LIGAND®
PHARMACEUTICALS

October 2005

Dear Health Care Professional:

Ligand Pharmaceuticals Inc. is writing to inform you of changes to the product labeling for AVINZA® (morphine sulfate extended-release capsules). These changes are being made to highlight and strengthen the WARNING that patients should not consume alcohol while taking AVINZA. Additionally, patients must not use prescription or non-prescription medications containing alcohol while on AVINZA therapy.

The following new and/or additional text has been added to the Package Insert for AVINZA.

- Black Box Warning, Warnings, and Dosage and Administration sections:

  Patients must not consume alcoholic beverages while on AVINZA therapy. Additionally, patients must not use prescription or non-prescription medications containing alcohol while on AVINZA therapy. Consumption of alcohol while taking AVINZA may result in the rapid release and absorption of a potentially fatal dose of morphine.

- Precautions, Information for Patients section:

  Patients should be informed that they must not consume alcoholic beverages while on AVINZA therapy. Additionally, patients should be informed that they must not use prescription or non-prescription medications containing alcohol while on AVINZA therapy. Consumption of alcohol while taking AVINZA may result in the rapid release and absorption of a potentially fatal dose of morphine.

- Clinical Pharmacology and Warnings sections:

  In vitro studies performed by the FDA demonstrated that when AVINZA 30 mg was mixed with 900 mL of buffer solutions containing ethanol (20% and 40%), the dose of morphine that was released was alcohol concentration-dependent, leading to a more rapid release of morphine. While the relevance of *in vitro* lab tests regarding AVINZA to the clinical setting remains to be determined, this acceleration of release may correlate with *in vivo* rapid release of the total morphine dose, which could result in the absorption of a potentially fatal dose of morphine.

The updated Package Insert for AVINZA is enclosed.

If you have any questions or are aware of adverse events related to AVINZA, please contact the AVINZA Information Service at 1-888-8-AVINZA.

Sincerely,

Richard Ghalie, M.D.
Vice President, Medical Affairs and Professional Services
Ligand Pharmaceuticals Inc.

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