News from the EMA

Activities of the CHMP

During its meeting from 10-13 December 2012 the Committee for Medicinal Products for Human Use (CHMP) adopted:

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

- **Adasuve** (loxapine) 4.5 mg and 9.1 mg, inhalation powder, pre-dispensed, from Alexza UK Ltd, intended for the rapid control of mild-to-moderate agitation in adult patients with schizophrenia or bipolar disorder.
- **Perjeta** (pertuzumab) 420 mg, concentrate for solution for infusion, from Roche, intended for use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.
- **Selincro** (nalmefene), 18.6 mg, film-coated tablet, from Lundbeck, intended for the reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level, without physical withdrawal symptoms and who do not require immediate detoxification.

- two negative opinions for**:**

- **Fanaptum** (iloperidone) tablets, from Vanda Pharmaceuticals, intended for the treatment of schizophrenia. The reasons for not recommending marketing authorisation were modest short-term effectiveness compared with placebo, no sufficient proof of longer-term effectiveness, a delayed onset of action and on the safety side QT prolongation.
- **Kynamro** (mipomersen) solution for s.c. injection, from Genzyme, intended to treat patients with inherited familial hypercholesterolaemia. The reasons for not recommending marketing authorisation were a high drop-out rate within two years due to side effects such as flu-like symptoms, injections site reactions and liver toxicity and concerns regarding potential cardiovascular risks.

- three positive opinions for the following extensions of indications:

- **Abilify (aripiprazole),** from Otsuka, is also indicated for the treatment up to 12 weeks of moderate to severe manic episodes in Bipolar I Disorder in **adolescents aged 13 years and older** (currently: for adults).
- **Ilaris (canakinumab),** from Novartis, is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults, adolescents and children aged **2** years and older with body weight **of 7.5 kg or** above (currently: aged 4 years/15 kg).
- **Ixiaro (Japanese encephalitis vaccine),** from Intercell, is indicated for active immunization against Japanese encephalitis in adults, **adolescents, children and infants aged 2 months and older** (currently: for adults).

Pharmacovigilance

New contraindication for Pradaxa (dabigatran etexilate):
For this medicine from Boehringer Ingelheim the following new contraindication was recommended: **“**Prosthetic heart valves requiring anticoagulant treatment”

Phosphate-containing eye drops:
Having completed an assessment of the use of phosphate buffers in eye drops and whether these can cause corneal calcification the CHMP considered that the benefits of phosphate-containing eye drops outweigh their risks but that in very rare cases patients with significant damage to the cornea may develop corneal calcification during treatment with eye drops that contain phosphate, and that this should be mentioned in the product information.

Finalisation of reviews:
For the following medicines reviews were finalised:
Fibrin sealants Tisseel, Tissucol, Artiss and Beriplast P (and associated names): The CHMP concluded that the benefits of these medicines continue to outweigh their risks, but that appropriate measures have to be put in place to optimise the safe use of these medicines when they are applied as a spray during surgery.
Monovalent and multivalent measles, mumps, rubella and/or varicella vaccines (MMRV): The CHMP concluded that these vaccines should continue to be avoided during pregnancy, but that inadvertent vaccination of pregnant women with measles-, mumps- and/or rubella-containing vaccines should not be a reason for termination of pregnancy. In addition MMRV should continue to be avoided in patients with the most severely weakened immune systems, but their use could be considered in less severe immune deficiency. The CHMP also recommended that some changes be made to the product information to clarify the risks and precautions to be taken.
Fenofibrato Pensa and Fenofibrato Ranbaxy: After re-examination of its initial opinion for these medicines, the CHMP reconfirmed its recommendation from the September meeting, that
some of the studies that supported their marketing authorisations could not be considered reliable and that therefore their marketing authorisations should be suspended until adequate data are provided.

Withdrawals of applications*:* On 27 November 2012 the EMA informed that Marvel LifeSciences has withdrawn the applications submitted on 5 December 2011 for the **biosimilar insulins Solumary, Isomary and Combimary solution** for injection containing 100 IU/ml human insulin (reference product: Humulin S from Lilly) for the treatment of diabetes. The company wrote in its letter that it would need some time to generate bioequivalence data in line with the new guideline for insulins. During assessment of these applications the CHMP had concerns regarding the manufacture and the similarity to Humilin and regarding the validity of the submitted study data. During a GCP inspection of the Indian study center and of the Marvel site in UK by inspectors of Germany, Sweden and UK, some critical and major findings had been made which give reason to doubt the validity of the clinical data and thus prevent their use for making a decision on risk benefit of these products.
On 30 November 2012 the EMA informed that MSD has withdrawn the application submitted on 25 June 2011 for **Jenzyl (ridaforolimus)** 10 mg tablets, an orphan medicine for maintenance therapy of patients with metastatic soft tissue sarcoma or bone sarcoma. The CHMP was of the preliminary opinion that in relation to the additional side effects the prolongation of the time to progression of the disease by Jenzyl was quite small.

Date of the next CHMP meeting: 14–17 January 2013.

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Guide to Drug Regulatory Affairs www.drugregulatoryaffairs.eu