ANMAT
Administración Nacional de Medicamentos, Alimentos y Tecnología Médica

INTERNATIONAL AND NATIONAL NEWS ON MEDICINES SAFETY

JANUARY 2013

NEWS FROM INTERNATIONAL REGULATORY AGENCIES

LENALINOMIDE – Immune modulator – Liver disorders in subjects with risk factors.

(MHRA, United Kingdom, December 10, 2012)
(IMB, Ireland, January 09, 2013)

A letter containing safety information about the use of lenalinomide has been sent to healthcare professionals:

- Hepatotoxicity cases, some serious, were reported in patients with myeloma treated with lenalinomide and dexamethasone.
- As lenalinomide is excreted by the kidneys, it is extremely important to adjust the doses in subjects with kidney impairment to prevent plasma levels from increasing too much and therefore increasing the risk of hematologic and hepatotoxicity adverse events.
- There are pre-existing risk factors for hepatoxicity, such as liver viral disease, high levels of baseline liver enzymes and, possibly, antibiotic treatment.
- Monitoring for hepatic function is recommended for lenalinomide-treated subjects, when there is a previous history of viral liver disease or when this drug is combined with other drugs known to cause liver dysfunction, such as paracetamol.

http://www.imb.ie/images/uploaded/documents/Revlimid%20DHCP%20Letter_HCPs_Ire_%20Final_10Dec12.pdf

http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con218766.pdf

ANMAT reminds the public that a Risk Management Plan has been established for this active pharmaceutical ingredient. The National Pharmacovigilance System has not received to date any reports of hepatotoxicity associated to the treatment with lenalinomide.

Likewise, File 1-47-1841-13-1 has been opened to require holders of marketing authorizations of lenalinomide-containing products to update patient information leaflets.

ZOLPIDEM – Non-benzodiazepine hypnotic drug – Reduction of bedtime dose.
(FDA, United States, January 10, 2013)

The United States drug regulatory agency has issued a safety communication to recommend reducing the bedtime dose of zolpidem as some patients may show high serum levels of the drug the morning after taking it, which prevents subjects from appropriately carrying out activities requiring alertness (e.g. driving). Women appear to be more susceptible to this effect which is more frequent when extended-release forms are used.

Recommendations are as follows:

- Reducing the dose for women from 10 mg to 5 mg when immediate release forms are used and from 12.5 mg to 6.25 mg in the case of extended-release forms.
- Using the lowest possible effective dose to treat insomnia.

http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm334738.htm?source=govdelivery

ANMAT is currently evaluating the safety profile of this drug and suggests the healthcare community that they should put these recommendations into practice. ANMAT reminds holders of marketing authorizations of zolpidem-containing products to keep updated patient information leaflets.

NIACIN/LAROPIPRANT – Hypolipemiant – Negative risk/benefit balance.

(EMA, European Union, January 10, 2013)
(IMB, Ireland, January 10, 2013)
(AEMPS, Spain, January 18, 2013)

The European Medicines Agency has published preliminary results of a study that suggest the the use of nicotic acid+laropiprant associated to a statin may not provide an additional benefit as a hypolipemiant as compared to a statin alone.

Likewise, a high frequency of adverse events in patients receiving these active pharmaceutical ingredients was observed, with a higher frequency of bleeding, muscle weakness, infections and diabetes. For all the above mentioned, the marketing of products containing niacin+laropiprant has been suspended.

http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Tredaptive_20/Recommendation_provided_by_Pharmacovigilance_Risk_Assessment_Committee/WC500137124.pdf

http://www.imb.ie/images/uploaded/documents/Tredaptive%20prac.pdf

http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/seguridad/2013/NI-MUH_FV_05-2013-tredaptive.htm

Only one product containing nicotic acid and laropiprant is marketed in Argentina. Its brand name is Cordaptive (manufacturer Merck, Sharp & Dohme). The National Pharmacovigilance System has not received to date any report of adverse events associated to the use of Cordaptive.

The product manufacture communicated ANMAT its decision to suspend the marketing of the product in our country, through File 1-47-41-13-1.

Patients treated with Cordaptive are to be evaluated by their doctors for treatment discontinuation purposes as the initiation of other therapies should be assessed for dyslipemia control.

DABIGATRAN – Anticoagulant – Not to be used in patients with mechanical heart valves.

(ANSM, France, January 18, 2013)

According to recent information from clinical trials, dabigatran is contraindicated for patients with mechanical heart valves. A higher rate of thromboembolism and hemorrhagic events associated to the use of dabigatran has been observed in dabigatran-treated patients as compared to those receiving warfin.

http://ansm.sante.fr/S-informer/Informations-de-securite-Lettres-aux-professionnels-de-sante/PRADAXA-contre-indication-chez-les-patients-porteurs-de-protheses-valvulaires-cardiaques-necessitant-un-traitement-anticoagulant-Lettre-aux-professionnels-de-sante

ANMAT reminds holders of marketing authorizations of dabigatran-containing products to keep updated patient information leaflets.

The drug regulatory agencies from the United States, Spain and Canada had already communicated this risk (see news from December 2012).

http://www.anmat.gov.ar/farmacovigilancia/Novedades_FVG_Diciembre2012.pdf

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ANAGRELIDE – Treatment of essential thrombocythemia – Serious cardiovascular events.

(MHRA, United Kingdom, January 23, 2013)

The manufacturer of anagrelide in the United Kingdom has informed about a review of the cardiovascular events reported in patients under 50 years old. Serious cardiovascular events have been reported in patients without heart disease prior to treatment and with controlled myeloproliferative disease. This new piece of safety information does not alter the risk/benefit balance, which remains favorable for the drug as a second-line treatment of essential thrombocythemia.

http://www.mhra.g'ov.uk/home/groups/commsic/documents/websiteresources/con228796.pdf

The National Pharmacovigilance System has not received to date any report of cardiovascular events associated to the use of anagrelide.

ANMAT recommends:

- Conducting a cardiologic examination prior to treatment.
- Seeing a cardiologist in case cardiovascular events occur of during treatment.

NATIONAL NEWS

GOOD PHARMACOVIGILANCE PRACTICES FOR THE PHARMACEUTICAL INDUSTRY

By means of Regulation 5358/12, ANMAT approved the Good Pharmacovigilance Practices for the pharmaceutical industry. Pharmacovigilance is an activity based on the joint responsibility of the agents who use the medicine, that is, the holders of the marketing and registration authorization (pharmaceutical industry); the health regulatory authority (ANMAT, Pharmacovigilance Department); healthcare professionals (doctors, pharmacists, etc.) and patients.

Holders of marketing and registration authorizations (TARC – Spanish acronym) are to assume their responsibilities and duties for their authorized medicines and ensure the adoption of timely measures, as necessary.

Among other duties each TARC shall:

- Keep a detailed record of all the suspicions of adverse reactions occurred with their medicines in Argentina.
- Notify ANMAT Pharmacovigilance Department when it has been detected that a pregnant woman was exposed to the medicine, even when no adverse event occurred.
- Make sure that the reports contain the minimum indispensable information. Said information includes: the start date of the adverse event, the start date of administration of the suspected medicine, the age of the patient, a complete description of the event and the name of the drug/s involved (Argentine Common Denomination – ACD - and brand).
- Carry out the Risk Management Plans established for each medicine.
- Refrain from communicating the public and healthcare professionals pharmacovigilance matters related to their authorized medicine, without a previous communication of such matters to ANMAT, at least 24 hours in advance.
- Ensure the availability in Argentina of an adequate qualified person for pharmacovigilance (QPPV) and inform the name of such person to ANMAT Pharmacovigilance Department.