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PRESS RELEASE
Meeting highlights from the Committee for Medicinal Products for Human Use, 16-18 October 2006

The Committee for Medicinal Products for Human Use (CHMP) concluded the review of **non-selective non-steroidal anti-inflammatory drugs (NSAIDs)**, which was initiated during the September 2006 meeting. A statement will be issued on Tuesday 24 October at 10h00 (London time).

Initial marketing authorisation applications
The Committee gave four positive opinions on initial marketing authorisation applications, including two opinions for medicinal products that are intended for the treatment of patients suffering from rare diseases:

- The Committee recommended the granting of a conditional marketing authorisation for **Diacomit** (stiripentol), from Laboratoires Biocodex, for the treatment of severe myoclonic epilepsy in infants in conjunction with clobazam and valproate. Conditional marketing authorisation has been recommended on the condition that further evidence regarding efficacy of stiripentol in combination with maximum safe doses of clobazam and valproate, and on the bioavailability of Diacomit sachets compared to capsules is provided at a later stage. The EMEA will re-assess Diacomit annually to confirm that the benefit-risk balance remains positive. Diacomit is the **32nd orphan medicinal product** to receive a positive CHMP opinion. EMEA review began on 18 May 2005 with an active review time of 201 days.
- The Committee recommended the granting of a marketing authorisation under exceptional circumstances for **Elaprase** (idursulfase), from Shire Human Genetics Therapies AB, for the long-term treatment of patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). Elaprase is the **33rd orphan medicinal product** to receive a positive CHMP opinion. EMEA review began on 28 December 2005 with an active review time of 207 days. Marketing authorisation under exceptional circumstances may be granted subject to certain specific obligations, to be reviewed annually. In the case of Elaprase, this relates to the fact that the indication applied for is so rare that the applicant cannot reasonably be expected to provide comprehensive data on the safety and efficacy of the medicinal product.
- **Tandemact** (pioglitazone hydrochloride/glimepiride), from Takeda Europe R & D Centre Ltd, is recommended for the treatment of patients with type-2 diabetes mellitus who show intolerance to metformine or for whom metformin is contraindicated and who are already treated with a combination of pioglitazone and glimepiride. EMEA review began on 17 August 2005 with an active review time of 196 days.
- **Adrovance** (alendronic acid and colecalciferol), from Merck Sharp & Dohme Ltd, is recommended for the treatment of postmenopausal osteoporosis in patients at risk of vitamin D insufficiency. Adrovance is the same medicinal product as Fosavance, also from Merck Sharp & Dohme Ltd, which is already authorised in the European Union. EMEA review began on 21 July 2006 with an active review time of 89 days.

Lifting of conditional marketing authorisation
The Committee recommended to lift the conditional marketing authorisation for **Sutent** (sunitinib malate), from Pfizer Ltd. Sutent was the first medicinal product to be granted a conditional marketing authorisation in the European Union. It is currently indicated for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumours after failure of imatinib mesylate treatment due

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to resistance or intolerance, and advanced and/or metastatic renal cell carcinoma (MRCC) after failure of interferon alfa or interleukin-2 therapy.
The marketing authorisation was granted under the condition that the marketing authorisation holder would provide further comprehensive data on Sutent's effect in terms of relevant clinical endpoints such as progression free survival in patients with MRCC.
Following evaluation of clinical data submitted by the marketing authorisation holder, the Committee recommended a switch from the conditional marketing authorisation to a full marketing authorisation. It also recommended to extend the indication to first-line treatment of advanced and/or metastatic renal cell carcinoma (MRCC).

Extension of indication
In addition to the extension of indication for Sutent, the Committee gave positive opinions for applications for extensions of indication, adding new treatment options for the following previously approved medicines:

- **Aldara** (imiquimod), from Laboratoires 3M Santé, received a positive opinion to include topical treatment of clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratosis in adults. Aldara was first granted a marketing authorisation in the European Union on 18 September 1998 and is currently indicated for the topical treatment of external genital and perianal warts and small superficial basal cell carcinomas in adults.
- **Glivec** (imatinib mesylate), from Novartis Europharm Ltd, received two positive opinions to include treatment of myelodysplastic syndromes and myeloproliferative diseases (MDS/MPD) as well as treatment of adult patients with hypereosinophilic syndrome and chronic eosinophilic leukaemia (HES/CEL). Glivec was first granted a marketing authorisation in the European Union on 7 November 2001 and is currently indicated for the treatment of adult and paediatric patients with Philadelphia chromosome (bcr-abl) positive chronic myeloid leukaemia, adult patients with Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL), adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST) and adult patients with dermatofibrosarcoma protuberans (DFSP).
- **Hycamtin** (topotecan), from SmithKline Beecham Plc, received a positive opinion to include treatment, in combination with cisplatin, of patients with carcinoma of the cervix recurrent after radiotherapy and for patients with Stage IVB disease. Patients with prior exposure to cisplatin require a sustained treatment-free interval to justify treatment with the combination. Hycamtin was first granted a marketing authorisation in the European Union on 12 November 1996 and is currently indicated as monotherapy for second-line treatment of patients with metastatic carcinoma of the ovary and patients with relapsed small cell lung cancer.
- **Rotarix** (live human rotavirus RIX4414), an oral vaccine from GlaxoSmithKline Biologicals, received a positive opinion to extend the therapeutic indication to include new information that protection against rotavirus serotypes G4P[8] and G2P[4] has also been demonstrated. Rotarix was first granted a marketing authorisation in the European Union on 21 February 2006 and indicated for the prevention of gastro-enteritis caused by Rotavirus of types G1P[8], G3P[8] and G9P[8].

New contraindications
The Committee recommended adding new contraindications for four medicinal products that contain duloxetine as active substance. For all four products, namely **Ariclaim** and **Xeristar**, from Boehringer Ingelheim International GmbH, and **Yentreve** and **Cymbalta**, from Eli Lilly Nederland, the Committee recommended that treatment should not be initiated in patients with uncontrolled hypertension that could expose patients to a potential risk of hypertensive crisis.
In addition, for Ariclaim and Yentreve, the Committee also recommended that these two products should not be used in patients with severe renal impairment. This contraindication is already included in the product information for Cymbalta and Xeristar.
Ariclaim and Yentreve were first granted marketing authorisations on 11 August 2004 and are currently authorised for the treatment of moderate to severe stress urinary incontinence in women. Cymbalta and Xeristar were first granted marketing authorisations on 17 December 2004 and are currently authorised for the treatment of major depressive episodes and the treatment of diabetic peripheral neuropathic pain in adults.

Summaries of opinions, including more detailed information on the new indications or contraindications for all products mentioned above are available and can be found here.

Referral procedures concluded

The Committee concluded a referral procedure for **Alendros 70** (alendronate sodium trihydricum), from Zentiva a.s., intended for the treatment of osteoporosis in postmenopausal women. The CHMP recommended the refusal of a marketing authorisation in the concerned Member States and a suspension of the marketing authorisation for Alendros 70 mg tablets in the reference Member State because bioequivalence with the reference product (Fosamax 70 mg tablets) has not been demonstrated. The procedure was initiated under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) by the Czech Republic because of disagreement among the Member States in the context of the mutual recognition procedure.

The Committee concluded a referral procedure recommending the suspension of a generic medicinal product called **Simvastatine** (simvastatine), from Neo Pharma Ltd, because of non-compliance with good clinical practice (GCP) in the conduct of the study used to demonstrate bioequivalence with the originator product. The procedure was initiated by the Netherlands under Article 36 of the Community code on human medicinal products (Directive 2001/83/EC as amended). These procedures are initiated where a Member State considers that there are public health concerns relating to a product that may require regulatory action in all Member States where the product is authorised.

Referral procedures started

The Committee started referral procedures for two generic medicinal products under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) because of disagreement among the Member States in the context of the mutual recognition procedure:

- The referral for **Cefuroximaxetil** 125 omhulde tabletten 125 mg, Cefuroximaxetil 250 omhulde tabletten 250 mg, Cefuroximaxetil 500 omhulde tabletten 500 mg, (cefuroxim (as axetil)), from Sandoz B.V., was initiated because of disagreements on whether the medicinal product should be indicated for the treatment of uncomplicated gonorrhoea (urethritis and cervicitis).
- The referral for **Fexofenadinhydrochlorid "Teva"** 120 mg and 180 mg film-coated tablets (fexofenadine hydrochloride), from Teva UK Ltd, was initiated because of disagreements regarding bioequivalence with the originator product.

A more detailed CHMP meeting report will be published shortly.

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