ACORDA®
THERAPEUTICS

Updated Safety Information: Contraindications to the use of Tizanidine

March 5, 2007

Dear Healthcare Professional:

Acorda Therapeutics would like to inform you that concomitant use of tizanidine with fluvoxamine or ciprofloxacin (potent CYP1A2 inhibitors) is contraindicated.

The interaction between tizanidine and either fluvoxamine or ciprofloxacin, characterized by markedly and potentially dangerously elevated serum tizanidine levels, is most likely due to inhibition of CYP1A2 by fluvoxamine or ciprofloxacin. Although there have been no clinical studies evaluating the effects of other CYP1A2 inhibitors on tizanidine, other CYP1A2 inhibitors may lead to substantial increases in tizanidine blood concentrations. Therefore, concomitant use of tizanidine with other CYP1A2 inhibitors, such as zileuton, other fluoroquinolones, antiarrythmics (amiodarone, mexiletine, propafenone, and verapamil), cimetidine, famotidine, oral contraceptives, acyclovir and ticlopidine should ordinarily be avoided. If their use is clinically necessary, they should be used with caution.

Addition of two contraindications to the CONTRAINDICATIONS section of the U.S. PI:

CONTRAINDICATIONS
Concomitant use of tizanidine with fluvoxamine or with ciprofloxacin, potent inhibitors of CYP1A2, is contraindicated. Significant alterations of pharmacokinetic parameters of tizanidine including increased AUC, t1/2, Cmax, increased oral bioavailability and decreased plasma clearance have been observed with concomitant administration of either fluvoxamine or ciprofloxacin. This pharmacokinetic interaction can result in potentially serious adverse events (See WARNINGS and CLINICAL PHARMACOLOGY: Drug Interactions). Zanaflex is contraindicated in patients with known hypersensitivity to Zanaflex or its ingredients.

Addition of two WARNINGS sections to the U.S. PI:

POTENTIAL INTERACTION WITH FLUVOXAMINE OR CIPROFLOXACIN
In a pharmacokinetic study, tizanidine serum concentration was significantly increased (Cmax 12-fold, AUC 33-fold) when the drug was given concomitantly with fluvoxamine. Potentiated hypotensive and sedative effects were observed. Fluvoxamine and tizanidine should not be used together. (See CONTRAINDICATIONS and CLINICAL PHARMACOLOGY: Drug Interactions).

In a pharmacokinetic study, tizanidine serum concentration was significantly increased (Cmax 7-fold, AUC 10-fold) when the drug was given concomitantly with ciprofloxacin. Potentiated hypotensive and sedative effects were observed. Ciprofloxacin and tizanidine should not be used together (See CONTRAINDICATIONS and CLINICAL PHARMACOLOGY: Drug Interactions).

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POSSIBLE INTERACTION WITH OTHER CYP1A2 INHIBITORS
Because of potential drug interactions, concomitant use of tizanidine with other CYP1A2 inhibitors, such as zileuton, other fluoroquinolones, antiarrythmics (amiodarone, mexiletine, propafenone, and verapamil), cimetidine, famotidine, oral contraceptives, acyclovir and ticlopidine (see CLINICAL PHARMACOLOGY: Drug Interactions) should ordinarily be avoided. If their use is clinically necessary, they should be used with caution.

Pharmacokinetics and Dosing Administration Considerations

Acorda Therapeutics also would like to remind you of the pharmacokinetic differences between Zanaflex Capsules™ (tizanidine hydrochloride) and Zanaflex® tablets (tizanidine hydrochloride) and generic tizanidine tablets. Zanaflex Capsules™ and Zanaflex® tablets are not bioequivalent when given in the fed state.

Food has complex effects on tizanidine hydrochloride pharmacokinetics. These pharmacokinetic differences may result in clinically significant differences when [1] switching administration of the tablet between the fed or fasted state, [2] switching administration of the capsule between the fed or fasted state, [3] switching between the tablet and capsule in the fed state, or [4] switching between the intact capsule and sprinkling the contents of the capsule on applesauce. These changes may result in increased adverse events or delayed/more rapid onset of activity, depending upon the nature of the switch. For this reason, the prescriber should be thoroughly familiar with the changes in kinetics associated with these different conditions.

Acorda Therapeutics is committed to ensuring that Zanaflex Capsules™ and Zanaflex® tablets are used safely and effectively. We look forward to working in collaboration with you for the safety and well-being of all patients. You should report any adverse events to Acorda's Medical Information System by calling toll free: 1 800 367-5109 or by email at: Acorda@medcomsol.com. You can also report all cases to the FDA MedWatch program by phone at: 1 800 FDA-1088, by fax at: 1 800 FDA-0178, by website at http://www.accessdata.fda.gov/scripts/medwatch/ or by mail:

MedWatch, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

A copy of the full prescribing information for Zanaflex Capsules™ and Zanaflex® is enclosed. Prescribing healthcare professions are advised to review this information carefully. Should you have any questions or require further information please contact the Acorda Medical Information System at 1 800 367-52109.

Sincerely,

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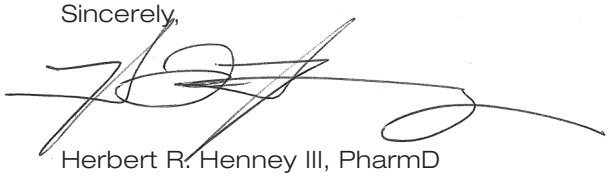

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