



European Medicines Agency
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PRESS RELEASE
Meeting highlights from the Committee for Medicinal Products for Human Use,
17-20 September 2007

Positive opinions

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted 6 positive opinions, including one for a generic medicine and one 'informed consent' application, recommending the granting of a marketing authorisation for the following medicinal products:

- **Cyanokit** (hydroxocobalamin), from Merck Santé s.a.s., for the treatment of known or suspected cyanide poisoning. EMA review began on 27 December 2006 with an active review time of 177 days.
- **Eucreas** (vildagliptin / metformin hydrochloride), from Novartis Europharm Limited, for the treatment of type 2 diabetes mellitus. EMA review began on 24 January 2007 with an active review time of 177 days.
- **Tasigna** (nilotinib), from Novartis Europharm Limited, for the treatment of Philadelphia chromosome positive chronic myelogenous leukaemia (CML). Tasigna is the 43rd orphan medicinal product* to receive a positive opinion. EMA review began on 25 October 2006 with an active review time of 200 days.
- **Torisel** (temsirolimus), from Wyeth Europa Ltd, for the first-line treatment of renal cell carcinoma. Torisel is the 44th orphan medicinal product* to receive a positive opinion. EMA review began on 25 October 2006 with an active review time of 203 days.

Positive opinion for a generic medicinal product

The CHMP adopted a positive opinion for **Olanzapine Neopharma** (olanzapine), from Neopharma Ltd, for the treatment of schizophrenia and moderate to severe manic episode. The reference product for Olanzapine Neopharma is Zyprexa, from Eli Lilly Nederland B.V., which is already authorised in the European Union (EU), in the applied indications. EMA review began on 25 October 2006 with an active review time of 205 days.

Positive opinion for 'informed consent' application

The CHMP adopted a positive opinion for **Pioglitazone / metformin hydrochloride** Takeda 15 mg/850 mg film-coated tablets (Pioglitazone / metformin hydrochloride), from Takeda Europe R&D Centre Ltd, for which an 'informed consent' application was submitted, intended for treatment of type 2 diabetes mellitus patients, particularly overweight patients, who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone. This type of application requires that reference is made to an authorised medicinal product and that the marketing authorisation holder of this reference product has given consent to the use of the dossier in the application procedure.

Negative opinion

The CHMP adopted a negative opinion recommending the refusal of a marketing authorisation for **Mylotarg** (gemtuzumab ozogamicin), from Wyeth Europa Limited. Mylotarg was intended to be used for the re-induction treatment of CD33-positive acute myeloid leukaemia patients in first relapse who are not candidates for other intensive re-induction chemotherapy regimens (e.g. high-dose ARA-C). EMA review began on 28 December 2005 with an active review time of 200 days.

* corr: The number of positive opinions for orphan medicinal products has been corrected.

A separate [question-and-answer document](#) explaining the grounds for the negative opinion for Mylotarg is available on the EMEA website.

Re-examination procedure concluded

Following the re-examination of the negative opinion adopted on 24 May 2007, the CHMP adopted a final positive opinion with specific obligations for **Vectibix** (panitumumab), from Amgen, intended as monotherapy for the treatment of patients with EGFR expressing metastatic colorectal carcinoma with non-mutated (wild-type) KRAS after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens. The CHMP recommended a 'Conditional Approval' for Vectibix, since there is more information to come about the medicine, in particular its safety and efficacy in patients according to their KRAS status.

A separate [question-and-answer document](#) with more information about the re-examination procedure is available on the EMEA website.

Extensions of indication

The CHMP gave positive opinions on applications for extensions of indication, adding new treatment options for the following previously approved medicines:

- **Combivir** (lamivudine/zidovudine), from GlaxoSmithKline, to extend the indication to paediatric patients and to replace film coated tablets by scored film coated tablets. Combivir is currently authorised for use in adults and adolescents (over 12 years of age) as part of a combination treatment for HIV infection.
- **Lamivudine/Zidovudine GSK** (lamivudine/zidovudine), from GSK, to extend the indication to paediatric patients and to replace film coated tablets by scored film coated tablets. Lamivudine/Zidovudine GSK is currently authorised for use in adults and adolescents (over 12 years of age) as part of a combination treatment for HIV infection. The opinion is given in accordance with Article 58 of Regulation (EC) No 726/2004, which allows the CHMP, in the context of cooperation with the World Health Organization (WHO), to adopt scientific opinions on medicinal products intended exclusively for markets outside the European Union.
- **Nexavar** (sorafenib), from Bayer Healthcare AG, to extend the indication to include treatment of patients with hepatocellular carcinoma. Nexavar is currently indicated for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.
- **Pegintron** and **ViraferonPeg** (peginterferon alfa-2b), from SP Europe, to extend the indication in combination with ribavirin to adult patients who have failed previous treatment with interferon alpha (pegylated or nonpegylated) and ribavirin combination therapy or interferon alpha monotherapy. Peginterferon alfa-2b is currently indicated for the treatment of adult patients with chronic hepatitis C. The best way to use peginterferon alfa-2b in this indication is in combination with ribavirin.
- **Rebetol** (ribavirin), from SP Europe, to extend the indication in combination with peginterferon alfa-2b to adult patients who have failed previous treatment with interferon alpha (pegylated or nonpegylated) and ribavirin combination therapy or interferon alpha monotherapy. Rebetol is currently indicated for the treatment of chronic hepatitis C and must only be used as part of a combination regimen with peginterferon alfa-2b in adults or with interferon alfa-2b in adults and children.
- **Remicade** (infliximab), from Centocor B.V., to change the indication for ankylosing spondylitis to include patients who have responded inadequately to conventional therapy, regardless of their HLA-B27 status or serological markers level. Remicade is currently indicated for treatment of rheumatoid arthritis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis.

Negative opinion for Nutropin AQ

The CHMP adopted a negative opinion, recommending the refusal of an extension of indication for **Nutropin AQ** (somatropin), from Ipsen Ltd. The indication applied for related to the inclusion of treatment of children with severe 'idiopathic' short stature (ISS) not explained by growth hormone deficiency (GHD) or other medical conditions and with a predicted adult height at least 1 SDS (Standard Deviation Score) below the target height.

A separate [question-and-answer document](#) explaining the grounds for the negative opinion for the extension of indication is available on the EMEA website.

Changes to contraindications

The Committee recommended a new contraindication for **Viracept** (nelfinavir mesilate), from Roche Registration Ltd, saying that Viracept should not be co-administered with omeprazole due to a reduction in exposure to nelfinavir and its active metabolite M8. This may lead to a loss of virologic response and possible resistance to Viracept.

The adoption of the contraindication is not related to the recommendation to lift the suspension of the marketing authorisation for Viracept (see below).

The CHMP recommended the removal of the contraindication for **Competact** (pioglitazone/metformin) and **Tandemact** (pioglitazone/glimepiride) from Takeda Europe R&D Centre Ltd, regarding the concurrent administration with insulin. Competact is currently authorised for the treatment of type 2 diabetes mellitus patients, particularly overweight patients, who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone. Tandemact is currently indicated for the treatment of patients with type 2 diabetes mellitus who show intolerance to metformin or for whom metformin is contraindicated and who are already treated with a combination of pioglitazone and glimepiride.

Summaries of opinions for all mentioned products, including their full indication, can be found [here](#).

Lifting of suspension for Viracept recommended

The CHMP recommended the lifting of the suspension of the marketing authorisation for Viracept (nelfinavir, as nelfinavir mesilate), from Roche, and the re-introduction of the medicine onto the market in the European Union.

A separate [press release](#) and a [question-and-answer document](#) with more detailed information are available on the EMEA website.

Referral procedures concluded

The CHMP finalised a referral procedure under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) for **Bicaluplex 150mg tablet** (Bicalutamide) and associated names, from Ingers Industrial Solutions s.r.o., indicated either alone or as adjuvant to radical prostatectomy or radiotherapy in patients with locally advanced prostate cancer at high risk of disease progression. The procedure was initiated due to concerns raised by Germany that a positive benefit-risk balance of this product had not been proven. The CHMP concluded that the benefits of Bicaluplex outweigh its risks and recommended the granting of the marketing authorisation for Bicaluplex.

Review procedures under Article 29 are normally initiated because of disagreement among the Member States in the context of the mutual recognition procedure related to a potential serious risk to public health.

Referral procedures started

The CHMP started a referral procedure under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended), for **Oracea** (doxycycline), from FGK Representative Service GmbH, intended to reduce inflammatory lesions in patients with rosacea.

The CHMP began two referrals under Article 30 of the Community code on human medicinal products (Directive 2001/83/EC as amended). This type of procedure is initiated with a view to harmonising product information for medicinal products authorised at Member State level. The two products concerned are:

- **Singulair** 4mg chewable tablets and oral granules, from Merck Sharp & Dohme Inc., intended for the treatment and prophylaxis of asthma.
- **Risperdal** and **Risperdal Consta** and associated names (risperidone), from Janssen-Cilag, intended for the treatment of schizophrenia, manic episodes associated with bipolar disorder, behavioural and psychological disturbances in patients with dementia, disruptive behaviour disorders and autistic disorders.

The CHMP started a referral procedure for oral formulation of **norfloxacin-containing medicinal products** in the treatment of acute or chronic complicated pyelonephritis due to susceptible organisms. The referral procedure was initiated by Belgium under Article 31 of the Community code on human medicinal products (Directive 2001/83/EC as amended) to re-assess the balance of benefits and risks of these medicinal products in the treatment of acute or chronic complicated pyelonephritis due to susceptible organisms. Referrals under Article 31 are initiated in cases involving the interests of the Community or concerns relating to the protection of public health.

The CHMP started to review the benefits and risks of all **Etoricoxib-containing medicinal products** because of concerns over cardiovascular safety when used in the long-term treatment of ankylosing spondylitis and rheumatoid arthritis. A review was initiated, under Article 6(12) of Commission Regulation EC No 1084/2003, for **Arcoxia** (etoricoxib), from Merck Sharp & Dohme Limited, because of disagreement between Member States on the safety of an extension of the indication of Arcoxia to include symptomatic treatment of ankylosing spondylitis in the context of the mutual recognition procedure. Furthermore a review under Article 31 of Directive 2001/83/EC for all Etoricoxib-containing medicinal products in the long-term treatment of ankylosing spondylitis and rheumatoid arthritis was initiated because the safety issue raised by France was considered to be of Community interest to protect public health.

The CHMP also started referral procedures for generic medicinal products containing **Cetirizine dihydrochloride** because of concerns over their bioequivalence. The procedures were initiated by the Netherlands under Article 36 of the Community code on human medicinal products (Directive 2001/83/EC as amended) for the following products and associated names: Cetirizine dihydrochloride-Apex 10mg, Cetirizine dihydrochloride Copyfarm 10mg, Cetirizine dihydrochloride Dermapharm 10mg and Cetirizine dihydrochloride Nordic Drugs 10mg film-coated tablets. Article 36 procedures are initiated where a Member State considers that there are public health issues relating to a product that may require further regulatory action.

Review procedures under Article 107

The CHMP finalised a procedure under Article 107, initiated as a result of the evaluation of pharmacovigilance data, for systemic formulations of **nimesulide**-containing medicinal products, intended for the treatment of pain, following the suspension of the marketing authorisation in Ireland, due to concerns over serious liver problems. The CHMP concluded that the benefit-risk of nimesulide continues to be positive and recommended the maintenance of the marketing authorisation, but that there is a need to restrict its use.

A separate [press release](#) and a [question-and-answer document](#) with more detailed information are available on the EMEA website.

The CHMP initiated two procedures under Article 107 for:

- **Carisoprodol**, intended for the treatment of several types of pain further to the plan to withdraw the product from the Norwegian market in May 2008 due to risks of intoxication, psychomotor impairment, addiction and misuse due to off-label prescribing.
- **Silomat** (clobutinol), from Boehringer Ingelheim, used for the treatment of cough, further to the decision by Germany to suspend all clobutinol-containing medicinal products in Germany on 31 August 2007 due to an increased risk of cardiac arrhythmia associated with clobutinol.

A more detailed CHMP meeting report will be published shortly.

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