

# Device Lowers Weight, Glucose in Type 2 Diabetes

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AMSTERDAM — A novel gastric electrical stimulation device can potentially improve glucose levels and induce weight loss in obese patients with type 2 diabetes on oral antihyperglycemic therapy, Dr. Christoph Rosak said in a poster presentation at the annual meeting of the European Association for the Study of Diabetes.

The implantable device, called the Tan-

talus system, is manufactured by MetaCure Ltd. It has met marketing requirements in Europe (CE marking) and is indicated for the treatment of both type 2 diabetes and obesity (defined as a body mass index of 30-50 kg/m<sup>2</sup>). It is currently in phase III trials in the United States.

The Tantalus system comprises a pulse generator and bipolar leads that are implanted laparoscopically in the antrum and fundus of the stomach. When food intake occurs, the system delivers nonexci-

tatory electrical stimulation to the gastric wall, thereby increasing the amplitude of the contractions and allowing the vagal nerve to send a signal to the brain, triggering earlier satiety. Previous data suggested that the device could safely produce clinically significant weight loss and reduce blood pressure in morbidly obese individuals at 1 year (Obes. Surg. 2006;16:627-34).

In the current phase II open-label study, 24 obese patients with type 2 diabetes were implanted with the Tantalus. Subjects in-

cluded 9 men and 15 women, with a mean BMI of 41.7. In all, 7 patients used insulin; the other 17 took oral antihyperglycemic medication. The 16 patients on oral diabetes drugs who completed a 1-year follow-up showed a significant mean weight loss of 5.5 kg and reductions in waist circumference, Dr. Rosak, of Krankenhaus Sachsenhausen, Frankfurt, Germany, said during the poster presentation.

A subset of eight patients who were initially not well controlled (hemoglobin A<sub>1c</sub> greater than 7%) on stable oral medications had a significant decrease in mean HbA<sub>1c</sub> from 8.34% to 7.44%, and a drop in fasting plasma glucose from 206 mg/dL to 158



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DR. ROSAK

mg/dL. Available data on self glucose monitoring showed a significant decrease in 2-hour postprandial levels from 176 mg/dL to 141 mg/dL. The other eight patients on oral agents either changed their medication regime during treatment or had been well controlled initially, Dr. Rosak said.

In contrast, the four insulin-treated subjects who completed the 1-year study showed no significant changes in HbA<sub>1c</sub> or weight. It's not clear why insulin-treated patients don't respond as well to the Tantalus, but one theory is that exogenous insulin may interfere with the vagal signal, he said.

Dr. Harold Lebovitz, professor of medicine at the State University of New York Downstate Medical Center, Brooklyn, and a consultant to MetaCure, said the Tantalus could "improve glycemic control with an associated weight loss in type 2 diabetic patients inadequately controlled on combinations of oral agents."

It may also work in insulin-treated patients, he said, noting that some of the insulin-treated patients in the study were adjusting their premeal bolus doses, which would have masked the device's effect. "The meaningful data were the results in the patients on oral agents since their medication doses were kept constant" he said. ■

## ENDO PHARMACEUTICALS LIDODERM® (Lidocaine Patch 5%)

**Brief Summary** (For full Prescribing Information and Patient Information, refer to package insert.)

**INDICATIONS AND USAGE**  
LIDODERM is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to intact skin.

**CONTRAINDICATIONS**  
LIDODERM is contraindicated in patients with a known history of sensitivity to local anesthetics of the amide type, or to any other component of the product.

**WARNINGS**  
**Accidental Exposure in Children**  
Even a used LIDODERM patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used LIDODERM patch, although the risk with this formulation has not been evaluated. It is important for patients to **store and dispose of LIDODERM out of the reach of children, pets, and others.** (See HANDLING AND DISPOSAL)

**Excessive Dosing**  
Excessive dosing by applying LIDODERM to larger areas or for longer than the recommended wearing time could result in increased absorption of lidocaine and high blood concentrations, leading to serious adverse effects (see ADVERSE REACTIONS, Systemic Reactions). Lidocaine toxicity could be expected at lidocaine blood concentrations above 5 µg/mL. The blood concentration of lidocaine is determined by the rate of systemic absorption and elimination. Longer duration of application, application of more than the recommended number of patches, smaller patients, or impaired elimination may all contribute to increasing the blood concentration of lidocaine. With recommended dosing of LIDODERM, the average peak blood concentration is about 0.13 µg/mL, but concentrations higher than 0.25 µg/mL have been observed in some individuals.

**PRECAUTIONS**  
**General**  
Hepatic Disease: Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of lidocaine, because of their inability to metabolize lidocaine normally.

Allergic Reactions: Patients allergic to para aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. However, LIDODERM should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain.

Non-intact Skin: Application to broken or inflamed skin, although not tested, may result in higher blood concentrations of lidocaine from increased absorption. LIDODERM is only recommended for use on intact skin.

Eye Exposure: The contact of LIDODERM with eyes, although not studied, should be avoided based on the findings of severe eye irritation with the use of similar products in animals. If eye contact occurs, immediately wash out the eye with water or saline and protect the eye until sensation returns.

**Drug Interactions**  
Antiarrhythmic Drugs: LIDODERM should be used with caution in patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic.

Local Anesthetics: When LIDODERM is used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**  
Carcinogenesis: A minor metabolite, 2, 6-xylylidine, has been found to be carcinogenic in rats. The blood concentration of this metabolite is negligible following application of LIDODERM.

Mutagenesis: Lidocaine HCl is not mutagenic in Salmonella/mammalian microsome test nor clastogenic in chromosome aberration assay with human lymphocytes and mouse micronucleus test.

Impairment of Fertility: The effect of LIDODERM on fertility has not been studied.

**Pregnancy**  
Teratogenic Effects: Pregnancy Category B. LIDODERM (lidocaine patch 5%) has not been studied in pregnancy. Reproduction studies with lidocaine have been performed in rats at doses up to 30 mg/kg subcutaneously and have revealed no evidence of harm to the fetus due to lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, LIDODERM should be used during pregnancy only if clearly needed.

**Labor and Delivery**  
LIDODERM has not been studied in labor and delivery. Lidocaine is not contraindicated in labor and delivery. Should LIDODERM be used concomitantly with other products containing lidocaine, total doses contributed by all formulations must be considered.

**Nursing Mothers**  
LIDODERM has not been studied in nursing mothers. Lidocaine is excreted in human milk, and the milk: plasma ratio of lidocaine is 0.4. Caution should be exercised when LIDODERM is administered to a nursing woman.

R<sub>x</sub> only

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### Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

### ADVERSE REACTIONS

**Application Site Reactions**  
During or immediately after treatment with LIDODERM (lidocaine patch 5%), the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritus, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours.

**Allergic Reactions**  
Allergic and anaphylactoid reactions associated with lidocaine, although rare, can occur. They are characterized by angioedema, bronchospasm, dermatitis, dyspnea, hypersensitivity, laryngospasm, pruritus, shock, and urticaria. If they occur, they should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

**Other Adverse Events**  
Due to the nature and limitation of spontaneous reports in postmarketing surveillance, causality has not been established for additional reported adverse events including:

Asthenia, confusion, disorientation, dizziness, headache, hyperesthesia, hypoesthesia, lightheadedness, metallic taste, nausea, nervousness, pain exacerbated, paresthesia, somnolence, taste alteration, vomiting, visual disturbances such as blurred vision, flushing, tinnitus, and tremor.

**Systemic (Dose-Related) Reactions**  
Systemic adverse reactions following appropriate use of LIDODERM are unlikely, due to the small dose absorbed (see CLINICAL PHARMACOLOGY, Pharmacokinetics). Systemic adverse effects of lidocaine are similar in nature to those observed with other amide local anesthetic agents, including CNS excitation and/or depression (light headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold, or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression, and arrest). Excitatory CNS reactions may be brief or not occur at all, in which case the first manifestation may be drowsiness merging into unconsciousness. Cardiovascular manifestations may include bradycardia, hypotension, and cardiovascular collapse leading to arrest.

**OVERDOSAGE**  
Lidocaine overdose from cutaneous absorption is rare, but could occur. If there is any suspicion of lidocaine overdose (see ADVERSE REACTIONS, Systemic Reactions), drug blood concentration should be checked. The management of overdose includes close monitoring, supportive care, and symptomatic treatment. Dialysis is of negligible value in the treatment of acute overdose with lidocaine.

In the absence of massive topical overdose or oral ingestion, evaluation of symptoms of toxicity should include consideration of other etiologies for the clinical effects, or overdosage from other sources of lidocaine or other local anesthetics.

The oral LD<sub>50</sub> of lidocaine HCl is 459 (346-773) mg/kg (as the salt) in non-fasted female rats and 214 (159-324) mg/kg (as the salt) in fasted female rats, which are equivalent to roughly 4000 mg and 2000 mg, respectively, in a 60 to 70 kg man based on the equivalent surface area dosage conversion factors between species.

**DOSE AND ADMINISTRATION**  
Apply LIDODERM to intact skin to cover the most painful area. Apply up to three patches, only once for up to 12 hours within a 24-hour period. Patches may be cut into smaller sizes with scissors prior to removal of the release liner. (See HANDLING AND DISPOSAL) Clothing may be worn over the area of application. Smaller areas of treatment are recommended in a debilitated patient, or a patient with impaired elimination.

If irritation or a burning sensation occurs during application, remove the patch (es) and do not reapply until the irritation subsides.

When LIDODERM is used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

**HANDLING AND DISPOSAL**  
Hands should be washed after the handling of LIDODERM, and eye contact with LIDODERM should be avoided. Do not store patch outside the sealed envelope. Apply immediately after removal from the protective envelope. Fold used patches so that the adhesive side sticks to itself and safely discard used patches or pieces of cut patches where children and pets cannot get to them. LIDODERM should be kept out of the reach of children.

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature].

Manufactured for:  
Endo Pharmaceuticals Inc.  
Chadds Ford, Pennsylvania 19317

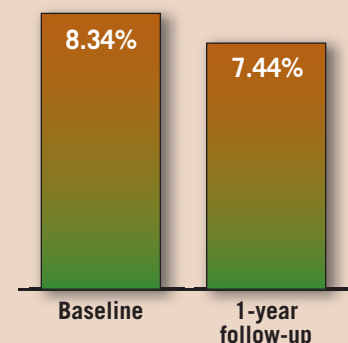
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**References:** 1. Lidoderm Prescribing Information. Chadds Ford, Pa: Endo Pharmaceuticals Inc; 2006. 2. Galer BS. Advances in the treatment of postherpetic neuralgia: the topical lidocaine patch. *Today's Therapeutic Trends* 2000; 18:1-20. 3. Argoff CE. Targeted topical peripheral analgesics in the management of pain. *Curr Pain Headache Rep*. 2003;7:34-38. 4. Rowbotham MC, Davies PS, Verkeimpinck C, Galer BS. Lidocaine patch: double-blind controlled study of a new treatment method for post-herpetic neuralgia. *Pain*. 1996;65:39-44. 5. Data on file. 6. Galer BS, Jensen MP, Ma T, Davies PS, Rowbotham MC. The lidocaine patch 5% effectively treats all neuropathic pain qualities: results of a randomized, double-blind, vehicle-controlled, 3-week efficacy study with use of the neuropathic pain scale. *Clin J Pain*. 2002;18:297-301.

## Mean HbA<sub>1c</sub> Levels in Eight Gastric Stimulation Patients



Note: Based on patients initially not well controlled on stable oral medications.  
Source: Dr. Rosak