Issue 19, N 2, December 2015

SAFETY OF MEDICINES

Drug safety monitoring department

In this issue:

Codeine: Not to be used in children below 12 years for cough and cold.

The CMDh has agreed by consensus new measures to minimize the risk of serious side effects, including breathing problems, with codeine-containing medicines when used for cough and cold in children. As a result of these new measures:

- Use of codeine for cough and cold is now contraindicated in children below 12 years. This means it must not be used in this patient group.
- Use of codeine for cough and cold is not recommended in children and adolescents between 12 and 18 years who have breathing problems.

The effects of codeine are due to its conversion into morphine in the body. Some people convert codeine to morphine at a faster rate than normal, resulting in high levels of morphine in their blood. High levels of morphine can lead to serious effects, such as breathing difficulties, even death.

The new measures follow a review by EMA's Pharmacovigilance Risk Assessment Committee (PRAC). The PRAC considered that, although morphine-induced side effects may occur in patients of all ages, the way codeine is converted into morphine in children below 12 years is more variable and unpredictable, making this population at special risk of such side effects. In addition, children who already have problems with their breathing may be more susceptible to respiratory problems due to codeine. The PRAC also noted that cough and cold are generally self-limiting conditions and the evidence that codeine is effective at treating cough in children is limited.

In addition to the new measures for children, codeine must also not be used in people of any age who are known to convert codeine into morphine at a faster rate than normal ('ultra-rapid metabolisers') nor in breastfeeding mothers, as codeine can harm the baby because it passes into breast milk.

Information for healthcare professionals

- Codeine for cough and cold is now contraindicated in children below 12 years,
- Codeine not recommended in children between 12 and 18 years with compromised respiratory function.
- Codeine is also contraindicated in women during breastfeeding and patients known to be CYP2D6 ultra-rapid metabolisers.

These new measures follow a review of available safety and efficacy data on codeine when used for cough and cold, including data from clinical studies, observational studies and meta-analyses, post-marketing data in Europe and other published literature on the use of codeine in children.

EMA (www.ema.europa.eu)

Mirabegron. New recommendations about the risk of increase in blood pressure.

European Medicines Agency (EMA) released new recommendations for the use of mirabegron.

- Mirabegron is now contraindicated in patients with severe uncontrolled hypertension defined as systolic blood pressure ≥180 mm Hg and diastolic blood pressure ≥110 mm Hg.
- It is essential to measure blood pressure before starting treatment and monitor it regularly during treatment, especially in patients with hypertension.
- It is necessary to register the serious cases of hypertension and increased blood pressure on mirabegron treatment.

The new recommendations follow a review by the EMA of cumulative data associated with mirabegron and increased blood pressure. Serious cases of hypertension and increased blood pressure have been reported in patients on mirabegron treatment. In addition, there have been some reports of hypertensive crisis and cerebrovascular and cardiac events associated with hypertension with a clear temporal relationship with the use of mirabegron.

Therefore, the use in patients with severe uncontrolled high blood pressure is now contraindicated. Blood pressure should be measured at the start of treatment and monitored regularly, especially in patients with hypertension.

As a new active substance, mirabegron is subject to additional monitoring. This supports enhanced reporting of adverse reactions and allows quick identification of new safety information to further inform safe and effective use.

EMA (www.ema.europa.eu)

Non-aspirin Nonsteroidal Anti-inflammatory Drugs (NSAIDs): Increased Risk of Heart Attack or Stroke.

FDA is strengthening an existing label warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) increase the chance of a heart attack or stroke. Based on FDAs comprehensive review of new safety information, FDA is requiring updates to the drug labels of all NSAIDs. Labels will be revised to reflect the following information:

- The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAID.
- The risk appears greater at higher doses.
- It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient for us to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.
- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied.
- In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.
- There is an increased risk of heart failure with NSAID use.

Drug Safety Communication, US FDA, 9 July 2015

Reminder.

Scientific centre of drug and medical technology expertise after academician E. Gabrielyan

(SCDMTE) continues to encourage and promote health professionals, pharmacists and patients to submit adverse reaction reports associated with the use of medicines.

These reports are important to highlight potential safety issues from medicines in use and ultimately assist the SCDMTE in monitoring the safety of medicines on the Armenian market.

There are several options in place for reporting suspected adverse reactions to the SCDTE. These are as follows:

- By following the links to the online reporting options accessible from the SCDMTE homepage (www.pharm.am)
- Using the downloadable report form also accessible from the SCDMTE website, which may be completed manually and submitted to the Centre
- By telephone to the SCDMTE Pharmacovigilance section (+374 10 237265; +37498773368).

Address: 49/4 Komitas av., 0051, Yerevan, Armenia

Tel.: (374 10) 23 21 32, 23 16 82

Fax: (374 10) 23 21 18

Email : vigilance@pharm.am

Web : http://www.pharm.am

You will help thousand of patients if you report about adverse drug reactions of medicines!