Recommendation to restrict the use of thiocolchicoside by mouth or injection

2.1.2014 | Circular Number P02/2014

Information on Thiocolchicosides

Thiocolchicoside is a muscle relaxant for use by mouth or intramuscular injection in the treatment of painful muscular disorders. It is thought to act on receptors in the nervous system that are involved in the regulation of muscle function. Thiocolchicoside is authorised through national procedures in several EU member states. In Malta, it is available in tablet form containing 4mg thiocolchicoside and marketed as Coltramyl®.

Information from European Medicines Agency about the safety concern

The review of thiocolchicoside was triggered by following new experimental evidence which suggested that thiocolchicoside was broken down in the body into a metabolite called M2 or SL59.0955 that could damage dividing cells, resulting in aneuploidy (an abnormal number or arrangement of chromosomes). The Committee on Human Medicinal Products (CHMP) reviewed the evidence, including the opinions of experts in the field of medicines safety, and concluded that aneuploidy could occur with M2 at levels not much greater than those seen after recommended doses of thiocolchicoside taken by mouth. Aneuploidy is a risk factor for harm to the developing fetus, reduced fertility in men and in theory could increase the risk of developing cancer. The CHMP therefore recommended measures to ensure thiocolchicoside-containing medicines are used as safely as possible. These include restricting the maximum dose and number of days of treatment when given by mouth or injection. Use is also contra-indicated in pregnancy and lactation or in women of childbearing potential not using contraception, as well as in children or for chronic (long-term) conditions. Preparations for local application to the skin, which do not produce substantial levels of M2 in the body, are not affected by this review.

The CHMP opinion will now be forwarded to the European Commission, which will issue a final decision in due course.

In Malta

For Healthcare Professionals

- Systemic thiocolchicoside is recommended only as adjuvant treatment for acute muscle contractures in spinal pathology, for adults and adolescents from 16 years of age.
- It is not recommended for longer-term treatment of chronic conditions.

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- The maximum recommended oral dose is 8 mg every 12 hours; treatment duration should be no more than 7 consecutive days. When given intramuscularly, the maximum dose should be 4 mg every 12 hours, for up to 5 days.
- Medicines containing thiocolchicoside should not be used during pregnancy and lactation, nor in women of childbearing potential who are not taking appropriate contraceptive measures.
- Patients being treated with systemic thiocolchicoside should have their treatment reviewed at the next scheduled appointment, and appropriate alternative treatments should be considered.
- Pharmacists should refer any patients who present a repeat prescription to their treating physician.
- Prescribers will be sent a letter giving them further information on the restriction of indication of systemic thiocolchicoside. Educational materials for prescribers and patients will also be prepared.
- The current findings do not apply to topical preparations of thiocolchicoside.

The Committee's recommendations were based on a review of available data from pre-clinical and clinical studies, published literature and post-marketing experience, and consultations with an expert working party on medicines safety. Preclinical studies indicated that the thiocolchicoside metabolite 3-demethylthiocolchicine (M2, SL59.0955) may be associated with aneuploidy (abnormal chromosome number and loss of heterozygosity) in dividing cells, at levels of exposure not much greater than those achieved in the body with maximum recommended oral doses. Aneuploidy is an established risk factor for teratogenicity, embryotoxicity or spontaneous abortion, and impaired male fertility. In theory it also increases the risk of cancer, although any significantly increased cancer risk would in general be dependent on long-term exposure to the causative substance. Thiocolchicoside metabolites were not associated with mutagenicity (changes to genes) or clastogenicity (structural damage to chromosomes). The Committee concluded that in the light of current evidence the benefit-risk for the medicine remained positive provided appropriate risk-mitigating measures were taken, including restricting the maximum dose and duration of use and contra-indicating use during pregnancy and lactation and in children.

Advice for Patients

- Medicines containing thiocolchicoside are now only recommended for short-term use as an addition to other treatment for pain due to permanent tightening of the muscles where there are problems with the spine, in adults and teenagers from 16 years of age.
- Treatment should now only be given for 7 days by mouth or 5 days by injection into the muscle. Patients who are taking thiocolchicoside for a long-term condition should have their treatment reviewed by their doctor at the next scheduled appointment.
- Medicines containing thiocolchicoside must never be taken if you are pregnant or breast-feeding. Women who might become pregnant must use contraception when taking these medicines.
- Thiocolchicoside-containing medicines are also available for application to the skin but these do not produce the same levels of M2 in the body and are not thought to affect the genetic material of cells. These medicines are therefore not affected by these recommendations.
- Patients who have any questions should discuss them with their doctor or pharmacist.

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For more information please visit **www.ema.europa.eu**

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Coltramyl. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Dr John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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