QSM/MC/IEA.103 01 October 2001

Information Exchange System

Alert No. 105

Olanzapine: associations with hyperglycemia resulting in diabetic ketoacidosis and coma

Japan's Ministry of Health, Welfare and Labour (MHLW) has issued an Emergency Press Release warning about the risk of serious hyperglycemia associated with Olanzapine therapy. The MHLW has directed Eli Lilly Japan K.K., the Marketing Authorization Holder (MAH) for Olanzepine in Japan, to revise the product insert for Olanzepine and to alert all health professionals to this safety information for Olanzapine. The MHLW initiated these measures since it has received 9 case reports of serious hyperglycemia including 2 deaths in patients being treated with olanzapine in the last 10 months. that have ebeen filed with the following a Olanzapine was approved as a psychotropic agent in Japan in December 2000. The MAH has been directed to include the following safety information in the HLW has directed issued this 9 serious case reports of serious hyperglycemiaAlthough no serious hyperglycemia cases had been reported in the clinical trials of Olanzepine in Japan, the product insert included hyperglycemia resulting in diabetic ketoacidosis or coma as a serious adverse reaction based on the safety information from other countries. MHLW has receueved 9 serious section of the included with olanzepine based on safety information tclinical trials conducted in japan before its approval, wa sdescribed in th serious of its package insert based on other available sfatey information in other countries. The Committee for Proprietary Medicinal Products (CPMP) at the European Medicines Evaluation Agency (EMEA) is of the opinion that there are serious deficiencies in the pivotal clinical studies on the safety issues for Nonacog alfa (Benefix), a human recombinant factor IX product used in treating hemophilia B patients.

The Committee considers that the benefit/risk balance for the treatment and prophylaxis of bleeding in previously treated patients is adequate but that the data on the frequency of some adverse reactions especially those linked to inhibitor formation and to allergic reactions are insufficient. The committee has therefore made recommendations to collect new efficacy and safety data from two additional clinical trials on the product in previously treated patients and to generate sufficient data on the use of Nonacog alfa in children under 6 years of age including previously treated and previously untreated patients.

Immediate measures will involve

1. Creating an intensive post-marketing surveillance for nonacog alfa that will register all new patients treated with nonacog alfa in Europe with careful monitoring for adverse reactions
2. Allowing patients already receiving nonacog alfa to carry on with the treatment with careful monitoring for any suspected adverse reactions that they may experience during the course of the treatment
3. Requiring all suspected adverse drug reactions to be reported to the Marketing Authorization Holder or the National Health Authorities.
4. Considering alternative haemostatic measures in the case of severe allergic reactions.

5. Switching patients to another factor IX product if doses higher than 100 IU/kg are needed for routine prophylaxis or treatment, even in the absence of inhibitor formation.

Reference:

EMEA Public Statement on Benefix (nonacog alfa), EMEA/CPMP/2777/01 dated 20 September 2001.