News from the EMA

Activities of the CHMP

During its meeting from 18–21 July 2011 the Committee for Medicinal Products for Human Use (CHMP) adopted:

- six positive opinions for the **granting of a marketing authorisation** for:

- **Dexdor** (dexmedetomidine), from Orion Corporation, intended for sedation of adult intensive care unit (ICU) patients. Dexdor allows more flexibility in the ICU setting for patients who do not require deep sedation and has shown the additional advantage of reducing the time for extubation compared with the standard of care. The review began on 20 October 2010; active review time: 210 days.
- **Incivo** (telaprevir), from Janssen-Cilag International N.V., intended for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease. Telaprevir belongs to a new class of medicines for the treatment of chronic hepatitis that can directly inhibit viral replication in infected host cells which can lead to the eradication of the virus, and thus effectively to a cure of chronic hepatitis C. The CHMP assessed this application under an accelerated timetable, because it considered that, as 70% of hepatitis C virus infections in the Western world are genotype 1, there would be an important public health gain in making this medicine available to patients as a treatment option. The review began on 19 January 2011; active review time: 150 days.
- **Mercaptopurine Nova Laboratories** (mercaptopurine monohydrate), an orphan medicine from Nova Laboratories Ltd, intended for the treatment of acute lymphoblastic leukaemia in adults, adolescents and children. The medicine has been formulated as a suspension, which provides better accuracy and ease of administration especially when used in small children. Development of an age-appropriate formulation to treat this disease was identified as a priority research area by the Agency's Paediatric Committee. The review began on 21 July 2010; active review time: 200 days.
- **Plenadren** (hydrocortisone), an orphan medicine from DuoCort Pharma AB, intended for the treatment of adrenal insufficiency in adults. The application dossier for Plenadren has been submitted as a 'hybrid application'. This means that the dossier contains administrative information, complete quality data, a clinical bioequivalence study with a reference medicine and non-clinical and clinical data based on the applicant's own tests and studies and/or bibliographic literature which can substitute or support certain tests or studies. The reference medicine for Plenadren is Hydrocortone. The review began on 23 June 2010; active review time: 210 days.
- **Vyndaqel** (tafamidis), from Pfizer Specialty UK Ltd, an orphan medicine intended for the treatment of transthyretin amyloidosis in adult patients with symptomatic polyneuropathy, a severe, progressive orphan disease. Vyndaqel is the first oral pharmacological treatment recommended for this rare disease. The CHMP recommended granting a marketing authorisation under exceptional circumstances because, due to the rarity of the disease, the applicant was not able to provide comprehensive evidence on the efficacy and safety of this medicine. The review began on 18 August 2010; active review time: 210 days.
- **Zytiga** (abiraterone acetate), from Janssen-Cilag International N.V., intended in combination with prednisone or prednisolone for the treatment of metastatic castration resistant prostate cancer in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen. The CHMP assessed this application under an accelerated timetable, because it considered that the poor prognosis of the target patient population represents a high unmet medical need while the novel mechanism of action of abiraterone has the potential to offer an alternative therapeutic option for these patients. The review began on 19 January 2011; active review time: 150 days.

- eleven positive opinions for the following generic medicines;

- Levetiracetam Accord (levetiracetam), from Accord Healthcare Ltd, intended for the treatment of partial onset seizures. Levetiracetam Accord is a generic of Keppra.
- Levetiracetam Actavis (levetiracetam), from Actavis Group PTC ehf, intended for the treatment of partial onset seizures. Levetiracetam Actavisis a generic of Keppra.
- Matever (levetiracetam), from Pharmathen S.A., intended for the treatment of partial onset seizures. Matever is a generic of Keppra.
- Pioglitazone Accord (pioglitazone hydrochloride), from Accord Healthcare Ltd, intended for the treatment of type 2 diabetes mellitus. Pioglitazone Accord is a generic of Actos.
- Pioglitazone ratiopharm (pioglitazone), from ratiopharm GmbH, intended for the treatment of type 2 diabetes mellitus. Pioglitazone ratiopharm is a generic of Actos.
- Pioglitazone ratiopharm GmbH (pioglitazone), from ratiopharm GmbH, intended for the treatment of type 2 diabetes mellitus. Pioglitazone ratiopharm GmbH is a generic of Actos.
- Pioglitazone ratio (pioglitazone), from ratiopharm GmbH, intended for the treatment of type 2 diabetes mellitus. Pioglitazone ratio is a generic of Actos.
- Paglitaz (pioglitazone), from Krka d.d. Novo mesto, intended for the treatment of type 2 diabetes mellitus. Paglitaz is a generic of Actos.
- Pioglitazone Krka (pioglitazone), from Krka d.d. Novo mesto, intended for the treatment of type 2 diabetes mellitus. Pioglitazone Krka is a generic of Actos.
- Pramipexole Accord (pramipexole), from Accord Healthcare Ltd, intended for the treatment of Parkinson's disease and restless legs syndrome. Pramipexole Accord is a generic of Mirapexin.
- Telmisartan Teva Pharma (telmisartan), from Teva Pharma B.V., intended for the treatment of essential hypertension in adults. Telmisartan Teva Pharma is a generic of Micardis.

- three positive opinions for extension of indications for:

- Afinitor (everolimus), from Novartis Europharm Ltd, to include treatment of patients with unresectable or metastatic, well- or moderately differentiated neuroendocrine tumours of pancreatic origin in adults with progressive disease.
- Enbrel (etanercept), from Wyeth Europa Ltd, to extend the lower age range in polyarticular juvenile idiopathic arthritis (JIA) from four to two years; and to extend the lower age range in paediatric plaque psoriasis from eight to six years.
- Tarceva (erlotinib), from Roche Registration Ltd, to include first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer with EGFR activating mutations.

- a negative opinion for the following medicine:

- Sumatriptan Galpharm (sumatriptan), from Galpharm Healthcare Ltd. Sumatriptan Galpharm was intended as an over-the-counter medicine for the treatment of migraine attacks. Sumatriptan is a generic of Imigran.

- **Three negative opinions for extension of therapeutic indications for:**
- **Ariclaim** (duloxetine), **Cymbalta** (duloxetine hydrochloride) and **Xeristar** (duloxetine hydrochloride), all from Eli Lilly Nederland B.V., recommending that the current therapeutic indications should not be extended to include the treatment of moderate to severe chronic somatic pain in patients not taking non-steroidal anti-inflammatory drugs (NSAIDs) regularly.

Pharmacovigilance:

Review of pioglitazone-containing medicines concluded; The CHMP confirmed that these medicines remain a valid treatment option for certain patients with type-2 diabetes but that there is a small increased risk of bladder cancer in patients taking these medicines. This risk could be reduced by appropriate patient selection and exclusion, including a requirement for periodic review of the efficacy and safety of the individual patient's treatment. Prescribers are advised not to use these medicines in patients with current or a history of bladder cancer and in patients with uninvestigated macroscopic haematuria. Risk factors for bladder cancer should be assessed before initiating pioglitazone treatment.

Review of Pandemrix regarding narcolepsy concluded; The CHMP recommended that in persons under 20 years of age the vaccine may only be used if the recommended seasonal trivalent influenza vaccine is not available and if immunisation against H1N1 is still needed (e.g. in persons at risk of the complications of infection). The CHMP confirmed that overall the benefit-risk balance of Pandemrix remains positive.

Advice on Vimpat agreed: The CHMP agreed to a recall of **Vimpat** 15mg/ml syrup because of a quality defect in some batches leading to uneven distribution of the active substance lacosamide in the syrup. Doctors will be receiving a letter in the next few days advising them to contact their patients to switch them to Vimpat film coated tablets whenever possible.

Update on benefit-risk review of Multaq: The CHMP continued its benefit-risk review to fully assess data from a clinical study (PALLAS) that show an increased risk of cardiovascular side effects such as cardiovascular death, stroke and cardiovascular hospitalisation in patients with permanent atrial fibrillation. Pending the outcome of the current review, prescribers in the EU are reminded to follow the recommendations in the product information with respect to patients indicated for treatment, defined contraindications and warnings. Specifically, prescribers are advised to monitor patients regularly in order to ensure that they remain within the authorised indication and do not progress to permanent atrial fibrillation. Further advice will be issued at the time of the conclusion of the assessment in September.

Update on Champix: The CHMP confirmed that the benefit-risk balance for **Champix** (varenicline) remains positive, despite the results of a recent meta-analysis of the medicine's side effects affecting the heart and blood vessels. The CHMP concluded that the slightly increased risk of cardiovascular events reported by the study's authors does not outweigh the benefits of Champix in helping people to stop smoking.

Supply shortage of Thyrogen continues: The CHMP has been informed by Genzyme Europe B.V that the supply shortage for **Thyrogen** (thyrotropin alfa), will continue for longer than anticipated. It was expected that it would be resolved by July 2011. However, the company now expects that supply of Thyrogen will continue to be restricted until 2012.

To deal with the ongoing shortage, the company should inform doctors of revised temporary treatment recommendations: No new patients should be prescribed Thyrogen; in countries where Thyrogen is still available, supply should be prioritised for patients already scheduled and who are not able to tolerate thyroid hormone withdrawal, or in whom thyroid hormone withdrawal would not be effective. Thyrogen is authorised for the diagnosis and treatment of thyroid tissue remnants post thyroidectomy in patients with thyroid cancer.

Arbitration procedure concluded: The CHMP completed an arbitration procedure initiated by Malta because of a disagreement among EU Member States regarding the

authorisation of the generic medicine **Dexamethasone Alapis** (dexamethasone), from Alapis S.A. This medicine is an anti-inflammatory, immunosuppressant agent. This procedure was initiated because of Germany's concerns that the bibliography referring to dexamethasone tablets is not considered relevant with respect to Dexamethasone Alapis oral solution, due to the fact that the submitted literature data mainly concerned tablets and that no bridging data had been provided to justify the extrapolation of the published data on the efficacy and safety of dexamethasone tablets to Dexamethasone Alapis 0.4 mg/ml oral solution. The CHMP concluded that the data submitted were sufficient to show that Dexamethasone Alapis could be used safely and effectively, based on the well-established use of dexamethasone. The CHMP concluded that the benefits of Dexamethasone Alapis outweigh its risks, and therefore the marketing authorisation for Dexamethasone Alapis should be granted in Malta and all concerned Member States.

Harmonisation referral concluded: The CHMP recommended harmonisation of the prescribing information for **Norvasc** (amlodipine besilate) and associated names, from Pfizer group of companies. This medicine is a calcium channel blocker used to treat hypertension, chronic stable angina and vasospastic or Prinzmetal's angina. This review was initiated because of differences in the summaries of product characteristics, labelling and package leaflets in the EU Member States where this product is marketed.

Date of the next CHMP meeting: 19 – 22 September 2011.

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Guide to Drug Regulatory Affairs www.drugregulatoryaffairs.eu