Malta, 05 April 2007
Circular No. P05/2007

Dear Healthcare Professional,

Re: Safety of Dopamine Agonists.

Following reports in the local media that the drug pergolide (marketed locally as Celance® and in other markets as Permax®) is being voluntarily withdrawn in the US following an agreement between its manufacturers and the Food and Drug Administration (FDA), the Medicines Authority would like to provide an update on the status of this medicinal product as well as other dopamine agonists in Malta.

Following the latest MA circular issued in February 2007[1], the Medicines Authority would like to stress again that pergolide is indicated as a second-line treatment for Parkinson's Disease in those patients who are intolerant or fail treatment with a non-ergot compound, as monotherapy, or as an adjunctive to levodopa. Furthermore, the current product information stresses that the benefit of continued therapy with pergolide should be regularly assessed taking into account the risk of fibrotic reactions and valvulopathy, which are adverse effects that are clearly outlined in the product information of this medicinal product. There are also various risk minimisation measures in place as agreed with the marketing authorisation holder of this product.

The evidence from the scientific literature[2][3] that has led the manufacturers to withdraw this product in the US is being evaluated by the Medicines Authority in collaboration with the regulatory competent authorities in the European Union. Regulatory action in the EU will be taken as appropriate following the discussion of this issue, at the Pharmacovigilance Working Party (PhVWP) at the European Medicines Agency (EMEA) in the next few weeks. Other dopamine agonists such as ropinirole and pramipexole are also being investigated for the possibility of a class effect. Any regulatory action will be immediately implemented in a harmonized manner across all Member States, including Malta, and local healthcare professional informed in a timely manner. Prescribers and patients alike should also be aware that in the US the drug will not be immediately made unavailable, but will be slowly phased out and will be made available to certain patients whose symptoms cannot be controlled by other medication on a named-patient basis.

The above-mentioned recent publications have reported a similar frequency of heart valve damage with the dopanmine agonist cabergoline as with pergolide and as a result, similar restrictions are being applied to the use of cabergoline (marketed in Malta by Arrow Pharmaceuticals and Teva) in Parkinson's Disease as for pergolide. However, it should be noted that currently no such restrictions are in place for Dostinex®, another cabergoline-containing medicinal product marketed in Malta for use in hyperprolactinaemia, not in Parkinson's Disease. Discussions are ongoing with the marketing authorisation holder of Dostinex® for information with regards to valve disorders to be implemented in the product information. The Medicines Authority advises patients who are concerned not to stop their medicine but to discuss their treatment with their doctor.

[1] Medicines Authority Circular No P02/2007 Re: Pergolide and the risk of cardiac valvulopahty and fibrotic reactions. - 15.02.2007
[2] Schade R et al. Dopamine Agonists and the Risk of Cardiac-Valve Regurgitation, N Engl J Med 2007; 356-29
[3] Zanettini R et al. Valvular Heart Disease and the Use of Dopamine Agonists for Parkinson's Disease, N Engl J Med 2007; 356-39

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