

Bosentan Label Changes Address Hepatotoxicity

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Reported cases of hepatotoxicity associated with bosentan therapy have prompted changes to the pulmonary arterial hypertension drug's prescribing information.

Actelion Pharmaceuticals US Inc., which manufactures bosentan (Tracleer), made the changes to highlight the importance of monthly liver function monitor-

ing for the duration of bosentan treatments and the need to adhere to the new dosage adjustment and monitoring guidelines. The new recommendations include:

► For alanine aminotransferase/aspartate aminotransferase (ALT/AST) levels greater than three and up to five times the upper limit of normal, confirm by another aminotransferase test. If confirmed, reduce the daily dose or interrupt treatment and monitor aminotransferase levels at least every 2 weeks. If the aminotransferase levels return

to pretreatment values, continue or reintroduce the treatment as appropriate.

► For ALT/AST levels greater than five and up to eight times the upper limit of normal, confirm by another aminotransferase test. If confirmed, stop treatment and monitor aminotransferase levels at least every 2 weeks. Once the aminotransferase levels return to pretreatment values, consider reintroduction of the treatment.

► For ALT/AST levels greater than eight times the upper limit of normal, treatment

should be stopped and reintroduction of the drug should not be considered. There is no experience with reintroduction of the drug in these circumstances.

For more information, contact the company by calling 888-835-5445. Report any serious adverse events that occur with the use of bosentan to the Food and Drug Administration's MedWatch Adverse Event Reporting program by calling 800-332-1088 or online at www.fda.gov/medwatch/report.htm. ■

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- **First and only**—prescription insomnia medication that targets the normal sleep-wake cycle¹
- **First and only**—prescription insomnia medication with no evidence of abuse potential in clinical studies¹
- **First and only**—prescription insomnia medication that does not act by CNS depression¹
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*A randomized, single-center, double-blind, dose run-up study (N=6) and a single-center, randomized, double-blind, placebo-controlled crossover study (N=14) specifically assessed the abuse liability of Rozerem in patients with a history of substance abuse.²

Rozerem is indicated for the treatment of insomnia characterized by difficulty with sleep onset. Rozerem can be prescribed for long-term use. Rozerem should not be used in patients with hypersensitivity to any components of the formulation, severe hepatic impairment, or in combination with fluvoxamine. Failure of insomnia to remit after a reasonable period of time should be medically evaluated, as this may be the result of an unrecognized underlying medical disorder. Hypnotics should be administered with caution to patients exhibiting signs and symptoms of depression. Rozerem has not been studied in patients with severe sleep apnea, severe COPD, or in children or adolescents. The effects in these populations are unknown. Exercise caution if consuming alcohol in combination with Rozerem. Rozerem has been associated with decreased testosterone levels and increased prolactin levels. Health professionals should be mindful of any unexplained symptoms possibly associated with such changes in these hormone levels. Rozerem should not be taken with or immediately after a high-fat meal. Rozerem should be taken within 30 minutes before going to bed and activities confined to preparing for bed. The most common adverse events seen with Rozerem that had at least a 2% incidence difference from placebo were somnolence, dizziness, and fatigue.

Please see adjacent Brief Summary of Prescribing Information.

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