INTERNATIONAL AND NATIONAL NEWS ON MEDICINES SAFETY

MARCH 2013

NEWS FROM INTERNATIONAL REGULATORY AGENCIES

AZITHROMYCIN – Macrolide antibiotic – Risk of heart arrhythmias. (See news of May 2012)

(FDA, United States. March 12, 2013)

United States drug agency has published a warning about the risk of serious heart electric alterations (QT interval prolongation, torsades de Pointes) in subjects treated with azithromycin. Patients at a higher risk of these disorders are those with known predisposing factors such as existing QT interval prolongation, low serum levels of potassium or magnesium, bradyarrythmias or those concomitantly using other QT prolonging drugs.

http://www.fda.gov/Drugs/DrugSafety/ucm341822.htm

For the last five years, the National Pharmacovigilance System has not received any report of cardiovascular adverse events suspected to be associated with the use of azithromycin.

Holders of marketing authorizations of azithromycin-containing products are being reminded of the importance of keeping updated information in patient leaflets.

To report any suspected adverse event related to any drug to the Pharmacovigilance Department, please, click on:

http://www.anmat.gov.ar/farmacovigilancia/Notificar.asp

INCRETIN-MIMETICS – Treatment of type II diabetes. Risk of acute pancreatitis and possible increased risk of pre-cancerous pancreatic lesions.

(FDA, United States. March 14, 2013)

(EMA, European Union. March 26, 2013)

The United States Food and Drug Administration and the European Medicines Agency informed about an increased risk of pancreatitis and pre-cancerous lesions (pancreatic duct metaplasia) in type II diabetic patients treated with incretin-mimetic drugs. So far neither of the above agencies has reached a final conclusion nor taken regulatory actions, as the findings come from the examination of a small number of specimens taken from pancreatic tissue of diabetic patients who died to causes other than diabetes or unspecified ones.

http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm343805.htm

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/03/news_detail_001753.jsp&mid=WC0b01ac058004d5c1

In March 2012, France drug agency informed about the risk of pancreatitis associated with the use of saxagliptin. Also in September 2012, the United Kingdom drug agency informed about the risk of pancreatitis associated with the use of dipeptidyl-peptidase 4 (DPP-4) inhibitors.

http://www.anmat.gov.ar/farmacovigilancia/Informe_marzo_2012.pdf

http://www.anmat.gov.ar/farmacovigilancia/Informe_septiembre_2012.pdf

To date, the National Pharmacovigilance System has received two reports of acute pancreatitis in patients treated with saxagliptin, two reports of pancreatitis in patients treated with vildagliptin (based on case review one was found as possible and another one as unrelated), two reports of pancreatitis in subjects treated with vildagliptin+metformin and three reports of suspected pancreatitis in patients treated with exenatide.
Products containing glucagon-like peptide-1 and DPP-4 enzyme inhibitors are included in a Risk Management Plan.

Holders of marketing authorizations of products containing glucagon-like peptide 1 and DPP-4 enzyme inhibitors are being reminded of the importance of keeping updated information in patient information leaflets.

POST-MARKETING STUDIES

CALCITONIN – Treatment of post-menopausal osteoporosis – Review of the benefit-risk profile of synthetic nasal spray salmon calcitonin. FDA Panel Says to Stop Marketing Salmon Calcitonin for Osteoporosis. Medscape. Mar 06, 2013. Published on-line.

United States FDA has carried out a review of the benefit-risk profile of the nasal spray synthetic salmon calcitonin for osteoporosis treatment in post-menopausal women. The meeting of an advisory panel concluded with a 12-to-9 vote decision in favor of suspending nasal spray calcitonin marketing based on the statement of absent significant benefits and a possible risk of malignancies.

http://www.medscape.com/viewarticle/780323

http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM343748.pdf

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CILOSTAZOL – Peripheral vasodilatador and platelet antiaggregant – Review of benefit-risk relation and use restrictions.
(AEMPS, Spain. March 22, 2013)

Spain drug regulatory agency has finished the review of the benefit-risk profile of cilostazol announced in May 2011, following a series of reports of suspected hemorrhagic and cardiovascular adverse reactions.

The review found the following:

. The clinical efficacy of cilostazol is moderate and its benefits outstrip its potential risks in a reduced subgroup of patients.
. The data stemming from suspected adverse reactions suggest a risk of hemorrhage and cardiovascular developments, even though the relevance of said risks has not been confirmed by clinical trials data. In clinical practice, cilostazol treatment should be avoided in patients at an increased risk of this type of adverse reactions.

Therefore, AEMPS has proposed changes in therapeutic indications, dosing, warnings and contraindications of cilostazol-containing products.

http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/seguridad/2011/NI-MUH_09-2011.htm

http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/seguridad/2013/NI-MUH_FV_08-2013-cilostazol.htm

To date, the National Pharmacovigilance System has received only one report of a cardiovascular event (myocardial infarction) in a Cilostazol-treated subject. Based on review, the report was regarded as possible and serious.

IMMUNOMODULATORY MEDICINES – Risk of Progressive Multifocal Leukoencephalopthy (PML). Progressive multifocal leukoencephalopathy – a rare but serious disease. Medicines Safety Update. Vol.4, Number 1, February 2013. TGA, Australia. Published on-line.

PML is a demyelinating and, sometimes fatal rare disease, that affects the central nervous system. It is caused by the human polyomavirus (JC) and approximately 50% of the population is infected by the age of 20. After the initial infection, the virus remains quiescent in the body. Immune-compromised patients using immune-modulators (rituximab, natalizumab, tacrolimus, mycophenolate, prednisone, among others) pose an increased risk of having the infection reactivated and spread on to the central nervous system.

http://www.tga.gov.au/hp/msu-2013-01.htm#pml

NATIONAL NEWS

DEXRAZOXANE RAFFO – Prevention of anthracycline cardiotoxicity – Risk of serious adverse events and lack of clinical evidence in children and adolescents up to 18 years old.

The holder of the marketing authorization of Dexrazoxane Raffo product has announced the issuing of a letter to doctors who are potential prescribers of said product to inform about the latest changes made to the patient information leaflet which state the following:

. Currently, the use of Dexrazoxane Raffo is contraindicated in children and adolescents. Such contraindication is based on the evidence of serious disorders associated to the use of dexrazoxane in children, including an increased risk of second primary malignant neoplasies (mainly, acute myeloid leukemia and myelodysplastic syndrome), serious myelosuppression, serious infection and lack of evidence of clinical efficacy.

. The use of Dexrazoxane Raffo is now restricted to adult patients with advanced or metastatic breast cancer.

. The use of Dexrazoxane Raffo is not recommended in an adjuvant combination therapy for breast cancer or chemotherapy intended as curative.

. The minimum cumulative dose of anthracycline prior to the use of dexrazoxane is 300/m2 of doxorubicin or 540mg/m2 of epirubicin.

. The dose ratio recommended for dexrazoxane: doxorubicin and dexrazoxane: epirubicin is: 10:1.

To date, the National Pharmacovigilance System has not received any report of adverse events of this type associated to the use of dexrazoxane.

QUETIAPINE – Atypical antipsychotic – Medical samples.

By means of its Circular 2/2013, ANMAT informed holders of medicinal products about the prohibition of delivering medical samples or samples for professionals of pharmaceutical products containing quetiapine as an active substance.

http://www.anmat.gov.ar/comunicados/circular_02-13.pdf

VACCINES

CERVARIX – Vaccine against human papillomavirus – Broadening of indication.
(EMA, European Union, February 21, 2013)

(AEMPS, Spain February, 2013)

The Committee of Medicinal Products for Human Use and the Spanish drug regulatory agency have announced the broadening of indication for Cervarix vaccine to include the prevention of pre-malignant genital lesions (cervical, vulvar and vaginal) caused by oncogenic types of the human papillomavirus.

It is worthy to mention that until recently, the indication authorized was the prevention of HPV-caused pre-malignant cervical lesions and womb neck cancer.

http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion/human/000721/WC500139202.pdf

http://www.aemps.gob.es/informa/informeMensual/2013/febrero/informe-medicamentos.htm

In Argentina, Cervarix is indicated as from ten years of age, under a three dose scheme with administration at time 0, 1 and 6 months.

http://www.msal.gov.ar/index.php/programas-y-planes/184-calendario-nacional-de-vacunacion-2013

If you would like to see Cervarix and other vaccines patient information leaflets, you can check ANMAT Drug Formulary at:

http://www.anmat.gov.ar/aplicaciones_net/applications/consultas/vademecum/vademecum.asp