25 June 2010
EMA/CHMP/272093/2010 corr.[1]
Press Office

Press release

Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP)

21-24 June 2010

Positive opinions for new medicines adopted

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

- **Brinavess** (vernakalant), from Merck Sharp & Dohme Ltd, intended for the rapid conversion of recent onset of atrial fibrillation to sinus rhythm in adults. The review for Brinavess began on 19 August 2009 with an active review time of 209 days.
- **Rapiscan** (regadenoson), from Gilead Sciences International Ltd, intended as pharmacological stress agent for radionuclide myocardial perfusion imaging. The review for Rapiscan began on 27 May 2009 with an active review time of 209 days.
- **Ruconest** (conestat alfa), previously known as Rhucin, from Pharming Group N.V., an orphan medicine intended for the treatment of angioedema attacks. The active substance in Ruconest, conestat alfa, is produced using recombinant DNA technology. It is extracted from the milk of rabbits that have had a gene (DNA) inserted, which makes them able to produce the human protein in their milk. The review for Ruconest began on 23 September 2009 with an active review time of 210 days. This was a resubmission of an application for a marketing authorisation following a negative opinion by the CHMP in December 2007.
- **Sycrest** (asenapine), from N.V. Organon, intended for the treatment of moderate to severe manic episodes associated with bipolar I disorder in adults. The review for Sycrest began on 27 May 2009 with an active review time of 210 days.

[1] * Ibandronate Teva reads now correctly as Ibandronic Acid Teva (page 2)
** The marketing authorisation holder of Fortiban Combi D reads now correctly as Warner Chilcott UK Ltd (page 3)

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8427 **Facsimile** +44 (0)20 7418 8416
E-mail press@ema.europa.eu **Website** www.ema.europa.eu

- **Vpriv** (velaglucerase alfa), from Shire Pharmaceutical Ireland Ltd, an orphan medicine intended for the treatment of Gaucher disease. The review for Vpriv began on 23 December 2009 with an active review time of 150 days. The Committee carried out an accelerated assessment of this medicine, due to a major public health interest. In the light of the ongoing shortage of the authorised medicine for the treatment of Gaucher disease, the CHMP found that Vpriv might constitute an alternative treatment option for this condition.

Positive opinion for a 'hybrid generic' medicine adopted

The Committee adopted a positive opinion recommending the granting of a marketing authorisation for **PecFent** (fentanyl), from Archimedes Development Ltd, intended for the treatment of breakthrough pain in adults who are already receiving maintenance opioid therapy for chronic cancer pain. PecFent is a 'hybrid generic' medicine. This means that this medicine contains a known active substance, but is presented in a new pharmaceutical form (nasal spray). The medicines Actiq lozenges and Effentora buccal tablets are the reference products. The review for PecFent began on 27 May 2009 with an active review time of 203 days.

Positive opinions for generic medicines adopted

The Committee adopted positive opinions recommending the granting of marketing authorisations for the following generic medicines:

- **Ibandronic Acid Teva** (ibandronic acid), from Teva Pharma B.V. The 50-mg tablets are intended for the prevention of skeletal events in patients with breast cancer and bone metastases, and the 150-mg tablets are intended for the treatment of osteoporosis in postmenopausal women at increased risk of fracture. Ibandronic Acid Teva 50 mg is a generic of Bondronat, and Ibandronic Acid Teva 150 mg* is a generic of Bonviva.
- **Telmisartan Actavis** (telmisartan), from Actavis Group PTC ehf, intended for the treatment of essential hypertension and reduction of cardiovascular morbidity. Telmisartan Actavis is a generic of Micardis.

Positive opinions for extensions of indications adopted

The Committee gave positive opinions for applications for extension of the therapeutic indications, adding new treatment options for medicines that are already authorised in the European Union:

- **Byetta** (exenatide), from Eli Lilly Nederland B.V., to include treatment of type 2 diabetes mellitus in combination with thiazolidinedione (with or without metformin).
- **Gardasil** and **Silgard** (human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)), from Sanofi Pasteur MSD SNC and Merck Sharp & Dohme Ltd, to include the prevention of premalignant genital lesions, cervical cancer and external genital warts in mid-adult women, from the age of 26 to 45 years.

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

Re-examination procedure on Zeftera concluded

The Committee confirmed its previous negative opinion and adopted a final negative opinion, recommending that **Zeftera** (ceftobiprole medocaril), from Janssen-Cilag International NV, should not

be granted a marketing authorisation. Zeftera is an antibiotic, intended for the treatment of complicated skin and soft-tissue infections.

More information about this re-examination procedure is available in a separate question-and-answer document here.

Arbitration procedures concluded

The Committee completed arbitration procedures initiated because of disagreement among EU Member States regarding the authorisation of **Fortipan Combi D** and **Norsed Combi D** (risedronate sodium, calcium carbonate and colecalciferol) and associated names, from Warner Chilcott UK Ltd** and Sanofi-Aventis S.p.A. These medicines are indicated for the treatment of post-menopausal osteoporosis. The procedures were initiated because of concerns regarding the efficacy of these medicines, in particular regarding claims of improved benefit of the combination pack as compared with the individual active substances and improved compliance compared with the standard treatment. The Committee concluded that the combination pack will simplify the correct dosage regimen and did not consider the demonstration of improved compliance to be an absolute requirement for the approval of these combination products. Therefore, the Committee concluded that the benefit-risk profile of these medicines was positive and recommended that marketing authorisations should be granted.

The Committee completed an arbitration procedure initiated because of disagreement among EU Member States regarding the extension of the therapeutic indications for **Genotropin** (somatropin) and associated names, from Pfizer ApS. These medicines are indicated for treatment of children with growth disturbances and adults with growth hormone deficiency. This procedure was initiated because of concerns regarding the efficacy of these medicines in children with severe forms of juvenile idiopathic arthritis (JIA) requiring long-term glucocorticoid treatment. The Committee concluded that the benefit-risk profile of these medicines was negative in children with JIA requiring long term glucocorticoid treatment and recommended that the therapeutic indications should not be extended.

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

Harmonisation referral on candesartan & hydrochlorothiazide concluded

The Committee recommended harmonisation of the prescribing information for **Atacand Plus** (candesartan/hydrochlorothiazide) and associated names, from AstraZeneca group of companies. The review was initiated because of differences in the summaries of product characteristics, labelling and package leaflets in the countries where the products are marketed. These medicines are authorised to treat essential hypertension in patients whose blood pressure is not optimally controlled with candesartan or hydrochlorothiazide monotherapy.

A question-and-answer document with more information about this referral can be found here.

Review of benefits and risks for Invirase started

The Committee started a review of the benefits and risks of Invirase (saquinavir), in view of the results of a study conducted by the marketing authorisation holder, Roche Registration Ltd, investigating the proarrhythmic effect of ritonavir-boosted saquinavir in healthy volunteers. The study showed that Invirase had a marked effect on QT interval prolongation and PR prolongation. These findings have been included in the product information of Invirase and the use of Invirase has been contra-indicated in patients at high risk of arrhythmia and in patients using other medicines that may cause QT or PR prolongation. Warnings over its use in patients at moderate risk of arrhythmia, together with

recommendations for ECG monitoring, have also been included in the product information. The review of the medicine's benefits and risks has been initiated to discuss any additional measures necessary to ensure the safe and effective use of Invirase and to determine how to balance the risks and benefits of the medicine. Ritonavir-boosted Invirase is indicated as combination treatment of HIV-infected adult patients.

Review of angiotensin II receptor inhibitors started

The Committee has begun looking at the possible risk of cancer in patients taking angiotensin II receptor inhibitors. This follows the publication of a meta-analysis reviewing nine randomised controlled trials involving almost 95,000 patients, which suggests that these medicines may be linked with a modestly increased risk of new diagnoses of cancer when compared with placebo or other heart medicines.

The CHMP will review the meta-analysis thoroughly, together with any other available non-clinical and clinical data (including data from clinical trials and epidemiological studies) on angiotensin II receptor inhibitors, to clarify whether there is an increased risk of cancer in patients taking these medicines. The Committee will also issue an opinion on whether a future change to the product information or risk-management plans for these medicines might be necessary.

Notes

1. A question-and-answer document and the CHMP assessment report on the December 2007 recommendation of the refusal of the marketing authorisation for Rhucin can be found here.
2. The arbitration procedures for Fortipan Comb and Norsed Combi were conducted under Article 29(4) of Directive 2001/83/EC.
3. The arbitration procedure for Genotropin was conducted under article 6(12) of Commission Regulation (EC) No 1084/2003.
4. The harmonisation referral of Atacand Plus was conducted under Article 30 of Directive 2001/83/EC, as amended.
5. The review of Invirase is being conducted in the context of a formal review, initiated by the European Commission under Article 20 of Regulation (EC) No 726/2004/EC. The Committee will make recommendations on whether the marketing authorisation for Invirase should be maintained, changed, suspended or revoked.
6. The review of angiotensin inhibitors was started at the request of Italy under Article 5(3) of Council Regulation (EC) No 726/2004.
7. The reference for the meta-analysis of angiotensin receptor blockers is as follows: Sipahi I et al. Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials. Lancet Oncol doi:10.1016/S0140-6736(08)61345-8.
8. Angiotensin receptor blockers are used to reduce blood pressure and have been available in the EU since the mid-1990s. The authorised angiotensin receptor blockers are candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan and valsartan.
9. A more detailed CHMP meeting report will be published shortly.

Contact our press officers

Martin Harvey Allchurch or Monika Benstetter

Tel. +44 (0)20 7418 8427

E-mail: press@ema.europa.eu