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SCIENCE MEDICINES HEALTH

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Press Office

Press release

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

19-22 July 2010

Update on the ongoing benefit-risk review of Avandia, Avandamet and Avaglim

The CHMP is currently reviewing the rosiglitazone-containing antidiabetes medicines **Avandia** (rosiglitazone), **Avaglim** (rosiglitazone/glimepiride) and **Avandamet** (rosiglitazone/metformin hydrochloride), from Smithkline Beecham Ltd, to determine the impact of new data, from recent publications on the risk of cardiovascular problems, on the benefit-risk profile of these medicines. While the Committee is reviewing all available data, prescribers in Europe are reminded to strictly follow the recommendations in the product information with respect to patients indicated for treatment, defined contraindications and warnings.

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

Positive opinion for a new medicine adopted

The Committee adopted a positive opinion recommending the granting of a marketing authorisation for **Twynsta** (telmisartan/amlodipine), from Boehringer Ingelheim International GmbH, intended for the treatment of essential hypertension. The review for Twynsta began on 23 September 2009 with an active review time of 210 days.

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Positive opinion for generic medicines adopted

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

- **Clopidogrel Teva Pharma B.V.** (clopidogrel, as hydrobromide), from Teva Pharma B.V., for the prevention of atherothrombotic events. Clopidogrel Teva Pharma B.V. is a generic of Plavix.
- **Clopidogrel HCS** and **Clopidogrel Teva Generics B.V.** (clopidogrel, as hydrochloride), from Teva Pharma B.V. and from HCS bvba, for the prevention of atherothrombotic events. Clopidogrel HCS and Clopidogrel Teva Generics B.V. are generics of Plavix.
- **Myclausen** (mycophenolate mofetil), from Herbert J. Passauer GmbH & Co. KG, for the prophylaxis of acute transplant rejection in combination with ciclosporin and corticosteroids. Myclausen is a generic of Cellcept.

Positive opinions for extensions of indications adopted

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

- **Arixtra** (fondaparinux sodium), from Glaxo Group Ltd, to include treatment of acute symptomatic spontaneous superficial vein thrombosis of the lower limbs without concomitant deep vein thrombosis.
- **M-M-RVAXPRO** (measles, mumps and rubella vaccine live), from Sanofi Pasteur MSD, SNC, to include vaccination of healthy children from 9 months of age under special circumstances, in accordance with official recommendations or when early protection is considered necessary.
- **Viread** (tenofovir disoproxil), from Gilead Sciences International Ltd, to include treatment of chronic hepatitis B in adults with decompensated liver disease.

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

New paediatric indication for Xalatan

The CHMP recommended an extension of the therapeutic indications of **Xalatan eye drops** and associated names (latanoprost), from Pfizer group of companies, to include the reduction of elevated intraocular pressure in the treatment of paediatric patients with elevated intraocular pressure and paediatric glaucoma.

The Committee's recommendation was made on the basis of data generated in accordance with an agreed paediatric investigation plan (PIP).

Update on the review of rotavirus vaccines

The CHMP finalised a review of the oral vaccine **Rotarix** (rotavirus vaccine, live) from GlaxoSmithKline Biologicals S.A., following the detection of porcine circovirus 1 (PCV1) DNA in the vaccine. The Committee concluded that the vaccine continues to have a positive benefit-risk balance and that the presence of a very small amount of viral particles does not present a risk to public health.

The review of the rotavirus vaccine, **Rotateq**, from Sanofi Pasteur MSD, SNC, following the detection of porcine virus in this vaccine is still ongoing and will be considered in September. The CHMP is awaiting further information from the manufacturer on the root cause of the findings and on measures to manufacture the vaccine free of porcine virus. While this review is still ongoing, the Committee confirmed its previous position that there is no need to restrict the use of Rotateq.

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

Review of topical formulations of ketoprofen concluded

Finalising a review of **topical formulations of ketoprofen**, a non-steroidal anti-inflammatory drug (NSAID), the Committee concluded that the benefits of these medicines continue to outweigh their risks. However, the Committee recommended that doctors should inform patients on how to use these medicines appropriately to prevent the occurrence of serious skin photosensitivity reactions.

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

Review of modafinil-containing medicines concluded

Finalising a review of **modafinil-containing medicines**, the Committee recommended restricting the use of these medicines to the treatment of sleepiness associated with narcolepsy. Doctors and patients should no longer use these medicines for the treatment of idiopathic hypersomnia, excessive sleepiness associated with obstructive sleep apnoea or chronic shift work sleep disorder.

Modafinil is a wakefulness promoting agent. The review had been initiated because of a number of safety concerns relating to neuropsychiatric disorders, skin and subcutaneous tissue reactions as well as significant off-label use and potential for abuse.

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

Review of modified-release oral opioids concluded

Finalising a review of **modified-release oral opioid products** in level III of the World Health Organization (WHO) scale for the management of pain, the Committee recommended the suspension of formulations using polymethacrylate-triethylcitrate controlled release systems because of their interaction with alcohol. The Committee concluded that other formulations had a positive benefit-risk balance, but recommended harmonising existing warnings regarding concomitant use of these medicines with alcohol.

Modified-release oral opioids of the WHO level III scale for the management of pain are strong painkillers used to treat pain that has not been controlled with other medicines.

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

Harmonisation referral on Daivobet concluded

The Committee recommended the harmonisation of the prescribing information for **Daivobet** and associated names (calcipotriol/betamethasone), from Leo Pharma and associated 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 psoriasis.

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

Review of dexrazoxane-containing medicines started

The Committee has begun looking at the possible risk of acute myelogenous leukaemia (AML), myelodyspastic syndrome (MDS) and solid tumours in paediatric patients taking **dexrazoxane-containing medicines** for the prevention of anthracycline-induced cardiotoxicity. This follows the review of published literature, together with the results of randomised clinical trials, which suggests that these medicines may be linked with a three-fold increased risk of secondary malignancies, especially AML and MDS. At the same time, the available clinical studies show only limited efficacy of these medicines in the prevention of cardiotoxicity, and the alternative treatment options of heart failure have been markedly improved.

The CHMP will review all available data thoroughly, including published data, non-clinical and clinical data (including data from clinical trials and epidemiological studies), to clarify the impact of the increased risk of secondary malignancies, coupled with limited data on efficacy, on the balance of risks and benefits of these medicines.

Notes

1. The review of Avandia, Avandamet and Avaglim is being conducted under Article 20 of Regulation (EC) No 726/2004.
2. The changes to the marketing authorisation for Xalatan were recommended under Article 29 of Regulation (EC) No 1901/2006, the Paediatric Regulation. This type of procedure allows companies to submit to the European Medicines Agency an application for a new indication, a new pharmaceutical form or a new route of administration for medicines that are already authorised at the level of the Member States. Once a CHMP opinion on such an application has been transformed into a decision by the European Commission, companies will be able to obtain approval for the new formulation and indication in all EU Member States where the medicine is authorised.
3. The review of Rotarix was conducted under Article 20 of Regulation (EC) No 726/2004.
4. The review of Rotateq is being conducted under Article 20 of Regulation (EC) No 726/2004.
5. The review of topical formulations of ketoprofen was conducted under Article 107 of Directive 2001/83/EC, as amended.
6. The review of modafinil-containing medicines was conducted under Article 31 of Directive 2001/83/EC, as amended.

7. The review of modified-release oral opioids was conducted under Article 31 of Directive 2001/83/EC, as amended.
8. The harmonisation referral on Daivobet was conducted under Article 30 of Directive 2001/83/EC, as amended.
9. The review of dexrazoxane-containing medicines is being conducted in the context of a formal review, initiated by the United Kingdom under Article 31 of Directive 2001/83/EC, as amended. The Committee will make recommendations on whether the marketing authorisations for dexrazoxane-containing medicines should be maintained, changed, suspended or revoked.

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