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Information Exchange System

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Mibefradil (Posicor®) – withdrawn from the market : potentially harmful interactions

United States of America. Roche Laboratories has announced that it is voluntarily withdrawing the antihypertensive and anti-anginal medication, mibefradil (Posicor®), from the market as a result of new information about potentially harmful interactions with other drugs. Mibefradil is a calcium-channel blocker, chemically unlike the other approved products in this class, that was approved in June 1997 for the treatment of patients with hypertension and chronic stable angina.

In many cases, drug interactions can be addressed by appropriate labelling changes and public education, but due to the complexity of the prescribing information needed in this case, and seriousness of adverse effects, the FDA and Roche agreed that it would be difficult to administer mibefradil safely.

Mibefradil reduces the activity of certain liver enzymes that are important in helping the body eliminate many other drugs. Inhibiting these enzymes can cause some of these other drugs to accumulate in the body to dangerous levels. When it was authorized for marketing in 1997, the enzyme-inhibiting properties of mibefradil were described in the labelling and three drugs were specifically listed (astemizole, cisapride, and terfenadine) that could be expected to accumulate to dangerous levels if mibefradil was coadministered.

In December 1997, after several cases were reported in which patients suffered serious adverse reactions after taking mibefradil with one or more of the other drugs, the FDA strengthened the labelling and two more drugs – lovastatin and simvastatin – were added to the list of drugs that should never be coadministered with mibefradil. The FDA also issued a public warning about this problem and the company issued a "Dear Doctor" letter to physicians [See WHO Pharmaceuticals Newsletter Nos.1&2, January&February 1998] .

From spontaneous reports and ongoing trials, the FDA and the company have subsequently learned of more adverse reactions related to coadministration of mibefradil with several other drugs. At present, more than 25 drugs are known to be potentially dangerous if used with mibefradil – a number and diversity of drugs that cannot be practically addressed by standard label warnings.

Since mibefradil has not been shown to offer special benefits (such as treating patients who do not respond to other antihypertensive and anti-anginal drugs), the problems associated with it are viewed as an unreasonable risk to patients.

Patients now taking mibefradil should not simply discontinue treatment because stopping medications can be dangerous, but should promptly consult with their physicians about appropriate alternative therapy. In addition, patients now taking mibefradil should not add any new medication to their current treatment without consulting their physician.

Roche Laboratories is providing information in a "Dear Doctor" letter to physicians, pharmacists, nurse practitioners, and other health care professionals.

The following (see overleaf) is a list of drugs that are known to have induced interactions when used concomitantly with mibefradil (Posicor®).

References:

1) FDA Talk Paper T98-33 dated 8 June 1998.

2) "Dear Doctor" letter from Roche Laboratories, 8 June 1998.

3) Internet: http://www.fda.gov/metwatch/safety/1998/poscor.htm

Generic name (INN)	Trade Name
amiodarone	Cordarone
astemizole	Hismanal
bepridil	Vesture
cisapride	Propulsid
ciclosporin	Neoral, Sandimmune
cyclophosphamide	Cytoxan
desipramine	Norpramin
erythromycin	Erythrocin, Ilosone, others
etoposide	VePesid
flecainide	Tambocor
flutamide	Eulexin
halofantrine	Halfan
ifosfamide	Ifex
imipramine	Tofranil
lovastatin	Mevacor
mexiletine	Mexitil
pimozide	Orap
propafenone	Rythmol
quinidine	Cardioquin, Quinaglute, Quinidex, others
simvastatin	Zocor
tacrolimus	Prograf
tamoxifen	Tamoxifen
terfenadine	Seldane
thioridazine	Mellaril
vinblastine	Velban
vincristine	Oncovin

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