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PRESS RELEASE

Meeting highlights from the Committee for Medicinal Products for Human Use, 21-24 July 2008

Initial evaluation

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted positive opinions, recommending the granting of a marketing authorisation, for the following medicines.

New medicinal products

- **Evicel** (human fibrinogen / human thrombin), from Omrix Biopharmaceuticals S.A., fibrin sealant for use as supportive treatment in surgery where standard surgical techniques are insufficient. EMA review began on 15 August 2007 with an active review time of 207 days.
- **Xarelto** (rivaroxaban), from Bayer Health Care, for the prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery. EMA review began on 23 November 2007 with an active review time of 181 days.

Generic medicinal products

- **Olanzapine Mylan** (olanzapine), from Generics (UK) limited, for the treatment of schizophrenia and the treatment of moderate to severe manic episodes. EMA review began on 26 December 2007 with an active review time of 177 days. The reference product for Olanzapine Mylan is Zyprexa, from Eli Lilly Nederland B.V., which is already authorised in the European Union (EU), in the applied indication.

'Informed consent' applications

This type of application requires that reference is made to an authorised medicine and that the marketing authorisation holder of this reference product has given consent to the use of the dossier in the application procedure. The medicines concerned are:

- **Duloxetine Boehringer Ingelheim** (duloxetine), from Boehringer Ingelheim International GmbH, for the treatment of moderate to severe stress urinary incontinence in women, and for the treatment of diabetic peripheral neuropathic pain in adults. EMA review began on 30 March 2008 with an active review time of 89 days. Reference medicine is Ariclim, from Eli Lilly Nederland B.V.
- **Fluticasone furoate GSK** (fluticasone furoate), from Glaxo Group Ltd., for the treatment of symptoms of allergic rhinitis in children aged 6 years or older, adolescents and adults. EMA review began on 28 May 2008 with an active review time of 57 days. Reference medicine is Avamys, from Glaxo Group Ltd.
- **Tadalafil Lilly** (tadalafil), from Eli Lilly Nederland B.V., for the treatment of erectile dysfunction. EMA review began on 28 May 2008 with an active review time of 57 days. Reference medicine is Cialis, from Eli Lilly Nederland B.V.
- **Prepandemic influenza vaccine** GlaxoSmithKline Biologicals (pre-pandemic influenza vaccine (H5N1) [(split virion, inactivated, adjuvanted) A/Vietnam/1194/2004 NIBRG-14], from GlaxoSmithKline Biologicals S.A., for active immunisation against H5N1 subtype of influenza A virus. EMA review began on 28 May 2008 with an active review time of 57 days. Reference medicine is Prepandrix (split inactivated, adjuvanted, H5N1 influenza vaccine containing antigens from A/VietNam/1194/2004 NIBRG-14), from GlaxoSmithKline Biologicals S.A.

Re-examination procedure concluded

Following the re-examination of the negative opinion adopted on 19 March 2008, the CHMP adopted a final positive opinion for **Ceplene** (histamine dihydrochloride), from EpiCept GmbH, intended to be used as maintenance treatment in combination with interleukin-2 in adults with acute myeloid leukaemia. Ceplene is **the 48th orphan medicine** to receive a positive opinion.

A separate question-and-answer document with more information about the re-examination procedure is available [here](#).

Revised positive opinion for Filgrastim ratiopharm, Ratiograstim, Biograstim and Tevagrastim

The CHMP adopted a revised positive opinion for Ratiograstim (filgrastim), from ratiopharm GmbH, Biograstim (filgrastim), from CT Arzneimittel GmbH, Tevagrastim (filgrastim), from Teva Generics GmbH, and Filgrastim ratiopharm (filgrastim), from ratiopharm GmbH, following a previous positive opinion issued in February 2008.

The European Commission requested that the CHMP evaluate whether data from a similar product (Grasalva), which has been marketed in Lithuania by Sicor Biotech UAB (part of Teva group), is relevant for the assessment of the marketing authorisation applications for the above products. Having reviewed these data, the CHMP concluded that the benefit-risk-balance for the use of Ratiograstim, Biograstim, Tevagrastim and Filgrastim ratiopharm in the treatment of neutropenia continues to be positive and recommended the granting of marketing authorisations.

Negative opinion

The CHMP adopted a negative opinion recommending the refusal of a marketing authorisation for **Sovrima**, from Santhera Pharmaceuticals (Deutschland) GmbH. Sovrima was intended to be used for treatment of Friedreich's Ataxia, an inherited condition that causes progressive damage to the nervous system and heart disease. It was designated as an orphan medicine. EMEA review began on 15 August 2007 with an active review time of 203 days

A separate question-and-answer document with more detailed information on the grounds for the negative opinion is available [here](#).

Extensions of indication

The CHMP gave positive opinions for applications for extension of indication, adding new treatment options for the following previously approved medicines:

- **Aclasta** (zoledronic acid), from Novartis Europharm Ltd, to extend the indication to include treatment of osteoporosis in post-menopausal women and men at increased risk of fracture, including those with a recent low-trauma hip fracture. Aclasta is currently indicated for the treatment of osteoporosis in post-menopausal women at increased risk of fracture and treatment of Paget's disease of the bone.
- **Humira*** (adalimumab), from Abbott Laboratories Ltd, to extend the indication to include treatment of active polyarticular juvenile idiopathic arthritis, in adolescents aged 13 to 17 years who have had an inadequate response to one or more disease-modifying anti-rheumatic medicines. Humira is currently indicated for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease and psoriasis.
- **Velcade** (bortezomib), from Janssen-Cilag International NV, to extend the indication for its use in combination with melphalan and prednisone for the treatment of patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with bone marrow transplant. Velcade is currently indicated as mono-therapy for the treatment of progressive multiple myeloma in patients who have received at least one prior therapy and who have already undergone or are unsuitable for bone marrow transplantation.

* Information concerning the extension of indication for Humira (adalimumab) has been included.

Negative opinion for extension of indication

The CHMP adopted a negative opinion for an extension of indication of **Taxotere** (docetaxel) and **Docetaxel Winthrop** (docetaxel), both from Aventis Pharma S.A. Both medicines were intended to be used to treat operable breast cancer whose tumours overexpress the protein HER2. Both medicines were expected to be used in addition to surgery to remove the tumour in combination with trastuzumab following treatment with doxorubicin and cyclophosphamide and in combination with trastuzumab and carboplatin. Taxotere and Docetaxel Winthrop are currently indicated for the treatment of advanced or metastatic breast cancer, in combination with other anticancer medicines, in patients previously or not previously treated with cytotoxic therapy and in breast cancer that can be treated with surgery. In these patients, Taxotere and Docetaxel Winthrop are used in addition to surgery to remove the tumour together with doxorubicin and cyclophosphamide. Taxotere and Docetaxel Winthrop are also indicated for the treatment of non-small cell lung cancer, prostate cancer, gastric adenocarcinoma and head and neck cancer.

A separate question-and-answer document with more detailed information on the grounds for the negative opinion is available [here](#).

Summaries of opinions for all mentioned products, including their full indication, can be found [here](#).

Referral procedures concluded

The CHMP finalised a procedure under Article 107 of the Community code on human medicinal products (Directive 2001/83/EC as amended) for **oral moxifloxacin-containing medicines**.

A separate [press release](#) and a [question-and-answer document](#) with more detailed information are available on the EMEA website.

The CHMP concluded a referral procedure under Article 31 of Directive 2001/83/EC, as amended, for oral **norfloxacin-containing medicines**.

A separate [press release](#) and a [question-and-answer document](#) with more detailed information are available on the EMEA website.

The CHMP concluded a number of referral procedures under Article 29 of Directive 2001/83/EC, as amended. This type of procedures 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 medicines concerned are:

- **Lisonorm** (amlodipine / lisinopril), from Gedeon Richter Plc, indicated as therapy for patients with blood pressure adequately controlled with lisinopril and amlodipine given concurrently at the same dose level. The procedure was initiated because of disagreement between the Member States on the grounds for approval of this medicine, in particular due to concerns over the bioequivalence with the reference product. The CHMP concluded that the benefits of Lisonorm outweigh its risks and recommended the granting of the marketing authorisation for Lisonorm.
- **Ribavirin “iQur”** (ribavirin), from iQur Pharmaceutical Ltd, is indicated for the treatment of chronic hepatitis C and to be used only in combination with peginterferon- α 2a or interferon- α 2a. The procedure was initiated because of disagreement between the Member States on the grounds for approval of this medicine. The concerns related to the application of the ‘well established use’ concept for the registration of Ribavirin due to its pharmacological characteristics. The CHMP considered that the company did not provide sufficient evidence for a systematic and documented use of the substance outside clinical trials, compassionate use and named patient supply to demonstrate the well established use of ribavirin in the claimed indication in the European Union. The Committee concluded that marketing authorisations should not be granted.

The CHMP finalised a number of referral procedures under Article 30 of Directive 2001/83/EC as amended. This type of procedure is initiated with a view to harmonising product information for medicinal products authorised at Member State level. The CHMP recommended for the three following medicines the amendment of the Summary of Product Characteristics, labelling and package leaflet:

- **Ciflox, Uniflox** (ciprofloxacin), from Bayer Pharma SA, used as antibacterial medicine**. The procedure was initiated by France.
- **Efexor and associated names (venlafaxine) and Efexor Depot and associated names** (venlafaxine), from Wyeth Europa Ltd., intended for the treatment of major depressive episodes and prevention of recurrence of major depressive episodes. The procedure was initiated by the European Commission.
- **Risperdal and associated names** (risperidone), from Janssen-Cilag, intended for the treatment of schizophrenia, moderate to severe manic episodes associated with bipolar disorders, persistent aggression in patients with moderate to severe Alzheimer's dementia and persistent aggression in conduct disorder. The procedure was initiated by the European Commission.
- **Risperdal Consta and associated names** (risperidone), from Janssen-Cilag, intended for the maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics. The procedure was initiated by the European Commission.

Re-examination procedure for referral concluded

The CHMP confirmed its previous position and recommended the refusal of the marketing authorisation and, where appropriate, the suspension of the marketing authorisation of the following **Fentanyl-containing transdermal patches** (Fentastad, Fentador, Fentrans, Matrigesic, Matripain), from STADA Arzneimittel AG.

The CHMP had adopted a negative opinion in November 2007, because it concluded that the product failed to show adequate characteristics which are key requirements for a product of this type in order to guarantee its safety and efficacy. In a re-examination procedure, requested by the company, the CHMP confirmed this outcome for all dose forms concerned.

The European Commission referred the opinion back to the CHMP in April 2008, requesting the Committee provide more clarity on the arguments to refuse the marketing authorisation for the lowest patch-strength, 25 micrograms/h patch. A revised opinion was adopted accordingly.

Referral procedure started

The CHMP started a referral procedure under Article 30 of Directive 2001/83/EC as amended for **Losec (omeprazole)** from AstraZeneca, used in the gastrointestinal therapeutic area, at the request of the European Commission, with a view to harmonising the product information for the medicines authorised at the level of the Member States.

A more detailed CHMP meeting report will be published shortly.

-- ENDS --

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**The information concerning the intended use of ciprofloxacin has been amended.