London, 22 April 1999
CPMP/1148/99

PUBLIC STATEMENT ON
VIAGRA & PATREX

In consultation with the EMEA the Marketing Authorisation Holders for Viagra (Pfizer Research Limited) and Patrex (Roerig Farmaceutici Italiana S.p.A.) have recently submitted variation applications to introduce changes to the Summary of Product Characteristics (SPC) and Package Leaflets of these products. The variation to the labelling adds, to the already existing information on interactions with other medicinal products and other forms of interaction.

The need to introduce these changes was identified as a precautionary measure following completion and review of two preliminary study reports investigating the pharmacokinetics of saquinavir and sildenafil and ritonavir and sildenafil when co-administered to healthy male volunteers.

Specific changes have been introduced to Section 4.2 – *Posology and method of administration*, 4.4 *Special warnings and special precautions for use* and 4.5 *Interaction with other medicinal products and other forms of interaction* of the SPC together with changes to the section "*Can Viagra/ Patrex be taken with other medicines"* in the Package Leaflet. These changes are summarised below:

Co-administration of the HIV protease inhibitor, ritonavir, which is a highly potent inhibitor of a broad range of P450 metabolic pathways, at steady state (500 mg bid) with sildenafil (100 mg single dose) resulted in a significant increase in sildenafil plasma concentrations (4-fold increase in Cmax and 11-fold increase in AUC). At 24 hours, the plasma levels of sildenafil were still significantly higher compared to administration of sildenafil alone. Sildenafil had no effect on ritonavir pharmacokinetics.

Having reviewed these results it was concluded that co-administration of sildenafil with ritonavir is not advised. However, if sildenafil must be prescribed for a patient on ritonavir, the maximum dosage of sildenafil should not exceed 25 mg within 48 hours.

For patients receiving concomitant treatment with potent CYP 3A4 inhibitors, such as saquinavir, other HIV protease inhibitors, erythromycin, ketoconazole and itraconazole, attention of prescribers is drawn to the current recommendation in the SPC that a starting dose of 25mg of sildenafil should be considered.

Patients currently being co-prescribed sildenafil and HIV protease inhibitors should contact their physician to receive further information and advice about their ongoing treatment.

The scientific committee of the EMEA, the CPMP, adopted positive opinions on the introduction of the above amendments to the SPC and Package Leaflet for Viagra and Patrex during the course of its April meeting (20-22 April 1999). These opinions will now be forwarded to the Commission to initiate the Decision-Making Process. In the interim the draft SPC and Package leaflet including these revisions may be found in the European Public Assessment Reports (EPARs) for these products (http://www.eudra.org/emea.html). The Marketing Authorisation Holders have also undertaken to write to concerned healthcare professionals in EU markets, to inform them of the introduction of this new information and to reinforce the instructions for appropriate use and administration of Viagra and Patrex.

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