European Medicines Agency
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PRESS RELEASE
Meeting highlights from the Committee for Medicinal Products for Human Use, 18-21 June 2007

Positive opinions
The European Medicines Agency's (EMEA) Committee for Medicinal Products for Human Use (CHMP) has adopted eleven positive opinions, three of which relate to similar biological medicinal products, recommending the granting of a marketing authorisation for the following medicinal products:

- **Atriance** (nelarabine), from Glaxo Group Limited, for the treatment of T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic leukaemia (T-LBL) of patients in second relapse. **Atriance is the 40th orphan medicinal product to receive a positive opinion.** EMEA review began on 21 June 2006 with an active review time of 203 days.
  Atriance is the first medicinal product for which an application was submitted using the Product Information Management (PIM) system. PIM enables the electronic exchange of the product information part of a marketing authorisation application in the European Union. Its aim is to increase efficiency of the management and exchange of the product information and to improve the quality and consistency of the published product information.
- **Gliolan** (5-aminolevulinic hydrochloride), from Medac, for the visualisation of malignant tissue during surgery for malignant glioma in adult patients. **Gliolan is the 41st orphan medicinal product to receive a positive opinion**. EMEA review began on 24 May 2006 with an active review time of 199 days.
- **Flebogammadif** [human normal immunoglobulin (IVIg)], from Instituto Grifols S.A., for replacement therapy in immunodeficiency and for immunomodulation in immune-mediated diseases. EMEA review began on 27 September 2006 with an active review time of 177 days.
- **Rasilez, Enviage, Sprimeo, Tekturna and Riprazo** (aliskiren), from Novartis Europharm Ltd, for the treatment of essential hypertension. EMEA review began on 27 September 2006 for Rasilez and on 25 March 2007 for Enviage, Sprimeo, Tekturna and Riprazo with an active review time of 194 for Rasilez and 77 days for Enviage, Sprimeo, Tekturna and Riprazo.

Positive opinion for similar biological medicinal products
The CHMP adopted positive opinions for three biosimilar medicinal products. **Binocrit** (Epoetin alfa), from Sandoz GmbH, **Epoetin alfa Hexal** (Epoetin alfa), from Hexal Biotech Forschungs GmbH, and **Abseamed** (Epoetin alfa), from Medice Arzneimittel Pütter GMBH & Co, are intended for the treatment of anaemia associated with chronic kidney disease and in oncology patients; and to reduce blood transfusion requirements in oncology patients and prior to elective orthopaedic surgery. All three medicinal products have been shown to be similar to Eprex/Erypo, the reference medicinal product already authorised in the EU, in the applied indications. EMEA review began on 29 March 2006 with an active review time of 205 days.

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

- **Arixtra** and **Quixidar** (fondaparinux sodium) 2.5 mg, from Glaxo Group, to extend the indication to add treatment of acute coronary syndromes in patients with unstable angina/non-ST segment elevation myocardial infarction (UA/NSTEMI) for whom an urgent (<120 min) invasive

management (PCI) is not indicated; and in patients with ST segment elevation myocardial infarction (STEMI) who are managed with thrombolytics or who initially are to receive no other form of reperfusion therapy. Arixtra 2.5mg is currently authorised for prevention of venous thromboembolic events (VTE) in patients undergoing major orthopaedic surgery; abdominal surgery and who are judged to be at high risk of thromboembolic complications, such as patients undergoing abdominal cancer surgery, and in patients who are judged to be at high risk for VTE and are immobilised. Arixtra (5, 7.5 and 10 mg) is also authorised for the treatment of acute deep vein thrombosis (DVT) and treatment of acute pulmonary embolism (PE), except in haemodynamically unstable patients or patients who require thrombolysis or pulmonary embolectomy.

- **Zostavax** (Zoster Vaccine, Live), from Sanofi Pasteur MSD, to extend the indication to individuals 50 years of age or older. Zostavax is currently indicated for prevention of herpes zoster and herpes zoster-related post-herpetic neuralgia (PHN) for individuals 60 years of age or older.

New contraindications
Following a literature review describing the interaction of four known inhibitors of CYP3A4 (ketoconazole, lopinavir/ritonavir, clarithromycin, saquinavir) with midazolam, the CHMP recommended to vary the product information for all protease inhibitors to contraindicate the concomitant use with *oral* midazolam and to provide further directions concerning co-administration with *parenteral* midazolam in the interaction section of the SPC.

The product information for the following protease inhibitors used in the treatment of AIDS/HIV-infections has now been amended: **Agenerase, Crixivan, Prezista, Kaletra, Norvir, Telzir** and **Viracept**.

Summaries of opinions for all mentioned products, including their full indication, can be found here.

Action plan following the recall of Viracept and recommendation to suspend the marketing authorisation
The CHMP agreed on an **action plan to follow-up patients who were exposed to contaminated Viracept** (nelfinavir), from Roche Registration Limited, **and recommended the suspension of the marketing authorisation to the European Commission**. Viracept is an antiretroviral medicine used to treat HIV-1 infected adults, adolescents and children of 3 years of age and older. The recommendation to suspend Viracept follows the recall of the medicinal product from the European market in early June 2007 because some batches had become contaminated during the manufacturing process with ethyl mesylate, a known genotoxic substance (harmful to DNA).

A separate press release and a question-and-answer document with more information are available.

Referral procedures concluded
The CHMP finalised a referral procedure under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) for **lansoprazole 15 and 30 mg Gastroresistant Capsules** (lansoprazole), from Teva. The CHMP concluded that bioequivalence with the originator medicinal product has been documented sufficiently and therefore recommended the medicinal product for approval for the treatment of gastro oesophageal reflux disease, ulcers, acid-related dyspepsia and as an adjuvant in the eradication of Helicobacter pylori.
Referrals under Article 29 are normally initiated because of disagreement among the Member States in the context of the mutual recognition procedure.

Referral procedures started
The CHMP started a referral procedure for **ergot-derived dopamine agonists** (bromocriptine, cabergoline, dihydroergocryptine, lisuride and pergolide), a class of medicines that is primarily used in the treatment of Parkinson's disease. The referral procedure was initiated by the United Kingdom under Article 31 of the Community code on human medicinal products (Directive 2001/83/EC as

amended) to re-assess the balance of benefits and risks of all these products in view of the risk of fibrotic disorders and cardiac valvulopathy reported with some of these medicines.
Referrals under Article 31 are initiated in cases involving the interests of the Community or concerns relating to the protection of public health.

The CHMP started a referral procedure for **Coxtral gel 3%** (nimesulide), from Zentiva, because of concerns regarding equivalence with the originator medicinal product. This procedure was initiated under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended).

The CHMP started a harmonisation referral for **Gemzar** (gemcitabine), from Lilly, on the request of the European Commission. The procedure was initiated under Article 30 of the Community code on human medicinal products (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.

A more detailed CHMP meeting report will be published shortly.

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