# iovera°®

## System User Guide

# Legal Notice

**Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician**

This user guide is the proprietary material of Pacira Pharmaceuticals, Inc. or its affiliates and is protected by laws of copyright. The customers of the iovera° system are hereby granted limited, non-exclusive rights to use this user guide solely for the purpose of operating the iovera° system. Unauthorized copying, renting, modifying, or creating derivatives of this user guide is prohibited.

Information in this document is subject to change without notice.

PACIRA PHARMACEUTICALS, INC. DISCLAIMS ALL WARRANTIES, EXPRESSED OR IMPLIED, WITH RESPECT TO THE iovera° SYSTEM (THE "PRODUCT"), INCLUDING BUT NOT LIMITED TO THOSE OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, TO THE FULLEST EXTENT ALLOWED BY LAW. IN NO EVENT SHALL PACIRA PHARMACEUTICALS, INC. BE LIABLE FOR MISREPRESENTATION (OTHER THAN WERE MADE FRAUDULENTLY) OR FOR ANY UNFORESEEABLE SPECIAL, INCIDENTAL, INDIRECT, PUNITIVE, MULTIPLE OR CONSEQUENTIAL DAMAGES IN CONNECTION WITH OR ARISING FROM THE PRODUCT, INCLUDING BUT NOT LIMITED TO THE USE THEREOF, WHETHER IN CONTRACT, TORT (INCLUDING BUT NOT LIMITED TO NEGLIGENCE), WARRANTY, OR UNDER ANY STATUTE OR ON ANY OTHER BASIS. NOTHING IN THE ABOVE SHALL EXCLUDE OR LIMIT LIABILITY FOR DEATH OR PERSONAL INJURY CAUSED BY THE NEGLIGENCE OF PACIRA PHARMACEUTICALS, INC.

# Trademarks

The trademarks mentioned herein, including iovera° and Focused Cold Therapy®, are the property of Pacira CryoTech, Inc. and are licensed to Pacira Pharmaceuticals, Inc. All other trademarks are the sole property of their respective owners.

# Patents

For information on patents and patents pending go to: http://iovera.com/company/patents/

# Contents

# Chapter 1 – Safety

## Introduction

Carefully read all instructions prior to using the iovera° system. Observe all contraindications, warnings, and cautions noted in this chapter and throughout the guide. Failure to do so may result in the possibility of injury to the patient or the operator, inferior treatment outcomes, or damage to the device.

## iovera° System Warnings and Cautions

The following symbols and descriptions are found at appropriate places throughout this document:

| | |
|---|---|
| **WARNING!** | **This symbol indicates a hazardous situation which, if not avoided, could result in patient or user injury.** |
| **CAUTION!** | This symbol indicates a hazardous situation, which, if not avoided, could result in equipment damage or malfunction. |
| NOTICE | This symbol is to provide information that helps to maintain the highest iovera° system performance. |

### General Warnings

| Warning | Description |
|---|---|
| Electrical | The iovera° system may be hazardous if misused. Only connect the device to a proper mains power outlet and use only the Electrical Adapter supplied by Pacira Pharmaceuticals, Inc. There is no user-serviceable parts in or on the iovera° system.<br>The effects of interference from radio frequency identification (RFID) readers have not been studied on the iovera° system. The iovera° system is not recommended for use in close proximity to RFID readers.<br>The iovera° system is not intended for use in a Magnetic Resonance Environment.<br>The iovera° system needs special precautions regarding electromagnetic compatibility (EMC) and needs to be installed and put into service according to the EMC information provided in this manual.<br>Portable and mobile radiofrequency (RF) communications equipment can affect the iovera° system.<br>The use of accessories other than those specified by Pacira Pharmaceuticals, Inc. may result in increased EMISSIONS or decreased IMMUNITY of the iovera° system, resulting in improper operation.<br>This iovera° system should not be used adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the iovera° system should be observed to verify normal operation in the configuration in which it will be used.<br>Operation of this equipment in environments not complying with the conditions specified in Appendix A may result in improper operation (e.g., excessive temperature in the skin warmer or excessive pressure in the Cartridge).<br>In the rare event that a cooling cycle fails to stop, you must immediately fully vent the remaining cryogen in the Cartridge or disengage the Smart Tip from the Handpiece.<br>**Danger: Explosion Hazard. Do Not Use in Presence of Flammable Anesthetics.** |
| iovera° System Components | The iovera° system is intended for use only with the provided components. Substituting different components (Cartridge, Smart Tip, Electrical Adapter for the Charging Dock, etc.) for those supplied by Pacira Pharmaceuticals, Inc. may damage the device and/or create a hazard to the patient or the operator. |

## General Warnings continued

| Warning | Description |
|---|---|
| Compatible 3rd Party Nerve Stimulator | When stimulation compatible components are used to facilitate target nerve location, the 3rd party nerve stimulator must have a maximum current output that is equal to or less than 5mA. |
| Nitrous Oxide | Nitrous oxide is an oxidizing agent that may accelerate combustion. DO NOT store Cartridges near flammable materials or igniters. Store only where temperatures do not exceed 50 °C (122 °F).<br>Nitrous oxide is under high pressure. A venting Cartridge may dislodge with high force if removed from the Handpiece. Allow system to depressurize completely before attempting to remove the Cartridge from the device. Store away from heat source. Keep away from sunlight.<br>Exercise caution when removing the Cartridge as it may be very cold. |
| iovera° Smart Tip | The iovera° Smart Tip houses the closed-end needle array used to deliver the treatment.<br>The iovera° system generates freezing temperatures that result in tissue destruction. The ends of the iovera° Smart Tip needles will reach subzero temperatures and could damage exposed tissues.<br>Do not use an expired iovera° Smart Tip. Check the sterile package for expiration date.<br>Carefully inspect the iovera° Smart Tip package prior to use for any breach of the sterile barrier or damage to the contents. If the sterile barrier integrity is compromised or the contents are damaged, DO NOT USE and contact a Pacira Pharmaceuticals, Inc. representative.<br>The iovera° Smart Tip is sterile. Touching the iovera° Smart Tip needles may compromise sterility. The iovera° Smart Tip comes protected in the Smart Tip Cap. DO NOT remove the Smart Tip Cap until the system is ready to perform a cycle.<br>The iovera° Smart Tip is single-patient-use. Do not reuse, reprocess or re-sterilize. |
| Treatment | Care should be taken when selecting the target treatment site. Treatment outside the intended target area could result in loss of motor function or unintended freezing of surrounding structures.<br>Minimize any movement of the Handpiece once the Smart Tip is in place and the cooling cycle has started. Excessive movement with the Smart Tip in place could result in damage to subcutaneous tissue.<br>Do not re-treat the same area immediately after a successful treatment cycle. Allow the skin to rewarm first to reduce the risk of skin injury.<br>As applicable, ensure that the Smart Tip needles are fully inserted into the skin so that the skin warming feature is touching the skin. Failure to fully insert the Smart Tip may result in skin injury. See supplemental instructions for use in Appendix C or D for details.<br>Do not reposition or remove the Smart Tip if resistance is felt. This may indicate the cooling zone is still attached to the Smart Tip and moving the Smart Tip may result in damage to subcutaneous tissue.<br>Do not attempt to remove the Smart Tip from the patient while cooling is in process. Doing so could result in damage to subcutaneous tissue. |

## General Cautions

| Caution | Description |
|---|---|
| iovera° System | Carefully read all instructions prior to using the iovera° system. Observe all contraindications, warnings and cautions noted in this chapter and throughout this guide. Failure to do so may result in the possibility of injury to the patient or the operator, subpar treatment outcomes, or damage to the device.<br>Never submerge the iovera° Handpiece or the Charging Dock into any liquids.<br>Do not allow liquids or particulates into the Cartridge chamber. Doing so could block nitrous oxide flow and prevent or limit cooling. |

## Symbols

The following symbols are associated with the iovera° system:

| Symbol | Description |
|---|---|
| CE 0344 | This marking on a product is a manufacturer's declaration that the product complies with the essential requirements of the relevant European health, safety, and environmental protection legislation. |
| MD | Medical Device |
| | For Single Use Only, Do Not Reuse |
| STERILE EO | Sterilized Using Ethylene Oxide — The iovera° Smart Tip is sterilized |
| | Do no Re-Sterilize |
| LOT | Lot Number |
| SN | Serial Number |
| REF | Catalog Number |
| | Contains electronics — Dispose according to local regulations or return to Pacira Pharmaceuticals, Inc. |
| 5V⎓/2.4A | 5 Volt Direct Current, 2.4 Amps, cylindrical connector with positive center |
| | User must follow Instructions for Use (this guide) |
| | Use By Date |
| | Storage Temperature Limitation |
| | Date of Manufacture |
| | Legal Manufacturer |
| | Caution — Refer to manual for important safety information |
| | Warning — Refer to manual for important safety information |
| | Keep Away from Sunlight |
| | Keep Dry |
| | Do Not Use if Package is Damaged |
| | Type BF Applied Part (designation for medical devices that come into contact with a patient) |
| | iovera° Smart Tip |
| | RF Transmitter |
| MR | MR Unsafe; Product is unsafe for use in a magnetic resonance environment |
| | Must wear protective gloves |
| | Warning — low temperatures/freezing conditions |
| Rx Only | The product is intended for use by, or under the direction of, a physician |

| Symbol | Description |
|---|---|
|  | Identifies the range of temperature to which the product can be safely exposed during transit and storage; The upper and lower temperature limits are shown adjacent to the upper and lower horizontal lines |
|  | Identifies range of atmospheric pressure to which the product can be safely exposed during transit and storage; The upper and lower atmospheric pressure limits are shown adjacent to the upper and lower horizontal lines |
|  | Identifies range of relative humidity to which the product can be safely exposed during transit and storage; The upper and lower relative humidity limits are shown adjacent to the upper and lower horizontal lines |

# Indications for Use

The iovera° system is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera° system is not indicated for treatment of central nervous system tissue.

When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a compatible 3rd party nerve stimulator.

# Intended User

The iovera° system is intended for use by, or under the direction of, a physician.

# Target Population

The iovera° system, when used for the relief of pain and symptoms associated with osteoarthritis of the knee, is intended for patients with Kellgren-Lawrence grade II or grade III osteoarthritis of the knee. The effects of the iovera° treatment in patients with Kellgren-Lawrence grade IV osteoarthritis of the knee have not been studied, nor have the effects of repeated treatments. Cryoneurolysis with the iovera° system has not been associated with secondary neuritis or neuroma formation in prior clinical experience, and there is no evidence that repeat cryoneurolysis treatments cause long-term changes to nerve function or structure[1,2].

# Important Safety Information

### Contraindications

The iovera° system is contraindicated for use in patients with the following:

- Cryoglobulinemia, paroxysmal cold hemoglobinuria, cold urticaria, Raynaud's disease, and open and/or infected wounds at or near the treatment site

### Potential Complications

As with any surgical treatment that uses needle-based therapy and local anesthesia, there is a potential for site-specific reactions, including, but not limited to:

- Ecchymosis, edema, erythema, local pain and/or tenderness, and localized dysesthesia

Proper use of the device as described in the User Guide can help reduce or prevent the following complications:

- At the treatment site(s): injury to the skin related to application of cold or heat, hyper- or hypopigmentation, and skin dimpling
- Outside the treatment site(s): loss of motor function

[1] Ilfeld BM, Preciado J, Trescot AM. Novel cryoneurolysis device for the treatment of sensory and motor peripheral nerves. *Expert Rev Med Devices*. 2016 Aug;13(8):713-25.

[2] Hsu M, Stevenson FF. Wallerian degeneration and recovery of motor nerves after multiple focused cold therapies. *Muscle Nerve*. 2015; 51(2):268-275.

# Clinical Study, Osteoarthritis of the Knee[3]

A multi-center, prospective, randomized, double-blind, sham-treatment controlled trial enrolling 180 subjects was conducted in subjects diagnosed with Grade II or III osteoarthritis of the knee (Kellgren-Lawrence classification grading scale) and washed out of all pain medication. A local anesthetic was used to create a diagnostic block of the infrapatellar branch of the saphenous nerve, as assessed by a 50% decrease in VAS pain upon standing from a seated position or walking upstairs, to confirm that the subject was a candidate for treatment.

121 subjects were treated with the iovera° system and 59 subjects were treated with a sham device, with ages ranging from 36 to 75 years. Data from all 180 subjects enrolled were collected and analyzed. The primary endpoint (superiority of the iovera° treatment over sham treatment for reducing pain and symptoms due to osteoarthritis in the knee as assessed by the Total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale from baseline to Day 30) was met, p=0.001, see Table 1 below. Subjects treated with the iovera° system reported substantially more pain and symptom relief as subjects treated with the sham device (55% improvement versus 33% improvement, respectively).

Secondary endpoints were also met, including statistically significant superiority of iovera° treatment over sham treatment for relief of pain and symptoms due to osteoarthritis of the knee on the Total WOMAC scale (pain, stiffness, function) at Day 60 and a statistically significant number of patients reported clinically significant pain relief (30% reduction in WOMAC pain score) through 90 days after treatment with the iovera° system, as shown in Table 1 below.

**Table 1**

| | | iovera° treatment group (n=121) | Sham control group (n=59) |
|---|---|---|---|
| Reduction in pain and symptoms on Total WOMAC scale 30 days post-treatment | | -73.31[1] | -42.18 |
| Percentage of patients reporting 30% improvement in pain and symptoms on Total WOMAC scale post-treatment | 30 days<br>60 days<br>90 days | 74.58%<br>76.79%<br>80.18% | 44.83%<br>56.90%<br>54.39% |

*LS Means and p-value were obtained by fitting an ANCOVA model with treatment as factor and WOMAC baseline score as a covariate.*

There were no serious device-related or procedure-related adverse events. All device-related adverse events were as anticipated per the device labeling. A summary of adverse reactions, including site-specific reactions and/or known effects from cryoanalgesia that lasted longer than 30 days follows.

**Table 2**

| Adverse Reaction | iovera° (n=121) | Sham (n=59) |
|---|---|---|
| Numbness | 18 (14.8%) | 1 (1.7%) |
| Tenderness upon palpitation | 14 (11.6%) | 8 (13.6%) |
| Local pain | 8 (6.6%) | 4 (6.8%) |
| Altered sensation/localized dysesthesia | 3 (2.5%) | 2 (3.4%) |
| Tingling | 3 (2.5%) | 1 (1.7%) |
| Swelling | 3 (2.5%) | 3 (5.1%) |
| Bruising | 3 (2.5%) | 2 (3.4%) |
| Itching | 2 (1.6%) | 0 |
| Vasovagal response | 1 (0.8%) | 0 |
| Knee pain | 1 (0.8%) | 2 (3.4%) |
| Redness/inflammation | 1 (0.8%) | 1 (1.7%) |

| Adverse Reaction | iovera° (n=121) | Sham (n=59) |
|---|---|---|
| Pain, aggravated | 0 | 1 (1.7%) |

*100% of subjects were subjected to a diagnostic lidocaine block to ensure that patients with an appropriate evaluation were enrolled in the study.*

[1] Ilfeld BM, Preciado J, Trescot AM. Novel cryoneurolysis device for the treatment of sensory and motor peripheral nerves. *Expert Rev Med Devices*. 2016 Aug;13(8):713-25.

[3] Radnovich R, Scott D, Patel AT, et al. Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. Osteoarthritis Cartilage. 2017;25(8):1247-1256.

# Chapter 2 – System Overview

**iovera° System Components**

| Handpiece | Charging Dock |
|---|---|
|  |  |
| **iovera° Smart Tip and Smart Tip Cap** | **Cartridge** |
|  |  |
| **Electrical Adapter ("Charger")** | |
|   **WARNING!** **Use only the electrical adapter (“charger”) and Charging Dock supplied with the iovera° system to charge Handpiece** | |

## Glossary

The terms and acronyms used in this guide are listed in the table below:

| Term or Acronym | Description |
|---|---|
| Cartridge | A small pressurized canister containing liquid nitrous oxide |
| Cartridge Holder | The space inside the Handpiece where the $N_2O$ Cartridge is placed |
| Charging Dock | The stand used to hold the Handpiece |
| Cooling Cycle | A single cryoanalgesia application using the iovera° system on a single site on a patient; One or more cooling cycles at different sites equal one treatment |
| Handpiece | A non-sterile, reusable, handheld device designed to control the flow of refrigerant from a disposable Cartridge into an iovera° Smart Tip to cool target tissues |
| LCD Display | The color graphic information display at the back of the Handpiece |
| Main Button | Button located on the Handpiece that is used to start and to stop a cooling cycle; the button may also be used to perform other functions |
| Refrigerant | A substance used to produce low temperatures; the iovera° system uses nitrous oxide ($N_2O$) |
| Reset Access | Located underneath the Handpiece access cover, this is an area that provides access to perform an iovera° system reset |
| Skin Warmer | A plate located at the base of the needles on the iovera° Smart Tip that is designed to keep the skin surface warm during a treatment; The needles must be fully inserted for the skin warmer to be effective |
| Smart Tip | The sterile tip that attaches to the end of the Handpiece in order to deliver a treatment |
| Smart Tip Cap | Protective cap that fully covers an iovera° Smart Tip when not in use |
| Storage Cap | Protective cap that can be used to cover the end of the Handpiece when a Smart Tip is not in use or when the Handpiece is charging |
| Treatment | One or more cooling cycles administered to one or more sites on a single patient |

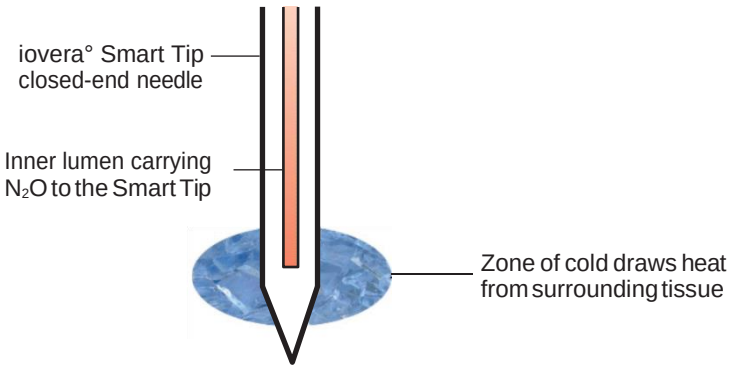
# Theory of Operation

The Pacira Pharmaceuticals, Inc. iovera° system is a handheld device that enables the use of closed-end needles (called Smart Tips) to treat the targeted peripheral nerves for a particular application. Cryoneurolysis has been well established as a successful and preferred non-toxic method of tissue destruction, while keeping the surrounding tissue structures intact. The iovera° consumables include nitrous oxide Cartridges and single-patient-use iovera° Smart Tips.

During a patient treatment, the iovera° Smart Tip needle(s) are inserted into the target tissue and liquid nitrous oxide ($N_2O$) is delivered from a pressurized cylinder at >850 psi through a control valve and into the closed-end needles of the iovera° Smart Tip. Within each closed end iovera° Smart Tip needle, the liquid nitrous oxide flows to the Smart Tip through an inner channel (lumen).

A combination of rapid pressure decreases, and evaporation of the nitrous oxide causes an endothermic event that rapidly draws heat from the surrounding tissue, thus causing focused cooling at the point of the inserted iovera° Smart Tip needle(s). The focused cooling can reach temperatures below -20 °C (-4 °F). By incorporating a skin warmer, the iovera° system focuses precise subdermal cooling while protecting the skin.

The iovera° Smart Tip closed-end needles leave nothing in the patient's body. The gas created from the evaporating $N_2O$ is vented back up through the needle and released harmlessly into the atmosphere.




Sensors within the iovera° Handpiece monitor the automated delivery of nitrous oxide and the rate of cooling to ensure consistency during treatment cycles.

When applied to nervous tissue, this freezing power is known as cryoneurolysis; freezing along the nerve axon causes distal disintegration of the axon and breakdown of the myelin sheath, while keeping the endoneurium and other connective tissue elements intact, which helps the nerve to re-grow along its original pathway. Lesioning of the nerve axon at the point of contact with the iovera° Smart Tip needle end is caused by rapid freezing at or below -20°C (-4°F). The rapid freeze causes mechanical and osmotic stresses which disrupt the tissue within the freezing zone and create axonal discontinuity that results in an immediate cessation of nerve signaling. Subsequently, the distal segment of the axon and myelin sheath degenerate (through the process known as Wallerian Degeneration). The endoneurium, epineurium, and perineurium remain intact, allowing subsequent regeneration of the nerve. Cryoneurolysis has not been associated with secondary neuritis or neuroma formation in prior clinical Experience.[4]

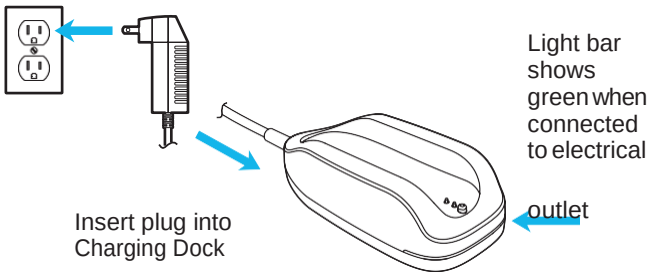
[4] Trescot, AM. Cryoanalgesia in an Interventional Pain Management Setting. *Pain Physician*. 2003;6:345-3

# Chapter 3 – iovera° System Set-Up

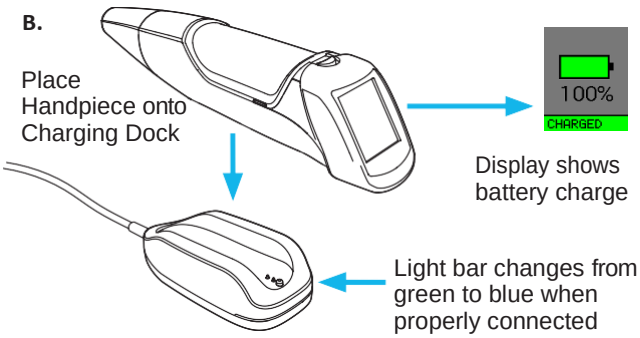
| IMPORTANT | Although the iovera° system arrives partially charged, the amount of charge at delivery may vary. It is recommended that the Handpiece be **FULLY CHARGED** before using the Handpiece for the first time. |
|---|---|

## Charging the Device

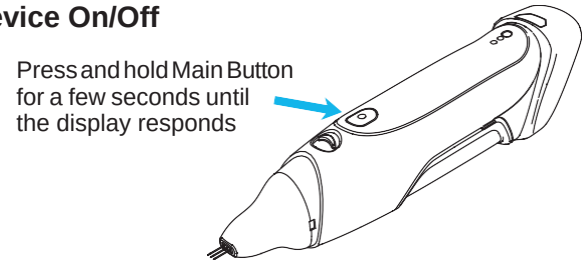
**A.** Plug adaptor into outlet
Plug charger cable into base of Charging Dock




**B.**



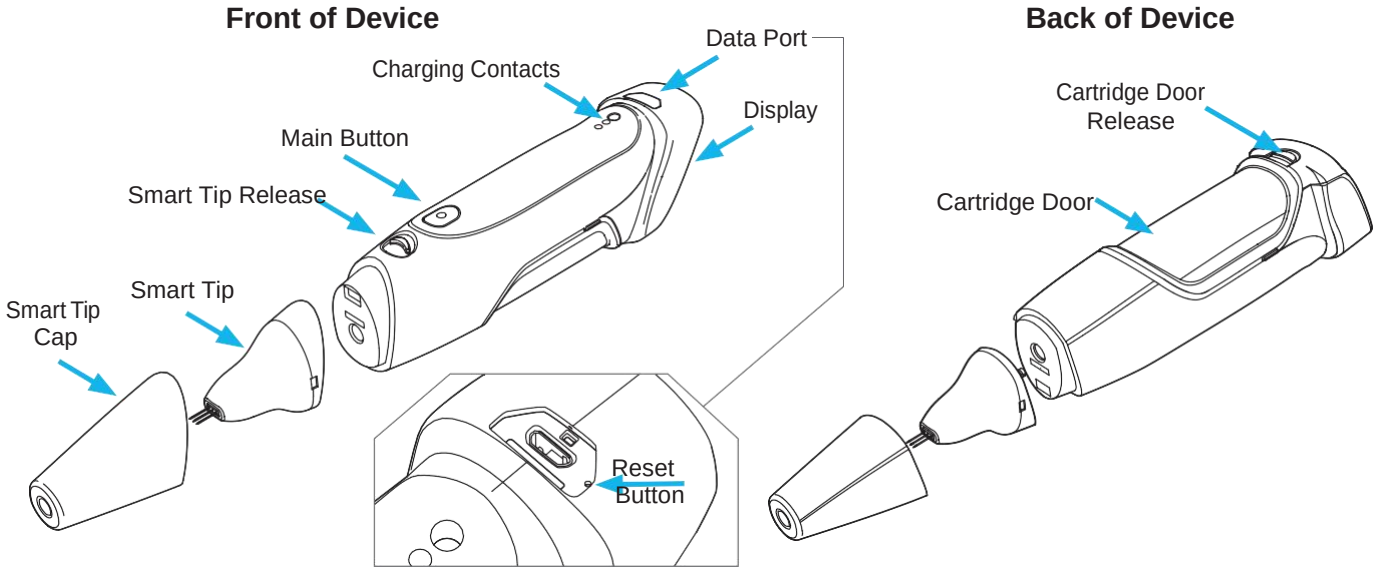

## Turning the Device On/Off




## iovera° Handpiece

The iovera° Handpiece is the control system that facilitates the transfer of nitrous oxide to the connected iovera° Smart Tip in order to enable treatment. The illustrations on the next two pages highlight the essential components of the Handpiece. To ensure that it is ready for use, always place the Handpiece into the Charging Dock when it is not in use.

### Handpiece Components: Expanded View

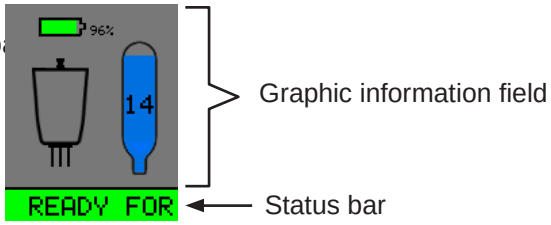


# Information Display

The LCD display is an integral component of the iovera° system. The displays are context-sensitive and include 3 main types:

- Main display
- Treatment display
- Charging display

Each display type consists of two sections – a graphic information field and a status ba



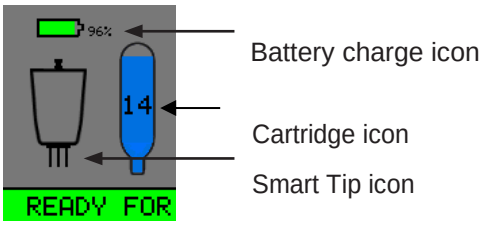

The messages on the status bar scroll to allow for sufficient content. The colors of the LCD status bar provide additional visual feedback of the Handpiece status:

- **Green:** Normal operation
- **Yellow:** Action indicated
- **Red:** System issue requiring attention

## Main Display

Cartridge icon:

- Number and height of **blue** field indicate how many cycles remain in the Cartridge for the current Smart Tip
- Icon flashes if no Cartridge is detected




Smart Tip icon:

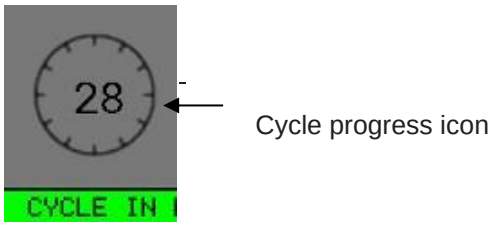
- Icon is solid when Smart Tip is present and functional
- Icon flashes when Smart Tip is missing

For battery charge icon, see **Battery Status** section below.

## Treatment Display

Cycle progress icon:

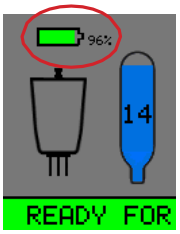
- Number indicates the number of seconds remaining in the current treatment cycle
- A check mark will appear if the cycle completes successfully



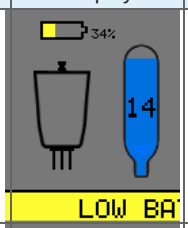
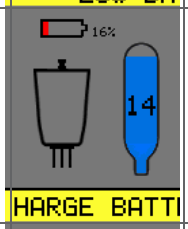
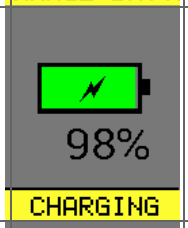
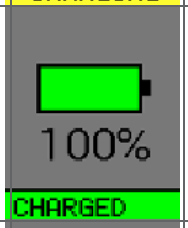
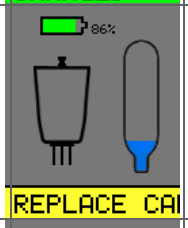
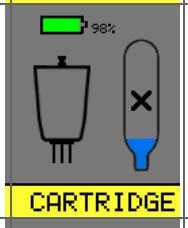
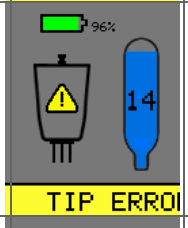
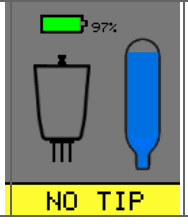

## Battery Status

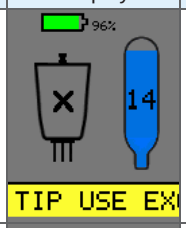
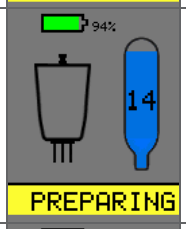
The LCD displays information indicating how much battery power is available, as well as an indication that the battery is being charged.

During normal use, the system will display the battery charge level on the main display as follows:




Battery charge level is shown in **green** in the icon, as well as in text to the right of the battery

| Message | Representative Display | Scrolling Text and Notes |
|---|---|---|
| LOW BATTERY |  | LOW BATTERY<br>(On yellow field)<br>Note: Yellow battery bar also flashes.<br>Message is displayed when battery charging is recommended. |
| RECHARGE BATTERY |  | RECHARGE BATTERY<br>(On yellow field)<br>Note: Red battery bar also flashes<br>Message is displayed when battery is too depleted to allow treatment cycles. |
| BATTERY CHARGING |  | CHARGING (on yellow field)<br>This display will only appear if Handpiece is receiving power from Charging Dock. Number shows current charge state of battery. Light bar on charger will appear blue during charging. |
| BATTERY CHARGED |  | CHARGED<br>(On green field)<br>Light bar on charger will appear green at end of charging. |
| REPLACE CARTRIDGE |  | REPLACE CARTIDGE<br>(On yellow field)<br>Cartridge shows minimum fill level and no cycle count.<br>If Cartridge is removed, empty Cartridge icon flashes on and off. |
| CARTRIDGE EXPIRED |  | CARTRIDGE EXPIRED<br>(On yellow field)<br>Message is displayed if Cartridge has been left in the Handpiece too long. |
| TIP ERROR |  | TIP ERROR - *nn*<br>(on yellow field)<br>Message is displayed if the tip is detected but is malfunctioning. |
| NO TIP |  | NO TIP<br>(On yellow field)<br>Tip icon flashes on and off.<br>Cartridge icon will not display a cycle count (as count is tip-dependent)<br>Blue cryogen level in icon will reflect current state. |

| Message | Representative Display | Scrolling Text and Notes |
|---|---|---|
| TIP USE EXCEEDED |  | TIP USE EXCEEDED<br>(On yellow field)<br>Message is displayed if no more cycles are allowed from this particular tip. |
| PREPARING FOR CYCLE |  | PREPARING FOR CYCLE<br>(On yellow field)<br>Message is displayed when system is warming up the cryogen Cartridge prior to allowing a treatment cycle. |
| READY FOR CYCLE |  | READY FOR CYCLE (on green field)<br>Number in Cartridge indicates the number of cycles remaining in the Cartridge for the currently attached tip. Cartridge number flashes for 2 or fewer remaining cycles.<br>Blue cryogen level in Cartridge drops as cryogen is used up. |
| CYCLE IN PROGRESS |  | CYCLE IN PROGRESS<br>(on green field)<br>Number in clock indicates number of seconds remaining in current treatment cycle. |
| CYCLE COMPLETE |  | CYCLE COMPLETE<br>(On green field)<br>This image is displayed for a few seconds, then display reverts to main display (with tip and Cartridge images). |
| CYCLE STOPPED (BY USER) |  | CYCLE STOPPED<br>(On yellowfield)<br>Message is displayed if user stops a cycle by pressing the Main Button while a cycle is in progress. |
| TILT HANDPIECE UP |  | TILT UP<br>(on yellow field)<br>Message is displayed when angle of Handpiece is not vertical enough for treatment.<br>Message is only displayed during treatment cycle. |
| SYSTEM FAULT |  | SYSTEM FAULT - *nn*<br>(On red field)<br>Message is displayed when a critical failure with the system is detected such that treatment cycles are not allowed. “nn” is a two-digit error code. |

# Handpiece Control Features

Functions using the Main Button on the front of the iovera° Handpiece are described below:

<table>
<tr><th>Event</th><th>Action Description</th></tr>
<tr><td>Start a Cycle</td><td>Press and release the Main Button to initiate a cycle.<br><br>NOTICE A cycle can only be initiated if the system detects an acceptable iovera Smart Tip, Cartridge and sufficient battery charge</td></tr>
<tr><td>Stop a Cycle</td><td>Press and release the Main Button once after the cycle has started.<br>Wait for the cycle to complete before withdrawing the needle(s) from the patient.<br><br>WARNING! Do not attempt to remove an inserted iovera° Smart Tip from a patient while the treatment is in process. Doing so could result in damage to subcutaneous tissue.</td></tr>
<tr><td>Standby Mode</td><td>Press and hold the Main Button for several seconds to place the system in low-power standby mode. (The system will momentarily show a crescent moon display when entering standby mode.)<br><br>NOTICE The iovera° Handpiece is shipped in standby mode. Also, when the Handpiece has been unused for more than 40 minutes, the Handpiece enters standby mode.</td></tr>
<tr><td>Wake Device from Standby Mode</td><td>When the Handpiece is in standby mode, press and hold the Main Button for several seconds to wake (display will show "iovera°" start screen.)<br>The system will also wake from standby mode when placed into the Charging Dock.</td></tr>
</table>

# Chapter 4 – Performing a Treatment Cycle

## Setting up for a Treatment Cycle

Before initiating a treatment, ensure that the iovera° system is clean and disinfected. See the "Cleaning the iovera° System" section of this guide for details.

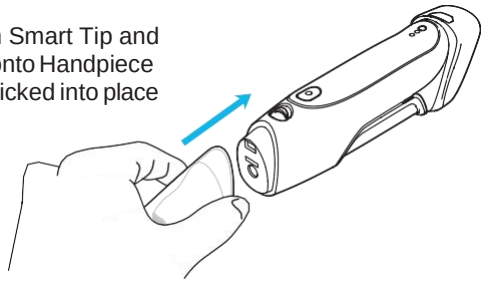
| | |
|---|---|
| **WARNING!** | **Inspect all components prior to use. Do not use component if the component or its package appears damaged.** |
| **WARNING!** | **Physician discretion should be exercised when patient presents with existing neuromuscular disease compromising the regeneration of peripheral nerves that may be involved in the treatment.** |

### Installing the iovera° Smart Tip

| | |
|---|---|
| **WARNING!** | **Carefully inspect the iovera° Smart Tip package prior to use for any breach of the sterile barrier or damage to the contents. If the sterile barrier integrity is compromised or the contents are damaged, DO NOT USE and contact a Pacira Pharmaceuticals, Inc. representative.** |

1. Remove the iovera° Smart Tip from the sterile package and push it firmly into the Handpiece as shown (Figure A).
2. Gently tug on the inserted Smart Tip to ensure it is properly latched into the Handpiece.

**A.** Align Smart Tip and snap onto Handpiece until clicked into place

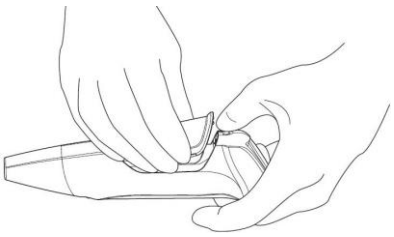


3. Do not remove the Smart Tip Cap until you are ready to use the iovera° Smart Tip.

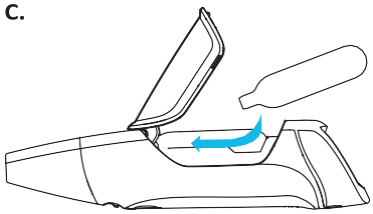
### Installing a Cartridge

1. Slide the Cartridge door release towards the display end to release the Cartridge door latch. The door will open slightly (Figure B).
2. Insert a new Cartridge into the Handpiece until it clicks into its holder (Figure C).
3. Firmly close the door until the latch engages (Figure D).

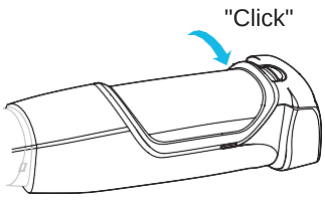
**B.**



**C.**



**D.**




| | |
|---|---|
| NOTICE | In order to ensure optimum performance, a Cartridge will expire after being in the Handpiece for several hours. Expired Cartridge symbol will appear on the display when the Cartridge expires. |

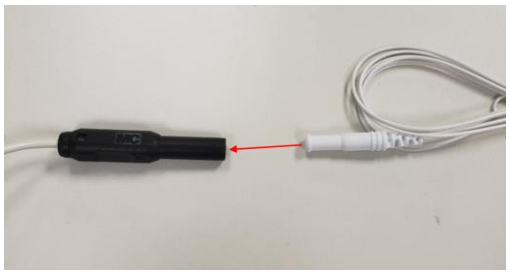
# Nerve Targeting

In applications where the nerve must be located without the aid of direct visualization and/or where the use of anatomical landmarks requires additional confirmation, a separate off-the-shelf nerve stimulator device may be used to identify the target nerve.

| | |
|---|---|
| **WARNING!** | **When using a nerve stimulator, follow the Instructions for Use (IFU) for that device, and observe all warnings, precautions, and contraindications** |

### Connecting the Stimulation Compatible Smart Tip to a 3rd Party Nerve Stimulator

Fully insert insulated connector of the supplied Stimulating Tip Cable (P/N 12358) into the black receptable of the connecting cable for the 3rd party nerve stimulator as shown:



Fully insert the other end of the Stimulating Tip Cable into the receptacle in the Smart Tip housing as shown:

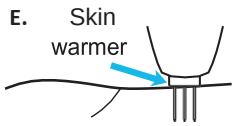
# Inserting the iovera° Smart Tip into the Target Site

| | |
|---|---|
| **WARNING!** | **The iovera° Smart Tip is sterile. Touching iovera° Smart Tip needles may compromise sterility. The Smart Tip comes protected in a Smart Tip Cap. DO NOT remove the Smart Tip Cap until ready to perform a cycle.** |
| **WARNING!** | **Smart Tips are for single patient use only and cannot be re-sterilized.** |
| **WARNING!** | **Do not straighten and attempt to use kinked needles.** |

1. Clean the treatment area with the antiseptic solution of choice.
2. Confirm the Handpiece is ready to start a cycle.
3. Remove the Smart Tip Cap.
4. Insert the iovera° Smart Tip into the target treatment site.

| | |
|---|---|
| **WARNING!** | **Care should be taken when selecting the target treatment site. Treatment outside the intended target area could result in loss of motor function or unintended freezing of surroundingstructures.** |

5. In applications where skin warming at the base of the iovera° Smart Tip is necessary (refer to Smart Tip-specific instructions in Appendix C and D), ensure that the needles are fully inserted into the skin so that the skin warmer is touching the skin (Figure E).




| | |
|---|---|
| **WARNING!** | **Failure to insert the iovera° Smart Tip sufficiently may result in skin injury in percutaneous applications.** |

6. If the Smart Tip has a minimum insertion depth mark on the needle, then the Smart Tip must be inserted into the tissue to at least the indicated minimum insertion depth to prevent skin damage.

# Completing the Treatment Cycle

1. Ensuring that the Handpiece is vertical or near vertical, press and release the Main Button once to begin the cooling cycle. A tone sounds when the cycle begins.

| | |
|---|---|
| **WARNING!** | **Minimize any movement of the Handpiece once the iovera° Smart Tip is in place and the cooling cycle has started. Excessive movement could result in damage to subcutaneous tissue.** |

| | |
|---|---|
| **WARNING!** | **Do not attempt to remove the iovera° Smart Tip from the patient while the cooling is in process. Doing so could result in damage to subcutaneous tissue.** |

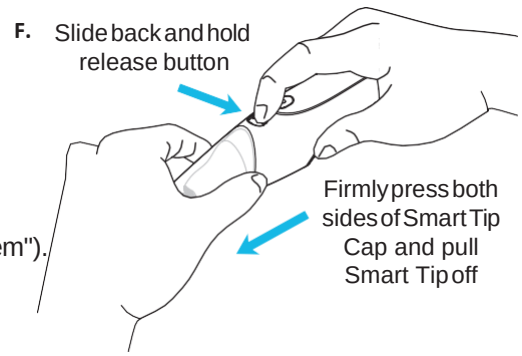
2. The LCD will provide a countdown timer when the cycle starts to indicate how many seconds remain in the cycle.
3. At the end of the cycle, the LCD will indicate that the cycle has completed, and a tone will sound. At this time, the iovera° Smart Tip may be removed from the treatment site and, if desired, repositioned at a different site for another treatment cycle.

| | |
|---|---|
| **WARNING!** | **For percutaneous application, do not to treat the same site more than once within 10 minutes. This allows the skin to warm and reduces risk of skin injury.** |

4. When the treatment is complete, remove the iovera° Smart Tip from the patient.

| | |
|---|---|
| **WARNING!** | **Do not reposition or remove the iovera° Smart Tip if there is any resistance. This may indicate that the cooling zone is still attached to the iovera° Smart Tip, which may result in damage to subcutaneous tissue if moved.** |

5. Replace the Smart Tip Cap back on the used Smart Tip.
6. Remove the Cartridge from the Handpiece (see below).
7. While pressing the sides of the Smart Tip Cap, slide the Smart Tip release actuator back and pull the used iovera° Smart Tip from the Handpiece (Figure F).
8. Place the used Smart Tip into a sharp's container.
9. Clean the iovera° Handpiece (see section "Cleaning the iovera° System").
10. Clean the Charging Dock, if necessary (see section "Cleaning the iovera° System").
11. Return the Handpiece to the Charging Dock.




# Stopping a Cycle

| | |
|---|---|
| **WARNING!** | **Do not reposition or remove the iovera° Smart Tip if there is any resistance. This may indicate that the cooling zone is still attached to the iovera° Smart Tip, which may result in damage to subcutaneous tissue if moved.** |

In the event that a cooling cycle must be terminated before the pre-programmed cycle is complete, press and release the Main Button on the Handpiece to terminate the cycle. Stopping a cycle may take a short time to complete in order to ensure safe removal of the iovera° Smart Tip.

| | |
|---|---|
| **WARNING!** | **It is imperative that you wait until the system signals that it is safe to remove the iovera° Smart Tip before doing so:**<br>**a. The LCD indicates that the cycle has been canceled.**<br>**b. A tone sounds as the cycle completes.** |

Once the display indicates that the cycle has been canceled and the tone sounds, it is safe to remove the iovera° Smart Tip from the treatment area.

### Performing an Emergency Cycle Stop

In the rare event that a cooling cycle fails to terminate, the Smart Tip may be released from the Handpiece while the cycle is in progress. Alternatively, the cryogen flow may be stopped by venting the Cartridge.

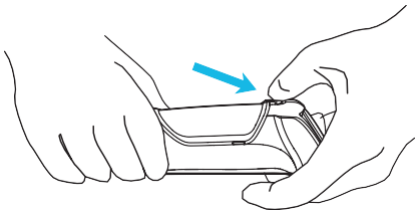
Be aware that a loud pop may be heard when the Smart Tip releases; this is an expected sound.

| | |
|---|---|
| **WARNING!** | **Do not reposition or remove the iovera° Smart Tip if there is any resistance. This may indicate that the cooling zone is still attached to the iovera° Smart Tip, which may result in damage to subcutaneous tissue if moved.** |

## Removing the Cartridge

1. Leave the Smart Tip on and replace the Smart Tip Cap before venting.
2. While wearing protective gloves, point the display away from the user, patient, and bystanders. Slide the Cartridge door release towards the display end. The door will open slightly (Figure G).
3. Ensure the LCD end of the Handpiece is not aimed at you or anyone else.

G.



| | |
|---|---|
| **WARNING!** | **If Smart Tip is removed before venting, venting will occur through the Handpiece outlet.** |

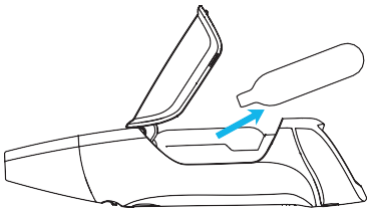
4. Grip the door near the display end of the door and SLOWLY rotate the door open until you hear the Cartridge start to vent. The rate of venting is controlled by the door position – open further to vent faster (Figure H).
5. Continue venting the Cartridge until all the cryogen in the Cartridge is expelled.
6. Open the door fully and remove the spent Cartridge (Figure I).

H.

**WARNING!**

**Wear protective gloves while venting the Cartridge. Keep exposed skin away from door openings and door hinge while Cartridge is venting, as the exhausting $N_2O$ is very cold.**

I.



- If nitrous oxide continues to vent from the Cartridge, firmly hold the Cartridge and allow the nitrous oxide to vent completely (use gauze to insulate against cold if necessary).

| | |
|---|---|
| **WARNING!** | **Nitrous oxide is under high pressure. A venting Cartridge may dislodge with high force if removed from the Handpiece before venting completes. Allow system to depressurize completely before fully removing Cartridge.** |
| **CAUTION!** | Exercise caution when removing the Cartridge. |

7. Dispose of the used Cartridge following local requirements and protocols.

| | |
|---|---|
| NOTICE | Always remove the Cartridge after completing treatments. If the Cartridge is left in the Handpiece for several hours, the Cartridge will expire. Replace the Cartridge prior to performing a treatment. |

# Cleaning the Iovera System

The iovera° system is a reusable cryoneurolysis device and must be thoroughly cleaned and disinfected after each patient use.

To clean the Handpiece:

- Remove contaminates with clean, pre-saturated 70% isopropyl alcohol (IPA) wipes. Repeat with new wipes until the device is clean.

| NOTICE | It is important that the Handpiece be cleaned immediately after each patient use. Cleaning immediately after use helps prevent accumulation of contaminants. |
|---|---|

| ⚠ CAUTION! | • Never submerge the iovera° Handpiece or the Charging Dock into any liquids.<br>• Never use compressed air on, around, or in the iovera° Handpiece.<br>• Do not allow liquids or particulates into the Cartridge chamber. Doing so could block nitrous oxide flow and prevent or limit cooling. |
|---|---|

### Detailed Instructions for Cleaning the Handpiece

Thoroughly cleaning the iovera° Handpiece involves the following:

- Remove conspicuous contamination. Inspect for any obvious signs of contamination (e.g., blood or other fluids, dirt/debris, other obvious contaminants).
- Use clean, pre-saturated 70% IPA wipes. Vigorously scrub the contaminated areas until the contamination is removed. Repeat as required using a new clean wipe.
- Limit scrubbing to conspicuously contaminated areas to reduce the possibility of spreading contaminants around the device.
- Pay special attention to these areas on the Handpiece:
  - Small gaps and lines on the outer Handpiece shell.
  - Gaps around the Main Button, Smart Tip release actuator, and Cartridge door release actuator.
- To ensure maximum disinfection, utilize sufficient, fresh wipes to ensure that all surfaces remain damp per manufacturer's recommendations.
- Discard soiled wipe and obtain a new wipe as required.
- Wipe gently and limit scrubbing to minimize abrasions on the Handpiece.

When complete, return the Handpiece to the Charging Dock and allow it to air dry for at least 5 minutes prior to the next use.

### Cleaning the Charging Dock

Use the same material and techniques described above to clean the Charging Dock.

# Handpiece Storage

1. If treatment is complete and if you are done using the Cartridge for the day, remove it and discard (see the Removing the Cartridge section).
2. Return the Handpiece to the Charging Dock.

# Chapter 5 – System Warnings and Troubleshooting

In the event that the iovera° system detects an unfavorable condition, an error message with a red background will appear on the LCD status display. Check the Troubleshooting section of this guide for additional information.

## Troubleshooting

The following table contains instructions for basic troubleshooting actions. In the event device malfunctions persist or malfunctions occur beyond those described below, users should not attempt to repair the device. Contact Pacira Pharmaceuticals, Inc. Customer Service for guidance at the number shown below.

| Issue | Possible Solution |
|---|---|
| Handpiece LCD is not on | 1. Press the Main Button for a minimum of 5 seconds to wake up device from standby mode.<br>2. If this does not resolve the issue, place the Handpiece on the Charging Dock and check the battery status to ensure it has sufficient battery charge.<br>3. If the issue is still not resolved, perform a hard reset by opening the data port cover and inserting the end of a paper clip into the small hole for several seconds to reset the system (refer to Chapter 3, "iovera° System Setup" for the location of the reset button).<br>If the issue continues to persist, contact Pacira Technical Support at 855-793-9727. |
| Cycle won't start/ system indicates no Smart Tip is present | Remove and replace the Smart Tip. Confirm that the system detects that a Smart Tip is present. If the issue persists, contact Pacira Technical Support at 855-793-9727. |
| Cycle won't start/ system indicates Smart Tip error | Refer to the "iovera° Smart Tip Errors" section of the guide.<br>NOTE: The device must be turned off and back on to clear the error. |
| Handpiece displays a System Fault error with a red background. | Refer to the "iovera° System Fault Errors" section of the guide. |
| System indicates a low battery condition with a yellow background | Battery power is low and only a few cycles remain. |
| Handpiece won't charge or wakeup while in Charging Dock | Check the dock power and make sure the light bar on the dock is illuminated. Make sure the dock light changes color from green to blue when the Handpiece is placed on the dock. If not, make sure the Handpiece charging contacts are positioned correctly with the pins on the dock.<br>If the issue persists, perform a system reset by opening the USB access cover and using a paperclip to press the reset button for at least 1 second. Then place the Handpiece on the dock for 2 to 3 hours.<br>If the issue persists, contact Pacira Technical Support at 855-793-9727. |
| Handpiece is leaking cryogen (may hear hissing) | Contact Pacira Technical Support at 855-793-9727 with details. |
| System indicates treatment was canceled | The treatment cycle was canceled (button was pressed or an error was detected). Wait until the system indicates the cycle is complete before attempting to remove the Smart Tip from the patient. |

# iovera° System Fault Errors

**NOTICE** All messages appear as scrolling text on the LCD screen.

| System Fault Error Number | Meaning | What To Do |
|---|---|---|
| 11 or 13 | Valve failed to open during treatment | Turn device off and on to clear the error. If error occurred following Cartridge venting, **wait at least 5 minutes** before attempting next treatment. |
| 14 | Valve leak detected after previous valve closure confirmed | Turn device off and on to clear the error. |
| 15 | Cartridge temperature exceeded 38°C | Turn device off and on to clear the error. If problem persists, turn off device, replace Cartridge, then turn device back on. |
| 16 | Difference between Cartridge heater temperatures too great | Turn device off and on to clear the error. |
| 17 | Cartridge pressure exceeded 1200 psi | Turn device off and on to clear the error. If problem persists, turn off device, replace Cartridge, then turn device back on. |
| 18 | Flash memory initialization failure | Contact Pacira Technical Support at 855-793-9727. |
| 19 | Persistent data in incorrect format | |
| 20 | Persistent data version too old | |
| 21 | Calibration data corrupted | |
| 22 | Reboot times exceeded | Turn device off and on to clear the error. |
| 23 | Cartridge temperature(s) exceeded hard limit | Turn device off, wait several minutes, then turn device back on to clear the error. |
| 24 | Valve failed to close during treatment | **Vent Cartridge or remove Smart Tip from Handpiece immediately**. Contact Pacira Technical Support at 855-793-9727. |
| 25 | Cartridge took too long to reach correct temperature | Turn device off and on to clear the error. If problem persists, replace Cartridge. |
| 26 | Cartridge thermistor 1 fault | Contact Pacira Technical Support at 855-793-9727. |
| 27 | Cartridge thermistor 2 fault | |
| 28 | Upstream pressure fault | |
| 29 | Downstream pressure fault | |

Pacira Pharmaceuticals, Inc. recommends that users fully charge the system prior to first use. Training on the operation and specific techniques is provided by Pacira Pharmaceuticals, Inc., and/or your local representative.
See contact information on the back cover of the user guide.

There are no user-serviceable parts in the iovera° system. Contact Pacira Customer Support for replacement parts.

**If any of the above System Fault errors persist, contact Pacira Technical Support at 855-793-9727**

# iovera° Smart Tip Errors

**NOTICE** All messages appear as scrolling text on the LCD screen.

| Smart Tip Error Number | Meaning | What To Do |
|---|---|---|
| 11 | Smart Tip temperature out of range | Turn device off and on or detach and re-attach Smart Tip to clear the error. Ensure Smart Tip is correctly inserted into patient during treatment. If problem persists, replace Smart Tip. |
| 12 | Smart Tip preheat timeout during cycle (Smart Tip did not reach temperature in allotted time) | Turn device off and on or detach and re-attach Smart Tip to clear the error. If problem persists, replace Smart Tip. |
| 13 | Smart Tip failed initial test upon insertion | |
| 14 | Smart Tip temperature(s) exceeded operating limits | Turn device off and on or detach and re-attach Smart Tip to clear the error. Wait several minutes to allow Smart Tip temperature to recover. If problem persists, replace Smart Tip. |
| 15 | Smart Tip temperature(s) exceeded hard limit | |
| 16 | Smart Tip authentication challenge message failed CRC check | Turn device off and on or detach and re-attach Smart Tip to clear the error. If problem persists, replace Smart Tip. |
| 17 | Smart Tip failed authentication | |
| 18 | Smart Tip descriptor message failed CRC check | |
| 19 | Smart Tip/Handpiece incompatibility detected | |
| 20 | Smart Tip descriptor version mismatch | |
| 22 | Smart Tip secure processor reset count exceeded | |
| 23 | Smart Tip occlusion | Turn device off and on to clear the error. Detach and re-attach Smart Tip to relieve any trapped pressure. If problem persists, replace Smart Tip. |
| 24 | Smart Tip thermistor 1 fault | Turn device off and on or detach and re-attach Smart Tip to clear the error. If problem persists, replace Smart Tip. |
| 25 | Smart Tip thermistor 2 fault | |
| 26 | $I^2C$ timeout error | |
| 27 | $I^2C$ reset error | |
| 28 | Difference between Smart Tip temperatures too great | Turn device off and on or detach and re-attach Smart Tip to clear the error. Ensure Smart Tip is correctly inserted into patient during treatment. If problem persists, replace Smart Tip. |

**If any of the above Smart Tip errors persist, contact Pacira Technical Support at 855-793-9727.**

# Appendix A – Guidance and Manufacturer's Declaration

| Table 1<br>Guidance and Manufacturer's Declaration – Electromagnetic Emissions | | |
|---|---|---|
| The iovera° system is intended for use in the electromagnetic environment specified below.<br>The customer or the user of the iovera° system should assure that it is used in such an environment. | | |
| **Emissions Test** | **Compliance** | **Comments** |
| Conducted Emissions<br>EN 55011:2009+A1:2010,<br>IEC/CISPR 11:2009<br>+A1:2010 | Class B<br>150 kHz to 30 MHz | The iovera° system uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment. |
| Radiated Emissions<br>EN 55011:2009+A1:2010,<br>IEC/CISPR 11:2009<br>+A1:2010 | Class B<br>30 MHz to 1 GHz | |
| Harmonics<br>IEC/EN 61000-3-<br>2:2006/A2:2014 | Per Clause 5 of the standard | |
| Flicker<br>IEC/EN 61000-3-3:2013 | Per Clause 5 of the standard | |

Table 2
Guidance and Manufacturer's Declaration – Electromagnetic Immunity

The iovera° system is intended for use in the electromagnetic environment specified below. The customer or the user of the iovera° system should assure that it is used in such an environment

| Test Type | IEC 60601 test level | Compliance Level | Electromagnetic Environment – Guidance |
|---|---|---|---|
| Electrostatic discharge (ESD) IEC/EN 61000-4-2 | ±8 kV contact discharge<br>±2, 4, 8 & 15 kV air discharge | ±8 kV contact discharge<br>±2, 4, 8 & 15 kV air discharge | Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%. |
| Radiated Immunity IEC/EN 61000-4-3 | 80 MHz - 2.7 GHz<br>3 V/m, 80% modulation @ 1 kHz | 80 MHz - 2.7 GHz<br>3 V/m, 80% modulation @ 1 kHz | Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the iovera° system, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result. |
| Proximity field from RF wireless communications equipment IEC 61000-4-3 | Spot frequencies, 385 MHz – 5.750 GHz,<br>Pulse Modulation | Spot frequencies, 385 MHz – 5.750 GHz,<br>Pulse Modulation | |
| Conducted Immunity (AC Power) IEC/EN 61000-4-6 | 0.15 - 80 MHz: 3 Vrms<br>ISM bands: 6 Vrms<br>80% AM modulation @1 kHz on AC Mains | 0.15 - 80 MHz: 3 Vrms<br>ISM bands: 6 Vrms<br>80% AM modulation @1 kHz on AC Mains | Mains power quality should be that of a typical commercial or hospital environment. |
| Electrical Fast Transients (AC Power) IEC/EN 61000-4-4 | ±2 kV (AC Mains)<br>5/50 ns pulses@100 kHz<br>(15 ms bursts repeated every 300 ms) | ±2 kV (AC Mains)<br>5/50 ns pulses@100 kHz<br>(15 ms bursts repeated every 300 ms) | Mains power quality should be that of a typical commercial or hospital environment. |
| Surge Line to Line (AC Power) IEC/EN 61000-4-5 | ±1 kV Line to Line<br>±2 kV Line to Ground | ±1 kV Line to Line<br>±2 kV Line to Ground | Mains power quality should be that of a typical commercial or hospital environment. |
| Magnetic Immunity IEC/EN-61000-4-8 | 3 A/m<br>50/60 Hz | 3 A/m<br>50/60 Hz | Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment. |
| Voltage Dips and Interruptions IEC/EN 61000-4-11 | 0% UT 0.5 cycle<br>0% UT 1 cycle<br>0% UT 5 sec<br>70% UT 25 cycles | 0% UT 0.5 cycle<br>0% UT 1 cycle<br>0% UT 5 sec<br>70% UT 25 cycles | If the user of the iovera° system requires continued battery charging operation during power mains interruptions, it is recommended that the Charging Dock be powered from an uninterruptible power supply. |

NOTE: UT is the AC mains voltage prior to application of the test level

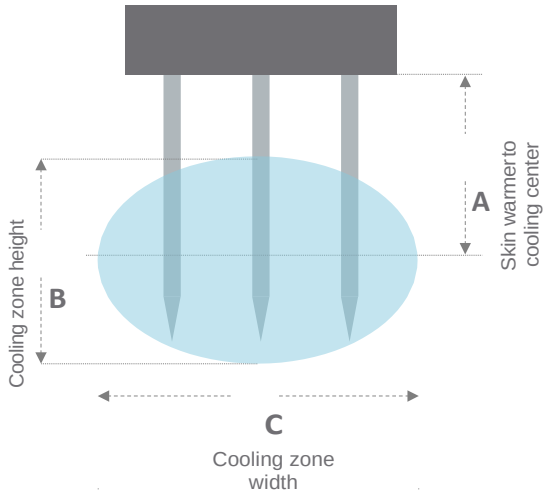
# Appendix B – System Specifications

| | |
|---|---|
| Handpiece Mass: | 252 g (0.555 lbs.) |
| Charging Dock Mass: | 205 g (0.452 lbs.) |
| IPX0: | No protection against ingress of fluids |
| Type of Refrigerant Used: | Nitrous Oxide ($N_2O$) |
| Minimum /Maximum Internal Operating Pressure: | 5650 to 6880 kPa (820 to 998 psi) |
| Power Requirements: | Input 100 - 240 VAC, 50/60 Hz, 0.35 – 0.15 A |
| Internal Battery (not serviceable): | 3.7V 3100mAh |
| Replaceable Parts: | Piercing point/Filter assembly |
| Manufacturer's Recommended Refrigerant Containers: | Only use Pacira Pharmaceuticals, Inc. provided refrigerant Cartridges (iovera° Cartridges) |
| Manufacturer's Recommended Electrical Mains Adapters: | Only use Pacira Pharmaceuticals, Inc. provided electrical mains adapter for the Charging Dock |
| Thermal Insulation: | Handpiece is designed to prevent excessive cooling and possible damage to the user. |
| Electrical Isolation: | Type  BF Applied Part |

Operating, Storage, and Transit Conditions:

| | Operating | Storage and Transit |
|---|---|---|
| Temperature | 15 - 28 °C (59 to 82 °F) | -20 - 50 °C (-4 - 122 °F) |
| Humidity | 30 - 60% RH | 10 - 85% RH |
| Pressure | 76 - 102 kPa (11 - 15 psi) | 50 - 106 kPa (7 - 15 psi) |

# Appendix C – Smart Tip (3x8.5 mm Sharp, 27 Gauge)




| h | A mm (in) | B mm (in) | C mm (in) |
|---|---|---|---|
| STT2309 | 6.3 mm (0.25 in) | 6.6 mm (0.26 in) | 7.9 mm (0.31 in) |

Dimensions are for informaton purposes only. They are based on 33-second cooling cycle performed in agarose gel. The ice ball size could vary based on anatomy/physiology of patients and should not affect the efficacy of treatment.

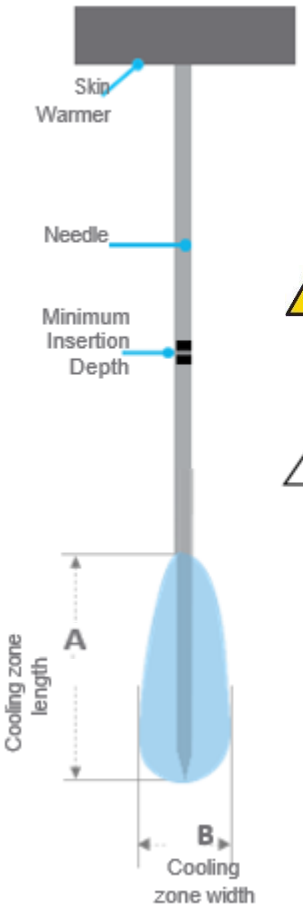
**Procedure:**

Insert needles until the skin warmer is in contact with the skin, then perform cooling cycle.

**WARNING!** To reduce likelihood of skin injury, skin warmer must be pressed against the skin when the needle is inserted before running a treatment cycle.

**WARNING!** Needles may contact bone in low BMI patients. Patient anatomy should be assessed prior to Smart Tip selection.

# Appendix D – Smart Tip (1x90 mm Sharp, 20 Gauge)




| h | mm (in) | |
|---|---|---|
| | A | B |
| STT2190 | 15.5 mm (0.61 in) | 7.5 mm (0.30 in) |

Dimensions are based on 60-second cooling cycle performed in agarose gel.

**WARNING!** To reduce likelihood of skin injury, insert needle at least 30 mm, denoted by the double marking (labeled minimum insertion depth on the image).

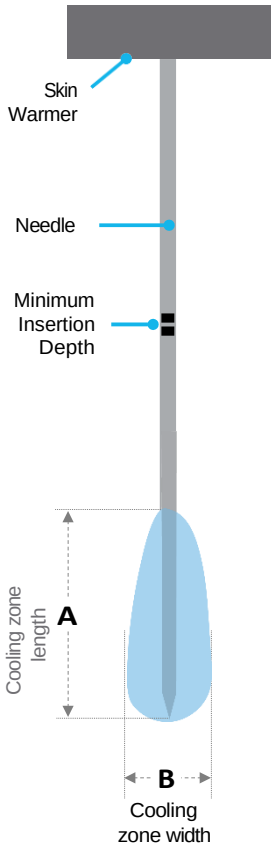
**CAUTION!** Small bend radii may affect performance.

- Do not kink or permanently deform needle.
- The minimum bend radius is 55mm.

**Procedure:**

- Pre-piercing of the skin may make Smart Tip insertion easier.
- Insert needle to maximum insertion desired, then perform cooling cycle.

# Appendix E – Smart Tip (1x90 mm Sharp, 20 Gauge) with Nerve Stim




| h | mm (in) | |
|---|---|---|
| | A | B |
| STT2190STIM | 15.5 mm (0.61 in) | 7.5 mm (0.30 in) |

Dimensions are based on 60-second cooling cycle performed in agarose gel.

**WARNING!** To reduce likelihood of skin injury, insert needle at least 30 mm, denoted by the double marking (labeled minimum insertion depth on the image).

**CAUTION!** Small bend radii may affect performance.

- Do not kink or permanently deform needle.
- The minimum bend radius is 55 mm.

**Procedure:**

- Pre-piercing of the skin may make Smart Tip insertion easier.
- Insert needle to maximum insertion desired, then perform cooling cycle.

**Optional Nerve Stimulation**

- This iovera° Smart Tip is enabled to be connected to a separate off-the-shelf nerve stimulator via the port on the side of the Smart Tip using the cable provided.
- When stimulation compatible components are used to facilitate target nerve location, the 3rd party nerve stimulator must have a maximum current output that is equal to or less than 5mA.
- Please refer to manufacturer-specific instructions for that device and observe all warnings, cautions, and precautions should the user choose to use this optional feature.

PACIRA
PHARMACEUTICALS, INC.
A Subsidiary of Pacira Biosciences, Inc.

**Manufacturer**
Pacira Pharmaceuticals, Inc.
A Subsidiary of Pacira Biosciences, Inc.
10410 Science Center Drive, Building A
San Diego, CA 92121 USA
Customer Service, 800-442-0989
Adverse Event Reporting, 855-793-9727
Medical Information, 855-793-9727
www.iovera.com

PN 12826 Rev F