

# Tricyclics Tied to 35% Higher Cardiovascular Risk

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FROM THE EUROPEAN HEART JOURNAL

A large population-based study has shown a link between tricyclic antidepressant medications and an increased risk of cardiovascular disease, adding to a growing body of evidence that the medications carry cardiovascular risks – both for people with and without existing disease.

In a cohort study of 14,784 adults without known CVD in Scotland, the use of tricyclic antidepressants for any amount of time and for any reason was associated with a 35% higher risk of being diagnosed with CVD within 8 years, even after accounting for potential confounders, including symptoms of anxiety and depression, which are also linked to CVD.

Tricyclic antidepressants have been shown to increase cardiac events, in-

cluding myocardial infarction, in patients with CVD; however, few population-based studies have examined the effects on people without known CVD, said Mark Hamer, Ph.D., of University College London, the lead author of the findings published in the *European Heart Journal* (doi:10.1093/eurheartj/ehq438). Now, “the evidence is starting to become overwhelming,” Dr. Hamer said.

Tricyclic antidepressants are an older

class of medication whose psychiatric use has fallen off in favor of newer agents such as selective serotonin reuptake inhibitors. However, TCAs are still used widely to treat headache, Dr. Hamer said, citing a recent meta-analysis (*BMJ* 2010;341:c5222) revealing tricyclics to be more effective than SSRIs and placebo in preventing migraine and tension headaches, and also to be increasingly effective with longer-term use.

For patients with type 2 diabetes whose blood glucose is uncontrolled with orals alone

**THIS IS NOT JUST A TIRE  
IT'S SOMETHING WE TAKE  
FOR GRANTED UNTIL IT'S  
WEARING OUT**



## Important Safety Information for Lantus® (insulin glargine [rDNA origin] injection) (cont'd)

### Warnings and Precautions (cont'd)

Do not dilute or mix Lantus® with any other insulin or solution. If mixed or diluted, the solution may become cloudy, and the onset of action/time to peak effect may be altered in an unpredictable manner. Do not administer Lantus® via an insulin pump or intravenously because severe hypoglycemia can occur. Insulin devices and needles must not be shared between patients.

Hypoglycemia is the most common adverse reaction of insulin therapy, including Lantus®, and may be life-threatening.

Severe life-threatening, generalized allergy, including anaphylaxis, can occur.

A reduction in the Lantus® dose may be required in patients with renal or hepatic impairment.

**Please see additional Important Safety Information for Lantus® continued on the next page.**

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For their research, Dr. Hamer and his colleagues used data from the Scottish Health Survey, an ongoing cohort study conducted every 3-5 years in Scottish households. They combined data from surveys in 1995, 1998, and 2003 in adults aged 35 years and older (age 52.4 + 11.9 years, 43.9% men) without clinically confirmed CVD. Of the total study group, 2.2%, 2.0%, and 0.7% reported taking TCAs, SSRIs, or other antidepressants (including monoamine oxidase inhibitors), respectively.

Over a mean follow-up of 8 years, there were 1,434 CVD events in the study

group, 26.2% of which were fatal, and 67.5% of the events were related to coronary heart disease. The risk of CVD events (including death, nonfatal myocardial infarction, coronary artery bypass, percutaneous transluminal coronary angioplasty, stroke, and heart failure) was elevated in TCA users, but this was not significant after adjusting for confounding factors. No associations were found between SSRI use and CVD. Dr. Hamer and his colleagues also found no significant associations between any antidepressant use and all-cause mortality.

However, the TCA users saw a 35%

higher risk of CVD (multivariate-adjusted hazard ratio 1.35, 95% confidence interval 1.03-1.77) even after adjustment for confounding factors, which included physical activity, smoking status, alcohol use, socioeconomic status, body mass index, marital status, a history of psychiatric illness, and the presence of pre-clinical CVD risk factors as measured by the use of cardiovascular medication and antihypertension drugs.

The investigators noted that tricyclic antidepressants have been associated with weight gain and have been shown to have cardiotoxic effects. These “might

explain the increased risk of CVD, including orthostatic hypotension, reduced heart rate variability, QT interval prolongation, and greater risk of hypertension,” they wrote in their analysis.

The Scottish Health Survey is funded by the Scottish Executive. Dr. Hamer's and his colleagues' research was funded in part by grant support from foundations, including the Wellcome Trust; the British Heart Foundation; the National Heart, Lung, and Blood Institute; and the National Institute on Aging. Neither Dr. Hamer nor his colleagues declared any conflicts of interest. ■

## ADVERTISEMENT



## JUST LIKE THE PANCREAS

By the time of diagnosis, patients may have lost up to 50% of  $\beta$ -cell function, and it may continue to decline, on average, by approximately 5% annually.<sup>1</sup>

Patients may not know that their pancreas is no longer making enough insulin and that their disease has progressed.<sup>2</sup>

Based on data from 2003-2004, about 40% of patients with diabetes nationwide were not adequately controlled<sup>a</sup>—and may have spent an average of 5 years with an A1C >8% from diagnosis to insulin initiation.<sup>3,4</sup>

You may be surprised that in a survey, about 80% of patients with type 2 diabetes taking oral antidiabetic drugs said they would consider taking insulin based on your recommendation.<sup>5</sup>

Patients may focus on blaming themselves for their uncontrolled blood glucose, but you can help them focus on turning this negative mindset into positive action for managing their disease.<sup>2</sup>

Insulin may help make a difference. Insulin is an effective medication for lowering blood glucose levels. It works as part of an overall treatment plan.<sup>b</sup>

So, consider prescribing insulin today to help lower blood glucose for your appropriate patients.

**Important Safety Information for Lantus<sup>®</sup>** (insulin glargine [rDNA origin] injection) (cont'd)

### Drug Interactions

Certain drugs may affect glucose metabolism, requiring insulin dose adjustment and close monitoring of blood glucose. The signs of hypoglycemia may be reduced in patients taking anti-adrenergic drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine).

### Adverse Reactions

Other adverse reactions commonly associated with Lantus<sup>®</sup> are injection site reaction, lipodystrophy, pruritus, and rash.

**Please see brief summary of full prescribing information for Lantus<sup>®</sup> on the following pages.**

<sup>a</sup>Glucose control defined as A1C <7%.

<sup>b</sup>Including diet, exercise, and other diabetes medications.

**References:** 1. Holman RR. *Diabetes Res Clin Pract.* 1998;40(suppl):S21-S25. 2. Polonsky WH, Jackson RA. *Clin Diabetes.* 2004;22(3):147-150. 3. Hoerger TJ, Segel JE, Gregg EW, Saaddine JB. *Diabetes Care.* 2008;31(1):81-86. 4. Brown JB, Nichols GA, Perry A. *Diabetes Care.* 2004;27(7):1535-1540. 5. Data on file, sanofi-aventis U.S. LLC.

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