

# Australian Diabetes Society

A.B.N. 13 053 787 965 A.C.N. 053 787 965

The Peak Medical and Scientific Health Professional Body for Diabetes in Australia

## **ADS Position Statement on Insulin Glargine (Lantus ®) and a Possible Link with Cancer: Data are Inconclusive Posted: December 15th, 2009**

In June 2009, online publications in the diabetes journal Diabetologia suggested an association between insulin glargine (Lantus ®), and increased risk of cancer. The articles were published in the September 2009 issue. A comprehensive Diabetologia commentary series can be found at <http://www.diabetologia-journal.org/>.

These population studies collectively included more than 350,000 patients and suggested that there may be a link between glargine (Lantus ®) and cancer risk. Specifically, there was an association between glargine (Lantus ®) when used alone and breast cancer.

ADS agree with the main summary points identified in the Diabetologia editorial and would like to make the points below:

- It is well-described that type 2 diabetes, the metabolic syndrome and obesity are associated with an increased risk of some cancers, including breast and colon cancer.
- The specific concern in the Diabetologia papers related to Lantus ® insulin used alone and not to insulin glargine in combination with rapid acting insulin analogues. Whether insulin use *per se* may be associated with increased cancer risk, and the nature of any such association, remains in research.
- These studies were confounded by the subjects using insulin glargine (Lantus ®) alone generally being older and more overweight compared with subjects using other insulins.
- In the 2 studies where a breast cancer signal was detected, the number of cases was small (~1-2 cases per 1000 users per year).
- Experimental evidence suggests that insulin glargine (Lantus ®) may be more mitogenic in vitro in some cell-based assays than other insulins but not in many other in vitro systems (1). There are no in vivo data to confirm this effect in mouse or man.
- There is no evidence suggesting a link between glargine and cancer in people with Type 1 diabetes.

### **Executive Committee**

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## **Since those publications, other reports have become available:**

An online publication summarising controlled trials in >10 000 type 1 or type 2 patients with diabetes reported no significant difference in the incidence of malignancies, including breast cancer (2). Most of the studies were 6 months or less in duration.

In a 5-year open-label randomised clinical trial in 1017 patients with type 2 diabetes, the overall rate of malignancies was similar in the insulin glargine and NPH groups (insulin glargine 23 (4.5%); NPH 32 (6.4%)). The number of patients with breast cancer was also similar (insulin glargine 3 (0.6%), NPH 4 (0.8%)). This trial has now been published (3).

The ADS have also been notified by Sanofi-aventis that its data include the following: **Post Marketing safety data:** The global exposure for insulin glargine since its release is estimated to be 23.7 million patient-years. Of the cancer cases that have been reported, there is no specific pattern with regard to cell type and no trends have been identified.

Interim review of the data related to cancers in the ORIGIN study, a large prospective trial of use of insulin glargine in early dysglycaemia concluded that “there is no cause for concern and no reason to alter the design of the study for safety reasons”. (4)

[http://en.sanofi-aventis.com/binaries/20090805\\_ORIGIN\\_en\\_pdf\\_tcm28-25953.pdf](http://en.sanofi-aventis.com/binaries/20090805_ORIGIN_en_pdf_tcm28-25953.pdf).

A position statement from the American Diabetes Association can be found at:

<http://www.diabetes.org/diabetesnewsarticle.jsp?storyId=20358264&filename=20090626/comtex20090626iw00001849KEYWORDMissingEDIT.xml>

## **The Australian Diabetes Society recommends that:**

Considering current evidence, patients with Type 2 diabetes taking insulin glargine (Lantus ®) alone should **not** cease nor do they need to change their insulin therapy.

In patients with breast cancer or at high risk of breast cancer (e.g. family history, previous breast cancer, BRCA mutations), an alternative insulin regimen should be considered.

**In summary**, while ADS do not consider that the current evidence allows a definitive recommendation on the use of insulin glargine (Lantus ®) in relation to cancer risk or presence, it is prudent practice for clinicians to consider discussion of these issues with their patients and to consider the on-going benefits and potential disadvantages on a case by case basis in patients who are using insulin glargine alone. It is also prudent practice to advise alternative management if after discussion a patient has ongoing concern.

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Potential conflict of interest statements relevant to insulin glargine (Lantus ®):

- ADS receives support for the ADS Annual Scientific Meeting from Sanofi-aventis as a principal sponsor and has standard commercial arrangements for Sanofi-aventis to display at the ADS Annual Scientific Meeting.
- Stephen Twigg, Michael D’Emden and Ashim Sinha have received honoraria, travel support and/or payment for participation in Sanofi-aventis advisory committees.

References:

- 1) Weinstein D, et al (2008) Insulin analogues display IGF-1-like mitogenic and anti-apoptotic activities in cultured cancer cells. *Diabetes Metab Res Rev* 25:41–49
- 2) Home PD and Lagarenne P. (2009) Combined randomised controlled trial experience of malignancies in studies using insulin glargine. *Diabetologia*  
<http://www.springerlink.com/content/r644844411g51752/fulltext.html>
- 3) Rosenstock J et al. (2009) Similar risk of malignancy with insulin glargine and neutral protamine Hagedorn (NPH) insulin in patients with type 2 diabetes: findings from a 5 year randomised, open-label study.  
<http://www.springerlink.com/content/131t04q531710g21/fulltext.html>

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