ANMAT
Administración Nacional de Medicamentos, Alimentos y Tecnología Médica

INTERNATIONAL AND NATIONAL NEWS ON DRUG PRODUCTS SAFETY - JULY 2012

INTERNATIONAL REGULATORY AGENCIES

ONDANSETRON – Antiemetic drug – QT Prolongation.

(FDA, USA, June 29, 2012)

The USA drug agency has reported that preliminary results of a clinical study suggest that a single 32mg intravenous dose of ondansetron can affect the heart electrical activity (QT interval prolongation). Label information will be updated to mention that ondansetron can still be used in children and adults for chemotherapy-induced nausea and vomit but that the single intravenous dose should not exceed 16mg. The FDA will evaluate the clinical study final results when available. The new information on the safety of a 32mg single dose does not change the oral or intravenous dosing regimens with the lower doses for preventing post-operative nausea and vomiting.

http://www.fda.gov/Drugs/DrugSafety/ucm310190.htm

The National Pharmacovigilance System has not received to date any ondansetron-associated QT prolongation report. VigiBase, the World Health Organization Uppsala Monitoring Center adverse reaction data base has received 48 reports of QT prolongation with the use of ondansetron. In 24 cases, ondansetron was reported as the single suspected drug and in other 11 cases other drugs used concomitantly could account for the QT prolongation. Conclusions on dosing and route of administration cannot be drawn as reported data are incomplete.

Patients with a higher risk for ondansetron-caused QT prolongation are those with heart failure, acute myocardial infarction or electrolyte alterations; or those concomitantly using QT-prolonging medicines.

This Administration requests holders of marketing authorizations of ondasetron-containing products without updated patient information leaflets to include the following information:

- **For single intravenous dose, indicate 16mg as the maximum dose.**
- **Correct any electrolyte alteration such as hypokalemia or hypomagnesemia prior to administering intravenous ondansetron.**

AMBRISENTAN – Treatment of pulmonary hypertension – Contraindication in pulmonary fibrosis.

(EMA, European Union, June 22, 2012)

(AEMPS, Spain, July 5, 2012)

(Afssaps, France, July 20, 2012)

Ambrisentan is a selective endothelin A receptor antagonist, indicated for treating functional class II and III pulmonary hypertension, as classified by the World Health Organization, to improve exercising capability. A clinical trial, ARTEMIS_IPF1, was early interrupted recently. It was a randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of ambrisentan in patients with idiopathic pulmonary fibrosis. The main objective was to determine the efficacy of ambrisentan in delaying the disease progress and reducing mortality. The evaluation of the main objective of the study revealed increased rates of respiratory-related hospitalization, mortality and compromised pulmonary function in ambrisentan-treated patients as compared to placebo-treated patients. Likewise, an ambrisentan-associated increasing tendency for disease progress and mortality was observed in the few patients with pulmonary hypertension at treatment start.

http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/seguridad/2012/NI-MUH_FV_12-2012.htm

http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion/human/000839/WC500129075.pdf

http://ansm.sante.fr/S-informer/Informations-de-securite-Lettres-aux-professionnels-de-sante/Communication-sur-l-ajout-d-une-nouvelle-contre-indication-concernant-l-utilisation-de-VOLIBRIS-lettre-aux-professionnels-de-sante

The National Pharmacovigilance System has received to date only one report of an ambrisentan-associated adverse event (peripheral edema). The Pharmacovigilance Department will continue the surveillance of this medicinal product.

ACITRETIN – Treatment of serious psoriasis and keratinization disorders – Pregnancy prevention program.

(Afssaps, France, July 13, 2012)

The French drug regulatory agency has informed that a pregnancy prevention program will be implemented for women with a child-bearing potential who use acitretine as this active pharmaceutical ingredient is a retinoid.
The above mentioned program includes a pregnancy test before, during and after finishing treatment (for two years after termination) and a monthly-based limited prescription. Likewise, patients are reminded not to use alcohol during treatment and up to two months after its termination as acitretin converts to etretinate, an equally teratogenic compound.

http://ansm.sante.fr/S-informer/Informations-de-securite-Lettres-aux-professionnels-de-sante/Soriatane-acitretine-Informations-importantes-sur-son-bon-usage-et-sa-securite-d-emploi-Lettre-aux-professionnels-de-sante

As is the case of other drug regulatory agencies, ANMAT is currently evaluating the benefits of implementing a Risk Management Plan for this drug product.

CALCITONIN – Regulator of the phosphocalcic metabolism – Evaluation of the risk-benefit balance.

(EMA, European Union, July 19, 2012)

(AEMPS, Spain, July 24, 2012)

Upon finishing a review of calcitonin risk-benefit balance, the European Medicines Agency concluded that the risk of cancer is slightly increased when used for a long time. Likewise, the EMA recommended using calcitonin only for treating Paget´s disease and neoplastic hypercalcemia but not for treating osteoporosis, due to its limited efficacy and the availability of other therapeutic alternatives.

The statements above are based on data provided by marketing authorization holders, post-marketing data and clinical trials, among others.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/public_health_alerts/2012/07/human_pha_detail_000065.jsp&mid=WC0b01ac058001d126

http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/seguridad/2012/NI-MUH_FV_13-2012.htm

Holders of marketing authorizations of drug products containing calcitonin as an active principle are reminded to keep updated patient information leaflets.

PANITUMUMAB – Treatment of colorectal cancer – Infectious complications of severe dermatologic reactions

(Afssaps, France, July 26, 2012)

The French drug regulatory agency has informed that panitumumab-associated severe skin adverse reactions were frequently reported. Also, five cases of necrotizing fasciitis were reported, of which three were fatal. Information for patients will be updated to include the risk of necrotizing fasciitis.

http://ansm.sante.fr/S-informer/Actualite/Association-du-panitumumab-Vectibix-R-avec-des-complications-infectieuses-de-reactions-dermatologiques-severes-engageant-le-pronostic-vital-ou-d-issue-fatale-dont-des-cas-de-fasciite-necrosante-Lettre-aux-professionnels-de-sante

To date, the National Pharmacovigilance System has not received any report of panitumumab-associated dermatologic adverse reactions.
Readers are reminded that this drug product is included in a Risk Management Plan that, among other activities, consists of handing in educational material with information about the most frequent adverse reactions, including dermatologic ones, to healthcare professionals.

SIGNAL, WHO COLLABORATING CENTRE FOR INTERNATIONAL DRUG MONITORING. JUNE 2012.

MOMETASONE – Topical, inhalation and intranasal corticosteroid – Risk of arrhythmias.

In VigiBase there have been 15 reports of arrhythmia and two of atrial arrhythmia associated with mometasome. The drug was withdrawn in 10 cases and in three cases, the reaction recurred on rechallenge. In 13 cases, mometasone was the only drug suspected and it was administered intranasally; in 2 cases it was administered by inhalatory route and in one case, it was administered topically.

The possibility of occurrence of a systemic adverse reaction with the use of topical, inhaled or intranasal corticosteroids is low. However, there is a literature report of atrial fibrillation associated with fluticasone. The National Pharmacovigilance System has not received to date any report of arrhymothmogenic events associated with mometasone. The Pharmacovigilance Department will continue surveillance on this adverse event.

NATIONAL NEWS

Anti-hepatitis B vaccine – Vaccination for all the public.

The World Health Organization established that the First World Hepatitis Day would be observed on July 28, 2012. Within this framework, it was announced that through the Argentine National Program for the Control of Vaccine-preventable Diseases (Pronacei) of the Ministry of Health, free-of-charge vaccination against hepatitis B would be provided to all the population, with a view to controlling and eradicating the disease from the country. The National Pharmacovigilance System will continue surveillance on this vaccine.