28 January 2011
EMA/CHMP/55372/2011

**Monthly Report**

# Committee for Medicinal Products for Human Use (CHMP)

17 – 20 January 2011

The Committee noted the following changes in the membership of the CHMP:

- Dr Dalibor Valik replaces Dr Ondřej Slanař as the new CHMP member from Czech Republic.
- Dr Dana Gabriela Marin as new Romanian Alternate replacing Dr Nela Vilceanu.

## Centralised procedure

### *Initial applications for marketing authorisation*

### New medicinal products

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

- **Gilenya** (fingolimod), from Novartis Europharm Ltd, intended for the treatment of adult patients with relapsing remitting multiple sclerosis with high disease activity. The review for Gilenya began on 21 January 2010 with an active review time of 181 days.
- **Halaven** (eribulin), from Eisai Europe Ltd, intended for the treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least two chemotherapeutic regimens for advanced disease. The review for Halaven began on 26 May 2010 with an active review time of 180 days.
- **Jevtana** (cabazitaxel), from Sanofi-aventis, intended in combination with prednisone or prednisolone for the treatment of patients with hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen. The review for Jevtana began on 26 May 2010 with an active review time of 208 days.
- **Pravafenix** (fenofibrate/pravastatin), from Laboratoires S.M.B. S.A., intended for the treatment of adult patients at high risk of coronary heart disease with mixed dyslipidaemia. The review for Pravafenix began on 18 November 2009 with an active review time of 210 days.

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- **Trobalt** (retigabine) from Glaxo Group Ltd, intended as adjunctive treatment of partial onset seizures in adults with epilepsy. The review for Trobalt began on 18 November 2009 with an active review time of 210 days.

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

## Negative opinion for Fampyra adopted

The Committee adopted a negative opinion by majority recommending that **Fampyra** (fampridine), from Biogen Idec Ltd, should not be granted a marketing authorisation. Fampyra was intended to be used to improve the walking ability of adult patients with multiple sclerosis.

*More information about this procedure is available in a separate question-and-answer document on the Agency's website.*

## Re-examination procedure on Movectro concluded

The Committee confirmed its previous negative opinion and adopted a final negative opinion by majority, recommending that **Movectro** (cladribine), from Serono Europe Ltd, should not be granted a marketing authorisation. Movectro was intended as disease-modifying therapy in relapsing remitting multiple sclerosis.

*More information about this re-examination procedure is available in a separate question-and-answer document on the Agency's website.*

## Positive opinion for informed consent application adopted

The Committee adopted a positive opinion by consensus recommending the granting of a marketing authorisation for **Riprazo HCT** (aliskiren/hydrochlorothiazide), from Novartis Europharm Ltd, intended for the treatment of adult patients with essential hypertension. The review for Riprazo HCT began on 21 November 2010 with an active review time of 60 days. This application was an informed consent application referring to the dossier of the authorised medicine Rasilez HCT.

## Withdrawals

The European Medicines Agency has been formally notified by Abbott Laboratories Limited of its decision to withdraw its application for a centralised marketing authorisation for the medicine **Ozespa** (briakinumab), 100 mg solution for injection. This medicine was intended to be used for the treatment of moderate to severe chronic plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA. The application for the marketing authorisation for Ozespa was submitted to the Agency on 2 September 2010. At the time of the withdrawal it was under review by the CHMP. A separate press release and a question-and-answer document with more information are available.

ChemGenex Europe SAS officially notified the CHMP that it wishes to withdraw its application for a marketing authorisation for **Tekinex** (omacetaxine mepesuccinate) intended to be used to treat patients with Philadelphia chromosome-positive chronic myeloid leukaemia who have the 'Bcr-Abl T315I kinase domain' mutation and whose previous treatment with imatinib had failed. At the time of the withdrawal it was under review by the CHMP. A separate press release and a question-and-answer document with more information are available.

## *Post-authorisation procedures*

## Extensions of indications and other recommendations

The Committee adopted three positive opinions by consensus for applications for extensions of the therapeutic indications, adding new treatment options for medicines already authorised in the European Union, for:

- **Baraclude** (entecavir), from Bristol-Myers Squibb Pharma EEIG, to include treatment of adult patients with chronic hepatitis B virus infection and decompensated liver disease.
- **INOmax** (nitric oxide), from INO Therapeutics AB, to include treatment of pulmonary hypertension peri- and post heart surgery.
- **Prezista** (darunavir), from Janssen-Cilag International N.V., to include the treatment of HIV infection in adults who have been previously treated with antiretroviral therapy to the 400 mg strength.

*The summaries of opinions for the mentioned medicines, including the full indications, 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 **Dukoral** (cholera vaccine (inactivated, oral)) from Crucell Sweden AB. Dukoral batches will be formulated using a higher content of bacteria, $125x10^9$ compared to $100x10^9$ bacteria per vaccine dose. The antigen content stays within the approved range which has proved efficacious and safe in a large number of clinical trials conducted with Dukoral and the dosage is not affected. The reason for this change is to give a greater assurance that the product fully meets the potency requirements over the entire shelf life. As a consequence of this recalibration the Product Information has been updated accordingly to reflect the change in the bacterial content prior to inactivation.

## Update on potential presence of endotoxins in Baxter peritoneal dialysis solutions

The Committee was informed by Baxter that the problem of endotoxins in **peritoneal dialysis solutions**[1] has not been solved and that it cannot guarantee the production of endotoxin-free solutions from a production line at its Castlebar plant in Ireland in the short-term. As a consequence, the CHMP, at the request of the European Commission, has started a full review of the manufacture of Baxter's dialysis solutions at the affected plant. The Committee has also updated its recommendations to healthcare professionals and patients which it had previously issued in the context of an Article 5(3) procedure which was concluded in its December plenary meeting.

*More information about this procedure is available in a separate press release and a question-and-answer document on the Agency's website*

[1] The review of peritoneal dialysis solutions is being conducted in the context of a formal review, initiated by the European Commission on 18 January 2011, under Article 31 of Directive 2001/83/EC, as amended. The Committee will make recommendations on whether the marketing authorisations for dialysis solutions should be maintained, changed, suspended or revoked.

# Other information on the centralised procedure

### *Lists of Questions*

The Committee adopted five Lists of Questions on initial applications (including three under the mandatory scope, one under the optional scope as per Regulation (EC) No. 726/2004 and one under Article 31 of Regulation (EC) No. 1901/2006), together with four 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 November is provided in **Annex 2**.

# Referral procedures

## Review on calcitonin-containing medicines started

The Committee has begun looking at the increased risk of prostate cancer progression and other types of malignancies in patients taking **calcitonin-containing medicines** for the prevention of acute bone loss[2]. This follows the review of two randomised, double-blind, placebo-controlled clinical trials, suggesting an increased frequency of malignancies.

The CHMP 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.

Calcitonin is a hypocalcaemic agent, which is authorised for the prevention of acute bone loss due to sudden immobilisation, such as in patients with recent osteoporotic fractures, Paget's disease and hypercalcaemia (when associated with malignant disease) and the treatment of established post-menopausal osteoporosis in order to reduce the risk of vertebral fractures. It is currently available in the EU in injectable and intranasal formulations of salmon or human calcitonin produced either by recombinant DNA technology or chemical peptide synthesis.

## Benefit-risk review of Multaq

Further to the report of two cases of serious liver injury in patients taking the anti-arrhythmic medicine **Multaq** (dronedarone), the European Commission has requested[3] that the CHMP assess all available data concerning the possible risks of liver injury associated with the use of Multaq and their impact on its benefit-risk balance.

The Committee discussed Multaq during its January 2011 meeting and concluded that there was a need for urgent regulatory action to help manage the possible risk of severe liver complications with the medicine. The Committee recommended that warnings and precautions be introduced into the medicine's prescribing information, to ensure that patients' liver function is tested before initiation of

[2] The review of calcitonin-containing medicines is being conducted in the context of a formal review, initiated by the United Kingdom on 19 January 2011, under Article 31 of Directive 2001/83/EC, as amended.
[3] The review of Multaq is being conducted in the context of a formal review, initiated by the European Commission under Article 20 of Regulation (EC) No 726/2004.

treatment and closely monitored during treatment, and that treatment is stopped if there are signs of potential liver damage.

A separate question-and-answer document with more information is available.

## Mutual-recognition and decentralised procedures - Human

The CHMP noted the report from the 58th CMDh (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 17-18 January 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 4–6 January 2011. For further details, please see **Annex 3**.

Documents adopted during the January 2011 CHMP meeting are listed in **Annex 4**.

## Upcoming meetings following the December 2010 CHMP plenary meeting

- The 74th meeting of the CHMP will be held at the Agency on 14-17 February 2011.
- The next Name Review Group meeting will be held at the Agency on 22 March 2011.
- The 59th CMDh (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the Agency on 14-15 February 2011.

## Organisational matters

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

- The election of Dr David Jonathan Wright as new Vice-Chair of the Biostatistics Working Party.
- The adoption of the CHMP Work Programme 2011 – 2013. The Work Programme will be published shortly on the EMA website.
- The adoption of the mandate, objectives and rules of procedure for the CHMP Guidelines Consistency Group. The Guidelines Consistency Group is composed of a small number of members/experts appointed by CHMP on the basis of their extensive clinical and methodological experience on the relevant scientific and regulatory matters. The group has been created to provide high-level scientific and regulatory peer review of concept papers, draft guidelines and reflection papers before they are adopted by the CHMP.
- A presentation on the preparation for the implementation of the pharmacovigilance legislation. The new pharmacovigilance legislation was published on 31 December 2010 and most measures will apply from July 2012. The availability of an appropriate governance structure to oversee and monitor the preparatory work for the new legislation was identified as an important prerequisite. Although the EMA has started to prepare for the implementation by establishing an internal Task Force in January 2010, a coordinated approach with the work undertaken by the European Commission and the Member States will be established.

# Procedural Announcement

## *Update of procedural advice for users of the centralised procedure for generic/hybrid applications*

An updated procedural advice for users of the centralised procedure for generic/hybrid applications, to reflect the experience gained with the handling of these applications, has been agreed by the Agency. The changes introduced pertain to the following main categories:

- A new set of questions and answers to provide guidance regarding handling of usage patents;
- An update of the references to the questions on safety variations, to take account of the new Variations Regulation;
- Clarification of issues where frequent queries have been received from Applicants, concerning identification of the reference medicinal product, consultation of the Name Review Group, user consultation, etc.;

In addition, it has also been clarified that the date of the notification of the marketing authorisation to the MAH should be used to determine the expiry of the protection period of the reference medicinal product.

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

# Annex 1 to CHMP Monthly Report January 2011

| Opinions for annual re-assessment applications | | |
|---|---|---|
| **Name of medicinal product (INN) MAH** | **Outcome** | **Comments** |
| **Ventavis** (iloprost), Bayer Schering Pharma AG | Positive Opinion | Marketing Authorisation remains under exceptional circumstances |

| Opinion for renewals of conditional Marketing Authorisation | | |
|---|---|---|
| **Name of medicinal product (INN) MAH** | **Outcome** | **Comments** |
| **Tyverb** (lapatinib), Glaxo Group Ltd. | Positive Opinion | Marketing Authorisation remains under conditional approval |

| Opinions for 5-Year Renewal applications | | |
|---|---|---|
| **Name of medicinal product (INN) MAH** | **Outcome** | **Comments** |
| **Evoltra** (clofarabine), Genzyme Europe B.V. | Positive Opinion | Recommending additional renewal |
| **Zostavax** (shingles (herpes zoster) vaccine (live)), Sanofi Pasteur MSD | Positive Opinion | Recommending additional renewal |
| **Proquad** (measles, mumps, rubella and varicella vaccine (live)), Sanofi Pasteur MSD | Positive Opinion | Recommending additional renewal |
| **HBVAXPRO** (hepatitis b vaccine (rdna)), Sanofi Pasteur MSD, SNC | Positive Opinion | Unlimited validity |

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

# Annex 2 to CHMP Monthly Report January 2011

***Medicinal products granted a community marketing authorisation under the centralised procedure since the December 2010 CHMP Monthly Report***

| Invented name | **Docetaxel Teva Pharma** |
|---|---|
| INN | docetaxel |
| Marketing Authorisation Holder | Teva Pharma B.V. |
| Proposed ATC code | L01CD 02 |
| Indication | Breast cancer<br><br>Docetaxel Teva Pharma monotherapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic therapy. Previous chemotherapy should have included an anthracycline or an alkylating agent.<br><br>Non-small cell lung cancer<br><br>Docetaxel Teva Pharma is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior chemotherapy.<br><br>Docetaxel Teva Pharma in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer, in patients who have not previously received chemotherapy for this condition.<br><br>Prostate cancer<br><br>Docetaxel Teva Pharma in combination with prednisone or prednisolone is indicated for the treatment of patients with hormone refractory metastatic prostate cancer. |
| CHMP Opinion date | 21/10/2010 |
| Marketing Authorisation Date | 21/01/2011 |

| Invented name | **Potactasol** |
|---|---|
| INN | topotecan |
| Marketing Authorisation Holder | Actavis Group PTC ehf. |
| Proposed ATC code | L01XX17 |
| Indication | Topotecan monotherapy is indicated for the treatment of:<br>- patients with metastatic carcinoma of the ovary after failure of first-line or subsequent therapy<br>- patients with relapsed small cell lung cancer (SCLC) for whom re-treatment with thefirst-line regimen is not considered appropriate (see section 5.1).<br><br>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 | 21/01/2010 |
| Marketing Authorisation Date | 06/01/2011 |

# Annex 3 to CHMP Monthly Report January 2011

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

| | 1995 - 2010 | 2011 | Overall total |
|---|---|---|---|
| Scientific Advice | 1368 | 20 | 1388 |
| Follow-up to Scientific Advice | 320 | 4 | 324 |
| Protocol Assistance | 297 | 4 | 301 |
| Follow-up to Protocol Assistance | 133 | 1 | 134 |
| | **2118** | **29** | **2147** |

| FDA Parallel Scientific Advice | 2006 - 2010 | 2011 | Overall total |
|---|---|---|---|
| Completed | 9 | 0 | 9 |
| Ongoing | 0 | 4 | 4 |
| Foreseen | 0 | 2 | 2 |
| | **9** | **6** | **15** |

## *Outcome of the January 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 type 2 diabetes mellitus. | *x* | | | | | | *x* | |
| Chemical | Prevention of nausea and vomiting associated with emetogenic cancer chemotherapy. | *x* | | | | *x* | *x* | *x* | |
| Chemical | Treatment of type 2 diabetes mellitus. | *x* | | | | | | *x* | |
| Chemical | Treatment of idiopathic pulmonary fibrosis. | *x* | | | | | *x* | *x* | |
| Advanced therapy | Treatment of soft-tissue sarcoma. | *x* | | | | *x* | *x* | *x* | |
| Chemical | Treatment of familial adenomatous polyposis. | | *x* | | | | | *x* | *x* |
| Chemical | Treatment of familial adenomatous polyposis. | | *x* | | | | *x* | *x* | |

| Substance | Intended indications(s) | Type of request | | | | Topic | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | New | | Follow-up | | Pharmaceutical | Pre-clinical | Clinical | Significant Benefit |
| | | SA | PA | SA | PA | | | | |
| Biological | Treatment of melanoma. | x | | | | x | x | x | |
| Other innovative | Treatment of acute lymphoblastic leukemia. | | | | x | | x | | |
| Biological | Treatment of cutaneous melanoma and non-small cell lung cancer. | x | | | | x | | | |
| Chemical | Treatment of metastatic prostate cancer. | | | 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, chronic lymphocytic leukaemia and rheumatoid arthritis. | x | | | | x | | x | |
| Chemical | Treatment of gastric cancer. | x | | | | | x | x | |
| Chemical | Treatment of metastatic breast cancer. | x | | | | x | x | x | |
| Chemical | Treatment of malaria. | | x | | | x | x | x | x |
| Chemical | Treatment of stage 2 human African trypanosomiasis or sleeping sickness due to T.b. gambiense. | x | | | | | | x | |
| Biological | Prophylaxis of leishmaniasis. | x | | | | x | x | x | |
| Biological | Treatment of leishmaniasis. | x | | | | x | x | x | |
| Biological | Treatment of haemophilia A. | x | | | | x | x | x | |
| Biological | Treatment of diabetic foot ulcers. | x | | | | x | x | x | |
| Biological | Immunisation against pneumonic plague resulting from aerosol exposure to Yersinia pestis. | x | | | | x | x | x | |
| Biological | Prevention of invasive meningococcal disease caused by N. meningitidis serogroup B. | | | x | | x | | x | |
| Biological | Immunization against moderate to severe diarrhoea caused by enterotoxigenic E. coli. | | | x | | x | | | |

| Substance | Intended indications(s) | Type of request | | | | Topic | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | New | | Follow-up | | Pharma ceutical | Pre-clinical | Clinical | Significant Benefit |
| | | SA | PA | SA | PA | | | | |
| Chemical | Treatment of nephropathy associated with type 2 diabetes. | *x* | | | | | *x* | *x* | |
| Chemical | Treatment of Duchenne muscular dystrophy. | | *x* | | | *x* | *x* | | |
| Advanced therapy | Treatment of spinal cord injury. | *x* | | | | *x* | *x* | *x* | |
| Chemical | Treatment of seasonal allergic rhinitis and perennial allergic rhinitis. | *x* | | | | *x* | *x* | *x* | |
| Other innovative | Renal transplantation. | *x* | | | | *x* | *x* | *x* | |

**SA: scientific advice**
**PA: protocol assistance**

The above-mentioned 20 Scientific Advice letters, 4 Protocol Assistance letters, 4 Follow-up Scientific Advice and 1 Follow-up Protocol Assistance letters were adopted at the 17 - 20 January 2011 CHMP meeting.

## New requests for scientific advice procedures

The Committee accepted 25 new Requests for which the procedure started at the SAWP meeting held on 4 – 6 January 2011. The new requests are divided as follows: 12 Initial Scientific Advice, 3 Follow-up Scientific Advice, 7 Initial Protocol Assistance and 3 Follow-up Protocol Assistance.

# Annex 4 to CHMP Monthly Report January 2011

***Documents adopted during the January 2011 CHMP meeting***

## Infectious Diseases Working Party

| Reference number | Document | Status |
|---|---|---|
| EMEA/CHMP/51240/ 2011 | Guideline on clinical evaluation of medicinal products for the treatment of chronic hepatitis C | **6-month public consultation**[4] |

## EMA

| Reference number | Document | Status |
|---|---|---|
| EMA/CHMP/683358/ 2010 | Mandate, objectives and rules of procedure for the CHMP Guidelines Consistency Group | **Adopted**[4] |
| EMA/CHMP/65166/2011 | CHMP Work Programme 2011 - 2013 | **Adopted**[5] |

[4] Adopted or release for consultation documents can be found at the European Medicines Agency website (under "Document library-Public Consultations" or under "Regulatory-Human Medicines").
[5] The CHMP Work Programme 2011-2013 will be published on the European Medicines Agency website under "About us-Committees-CHMP-Overview".