AMBIEN and AMBIEN CR DEAR HEALTHCARE PROFESSIONAL LETTER

March 2007

Dear Healthcare Professional:

Sanofi-aventis U.S. would like to inform you of important updated information regarding AMBIEN ® (zolpidem tartrate) CIV Tablets and AMBIEN CR ™ (zolpidem tartrate extended-release) CIV Tablets. The prescribing information for these 2 drug products has been revised to include safety recommendations resulting from a U.S. Food and Drug Administration (FDA) class labeling initiative for the sedative hypnotic drug products indicated for the treatment of insomnia. These changes have been reviewed and agreed to by the FDA.

The AMBIEN and AMBIEN CR Prescribing Information have been updated to:

1. Revise the **WARNINGS** section for complex behaviors;
2. Revise the **WARNINGS** section for severe anaphylactic and anaphylactoid reactions;
3. Revise the **PRECAUTIONS: Information for patients** section to include a section concerning "Sleep Driving" and other complex behaviors

The specific revisions to the prescribing information for AMBIEN and AMBIEN CR are indicated in italics as follows:

AMBIEN ® (zolpidem tartrate) CIV Tablets

WARNINGS

Because sleep disturbances may be the presenting manifestation of a physical and/or psychiatric disorder, symptomatic treatment of insomnia should be initiated only after a careful evaluation of the patient. **The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated**. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with sedative/hypnotic drugs, including Ambien. Because some of the important adverse effects of Ambien appear to be dose related (see Precautions and Dosage and Administration), it is important to use the smallest possible effective dose, especially in the elderly.

A variety of abnormal thinking and behavior changes have been reported to occur in association with the use of sedative-hypnotics. Some of these changes may be characterized by decreased inhibition (e.g., aggressiveness and extroversion that seemed out of character), similar to effects produced by alcohol and other CNS depressants. Visual and auditory hallucinations have been reported as well as behavioral changes such as bizarre behavior, agitation, and depersonalization. *Complex behaviors such as "sleep-driving"(i.e., driving while not fully awake after ingestion of a sedative-hypnotic, with amnesia for the event) have been reported. These events can occur in sedative- hypnotic-naive as well as in sedative-hypnotic-experienced persons. Although behaviors such as" sleep-driving" may occur with Ambien alone at therapeutic doses, the use of alcohol and other CNS depressants with Ambien appears to increase the risk of such behaviors, as does the use of Ambien at doses exceeding the maximum recommended dose. Due to the risk to the patient and the community, discontinuation of Ambien should be strongly considered for patients who report a "sleep-driving" episode. Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with "sleep-driving", patients usually do not remember these events.*

Amnesia, anxiety and other neuro-psychiatric symptoms may occur unpredictably. In primarily depressed patients, worsening of depression, including suicidal thinking has been reported in association with the use of sedative-hypnotics.

It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above is drug induced, spontaneous in origin, or a result of an underlying psychiatric or physical disorder. Nonetheless, the emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

Following the rapid dose decrease or abrupt discontinuation of sedative/ hypnotics, there have been reports of signs and symptoms similar to those associated with withdrawal from other CNS-depressant drugs (see Drug Abuse and Dependence).

Ambien, like other sedative/hypnotic drugs, has CNS-depressant effects. *Due to the rapid onset of action, Ambien should only be ingested immediately prior to going to bed*. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness or motor coordination such as operating machinery or driving a motor vehicle after ingesting the drug, including potential impairment of the performance of such activities that may occur the day following ingestion of Ambien. Ambien showed additive effects when combined with alcohol and should not be taken with alcohol. Patients should also be cautioned about possible combined effects with other CNS-depressant drugs. Dosage adjustments may be necessary when Ambien is administered with such agents because of the potentially additive effects.

Severe anaphylactic and anaphylactoid reactions

Rare cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses of sedative-hypnotics, including Ambien. Some patients have had additional symptoms such as dyspnea, throat closing, or nausea and vomiting that suggest anaphylaxis. Some patients have required medical therapy in the emergency department. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Patients who develop angioedema after treatment with Ambien should not be rechallenged with the drug.

PRECAUTIONS: Information for patients

Patient information is printed at the end of this insert. To assure safe and effective use of Ambien, this information and instructions provided in the patient information section should be discussed with patients.

"Sleep-Driving" and other complex behaviors:

There have been reports of people getting out of bed after taking a sedative-hypnotic and driving their cars while not fully awake, often with no memory of the event. If a patient experiences such an episode, it should be reported to his or her doctor immediately, since "sleep-driving" can be dangerous. This behavior is more likely to occur when Ambien is taken with alcohol or other central nervous system depressants (see WARNINGS). Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with "sleep-driving", patients usually do not remember these events.

Please refer to the enclosed **FULL PRESCRIBING INFORMATION**, including patient information, for a complete discussion of **WARNINGS** and **PRECAUTIONS.**

AMBIEN CR ™ (zolpidem tartrate extended-release) CIV Tablets

The specific changes in the prescribing information relating to AMBIEN CR ™ (zolpidem tartrate extended-release) CIV Tablets are **identical** those as outlined above for AMBIEN ® (zolpidem tartrate) CIV Tablets **except** that the word "*zolpidem*" or "*Ambien CR"* is used in place of the word "*Ambien*" throughout the prescribing information as reference to the product name.

Please refer to the enclosed **FULL PRESCRIBING INFORMATION**, including patient information, for a complete discussion of **WARNINGS** and **PRECAUTIONS.**

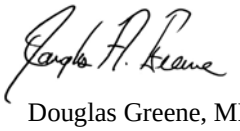
Patient safety is our highest priority at sanofi-aventis U.S., and we are committed to ensuring that healthcare professionals continue to have the information necessary to prescribe AMBIEN and AMBIEN CR appropriately. Please carefully review this information and contact sanofi-aventis if you should have any questions about this information or the safe and effective use of AMBIEN and AMBIEN CR.

We also encourage you to report any adverse events experienced by your patients. To report adverse events occurring in connection with the use of AMBIEN or AMBIEN CR call 1-800-633-1610 (option #2). Alternatively, this information may be reported to FDA's MedWatch Reporting System by phone at 1-800-FDA-1088, by facsimile at 1-800-FDA-0178, or by mail using the Form 3500 at http://www.fda.gov/medwatch/index.html.

The revised product information will be included in AMBIEN (zolpidem tartrate) CIV Tablets packages manufactured after March 31, 2007 and AMBIEN CR ™ (zolpidem tartrate extended-release) CIV Tablet packages manufactured after March 31, 2007. This information is also available on the company and product websites (www.sanofi-aventis.us, www.ambien.com , and www. ambiencr.com) or by calling Customer Information at 1-800-633-1610.

If you have further questions or require additional information, please contact our Medical Information Department at 1-800-633-1610 (option #1) from 9am to 5pm (EST) Monday–Friday.

Sincerely,



Douglas Greene, MD
Senior Vice President
US Medical Affairs & Chief Medical Officer
Sanofi-aventis U.S.

Enclosures: AMBIEN (zolpidem tartrate) CIV Tablets Full Prescribing Information
AMBIEN CR ™ (zolpidem tartrate extended-release) CIV Tablets Full Prescribing Information

US.ACR.07.03.026

sanofi aventis