EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 September 2010
EMA/CHMP/394406/2010
Press Office

Press release

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

20-23 September 2010

Suspension of rosiglitazone-containing medicines recommended

Finalising a review of the rosiglitazone-containing anti-diabetes medicines **Avandia** (rosiglitazone), **Avaglim** (rosiglitazone / glimepiride), and **Avandamet** (rosiglitazone / metformin), the Committee recommended the suspension of their marketing authorisations. These medicines will stop being available in Europe within the next few months. Patients who are currently taking these medicines should make an appointment with their doctor to discuss suitable alternative treatments. Patients are advised not to stop their medication without speaking to their doctor.

The review was initiated following the availability of new studies questioning the cardiovascular safety of the medicine.

More information about this review is available in a separate press release and a question-and-answer document.

Update on the review of Pandemrix

The Committee reviewed all available data on the suspected link between narcolepsy and **Pandemrix**, an (H1N1)v influenza vaccine, from GlaxoSmithKline Biologicals S.A. The Committee concluded that the available evidence is insufficient to determine whether there is any link between Pandemrix and reports of narcolepsy, and that further studies are necessary to fully understand this issue.

The Committee agreed that, at present, the benefit-risk balance of Pandemrix continues to be positive and that while the review is still ongoing, there is no need for Europe-wide restrictions on use.

More information about this review is available in a separate press release.

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Positive opinion for new medicines adopted

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

- **Aflunov** and **Prepandemic influenza vaccine (H5N1) Novartis** (prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)), from Novartis Vaccines and Diagnostics S.r.l., intended for immunisation against H5N1 subtype of influenza A virus. The review for Aflunov and Prepandemic influenza vaccine (H5N1) Novartis began on 23 December 2009 with an active review time of 210 days. The Aflunov application was a resubmission of an application that was withdrawn by the applicant on 13 June 2008, because at that time the company could not meet the Committee's request for additional clinical data, as required by the prepandemic guideline.
- **Brilique** and **Possia** (ticagrelor), from AstraZeneca AB, intended, in co-administration with acetylsalicylic acid, for the prevention of atherothrombotic events in adult patients with acute coronary syndromes. The review for Brilique began on 18 November 2009 with an active review time of 206 days. The review for Possia began on 26 May 2010 with an active review time of 86 days
- **TOBI Podhaler** (tobramycin), an orphan medicine from Novartis Europharm Ltd, intended for the suppressive therapy of chronic pulmonary infection due to *Pseudomonas aeruginosa* in adults and children aged 6 years and older with cystic fibrosis. The review for TOBI Podhaler began on 23 December 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 a new medicine adopted

The Committee adopted a negative opinion, recommending that **Movectro** (cladribine), from MerckSerono Europe Ltd, should not be granted a marketing authorisation. Movectro was intended for the treatment of multiple sclerosis.

More information about Movectro is available in a question-and answer-document.

Positive opinion for a generic medicine adopted

The Committee adopted a positive opinion recommending the granting of a marketing authorisation for the generic medicine **Leflunomide ratiopharm** (leflunomide), from ratiopharm GmbH, for the treatment of adult patients with active rheumatoid arthritis. Leflunomide ratiopharm is a generic of Arava.

Positive opinions for extensions of therapeutic indications adopted

The Committee adopted positive opinions for applications for extensions of the therapeutic indications, adding new treatment options for medicines that are already authorised in the European Union (EU), for:

- **Mabthera** (rituximab), from Roche Registration Ltd, to include the treatment of follicular lymphoma patients responding to induction therapy.
- **Tasigna** (nilotinib), from Novartis Europharm Ltd, to include the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukaemia in the chronic phase.

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

Suspension of Octagam recommended

Finalising a review of **Octagam** (human normal immunoglobulin), from Octapharma, the Committee recommended the suspension of the marketing authorisations, and a recall of Octagam currently on the market in Europe. As the medicine will no longer be available, the Agency recommended that doctors should stop using Octagam and should switch their patients to the most appropriate alternative treatment.

Octagam is an intravenous solution used to strengthen the body's immune system to lower the risk of infection in patients with a weakened immune system.

The review was initiated following an unexpected increase in reports of thromboembolic reactions, including stroke, myocardial infarction and pulmonary embolism in patients receiving the medicine. This increase is thought to be related to problems with the medicine's manufacturing process.

More information about this review is available in a separate press release and a question-and-answer document.

Review of RotaTeq concluded

The Committee finalised a review of the oral vaccine **RotaTeq**, from Sanofi Pasteur MSD, following the detection of porcine circovirus (PCV) DNA fragments. The Committee concluded that the presence of very low levels of viral DNA fragments in the vaccine does not present a risk to public health and that the vaccine continues to have a positive benefit-risk balance.

More information about the review of Rotateq is available in a separate press release and a question-and-answer document.

Arbitrations concluded

The Committee completed arbitration procedures initiated because of disagreement among EU Member States regarding the authorisation of

- **Galantamine Stada** (galantamine), from Alfred E. Tiefenbacher GmbH & Co KG. This medicine is indicated for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer type. This procedure was initiated because of concerns that this medicine was not bioequivalent to

the reference product, and that this could thus result in suboptimal dosing. The Committee concluded that bioequivalence with the reference product has not been shown and that the benefit-risk balance of this medicine is negative, and recommended that marketing authorisations should not be granted.

- **Prevora** (chlorhexidine diacetate), from CHX Technologies Europe Ltd. This procedure was initiated because of concerns that the results from the main study with Prevora were not sufficient to support the proposed indication. The Committee concluded that based on evaluation of the newly available data from a Phase IIIB controlled study, that the benefit-risk balance of this medicine in the prevention of coronal and root caries in adult patients at high-risk of dental caries was positive and recommended that marketing authorisations should be granted.

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

Harmonisation referral concluded

The Committee recommended harmonisation of the prescribing information for **Lipitor** and associated names (atorvastatin), from Pfizer and associated companies. This medicine is authorised to treat hypercholesterolaemia and to prevent cardiovascular disease. The review was initiated because of differences in the summaries of product characteristics, labelling and package leaflets in the countries where the product is marketed.

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

Review of benefits and risks of Avastin started

The Committee has started a review of the benefits and risks of **Avastin** (bevacizumab), in view of the results of a study conducted by the marketing authorisation holder, Roche Registration Ltd. The study was submitted in support of an application of Avastin in the treatment of breast cancer in combination with anthracycline-based or capecitabine cytotoxic chemotherapy.

In comparison to results of previous studies, this study points to inconsistencies between different trials relevant for the currently approved breast cancer indication, particularly in terms of efficacy.

The review of Avastin has been initiated to assess the new data and their impact on the benefit-risk balance of Avastin as regards the indication 'combination treatment with paclitaxel or docetaxel as first line treatment of patients with metastatic breast cancer'.

Review of bisphosphonates started

The Committee has begun looking at the possible increased risk of atypical stress fractures in patients taking **bisphosphonate-containing medicines** for the treatment and prevention of bone disorders. This follows the review of published literature and post-marketing reports, suggesting that atypical stress factures may be a class effect of bisphosphonates.

A warning about atypical stress fractures of the proximal femoral shaft has been included in the product information for alendronate-containing medicines across Europe, since a review in 2008.

The CHMP will now review all available data thoroughly, including published data, non-clinical and clinical data and post-marketing reports, to clarify whether atypical stress fractures are a class effect of bisphosphonates, and will assess their impact on the balance of risks and benefits of these medicines.

Notes

1. The review of Avandia, Avandamet and Avaglim was conducted under Article 20 of Regulation (EC) No 726/2004.
2. The review of Pandemrix is being conducted under Article 20 of Regulation (EC) No 726/2004.
3. On 16 August 2008, the European Medicines Agency published a press release informing of the withdrawal of the marketing authorisation application for the pre-pandemic vaccine Aflunov.
4. The review of Octagam was conducted under Article 107 of Directive 2001/83/EC, as amended.
5. The review of RotaTeq was conducted under Article 20 of Regulation (EC) No 726/2004.
6. The review of Galantamin Stada was conducted under Article 29(4) of Directive 2001/83/EC, as amended.
7. The review of Prevora was conducted under Article 29(4) of Directive 2001/83/EC, as amended.
8. The harmonisation referral on Lipitor was conducted under Article 30 of Directive 2001/83/EC, as amended.
9. The review of Avastin is being conducted in the context of a formal review under Article 20 of Regulation (EC) No 726/2004. The Committee will make recommendations on whether the marketing authorisation for Avastin should be maintained, changed, suspended or revoked.

   Avastin was first authorised in 2005 for first line treatment of metastatic colon or rectum cancer in combination with fluoropyrimidine-based chemotherapy. Subsequently the therapeutic indication had been extended to include the first-line treatment of metastatic breast cancer in combination with paclitaxel or docetaxel.
10. Bisphosphonates include alendronate, clodronate, etidronate, ibandronate, neridronate, pamidronate, risedronate, tiludronate and zoledronate.

    The review of nationally authorised bisphosphonates is being conducted in the context of a formal review under Article 31 of Directive 2001/83/EC, as amended. The Committee will make recommendations on whether the marketing authorisations for bisphosphonates should be maintained, changed, suspended or revoked.
11. A more detailed CHMP meeting report will be published shortly.

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