

Wedge Insoles Didn't Take the Load Off Knee OA

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FROM THE WORLD CONGRESS
ON OSTEOARTHRITIS

BRUSSELS – Lateral wedge insoles placed in the shoes of patients with knee osteoarthritis gave no benefit and produced foot discomfort in a controlled study with 179 participants who completed 1 year of treatment.

The finding means that knee os-

teoarthritis (OA) treatment recommendations from the European League Against Rheumatism (EULAR) and from the Osteoarthritis Research Society International (OARSI) need revision, Kim Bennell, Ph.D., said. The withdrawal of wedge insoles as a recommended treatment option seems likely, as the new findings make the fourth – and largest – study to show no benefit in either pain or function and

the first to show an absence of cartilage benefit by MRI examination.

Based on the consistent results from the four studies, “we can say [wedges] are not effective,” Dr. Bennell, professor of physiotherapy and director of the center for health, exercise, and sports medicine at the University of Melbourne, said at the congress, which was organized by OARSI.

Even though three previous studies

showed wedge ineffectiveness, Dr. Bennell thought her study might show something different. “There are good biomechanical data in the lab showing that insoles reduce load” on the knee.

In the Melbourne study reported here, the researchers used full-length wedges, which Dr. Bennell thought would work better than heel insoles. The study also used MRI to assess structural outcomes, whereas prior studies used less-sensitive

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.

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® are injection site reaction, lipodystrophy, pruritus, and rash.

References: 1. Holman RR. *Diabetes Res Clin Pract.* 1998;40(suppl):S21-S25. 2. DeFronzo RA. *Diabetes.* 2009;58(4):773-795. 3. Polonsky WH, Jackson RA. *Clin Diabetes.* 2004;22(3):147-150. 4. American Diabetes Association. *Clin Diabetes.* 2007;25(1):39-40. 5. Hoerger TJ, Segel JE, Gregg EW, Saaddine JB. *Diabetes Care.* 2008;31(1):81-86. 6. Hirsch IB, Bergenstal RM, Parkin CG, Wright E, Buse JB. *Clin Diabetes.* 2005;23(2):78-86. 7. Egede LE, Ellis C. *Diabetes Technol Ther.* 2008;10(3):213-219. 8. Data on file, sanofi-aventis U.S. LLC. 9. Brunton SA, Davis SN, Renda SM. *Clin Cornerstone.* 2006;8(suppl 2):S19-S26. 10. Nathan DM, Buse JB, Davidson MB, et al. *Diabetes Care.* 2009;32(1):193-203. 11. AACE/ACE Consensus Statement. *Endocr Pract.* 2009;15(6):540-559.

Please see brief summary of full prescribing information for Lantus® on the following pages.

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From the maker of
LANTUS® SoloSTAR®



INSULIN

IMPROVING BLOOD GLUCOSE
CONTROL SHOULDN'T WAIT

Major Finding: Knee osteoarthritis patients who placed wedge insoles in their shoes daily for 1 year had no benefit in pain or function, compared with control patients. These and other data appear to rule out the efficacy of wedge insoles for osteoarthritis.

Data Source: Randomized, controlled trial of 179 osteoarthritis patients.

Disclosures: Dr. Bennell said that she has no disclosures for this study. She said that she had received research support for other studies from Essex, an Australian running-shoe manufacturer.

x-rays, she said in an interview.

The study recruited patients (aged 50 years and older) from the community who had knee pain on walking over the medial region with medial osteophytes

and joint narrowing, a mechanical axis of 182 degrees or less, and a Kellgren-Lawrence (KL) grade of 2 or 3. The 200 patients who entered the study averaged 64 years old, about 60% were women,

their average symptom duration was 7 years, their average body mass index was about 29 kg/m², and they split evenly between having KL grade 2 or 3 disease.

Every day, the randomized patients placed in their shoes either a wedge insole with a 5-degree pitch, or a flat, fully compressible control insole. Treatment ran for 1 year, with the insoles replaced quarterly. Patients in the wedge group reported wearing their insoles for an average of 7 hours daily, whereas the controls used theirs for an average of 9 hours daily.

The study's primary outcomes (as-

sessments of pain and cartilage structure) showed no significant differences between the 89 patients who completed 1 year in the wedge group and the 90 control patients who finished 1 year. The two groups also had no significant differences in measures of function.

The main difference between the treatment groups was that 47% of wedge users and 23% of controls self-reported problems with the insoles. Reports of foot pain came from 36% of wedge users and 16% of controls. The discomfort was rated as severe by 10% of wedge users and 1% of controls. ■

LANTUS® (insulin glargine [rDNA origin] injection) solution for subcutaneous injection

Rx Only

Brief Summary of Prescribing Information

1. INDICATIONS AND USAGE

LANTUS is indicated to improve glycemic control in adults and children with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus.

Important Limitations of Use:

- LANTUS is not recommended for the treatment of diabetic ketoacidosis. Intravenous short-acting insulin is the preferred treatment for this condition.

2. DOSAGE AND ADMINISTRATION

2.1 Dosing

LANTUS is a recombinant human insulin analog for once daily subcutaneous administration with potency that is approximately the same as the potency of human insulin. LANTUS exhibits a relatively constant glucose-lowering profile over 24 hours that permits once-daily dosing.

LANTUS may be administered at any time during the day. LANTUS should be administered subcutaneously once a day at the same time every day. The dose of LANTUS must be individualized based on clinical response. Blood glucose monitoring is essential in all patients receiving insulin therapy.

Patients adjusting the amount or timing of dosing with LANTUS, should only do so under medical supervision with appropriate glucose monitoring [see Warnings and Precautions (5.1)].

In patients with type 1 diabetes, LANTUS must be used in regimens with short-acting insulin.

The intended duration of activity of LANTUS is dependent on injection into subcutaneous tissue [see Clinical pharmacology (12.2) in the full prescribing information]. LANTUS should not be administered intravenously or via an insulin pump. Intravenous administration of the usual subcutaneous dose could result in severe hypoglycemia [see Warnings and Precautions (5.3)].

As with all insulins, injection sites should be rotated within the same region (abdomen, thigh, or deltoid) from one injection to the next to reduce the risk of lipodystrophy [See Adverse Reactions (6.1)].

In clinical studies, there was no clinically relevant difference in insulin glargine absorption after abdominal, deltoid, or thigh subcutaneous administration. As for all insulins, the rate of absorption, and consequently the onset and duration of action, may be affected by exercise and other variables, such as stress, intercurrent illness, or changes in co-administered drugs or meal patterns.

2.2 Initiation of LANTUS therapy

The recommended starting dose of LANTUS in patients with type 1 diabetes should be approximately one-third of the total daily insulin requirements. Short-acting, premeal insulin should be used to satisfy the remainder of the daily insulin requirements.

The recommended starting dose of LANTUS in patients with type 2 diabetes who are not currently treated with insulin is 10 units (or 0.2 Units/kg) once daily, which should subsequently be adjusted to the patient's needs.

The dose of LANTUS should be adjusted according to blood glucose measurements. The dosage of LANTUS should be individualized under the supervision of a healthcare provider in accordance with the needs of the patient.

2.3 Converting to LANTUS from other insulin therapies

If changing from a treatment regimen with an intermediate- or long-acting insulin to a regimen with LANTUS, the amount and timing of shorter-acting insulins and doses of any oral anti-diabetic drugs may need to be adjusted.

- If transferring patients from once-daily NPH insulin to once-daily LANTUS, the recommended initial LANTUS dose is the same as the dose of NPH that is being discontinued.
- If transferring patients from twice-daily NPH insulin to once-daily LANTUS, the recommended initial LANTUS dose is 80% of the total NPH dose that is being discontinued. This dose reduction will lower the likelihood of hypoglycemia [see Warnings and Precautions (5.3)].

4. CONTRAINDICATIONS

LANTUS is contraindicated in patients with hypersensitivity to LANTUS or one of its excipients.

5. WARNINGS AND PRECAUTIONS

5.1 Dosage adjustment and monitoring

Glucose monitoring is essential for all patients receiving insulin therapy. Changes to an insulin regimen should be made cautiously and only under medical supervision.

Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in insulin dose or an adjustment in concomitant oral anti-diabetic treatment.

As with all insulin preparations, the time course of action for LANTUS may vary in different individuals or at different times in the same individual and is dependent on many conditions, including the local blood supply, local temperature, and physical activity.

5.2 Administration

Do not administer LANTUS intravenously or via an insulin pump. The intended duration of activity of LANTUS is dependent on injection into subcutaneous tissue. Intravenous administration of the usual subcutaneous dose could result in severe hypoglycemia [see Warnings and Precautions (5.3)].

Do not dilute or mix LANTUS with any other insulin or solution. If LANTUS is diluted or mixed, the solution may become cloudy, and the pharmacokinetic or pharmacodynamic profile (e.g., onset of action, time to peak effect) of LANTUS and the mixed insulin may be altered in an unpredictable manner. When LANTUS and regular human insulin were mixed immediately before injection in dogs, a delayed onset of action and a delayed time to maximum effect for regular human insulin was observed. The total bioavailability of the mixture was also slightly decreased compared to separate injections of LANTUS and regular human insulin. The relevance of these observations in dogs to humans is unknown.

Do not share disposable or reusable insulin devices or needles between patients, because doing so carries a risk for transmission of blood-borne pathogens.

5.3 Hypoglycemia

Hypoglycemia is the most common adverse reaction of insulin, including LANTUS. The risk of hypoglycemia increases with intensive glycemic control. Patients must be educated to recognize and manage hypoglycemia. Severe hypoglycemia can lead to unconsciousness or convulsions and may result in temporary or permanent impairment of brain function or death. Severe hypoglycemia requiring the assistance of another person or parenteral glucose infusion or glucagon administration has been observed in clinical trials with insulin, including trials with LANTUS.

The timing of hypoglycemia usually reflects the time-action profile of the administered insulin formulations. Other factors such as changes in food intake (e.g., amount of food or timing of meals), exercise, and concomitant medications may also alter the risk of hypoglycemia [See Drug Interactions (7)].

The prolonged effect of subcutaneous LANTUS may delay recovery from hypoglycemia. Patients being switched from twice daily NPH insulin to once-daily LANTUS should have their initial LANTUS dose reduced by 20% from the previous total daily NPH dose to reduce the risk of hypoglycemia [see Dosage and Administration (2.3)].

As with all insulins, use caution in patients with hypoglycemia unawareness and in patients who may be predisposed to hypoglycemia (e.g., the pediatric population and patients who fast or have erratic food intake). The patient's ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating other machinery.

Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as longstanding diabetes, diabetic neuropathy, use of medications such as beta-blockers, or intensified glycemic control. These situations may result in severe hypoglycemia (and, possibly, loss of consciousness) prior to the patient's awareness of hypoglycemia.

5.4 Hypersensitivity and allergic reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including LANTUS.

5.5 Renal impairment

Due to its long duration of action, Lantus is not recommended during periods of rapidly declining renal function because of the risk for prolonged hypoglycemia.

Although studies have not been performed in patients with diabetes and renal impairment, a reduction in the LANTUS dose may be required in patients with renal impairment because of reduced insulin metabolism, similar to observations found with other insulins. [See Clinical Pharmacology (12.3) in the full prescribing information].

5.6 Hepatic impairment

Due to its long duration of action, Lantus is not recommended during periods of rapidly declining hepatic function because of the risk for prolonged hypoglycemia. Although studies have not been performed in patients with diabetes and hepatic impairment, a reduction in the LANTUS dose may be required in patients with hepatic impairment because of reduced capacity for gluconeogenesis and reduced insulin metabolism, similar to observations found with other insulins. [See Clinical Pharmacology (12.3) in the full prescribing information].

5.7 Drug interactions

Some medications may alter insulin requirements and subsequently increase the risk for hypoglycemia or hyperglycemia [See Drug Interactions (7)].

6. ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere:

- Hypoglycemia [See Warnings and Precautions (5.3)]
- Hypersensitivity and allergic reactions [See Warnings and Precautions (5.4)]

6.1 Clinical trial experience

Because clinical trials are conducted under widely varying designs, the adverse reaction rates reported in one clinical trial may not be easily compared to those rates