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Press Office

Press release

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

14-17 March 2011

Positive opinions for new medicines adopted

The Committee adopted positive opinions 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 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 composition and pharmaceutical form and overlapping indications with Cinryze. This may preclude the granting of a marketing authorisation for Cinryze.

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Positive opinions for extensions of therapeutic indications adopted

The Committee adopted positive opinions 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 opinion for all medicines, including their full therapeutic indications, can be found on the Agency's website.

Negative opinion for extension of therapeutic indications adopted

The Committee adopted a negative opinion 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 available on the Agency's website.

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.

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.

Arbitration procedure concluded

The Committee completed an arbitration procedure 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.

Harmonisation procedure concluded

The Committee recommended the harmonisation 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.

Review of pioglitazone-containing medicines started

The Committee has begun looking at the benefit-risk balance of the antidiabetic **pioglitazone-containing medicines**, 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.

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** (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** 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 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), 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.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. The arbitration procedure for Canazole was conducted under Article 29 of Directive 2001/83/EC.
3. The harmonisation procedure for Arimidex was conducted under Article 30 of Directive 2001/83/EC.
4. 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.
5. 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.
6. 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.
7. 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.
8. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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