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PRESS RELEASE
Meeting highlights from the Committee for Medicinal Products for Human Use, 20-23 April 2009

Initial evaluation – positive opinions
The European Medicines Agency's (EMEA) Committee for Medicinal Products for Human Use (CHMP) adopted positive opinions, recommending the granting of a marketing authorisation, for the following medicines:

- **Instanyl** (fentanyl citrate), from Nycomed Danmark ApS, indicated as a nasal spray for the treatment of breakthrough pain in cancer patients who receive chronic opioid treatment for the management of their background pain. EMEA review began on 2 December 2007, with an active review time of 205 days.
- **Iressa** (gefitinib), from AstraZeneca AB, indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with activating mutations of EGFR-TK. EMEA review began on 28 May 2008, with an active review time of 210 days.
- **Nymusa** (caffeine citrate), from Chiesi Farmaceutici SpA, indicated for the treatment of primary apnoea in premature newborns. EMEA review began on 28 May 2008, with an active review time of 204 days. Nymusa is the **54th orphan medicine** to receive a positive opinion from the CHMP.
- **Victoza** (liraglutide), from Novo Nordisk A/S, indicated for the treatment of type-2 diabetes mellitus. EMEA review began on 25 June 2008, with an active review time of 204 days.

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

Generic medicinal products
The Committee adopted positive opinions recommending a marketing authorisation for the following generic medicines for which a reference medicine is already authorised in the European Union:

- **Repaglinide Teva** (repaglinide), from Teva Pharma B.V., indicated for the treatment of type-2 diabetes mellitus. The reference medicine for Repaglinide Teva is Novonorm, which is already authorised in the European Union in the indication applied for. EMEA review began on 24 September 2008, with an active review time of 177 days.
- **Ribavirin Teva Pharma BV** (ribavirin), from Teva Pharma B.V., indicated for the treatment of chronic hepatitis C. The reference medicine for Ribavirin Teva Pharma BV is Rebetol, which is already authorised in the European Union in the indication applied for. EMEA review began on 24 September 2008, with an active review time of 177 days.

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

Extension of indication – positive opinions
The Committee gave positive opinions for applications for the extension of indication, adding a new treatment option, for the following medicines:

- **Aptivus (**tipranavir), from Boehringer Ingelheim, to extend the indication to the treatment of human immunodeficiency virus (HIV-1) infection in highly pre-treated adolescents with virus resistant to multiple protease inhibitors above the age of 12, and also to extend the indication in highly pre-treated children aged 2 to 12. The latter indication comes with a new oral solution formulation. Aptivus is currently indicated for combination antiretroviral treatment of HIV-1 infection in highly pre-treated adult patients with virus resistant to multiple protease inhibitors.
- **Prezista (**darunavir), from Tibotec, to extend the indication to include the treatment of human immunodeficiency virus (HIV-1) infection in treatment-experienced children and adolescents

above the age of 6. This indication also comes with the new strengths 75mg and 150mg film-coated tablets. Prezista is currently indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in treatment-experienced adult patients.

- **Janumet**, **Efficib** and **Velmetia** (sitagliptin phosphate monohydrate / metformin hydrochloride), and **Januvia**, **Tesavel** and **Xelevia** (sitagliptin), from Merck Sharp & Dohme Ltd, to extend the indication of these medicines to use in combination with a PPARγ agonist and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. Janumet, Efficib and Velmetia are currently authorised for the treatment of type-2 diabetes mellitus, as an adjunct to diet and exercise, to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of metformin. Additionally, they are also indicated as triple combination with a sulphonylurea in patients inadequately controlled on their maximal tolerated dose of metformin and sulphonylurea. Januvia, Tesavel and Xelevia are currently authorised for the treatment of type-2 diabetes mellitus, in combination with metformin, in combination with a sulphonylurea, in combination with a PPARγ agonist or in triple combination with a sulphonylurea and metformin, as an adjunct to diet and exercise, to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of the previously mentioned agents.

Summaries of opinion for all mentioned medicines, including their full indication, can be found here.

Extension of indication – negative opinion

The Committee adopted a negative opinion, recommending the refusal of an extension of the indication to the treatment of fibromyalgia in adults experiencing moderate to severe pain, for **Lyrica** (pregabalin), from Pfizer Ltd. Lyrica is currently authorised for the treatment of neuropathic pain, epilepsy and generalised anxiety disorder in adults.

A question-and-answer document with more information on the negative opinion can be found here.

Abacavir and the risk of heart attack

Finalising a review of recent data on the risk of heart attack (myocardial infarction) associated with the use of abacavir in HIV-infected patients, the CHMP has concluded that there is insufficient evidence to recommend changes to the therapeutic management of patients. This follows the Committee's review of findings from the D:A:D study in April 2008, which concluded that further data were needed to determine this risk.

Data from observational studies that have become available since April 2008, including the French Hospital Database on HIV, have continued to show a possible link between myocardial infarction and the use of abacavir. Data from clinical trials showed low numbers of myocardial infarction and could not exclude a small increase in risk.

However, the CHMP has concluded that there were inconsistencies between the different studies' findings, and that a causal relationship between treatment with abacavir and the risk of myocardial infarction can neither be confirmed nor refuted. To date, there is no established biological mechanism that could explain a potential increase in risk.

Nevertheless, when prescribing abacavir-containing medicines, prescribers should take action to minimise modifiable risk factors, such as smoking, high blood pressure and high blood-fat levels. The product information for abacavir-containing medicines will be updated to reflect this information.

Abacavir is a nucleoside reverse transcriptase inhibitor (NRTI) indicated in antiretroviral combination therapy for the treatment of HIV infection. In the European Union, it is available as Ziagen, in combination with lamivudine as Kivexa, and in combination with lamivudine and zidovudine as Trizivir.

The press release 'Further data needed to determine risk of heart attack with abacavir', from April 2008, is available here.

Referral procedures concluded

The CHMP concluded a number of referral procedures under Article 29 of Directive 2001/83/EC, as amended. This type of procedure is initiated by one or more Member States in cases where an agreement cannot be reached in the context of the mutual-recognition procedure or the decentralised procedure. The medicinal products concerned are:

- **Ciclosporine IDL and associated names** (ciclosporin), 25mg, 50mg and 100mg capsules, from International Drug Licensing, used as an immunosuppressant drug. The procedure was initiated as a result of disagreements between some Member States regarding the bioequivalence of this medicine with the reference medicine. The CHMP concluded that the data and the justification presented were not adequate to confirm the bioequivalence. The CHMP recommended the refusal of the marketing authorisation in the concerned Member States, and the suspension of the marketing authorisation for Ciclosporin IDL in the Member States where the medicine is currently authorised.
- **Prokanazol and associated names** (itraconazole), 100mg hard capsules, from PRO.MED.CS Praha a.s., intended for the treatment of certain fungal infections. The procedure was initiated because of concerns by some Member States over bioequivalence of the medicine with the reference medicine. The CHMP concluded that bioequivalence with the reference medicine has not been demonstrated. The CHMP recommended the refusal of the marketing authorisations in the concerned Member States, and the suspension of the marketing authorisation in the Member States where the product is currently authorised.

Separate question-and-answer documents with more information about the abovementioned procedures are available here.

Referral procedure started

The CHMP started a referral for **valproate-containing medicines**, on the request of the Netherlands, because of concerns related to the efficacy of these medicines when used in the treatment of manic episodes in patients with bipolar disorder. The referral was initiated under Article 31 of Directive 2001/83/EC, as amended.

A more detailed CHMP meeting report will be published shortly.

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