

Malta, 10 June 2005
Circular No. P14/2005

Re: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and their recent association with an increased risk of myocardial infarction (heart attack).

Non-steroidal anti-inflammatory drugs (NSAIDs) are important medicines in the treatment of arthritic and other painful conditions. The known side effects are described in product information, including patient information leaflets.

The Medicines Authority continually reviews the safety of all licensed medicines in Malta. Following the publication of an epidemiological study¹ whose aims were to compare the risk of myocardial infarction (MI) in patients taking selective COX-2 inhibitors and (non-selective) NSAIDs, the Medicines Authority has taken immediate steps to review the data emerging from this study, which suggests an increased risk of MI with both COX-2 inhibitors and the NSAIDs diclofenac² and ibuprofen³.

The Medicines Authority concludes that this new study, which has limitations as identified by the author, will be reviewed in the context of a number of other studies which have not shown an increased risk of MI with ibuprofen. Ibuprofen has an excellent safety record which is why it has been made available as an over-the-counter medicine. There are a number of epidemiological studies regarding the cardiovascular safety of ibuprofen. The Medicines Authority will participate in a detailed European-wide review of the cardiovascular safety of NSAIDs at the European Medicines Agency.

The Medicines Authority has also been participating in the ongoing European-wide review of COX-2 inhibitors following last year's withdrawal of rofecoxib (Vioxx®) which resulted in the modification of the product information of the COX-2 inhibitors to include a contra-indication in patients with established ischaemic heart disease and/or cerebrovascular disease⁴. Another COX-2 inhibitor, valdecoxib (Bextra®) has recently been withdrawn because of an increased risk of serious skin reactions⁵.

Until further data is available, the Medicines Authority advises prescribers and patients alike that the **lowest effective dose should be used for the shortest period of time necessary for treatment**. Patients are reminded that when using an over-the-counter NSAID such as ibuprofen (i.e. available without prescription), the information on the lowest effective dose can be obtained from their doctor or pharmacist or alternatively can be obtained from the patient-information leaflet inside the package

¹ Hippisley-Cox J. Risk of Myocardial infarction in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. *BMJ* 2005;330:1366.

² The following diclofenac-containing medicinal products are marketed in Malta: Voltaren®, Cataflam®, Arthrotec®, Diclomelan®, Remethan®, Olfen®, Vostar®, Urigon®.

³ The following ibuprofen-containing medicinal products are marketed in Malta: Nurofen®, Nurofen Cold and Flu®, Nurofen Plus®, Irfen®, Fenbid®, Lemsip Flu®, Cuprofen®, Advil Cold and Flu®, Anadin Ibuprofen®, Ibufen®, Ibukod®, Dolgit®, Moment®, Solpaflex®.

⁴ MA Statement P03/2005 (18 February 2005): Celecoxib (Celebrex®/Onsenal®), etoricoxib (Arcoxia®), valdecoxib (Bextra®/Valdyn®) & parecoxib (Prexige®) and cardiovascular safety.

⁵ MA Statement P10/2005 (8 April 2005): Suspension of Bextra® (valdecoxib) as an interim measure.

of the medicinal product.. Prescribers and patients are finally reminded that the current evidence does not warrant that any prescribed NSAID treatment is stopped.