

NTARCIA PLATFORM TECHNOLOGY



Intarcia's platform technology is known as the DUROS® subcutaneous delivery system. The DUROS system is comprised of a small, matchstick-sized osmotic pump that is inserted subcutaneously (just beneath the skin) to deliver a slow and consistent flow of medication. Each device contains an appropriate volume of drug product to treat a patient for a predetermined extended duration of time. The DUROS device is activated when subcutaneous tissue fluid passes through the device inlet, expanding the osmotic engine. The osmotic engine drives the piston at a constant rate, delivering consistent drug levels through the device outlet. The device can be inserted in a subcutaneous space in various locations on the arms and abdomen during a reimbursable in-office procedure, in as little as five minutes by a physician or physician's assistant, and ensures 100 percent patient adherence to therapy.

Delivering drugs via the DUROS technology avoids unwanted peak drug levels often associated with toxicities and sub-therapeutic troughs often associated with suboptimal therapeutic effects. Another key aspect of the DUROS technology is the unique formulations that maintain stability of proteins and peptides at human body temperature for extended periods of time. This advance in formulations allows continuous delivery of effective therapy with less frequent administration thereby ensuring compliance and improving patient convenience. The DUROS device was first used as a drug delivery technology for the FDA-approved product Viadur® in the delivery of leuprolide acetate.



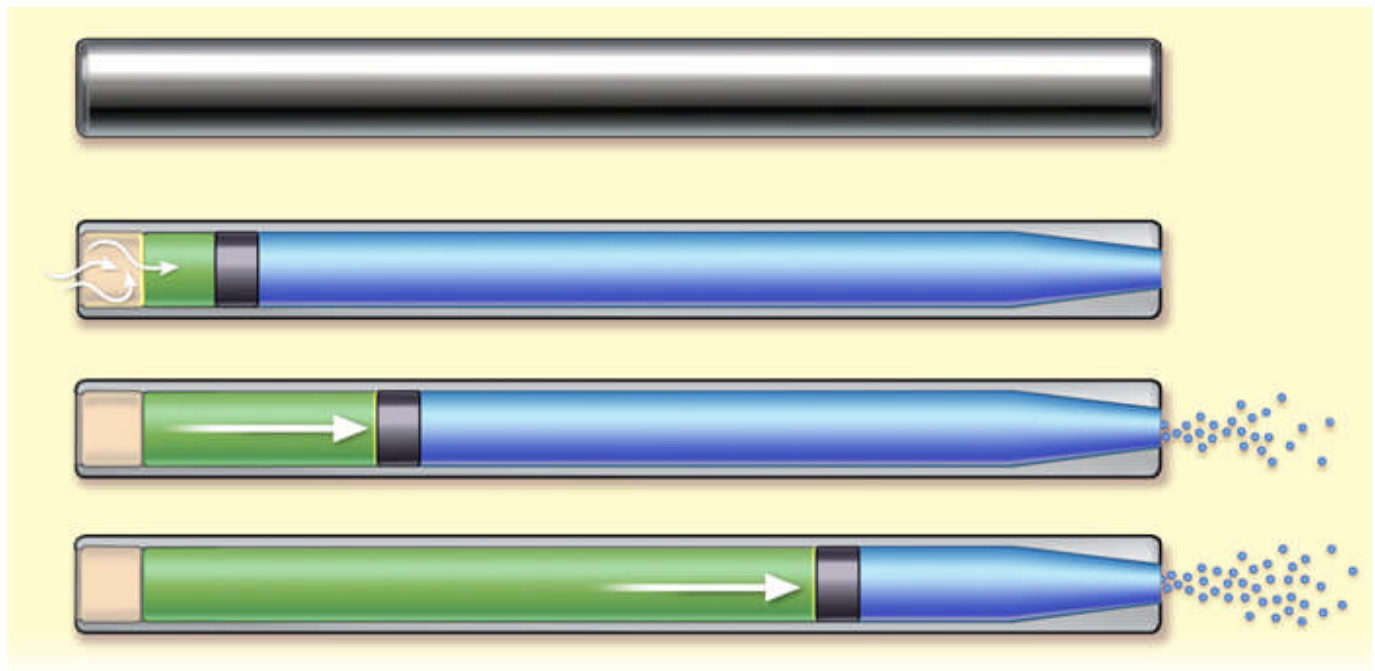
DUROS Technology: Revolutionizing How Type 2 Diabetes is Treated



Overview

Type 2 diabetes is currently one of the largest public health threats facing the U.S. over the next decade, and existing treatment options fail to address the myriad of complications patients endure including weight gain, suboptimal blood glucose control, nausea, and poor adherence with treatment. Many patients take several doses of oral medications daily and/or must inject themselves daily. Intarcia recognized the potential for the DUROS delivery system to reshape the way diabetes is treated by offering patients and their health care providers with a more convenient long term treatment regiment. The result is the investigational treatment now in late stage development – ITCA 650.

As part of a robust clinical trial program to develop ITCA 650, Intarcia paired the DUROS device with exenatide, a proven safe and effective drug commonly used for type 2 diabetes. ITCA 650 is a matchstick-sized, miniature osmotic pump that is inserted subcutaneously to provide continuous and consistent treatment of exenatide therapy for up to a year. Exenatide, the active agent in ITCA 650, has been approved in the U.S., Europe and many other markets and is currently marketed as a twice-daily self-injection therapy for type 2 diabetes.



How the Device Works

Intarcia's clinical stage type 2 diabetes candidate, ITCA 650 involves the delivery of exenatide, an approved incretin mimetic using the DUROS delivery system. The DUROS delivery system is a matchstick-sized device consisting of a cylindrical titanium alloy reservoir. Once inserted under the skin, water from the extracellular fluid enters the device at one end, by diffusing through a semipermeable membrane directly into a salt osmotic engine that expands to drive a piston at a controlled rate of travel. This forces the drug formulation to be released in a slow and consistent fashion through the exit port, or diffusion moderator at the other end of the device.

[Watch Video](#)

Phase 2 Trial Results

Results of a 24-week phase 2 clinical trial were presented at the 2010 European Association for the Study of Diabetes Annual Meeting demonstrating that continuous subcutaneous delivery of exenatide resulted in a reduction in glycated hemoglobin (HbA1c) levels and body weight, with 100 percent compliance.

The multicenter clinical trial randomized 155 type 2 diabetic patients who were inadequately controlled on metformin therapy to 3 initial treatment groups (51 to 53 patients per group) for 12 weeks, and then rerandomized each group in a 1:1 manner for another 12 weeks.

Treatment Groups

Initial Treatment Groups (Weeks 1 to 12)

ITCA 650 20 µg/day

ITCA 650 40 µg/day

Exenatide injections twice daily*

Rerandomization Groups (Weeks 13 to 24)

ITCA 650 20 µg/day or 60 µg/day

ITCA 650 40 µg/day or 80 µg/day

ITCA 650 40 µg/day or 60 µg/day

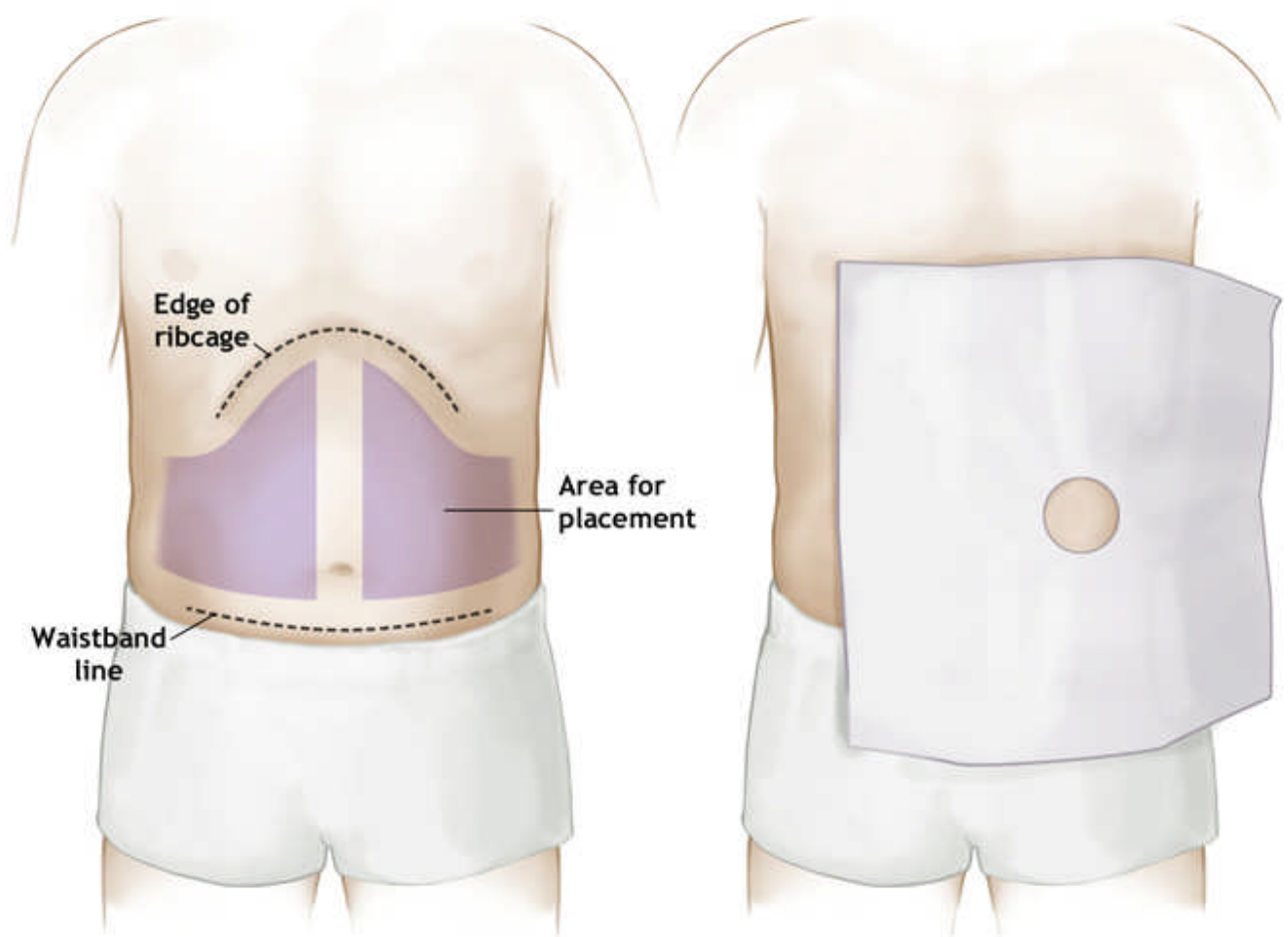
*5 µg twice daily for 4 weeks followed by 10 µg twice daily for 8 weeks

The aims of the trial were to investigate the effectiveness, safety, and tolerability of ITCA 650, and the feasibility of switching patients from injected exenatide to ITCA 650.

All doses of ITCA 650 resulted in substantial reductions in HbA1c and body weight. A starting dose of 20 µg/day showed the best tolerability, and switching to 60 µg/day for weeks 13 to 24 provided further reductions in HbA1c and weight at week 24. A phase 3 trial of ITCA 650 will use this dosing regimen.

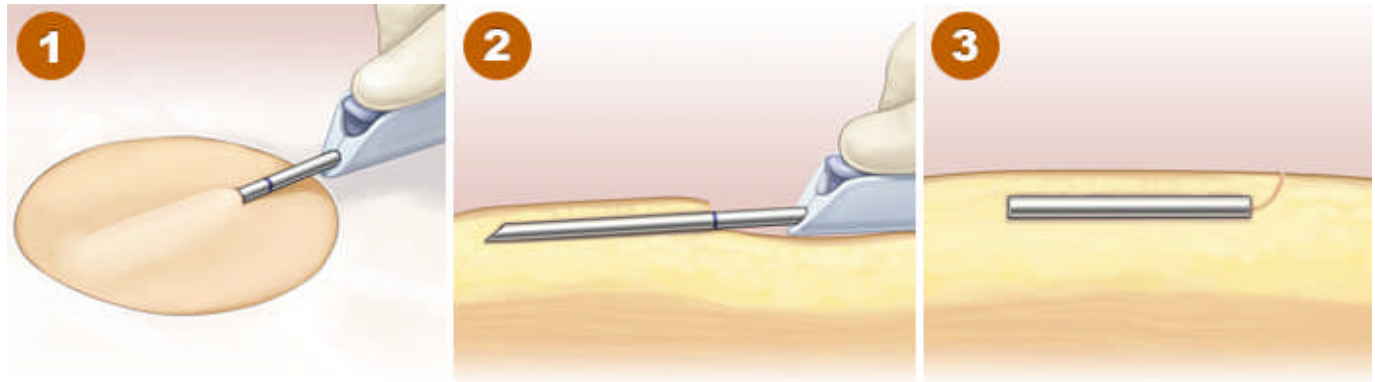
Tolerability of ITCA 650 20 µg/day than observed with exenatide injections of 20 µg/day or ITCA 650 40 µg/day during treatment weeks 1 -12. Dose escalation of to ITCA 650 to 60 µg/day after week 12 was well tolerated. Patient-assessed treatment satisfaction scores were higher among patients taking either 20 µg/day or 40 µg/day of ITCA 650 compared with exenatide injections and patient satisfaction scores increased when patients switched from 20 µg/day exenatide injections to ITCA 650 doses of 40 or 60 µg/day. In summary, an initial treatment with ITCA 650 20 µg/day for 12 weeks and then escalating to ITCA 650 60 µg/day resulted in the best tolerability glycemic control and weight profile through 24 weeks. At the end of the 24-week study, patients were offered an additional 24 week extension of treatment and 86% of patients offered the opportunity elected to continue their ITCA 650 treatment.

Insertion and Removal of DUROS Technology



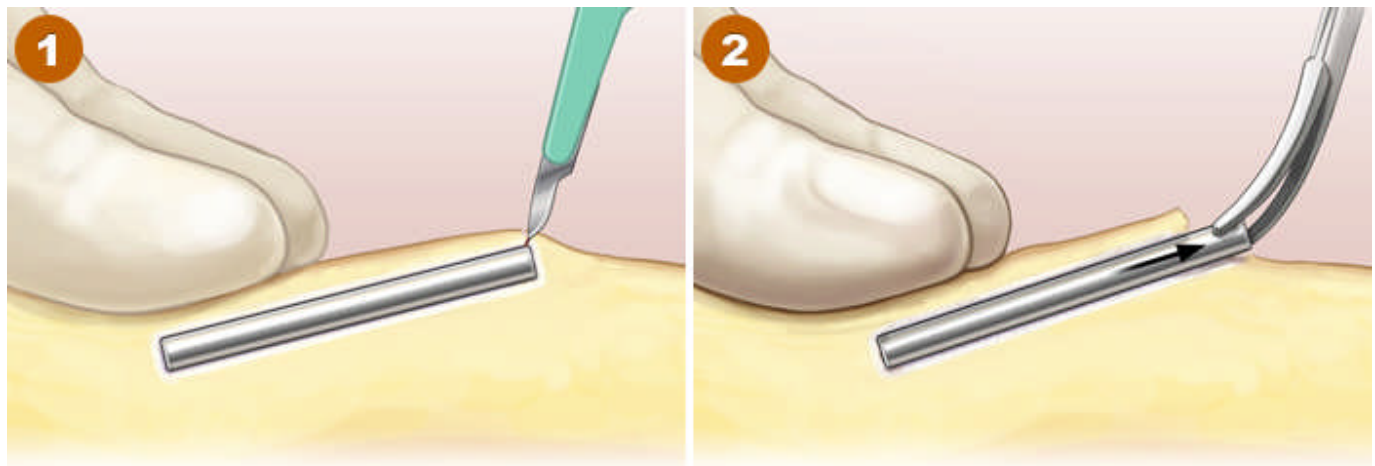
Device Location

The basis for the successful use and removal of ITCA 650 is a simple but carefully performed subcutaneous insertion. The insertion process is typically a 5-10 minute, painless procedure done in the doctor's office. ITCA 650 is inserted subcutaneously into one of four quadrants of the abdomen in the area extending below the ribs and above the beltline. The device is inserted at a depth of 0.5 centimeters just under the skin, so once fully inserted, the skin is not raised and the device is not visible or felt by the patient.



Device Insertion

The physician will first mark the location of the insertion site on the patient's abdomen to assist with the correct placement of the ITCA 650. The physician will then clean the insertion sight and will use a local aesthetic agent to numb the area. After making a very small incision, and using a surgical insertion tool, the physician will place the ITCA 650 at a depth of 0.5 centimeters below the skin. Once inserted, the physician will clean the skin, apply a skin protectant and cover with a sterile adhesive bandage. The patient should then be sure to keep the area clean and dry for 24-hours, and avoid heavy lifting for 48-hours. The incision typically takes 2-3 days to heal.



Device Removal

The physician will first inspect the insertion site and identify the location of the ITCA 650. Once the ITCA 650 has been identified, the physician will mark the location with a marking pen to assist with administering a local anesthetic and to assist in making the removal incision. After applying the

anesthetic, the physician will then make a small incision at the insertion site, to promote expulsion of the ITCA 650.

When the end of ITCA 650 is visible in the incision, the physician will grasp the device and remove it from the patient's abdomen. Once removed, the physician will clean the skin, apply a skin protectant and cover with a sterile adhesive bandage. The patient should then be sure to keep the area clean and dry for 24-hours, and avoid heavy lifting for 48-hours. The incision typically takes 3-4 days to heal and the sterile bandage should remain intact for this time.