Direct Healthcare Professional Communication

Diclofenac - new contraindications and warnings after a Europe-wide review of cardiovascular safety

Dear Healthcare professional,

This letter is sent in agreement with European Medicines Agency (EMA) and the Medicines Authority to inform you of important restrictions to the use of diclofenac-containing medicines (systemic formulations), following completion of a Europe-wide review of its cardiovascular safety.

Medochemie Ltd., who is the Marketing Authorisation Holder of the following products containing diclofenac, would like to inform you on these important restrictions.

The products that have a Marketing Licence in Malta are Areston 50mg Film-coated tablets, Almiral 25mg Gastro-resistant tablets, Almiral 50mg Gastro-resistant tablets and Almiral injection 75mg/3ml.

Summary

- **The benefits of diclofenac outweigh the risks, however, currently available data indicate an increase in arterial thrombotic risks associated with diclofenac, similar to that for selective COX-2 inhibitors.**
- **Diclofenac is now contraindicated in patients with established congestive heart failure (New York Heart Association, NYHA, classification II–IV), ischaemic heart disease, peripheral arterial disease or cerebrovascular disease. Patients with these conditions should have their treatment reviewed.**
- **Diclofenac treatment should only be initiated after careful consideration for patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, and smoking).**
- **The lowest effective dose of diclofenac should be used for the shortest duration necessary to control symptoms in all patients.**

Further information

Diclofenac is a widely used NSAID for relief of pain and inflammation. In 2012, the European Committee on Medicinal Products for Human Use (CHMP) considered the latest available data for the risk of cardiovascular side effects (such as heart attack or stroke) with non-selective NSAIDs. The Committee concluded that these data provided further evidence on the known risk with these medicines. Overall, the studies consistently indicated a small increased risk of cardiovascular side effects with diclofenac, similar to that seen with the COX-2 inhibitors.

As this conclusion raised safety concerns for diclofenac, the European Pharmacovigilance Risk Assessment Committee (PRAC) began an in-depth review on the cardiovascular safety of diclofenac in October 2012.

Academic research has been a central element of the reviews of NSAIDs and diclofenac. This includes an independent research project called 'safety of non-steroidal anti-inflammatory drugs' (SOS)[1], set up and funded by the European Commission's Seventh Framework Programme. Other groups have also been investigating the cardiovascular safety of NSAIDs, notably the Coxib and traditional NSAID Trialists' (CNT) collaborative group[2], who shared their results from a large meta-analysis of more than 600 randomised clinical trials with the Agency, and these were included in the PRAC's assessment of diclofenac. The group found that of 1000 patients allocated to diclofenac for a year, three more had major vascular events, compared to placebo.

Considering all evidence available, the PRAC supported the conclusions of the previous CHMP review and concluded that the benefits of diclofenac are considered to outweigh the risks. However, there is an increase in the risk of arterial thrombotic events associated with diclofenac, similar to that for selective COX-2 inhibitors. Therefore, new contraindications have been recommended in the product information for diclofenac, in line with measures in place for COX-2 inhibitors to help minimise cardiovascular risk.

The Summary of Product Characteristic (SmPC) and Package leaflet (PL) will be updated accordingly.

Call for reporting of adverse reactions
Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Alternatively Adverse reactions can be reported to Medochemie Ltd.
Pharmacovigilance department

Address: P.O.Box 51409, 3505 – Limassol, Cyprus
Tel: +357 25 86 7600
Fax: +357 25 560863
Email: pharmacovigilance@medochemie.com

Yours sincerely,

Marina Couva

[1] See www.sos-nsaids-project.org.
[2] See http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)60900-9/abstract