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IMPORTANT DRUG WARNING

The purpose of this communication is to inform healthcare professionals about a change in the prescribing information for Zoloft® (sertraline hydrochloride) tablets and oral concentrate. This change, made at the request of the Food and Drug Administration, articulates a pimozide/sertraline interaction and arises from the results of the study entitled, "Phase 1 Open Study Designed to Determine the Potential Interaction of Sertraline With Cisapride or Pimozide in Healthy Male and Female Subjects."

Based upon these study results, the CONTRAINDICATIONS and PRECAUTIONS sections of the Zoloft prescribing information have been revised as follows (underlined text indicates new text):

CONTRAINDICATIONS

Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated (see WARNINGS). Concomitant use in patients taking pimozide is contraindicated (see PRECAUTIONS).

PRECAUTIONS—Drug Interactions—CNS Active Drugs

In a study comparing the disposition of intravenously administered diazepam before and after 21 days of dosing with either ZOLOFT (50 to 200 mg/day escalating dose) or placebo, there was a 32% decrease relative to baseline in diazepam clearance for the ZOLOFT group compared to a 19% decrease relative to baseline for the placebo group ($p<0.03$). There was a 23% increase in Tmax for desmethyldiazepam in the ZOLOFT group compared to a 20% decrease in the placebo group ($p<0.03$). The clinical significance of these changes is unknown.

In a placebo-controlled trial in normal volunteers, the administration of two doses of ZOLOFT did not significantly alter steady-state lithium levels or the renal clearance of lithium.

Nonetheless, at this time, it is recommended that plasma lithium levels be monitored following initiation of ZOLOFT therapy with appropriate adjustments to the lithium dose.

In a controlled study of a single dose (2 mg) of pimozide, 200 mg sertraline (q.d.) co-administration to steady state was associated with a mean increase in pimozide AUC and Cmax of about 40%, but was not associated with any changes in EKG. Since the highest recommended pimozide dose (10 mg) has not been evaluated in combination with sertraline, the effect on QT interval and PK parameters at doses higher than 2 mg at this time are not known. While the mechanism of this interaction is unknown, due to the narrow therapeutic index of pimozide and due to the interaction noted at a low dose of pimozide, concomitant administration of ZOLOFT and pimozide should be contraindicated (see CONTRAINDICATIONS).

The risk of using ZOLOFT in combination with other CNS active drugs has not been systematically evaluated. Consequently, caution is advised if the concomitant administration of ZOLOFT and such drugs is required.

There is limited controlled experience regarding the optimal timing of switching from other drugs effective in the treatment of major depressive disorder, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, and premenstrual dysphoric disorder to ZOLOFT. Care and prudent medical judgment should be exercised when switching, particularly from long-acting agents. The duration of an appropriate washout period which should intervene before switching from one selective serotonin reuptake inhibitor (SSRI) to another has not been established.

Zoloft was launched in 1992 for the treatment of major depressive disorder. It is also approved for the treatment of panic disorder, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), and premenstrual dysphoric disorder (PMDD). It has been shown to be safe in the long-term treatment of pediatric OCD. Zoloft is the only SSRI approved for the long-term treatment of PTSD. Over the past decade, Zoloft has been used for more than 10.2 billion patient days of therapy worldwide.*

We trust this information is useful in providing guidance on the appropriate use of sertraline concomitantly with pimozide.

Sincerely,

Cathryn M. Clary, MD
Senior Medical Director
Medical and Scientific Affairs
Pfizer Inc.

*IMS America Global Sales Audits. Dec. 1990-June 2002.

Please see enclosed prescribing information.

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