WORLD HEALTH ORGANIZATION ORGANISATION MONDIALE DE LA SANTE

DRS/MtH/IEA.54 16 January 1997

DRS Information Exchange Service

ALERT No. 54

TERFENADINE (SELDANE®): PROPOSED WITHDRAWAL – SAFER ALTERNATIVE AVAILABLE

United States of America. The Food and Drug Administration has announced its intention to withdraw the approval of the antihistamine, terfenadine (Seldane®: Hoechst Marion Roussel), terfenadine in combination with pseudoephedrine (Seldane ® D) and generic versions of terfenadine.

Until recently, the agency had considered the benefits of terfenadine to outweigh the risks, despite its known serious cardiac adverse effects when used inappropriately, but now fexofenadine (Allegra®: Hoechst Marion Roussel) has become available. Fexofenadine – the primary active metabolite of terfenadine produced in the body – provides essentially all of the beneficial effects of terfenadine but, unlike terfenadine, it does not appear to cause a potentially fatal heart condition when taken with some other commonly prescribed medications.

After the approval of terfenadine in 1985 as the first prescription antihistamine to relieve the symptoms of allergic rhinitis without causing drowsiness, the FDA started to receive reports of serious and sometimes fatal cardiac arrhythmias associated with terfenadine when taken with certain antimicrobials or in patients with significant liver dysfunction. Normally very little terfenadine circulates in the plasma because orally administered terfenadine undergoes extensive first-pass metabolism in the liver. This pathway may be impaired in patients with liver dysfunction (e.g. alcoholic cirrhosis) or those who are taking drugs such as ketoconazole, itraconazole, or macrolide antibiotics (e.g. clarithromycin, erythromycin, or troleandomycin), which all are inhibitors of liver enzymes. As a consequence, blood levels of terfenadine may become elevated, resulting in severe adverse cardiac effects.

Since the serious cardiac risks of terfenadine were identified, both the company and the FDA have undertaken to inform health care providers and patients about the dangers of these drug interactions. Although these efforts have reduced inappropriate prescribing and dispensing of terfenadine with other drugs, such events have not been eliminated.

In view of these developments, the FDA has determined that terfenadine-containing products should be removed from the market. Manufacturers of these products have been given 30 days to request a hearing to show why approval of terfenadine should not be withdrawn. In the meantime, the FDA is advising patients currently taking terfenadine-containing products to consult their doctor about switching to alternative medications.

Terfenadine is available in many countries and in several of them it may be obtained without prescription.

Reference: FDA Talk Paper T97-3 dated 13 January 1997.

❖