthritis.	x				x	x	x	
Biological	Treatment of moderate to severe chronic plaque-type psoriasis.	x				x	x	x	
Chemical	Acute treatment and long-term prevention of recurrent venous thromboembolism, including deep venous thrombosis and pulmonary embolism.			x				x	
Biological	Treatment and prophylaxis of bleeding in haemophilia B.				x			x	
Chemical	Treatment of primary myelofibrosis.		x					x	x
Chemical	Treatment of post-essential thrombocythemia myelofibrosis.		x					x	
Chemical	Treatment of post-polycythemia vera myelofibrosis.		x					x	

Substance	Intended indications(s)	Type of request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Prevention and treatment of haemorrhage or surgical bleeding in von Willebrand disease.		x				x	x	x
Biological/ Other innovative	Prevention and treatment of infected diabetic skin ulcers.	x					x	x	
Biological	Prevention of all subtypes of hepatitis B infection.			x				x	
Chemical	Treatment for postcardiotomy right ventricular failure.		x					x	
Biological	Treatment of Hypophosphatasia.		x			x			
Chemical	Treatment of cognitive impairment in Down Syndrome.	x					x		
Chemical	Treatment of Alzheimer's Disease.	x					x	x	
Chemical	Delay of the onset of Alzheimer's Disease.	x					x	x	

SA: scientific advice
PA: protocol assistance

The above-mentioned 13 Scientific Advice letters, 9 Protocol Assistance letters, 5 Follow-up Scientific Advice and 3 Follow-up Protocol Assistance letters were adopted at the 14 – 17 March 2011 CHMP meeting.

New requests for scientific advice procedures

The Committee accepted 31 new Requests for which the procedure started at the SAWP meeting held on 2 – 4 March 2011. The new requests are divided as follows: 22 Initial Scientific Advice, 4 Follow-up Scientific Advice, 3 Initial Protocol Assistance and 2 Follow-up Protocol Assistance.

Annex 5 to CHMP Monthly Report March 2011

Documents adopted during the March 2011 CHMP meeting

Biologics Working Party (BWP)

Reference number	Document	Status[8]
EMA/CHMP/BWP/156215/2011	EU Recommendations for the Seasonal Influenza Vaccine Composition for the Season 2011/2012	**adopted**

Safety Working Party (SWP)

Reference number	Document	Status[8]
EMA/CHMP/SWP/44609/2010	Q&A on the Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use (EMEA/CHMP/SWP/4447/00) • Comments received (EMA/CHMP/SWP/739571/2010)	**adopted**
EMA/CHMP/SWP/169839/2011	Concept Paper on the Need for Revision of the Position on Replacement of Animal Studies by In-vitro Models (CPMP/SWP/728/95)	**3-month public consultation**
EMA/CHMP/SWP/336670/2010	Q&A on the Guideline on Photosafety Testing (CPMP/SWP/398/01) • Comments received (EMA/CHMP/SWP/170012/2011)	**adopted**
EMA/CHMP/SWP/100094/2011	Reflection Paper on Non-clinical studies for Generic Nanoparticle Iron Medicinal Product Applications	**adopted**

ICH

Reference number	Document	Status[8]
EMA/CHMP/ICH/82260/2006	ICH Q3C (R5) - Impurities: Guideline for residual solvents, Step 4	**adopted**

Gastroenterology Drafting Group

Reference number	Document	Status[8]
EMA/CHMP/EWP/342691/2009	Guideline on the evaluation of drugs for the treatment of gastro-oesophageal reflux disease (GORD) • Comments received (EMA/131448/2011)	**adopted**

[8] Adopted or released for consultation documents can be found at the European Medicines Agency website (under "Document library-Public Consultations" or under "Regulatory-Human Medicines").

Respiratory Drafting Group (RDG)

Reference number	Document	Status[8]
EMA/CHMP/EWP/165079/2011	Revised guideline on the clinical development of medicinal products for the treatment of cystic fibrosis	**adopted**

Radiopharmaceutical Drafting Group

Reference number	Document	Status[8]
EMA/CHMP/167834/2011	Revised Core SmPC and Package Leaflet for Radiopharmaceuticals	**1-month public consultation**

Quality Review of Documents Group

Reference number	Document	Status[8]
EMA/275297/2010	QRD recommendations on pack design and labelling for centrally authorised non-prescription human medicinal products	**3-month public consultation**