



May 23, 2019

Novocure, Ltd.  
% Jonathan Kahan  
Regulatory Counsel  
Hogan Lovells US LPP  
555 13th Street, NW  
Washington, District of Columbia 20004

Re: H180002

HUD Number: DEV 2017-0381

Trade/Device Name: NovoTTF™-100L System

Product Code: QGZ

Filed: October 23, 2018

Amended: November 14, 2018, November 27, 2018, March 8, 2019

Dear Jonathan Kahan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your humanitarian device exemption (HDE) application for the NovoTTF™-100L System. This device is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy. We are pleased to inform you that the HDE is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm> identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device and insofar as the sale and distribution of the device are restricted to oncologists and surgical oncologists. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and probable benefit of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 9 months for the transducer arrays. This is to advise you that the protocol you used to establish this expiration dating is considered an approved

protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.108 and 21 CFR 814.39(a)(7).

Continued approval of the HDE is contingent upon the submission of periodic reports, required under 21 CFR 814.126, at intervals of one year (unless otherwise specified) from the date of approval of the original HDE. This report, identified as "Annual Report" and bearing the applicable HDE reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.126.

In addition to the above an HDE holder is required to maintain records of the names and addresses of the facilities to which the humanitarian use device (HUD) has been shipped, correspondence with reviewing institutional review boards (IRBs), as well as any other information requested by a reviewing IRB or FDA.

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). For more information on these requirements, please see the UDI website, <http://www.fda.gov/udi>.

Before making any change affecting the safety or probable benefit of the HDE device, you must submit an HDE supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.108 and 814.39 except a request for a new indication for use of a humanitarian use device (HUD). A request for a new indication for use for an HUD shall comply with the requirements set forth in 21 CFR 814.110 which includes obtaining a new designation of HUD status for the new indication for use and submission of an original HDE application in accordance with §814.104. The application for the new indication for use may incorporate by reference any information or data previously submitted to the agency.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> and on combination product postmarketing safety reporting is available at (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at

<http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm>.

FDA has determined that this device meets the conditions of either (I) or (II) under section 520(m)(6)(A)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This device may be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (i.e., for profit) as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). The ADN for this device is determined to be 24,000. This ADN was calculated based on the estimated number of NovoTTF-100L devices needed per patient in a year. You must immediately notify the agency by submitting an HDE amendment (21 CFR 814.126) whenever the number of devices shipped or sold in a year exceeds the ADN. FDA may also inspect the records relating to the number of your devices distributed during any calendar year. See section 520(m)(6)(B) of the FD&C Act. If you notify the FDA that the ADN has been exceeded, or if FDA discovers through an inspection that the ADN has been exceeded, then you are prohibited to sell your device for profit for the remainder of the year. See section 520(m)(6)(D) of the FD&C Act. If additional information arises regarding the ADN for your device, you may submit an HDE supplement (21 CFR 814.108) requesting that FDA modify the ADN based upon this additional information. See section 520(m)(6)(C) of the FD&C Act.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your HDE by making available, among other information, a summary of the safety and probably benefit data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at

<http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm>. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the HDE number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a HDE. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this HDE submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above HDE number to facilitate processing.

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Control Center - WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Rachana Visaria at 240-402-5628 or [Rachana.Visaria@fda.hhs.gov](mailto:Rachana.Visaria@fda.hhs.gov).

Sincerely,

Michael J. Ryan -S

for Malvina Eydelman, M.D.

Director

OHT1: Office of Ophthalmic, Anesthesia,  
Respiratory, ENT and Dental Devices

Office of Product Evaluation and Quality  
Center for Devices and Radiological Health



Optune Lua®—For unresectable, locally advanced or metastatic, MALIGNANT PLEURAL MESOTHELIOMA (MPM)<sup>1</sup>

# ENTER AN EXCITING ERA IN SURVIVAL



## Indications For Use

Optune Lua® is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy.

## Selected Important Safety Information

### Contraindications

Do not use Optune Lua in patients with implantable electronic medical devices such as pacemakers or implantable automatic defibrillators, etc. Use of Optune Lua together with implanted electronic devices has not been tested and may lead to malfunctioning of the implanted device.

Do not use Optune Lua in patients known to be sensitive to conductive hydrogels. Skin contact with the gel used with Optune Lua may commonly cause increased redness and itching, and may rarely lead to severe allergic reactions such as shock and respiratory failure.

**Please see the Important Safety Information for Optune Lua throughout and on page 10 and the Optune Lua Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings and precautions at [OptuneLua.com/hcp](https://OptuneLua.com/hcp).**

**Caution:** Federal law restricts this device to sale by or on the order of a physician. Humanitarian Device. Authorized by Federal Law for use in the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma concurrently with pemetrexed and platinum-based chemotherapy. The effectiveness of this device for this use has not been demonstrated.

 **OPTUNE**  
LUA®



# Optune Lua<sup>®</sup> is a wearable and portable treatment for MPM<sup>1,2</sup>

FDA-approved, second-generation device—  
smaller, lighter, and designed to better fit your patient's everyday life



Weighs half as much, at just 2.7 pounds.

Easy access sleeve bag

Electric field generator and battery

Transducer arrays

## Loco-regional delivery of Tumor Treating Fields (TTFields) via transducer arrays provides antimitotic activity directly at the site of the malignancy<sup>1</sup>



- TTFields are added to pemetrexed + cisplatin or carboplatin systemic therapies
- The size and placement of arrays are customized based on gender, body type, and tumor location
- It is recommended that Optune Lua is turned on at least 75% of the time (18 hours per day)<sup>1</sup>
  - Patients have flexibility to decide which times of the day are best for them, including at night when sleeping<sup>2</sup>

Novocure<sup>®</sup> will provide a customized map for array placement based on patient-specific measurements and tumor location (determined via CT scans). FDA, US Food and Drug Administration; CT, computed tomography; MPM, malignant pleural mesothelioma.

Optune Lua allows patients to go about their daily routine while continuously receiving treatment for MPM<sup>3</sup>

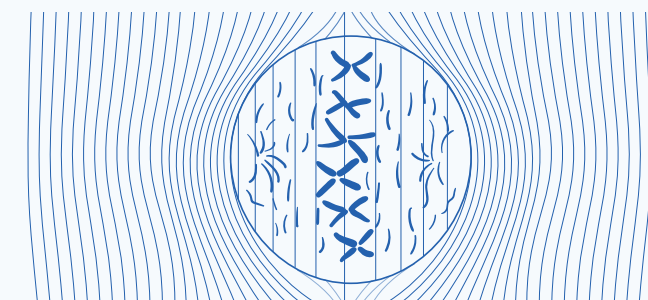
# Optune Lua is a noninvasive, antimitotic cancer treatment for MPM<sup>1</sup>

## Optune Lua delivers TTFields

- Optune Lua is a noninvasive, antimitotic cancer treatment for MPM that delivers Tumor Treating Fields (TTFields). TTFields are electric fields that continuously and selectively disrupt cancer cell division in solid tumors
  - TTFields disrupt cell division through physical interaction with key molecules during multiple phases of mitosis<sup>1,4</sup>

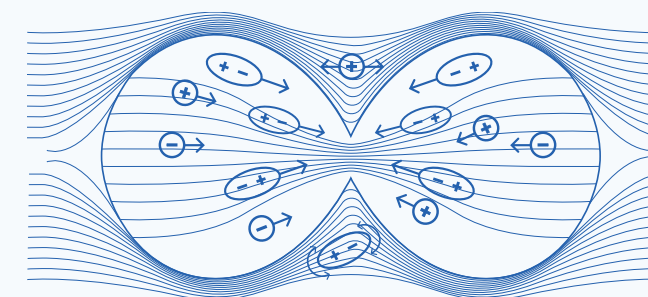
### TTFields target dividing cells, leading to apoptosis<sup>1,4</sup>

#### Metaphase – Uniform electric fields (TTFields)



- Disrupt alignment of highly polarized tubulin subunits<sup>4</sup>
- Disrupt microtubule spindle formation during mitosis and may ultimately lead to apoptosis<sup>4,5</sup>

#### Telophase – Nonuniform electric fields



- A change in cell shape during telophase causes a nonuniform electric field<sup>4,6</sup>
- Polar components move toward cleavage furrow<sup>4</sup>
- Cell cannot divide properly, which may ultimately lead to apoptosis<sup>4,5</sup>

MPM, malignant pleural mesothelioma; TTFields, Tumor Treating Fields.

## Selected Important Safety Information

### Warnings and Precautions

Optune Lua can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure<sup>®</sup>.

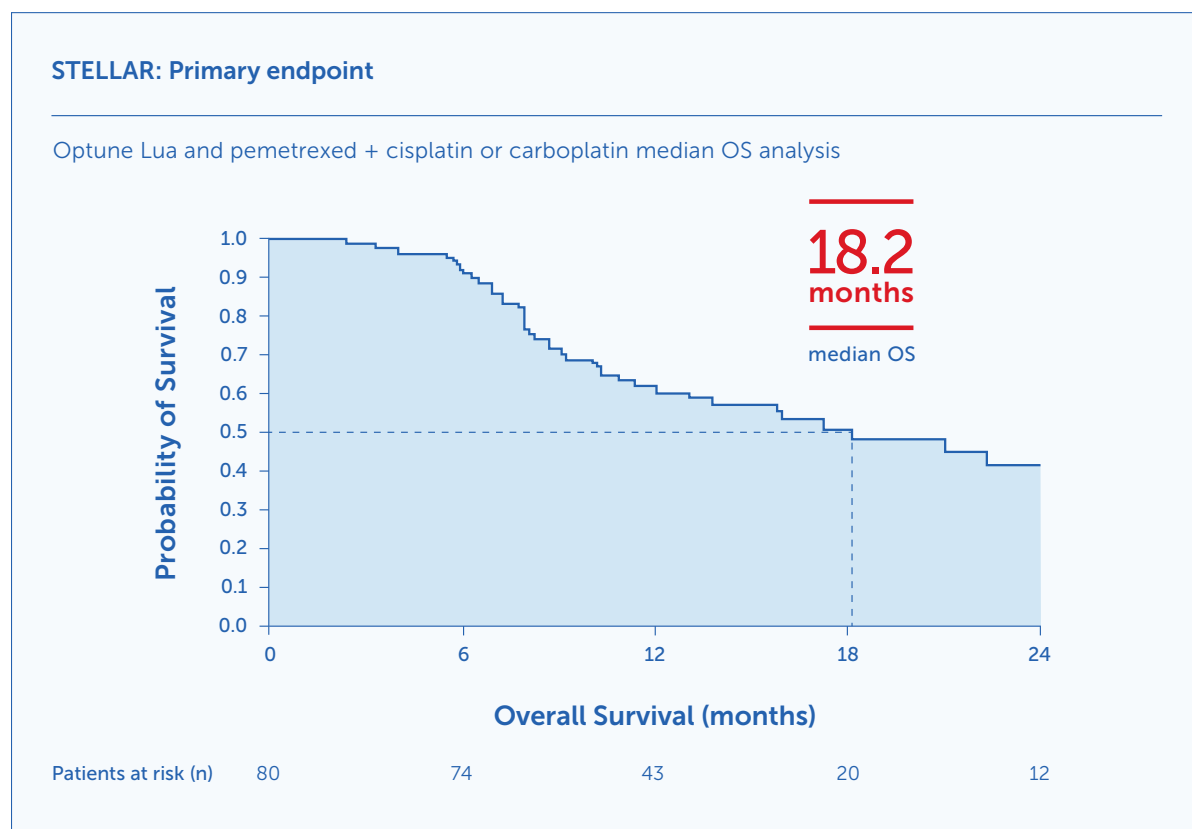
The most common (≥10%) adverse events involving Optune Lua in combination with chemotherapy were anemia, constipation, nausea, asthenia, chest pain, fatigue, medical device site reaction, pruritus, and cough.





# An exciting era in overall survival (OS) starts with Optune Lua®

STELLAR Clinical Results: Patients who used Optune Lua as first line together with pemetrexed + cisplatin or carboplatin achieved 18.2 months median OS with no added systemic AEs<sup>1,3</sup>



Kaplan-Meier OS curve for the 80 study patients (95% CI, 12.1-25.8).

## Study design

The STELLAR study was a prospective, single-arm, phase 2 trial to study the safety and efficacy of Optune Lua first line in patients with unresectable, locally advanced or metastatic, MPM (N=80). Patients were ≥18 years of age, had an ECOG performance status of 0-1, and at least 1 measurable or evaluable lesion according to mRECIST for MPM. Patients received continuous TTFIELDS to the thorax at a frequency of 150 kHz for at least 18 hours/day and concomitant chemotherapy every 21 days for up to 6 cycles.\*

\*Concomitant chemotherapy used in the STELLAR study was a combination of pemetrexed and platinum-based chemotherapy.

AEs, adverse events; ECOG, Eastern Cooperative Oncology Group; MPM, malignant pleural mesothelioma; mRECIST, modified Response Evaluation Criteria In Solid Tumors; TTFIELDS, Tumor Treating Fields.

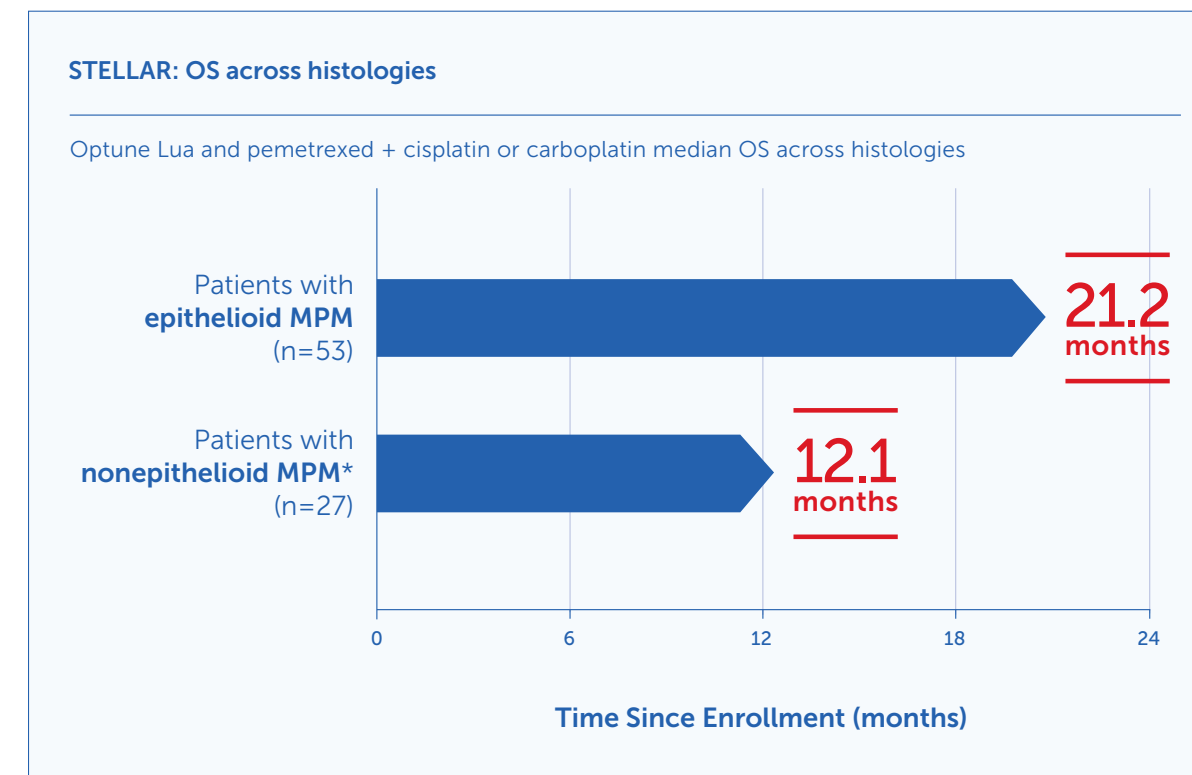
## Selected Important Safety Information

Other potential adverse effects associated with the use of Optune Lua include: treatment related skin toxicity, allergic reaction to the plaster or to the gel, electrode overheating leading to pain and/or local skin burns, infections at sites of electrode contact with the skin, local warmth and tingling sensation beneath the electrodes, muscle twitching, medical device site reaction and skin breakdown/skin ulcer.

# Median OS across MPM histologies

Optune Lua and pemetrexed + cisplatin or carboplatin median OS results shown across histologies<sup>1,3</sup>

- 21.2 months median OS in 66% of patients with epithelioid histology (2/3 of participants) and 12.1 months in 34% of less responsive, harder-to-treat nonepithelioid histology (1/3 of patients)\*



\*Nonepithelioid histology includes sarcomatoid or biphasic and unknown tumor pathology.

## Baseline patient characteristics

The STELLAR study included male (84%) and female (16%) patients with a median age of 67 years who had locally advanced (84%) and metastatic (16%) tumor stage. Tumor histology included epithelioid (66%), sarcomatoid or biphasic (26%), and unknown (8%). ECOG performance status for all patients was 0 (56%) or 1 (44%).

ECOG, Eastern Cooperative Oncology Group; MPM, malignant pleural mesothelioma; OS, overall survival.



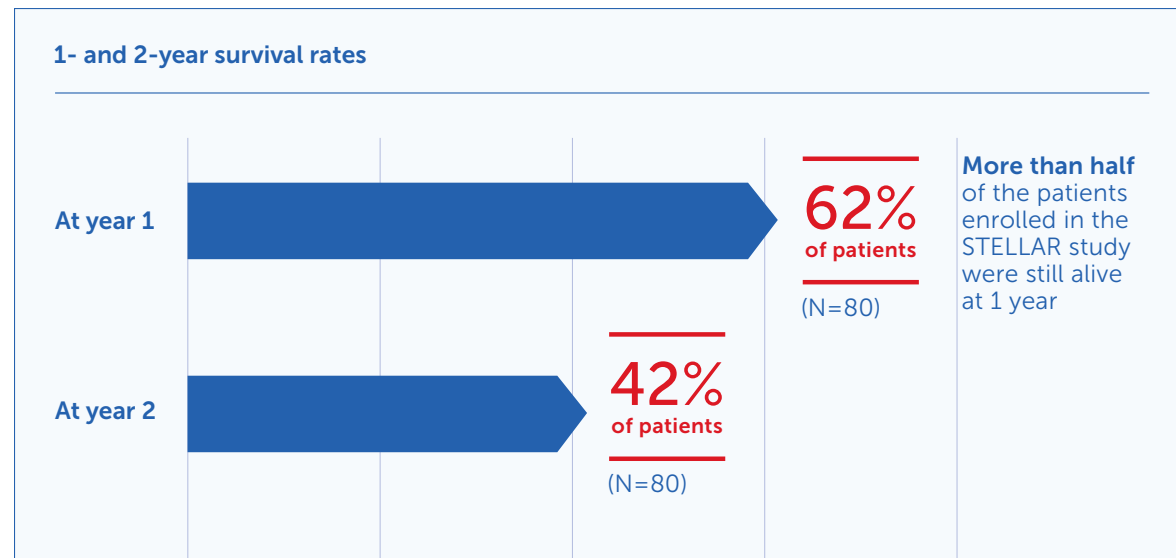
# STELLAR: Secondary endpoints

## Progression-free survival (PFS)<sup>1</sup>

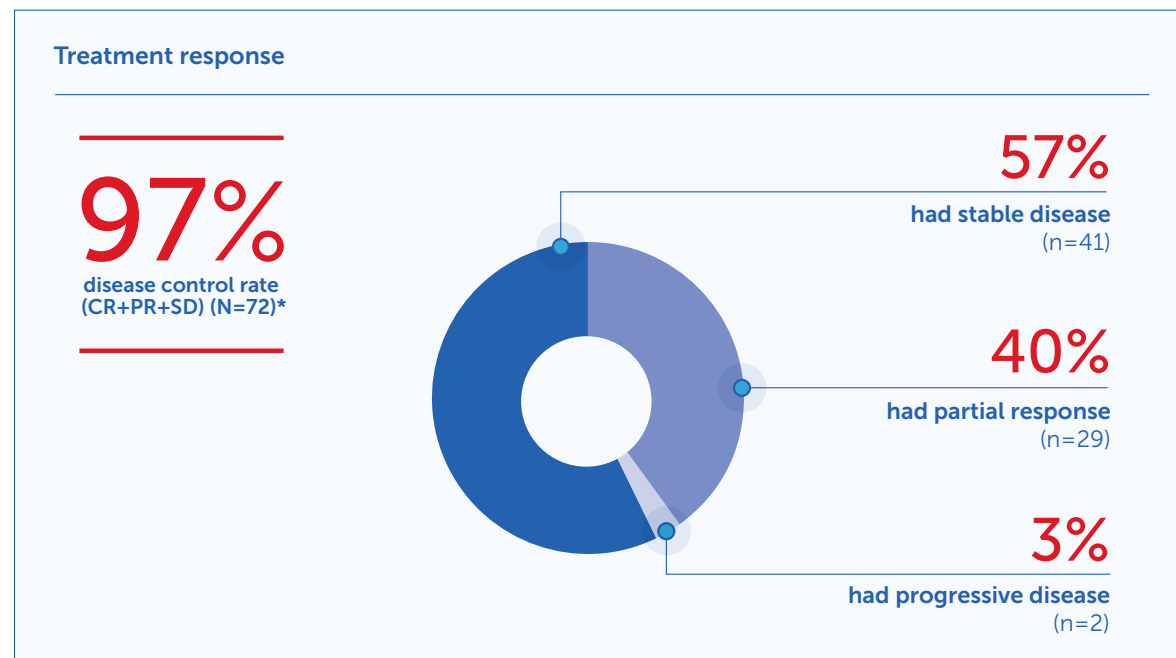
Patients using Optune Lua<sup>®</sup> together with pemetrexed + cisplatin or carboplatin as first-line treatment (N=80) achieved 7.6 months median PFS.

- 95% CI, 6.7-8.6, across all patients treated

## Survival rates<sup>1,3</sup>



## Radiological response rate<sup>1,3</sup>



CR, complete response; CT, computed tomography; mRECIST, modified Response Evaluation Criteria In Solid Tumors; PR, partial response; SD, stable disease.

# No systemic AEs were considered to be related to the use of Optune Lua

Mild-to-moderate skin irritation was the only device-related side effect with Optune Lua<sup>1,3</sup>

Severe (Grade 3-4) AEs by body system seen in >1 patient:			
System organ class/ preferred term	Optune Lua and pemetrexed + cisplatin or carboplatin (N=80)	System organ class/ preferred term	Optune Lua and pemetrexed + cisplatin or carboplatin (N=80)
<b>Number of patients with ≥1 AE</b>	<b>32 (40%)</b>	<b>General disorders and administration site conditions</b>	<b>6 (8%)</b>
<b>Blood and lymphatic system disorders</b>	<b>18 (23%)</b>	Fatigue	3 (4%)
Anemia	9 (11%)	<b>Infections and infestations</b>	<b>2 (3%)</b>
Leukopenia	3 (4%)	<b>Investigations</b>	<b>2 (3%)</b>
Neutropenia	7 (9%)	<b>Respiratory, thoracic, and mediastinal disorders</b>	<b>4 (5%)</b>
Thrombocytopenia	4 (5%)	Dyspnea	2 (3%)
<b>Cardiac disorders</b>	<b>3 (4%)</b>	<b>Skin and subcutaneous tissue disorders</b>	<b>4 (5%)</b>
Pericardial effusion	2 (3%)	Medical device site reaction (rash beneath transducer arrays)	4 (5%)
<b>Gastrointestinal disorders</b>	<b>3 (4%)</b>		
Vomiting	2 (3%)		

- The only AE attributed to Optune Lua use was skin irritation (71% of patients); 66% mild-to-moderate and 5% severe<sup>1,3</sup>
- No SAEs were considered related to device use

AEs, adverse events; SAEs, serious adverse events.

## Selected Important Safety Information

If the patient has an underlying serious skin condition on the chest, evaluate whether this may prevent or temporarily interfere with Optune Lua treatment.

Do not prescribe Optune Lua for patients that are pregnant, you think might be pregnant or are trying to get pregnant, as the safety and effectiveness of Optune Lua in these populations have not been established.





# Optune Lua<sup>®</sup> has the same mechanism of action as Optune Gio<sup>®1,7,8</sup>

Optune Gio, which has been approved for glioblastoma multiforme (GBM) since 2011, offers real-world experience and clinical evidence delivering Tumor Treating Fields (TTFields) in patients with both recurrent and newly diagnosed GBM<sup>9</sup>



MORE THAN **30,000 PATIENTS** HAVE BEEN TREATED WITH TTFields IN GBM SINCE THE FDA APPROVAL OF OPTUNE GIO IN 2011<sup>7,10</sup>

In newly diagnosed patients with GBM, the addition of Optune Gio + maintenance temozolomide (TMZ) **significantly improved PFS and OS with QoL maintained over time**<sup>9,10,\*†</sup>

In recurrent GBM, patients treated with Optune Gio experienced **similar efficacy, improved cognitive and emotional functioning, and fewer systemic AEs** compared with physician's choice of chemotherapy<sup>8,12,‡</sup>

- Optune Gio was approved under the Premarket Authorization (PMA) pathway<sup>13</sup>

**Optune Lua for MPM is FDA approved under the Humanitarian Device Exemption (HDE) pathway and is classified as an Humanitarian Use Device (HUD)**<sup>1,3</sup>

- An HDE may be granted if:
  - The device will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use while taking into account the probable risks and benefits of currently available devices or alternative forms of treatment<sup>14</sup>
  - The device would not be available to a person with the disease or condition in question without the HDE<sup>14</sup>
  - The device is designed to treat or diagnose a disease or condition that affects not more than 8,000 individuals in the United States annually<sup>14</sup>

\*Patient-reported QoL data collected per EORTC QLQ-C30 at baseline and Months 3, 6, 9, and 12. The 30-question survey covered 5 daily-functioning domains (physical, role, social, emotional, and cognitive).<sup>9,11</sup>

†EF-14 was a prospective, randomized, open-label, phase 3 clinical trial that was designed to evaluate the efficacy and safety of TTFields + TMZ vs maintenance TMZ in patients newly diagnosed with supratentorial GBM who completed radiation therapy and adjuvant TMZ. Patients (N=695) were randomized in a 2 to 1 ratio to receive either TTFields + TMZ or TMZ alone. Treatment began 4 to 7 weeks after the end of chemotherapy and radiation therapy. The specific objectives of the study included: PFS (primary endpoint), overall survival (powered secondary endpoint), 1- and 2-year survival rate, overall response rate, QoL, and safety.<sup>9</sup>

‡EF-11 was a prospective, randomized, open-label, phase 3 clinical trial that was designed to evaluate the efficacy and safety of TTFields as a monotherapy vs physician's best choice for chemotherapy (including bevacizumab) in patients with supratentorial recurrent GBM. The best available therapy was prescribed according to local practice and depending on prior treatment exposure. Adult patients (N=237) were randomized in a 1:1 manner to either TTFields or chemotherapy. The primary endpoint was OS. Secondary objectives included: PFS, 1-year survival rate, radiological response rate, QoL, and safety.<sup>8</sup>

AEs, adverse events; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer core quality of life questionnaire; FDA, US Food and Drug Administration; OS, overall survival; PFS, progression-free survival; QoL, quality of life.

## Selected Important Safety Information

### Contraindications

Do not use Optune Lua in patients known to be sensitive to conductive hydrogels. Skin contact with the gel used with Optune Lua may commonly cause increased redness and itching, and may rarely lead to severe allergic reactions such as shock and respiratory failure.

# MyNovocure<sup>®</sup> is an award-winning\* support program with comprehensive services



For patients using Optune Lua, MyNovocure partners with your patients and your practice every step of the treatment journey—offering customized support based on patient and caregiver needs

We are committed to identifying resources and programs to minimize the cost of Optune Lua for patients

- Support your patients and your practice through the reimbursement process, starting with an investigation of benefits

## Support includes



In-person device education



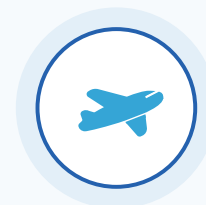
Resources and tips for using Optune Lua



24/7 technical support



Reordering supplies



Travel support



Call us:  
**1-855-281-9301** (toll-free)



Or email:  
**support@mynovocure.com**

\*Eyeforpharma 2018 North American Winner, Most valuable patient initiative or service.

MyNovocure<sup>®</sup>

OPTUNE<sup>®</sup>  
LUA<sup>®</sup>



# Important Safety Information

## Indications For Use

Optune Lua® is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy.

Optune Gio® is intended as a treatment for adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme (GBM).

Optune Gio with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery, and completion of radiation therapy together with concomitant standard of care chemotherapy.

For the treatment of recurrent GBM, Optune Gio is indicated following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

## Important Safety Information

### Contraindications

Do not use Optune Lua in patients with MPM with implantable electronic medical devices such as pacemakers or implantable automatic defibrillators, etc. Do not use Optune Gio in patients with GBM with an implanted medical device, a skull defect (such as, missing bone with no replacement), or bullet fragments. Use of Optune Gio together with skull defects or bullet fragments has not been tested and may possibly lead to tissue damage or render Optune Gio ineffective.

Use of Optune Lua for MPM or Optune Gio for GBM together with implanted electronic devices has not been tested and may lead to malfunctioning of the implanted device.

Do not use Optune Lua for MPM or Optune Gio for GBM in patients known to be sensitive to conductive hydrogels. Skin contact with the gel used with Optune Lua and Optune Gio® may commonly cause increased redness and itching, and may rarely lead to severe allergic reactions such as shock and respiratory failure.

### Warnings and Precautions

Optune Lua and Optune Gio can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure®.

The most common (≥10%) adverse events involving Optune Lua in combination with chemotherapy in patients with MPM were anemia, constipation, nausea, asthenia, chest pain, fatigue, medical device site reaction, pruritus, and cough.

Other potential adverse effects associated with the use of Optune Lua include: treatment related skin toxicity, allergic reaction to the plaster or to the gel, electrode overheating leading to pain and/or local skin burns, infections at sites of electrode contact with the skin, local warmth and tingling sensation beneath the electrodes, muscle twitching, medical device site reaction and skin breakdown/skin ulcer.

The most common (≥10%) adverse events involving Optune Gio in combination with chemotherapy in patients with GBM were thrombocytopenia, nausea, constipation, vomiting, fatigue, convulsions, and depression.

The most common (≥10%) adverse events related to Optune Gio treatment alone in patients with GBM were medical device site reaction and headache. Other less common adverse reactions were malaise, muscle twitching, and falls related to carrying the device.

If the patient has an underlying serious skin condition on the treated area, evaluate whether this may prevent or temporarily interfere with Optune Lua and Optune Gio treatment.

Do not prescribe Optune Lua or Optune Gio for patients that are pregnant, you think might be pregnant or are trying to get pregnant, as the safety and effectiveness of Optune Lua and Optune Gio in these populations have not been established.

# References

1. Optune Lua. Instructions For Use for Unresectable Malignant Pleural Mesothelioma. Novocure; 2021.
2. Optune Lua. Patient Information and Operation Manual for Unresectable Malignant Pleural Mesothelioma. Novocure; 2021.
3. Ceresoli GL, Aerts JG, Dziadziuszko R, et al. Tumour Treating Fields in combination with pemetrexed and cisplatin or carboplatin as first-line treatment for unresectable malignant pleural mesothelioma (STELLAR): a multicentre, single-arm phase 2 trial. *LancetOncol*. 2019;20(12):1702-1709.
4. Kirson ED, Gurvich Z, Schneiderman R, et al. Disruption of cancer cell replication by alternating electric fields. *CancerRes*. 2004;64(9):3288-3295.
5. Giladi M, Schneiderman RS, Voloshin T, et al. Mitotic spindle disruption by alternating electric fields leads to improper chromosome segregation and mitotic catastrophe in cancer cells. *SciRep*. 2015;5:18046.
6. Gutin PH, Wong ET. Noninvasive application of alternating electric fields in glioblastoma: a fourth cancer treatment modality. *AmSocClinOncolEducBook*. 2012;126-131.
7. Summary of Safety and Effectiveness Data (SSED). US FDA Website. Accessed September 11, 2023. [https://www.accessdata.fda.gov/cdrh\\_docs/pdf10/p100034s013b.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf10/p100034s013b.pdf)
8. Optune Gio. Instructions For Use. Novocure; 2023.
9. Stupp R, Taillibert S, Kanner A, et al. Effect of Tumor-Treating Fields plus maintenance temozolomide vs maintenance temozolomide alone on survival in patients with glioblastoma: a randomized clinical trial. *JAMA*. 2017;318(23):2306-2316.
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**Please see the Important Safety Information for Optune Lua on page 10 and the Optune Lua Instructions for Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions at [OptuneLua.com/hcp](http://OptuneLua.com/hcp).**

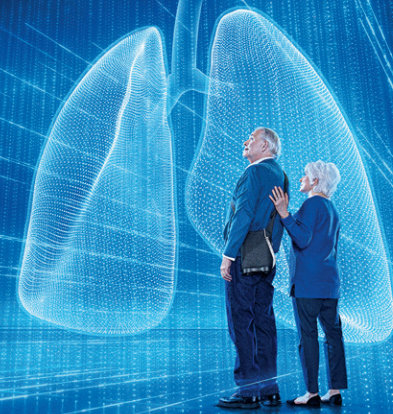
**Please see the Optune Gio® Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions at [OptuneGio.com/IFU](http://OptuneGio.com/IFU)**





Optune Lua®—For unresectable, locally advanced or metastatic,  
MALIGNANT PLEURAL MESOTHELIOMA (MPM)<sup>1</sup>

# ENTER AN EXCITING ERA OF SURVIVAL



Optune Lua together with pemetrexed + cisplatin or carboplatin showed encouraging overall survival (OS) results in the STELLAR clinical study with no added systemic AEs<sup>1,3</sup>

[OptuneLua.com/hcp](https://OptuneLua.com/hcp)

## Median OS

**18.2 months**

Median OS with no added chemotherapy-related side effects was achieved in patients using Optune Lua first line together with pemetrexed + cisplatin or carboplatin<sup>1,3</sup>

## Median OS shown across histologies

**21.2 months**

in 66% of patients with **epithelioid** histology (n=53)<sup>1</sup>

**12.1 months**

in 34% of patients with **nonepithelioid** histology (n=27)<sup>1</sup>

## No added systemic AEs

No added systemic AEs were considered to be related to the use of Optune Lua.<sup>1</sup>

- The only AE attributed to Optune Lua use was skin irritation (71% of patients); 66% mild-to-moderate and 5% severe<sup>1,3</sup>
- No SAEs were considered related to device use<sup>1,3</sup>

## MyNovocure®



MyNovocure is an award-winning support program with comprehensive services for your patients using Optune Lua

## MyNovocure®



Call us:  
**1-855-281-9301** (toll-free)



Or email:  
[support@mynovocure.com](mailto:support@mynovocure.com)

AEs, adverse events; SAEs, serious adverse events.

## Important Safety Information

Optune Lua and Optune Gio® can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure®.

**Please see the Important Safety Information for Optune Lua on page 10 and the Optune Lua Instructions for Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions at [OptuneLua.com/hcp](https://OptuneLua.com/hcp).**

Depictions of patients and caregivers are actor portrayals.

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**OPTUNE**  
LUA®

# Description of the Optune Lua<sup>®</sup> system



Discuss Optune Lua with your next patient

## Optune Lua overview

- For the first-line **treatment of unresectable, locally advanced or metastatic, MALIGNANT PLEURAL MESOTHELIOMA (MPM)**, the FDA has approved Optune Lua together with pemetrexed + cisplatin or carboplatin<sup>1,2</sup>
- When using Optune Lua, **loco-regional delivery of Tumor Treating Fields (TTFields) via transducer arrays** provides antimitotic activity directly at the site of the malignancy<sup>1</sup>

## How Optune Lua is used

- Transducer arrays are applied to the torso and need to be replaced at least twice per week (every 4 days at most) to help minimize the risk of skin irritation<sup>3</sup>
- Portable for use during normal daily activities<sup>3</sup>
  - Patients should avoid activities that may result in Optune Lua or the transducer arrays becoming wet, as this may cause damage<sup>3</sup>
- It is recommended to use TTFields continuously, averaging at least 18 hours a day<sup>1,4</sup>
- Patients should refer to the Skin Care Guidelines for specific information regarding taking care of their skin and array placement instructions

## Introducing the second-generation Optune Lua system<sup>3</sup>

Easy-access sleeve bag

Electric field generator and battery

Transducer arrays



## Second-generation Optune Lua system

Optune Lua is a wearable, portable treatment for MPM and has been redesigned for carrying comfort and usability. Note that the Optune Lua system is<sup>1,3</sup>:

### More compact

- Smaller-profile carrying case with easy-grip texture

### More convenient

- Weighs half as much and now has 5 different ways to carry the device, including a backpack and shoulder strap

### Equipped with smart technology

- Battery indicator alerts patients to change battery, and light sensor auto-dims for night use

Note: Transducer arrays are customized based on gender, body type, and tumor location.

## How Optune Lua works

Optune Lua is a noninvasive, antimitotic cancer treatment for MPM that delivers TTFields. TTFields are low-intensity (1-3 V/cm) alternating electric fields tuned to a specific frequency (150 kHz) to disrupt cancer cell division in solid tumors.<sup>1</sup>

TTFields disrupt cell division through physical interaction with key molecules during multiple phases of mitosis.<sup>1,5</sup>

**Caution:** Federal law restricts this device to sale by or on the order of a physician. Humanitarian Device. Authorized by Federal Law for use in the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma concurrently with pemetrexed and platinum-based chemotherapy. The effectiveness of this device for this use has not been demonstrated.

Please see the complete Important Safety Information for Optune Lua on the back and the Optune Lua Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions at [OptuneLua.com/hcp](http://OptuneLua.com/hcp).

US-OPL-00049v2.0 July 2024



Visit [OptuneLuaHCP.com/mpm/home](http://OptuneLuaHCP.com/mpm/home) for more information



## Indications For Use

Optune Lua® is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy.

## Important Safety Information

### Contraindications

Do not use Optune Lua in patients with implantable electronic medical devices such as pacemakers or implantable automatic defibrillators, etc. Use of Optune Lua together with implanted electronic devices has not been tested and may lead to malfunctioning of the implanted device.

Do not use Optune Lua in patients known to be sensitive to conductive hydrogels. Skin contact with the gel used with Optune Lua may commonly cause increased redness and itching, and may rarely lead to severe allergic reactions such as shock and respiratory failure.

### Warnings and Precautions

Optune Lua can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure®.

The most common (≥10%) adverse events involving Optune Lua in combination with chemotherapy were anemia, constipation, nausea, asthenia, chest pain, fatigue, medical device site reaction, pruritus, and cough.

Other potential adverse effects associated with the use of Optune Lua include: treatment related skin toxicity, allergic reaction to the plaster or to the gel, electrode overheating leading to pain and/or local skin burns, infections at sites of electrode contact with the skin, local warmth and tingling sensation beneath the electrodes, muscle twitching, medical device site reaction and skin breakdown/skin ulcer.

If the patient has an underlying serious skin condition on the chest, evaluate whether this may prevent or temporarily interfere with Optune Lua treatment.

Do not prescribe Optune Lua for patients that are pregnant, you think might be pregnant or are trying to get pregnant, as the safety and effectiveness of Optune Lua in these populations have not been established.

**Please see the Optune Lua Instructions For Use (IFU) included in the Information Kit for complete information regarding the device's indications, contraindications, warnings, and precautions.**

**References:** **1.** Optune Lua. Instructions For Use for Unresectable Malignant Pleural Mesothelioma. Novocure; 2021. **2.** FDA Approves the NovoTTF-100L™ System in Combination with Chemotherapy for the Treatment of Malignant Pleural Mesothelioma [press release]. St. Helier, Jersey: Business Wire; May 23, 2019. **3.** Optune Lua. Patient Information and Operation Manual for Unresectable Malignant Pleural Mesothelioma. Novocure; 2021. **4.** Ceresoli GL, Aerts JG, Dziadziuszko R, et al. Tumour Treating Fields in combination with pemetrexed and cisplatin or carboplatin as first-line treatment for unresectable malignant pleural mesothelioma (STELLAR): a multicentre, single-arm phase 2 trial. *Lancet Oncol.* 2019;20(12):1702-1709. **5.** Kirson ED, Gurvich Z, Schneiderman R, et al. Disruption of cancer cell replication by alternating electric fields. *Cancer Res.* 2004;64(9):3288-3295.



## Instructions for Use

### for Unresectable Malignant Pleural Mesothelioma

**novocure®**

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This manual is intended for physicians prescribing the use of Optune Lua™. Additional information is found in the following materials:

- Patient Information and Operation Manual
- Clinical Practice Guidelines: layout optimization in thoracic malignancies

Caution: Federal law restricts this device to sale by or on the order of a physician Humanitarian Device. Authorized by Federal Law for use in the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma concurrently with pemetrexed and platinum based chemotherapy. The effectiveness of this device for this use has not been demonstrated.

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## Indications for Use

Optune Lua™ is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy.



# Contraindications, Warnings and Precautions

## Contraindications

Do not use Optune Lua if you have implantable electronic medical devices including a pacemaker, implantable automatic defibrillator, etc. Use of Optune Lua together with implanted electronic devices has not been tested and may lead to malfunctioning of the implanted device.

Do not use Optune Lua if you are known to be sensitive to conductive hydrogels like the gel used on electrocardiogram (ECG) stickers or transcutaneous electrical nerve stimulation (TENS) electrodes. In this case, skin contact with the gel used with Optune Lua may commonly cause increased redness and itching, and rarely may even lead to severe allergic reactions such as shock and respiratory failure.

## Warnings

**Warning** – Use Optune Lua only after receiving training from qualified personnel, such as your doctor, a nurse, or other medical personnel who have completed a training course given by Novocure (the device manufacturer). Ask to see a certificate signed by Novocure that says they completed a training course. Your training will include a detailed review of this manual and practice in the use of the system. In addition, you will be trained in what to do if there are problems with treatment. Use of Optune Lua without receiving this training can result in breaks in treatment and may rarely cause increased skin irritation, open sores on your chest or back, allergic reactions or even an electric shock.

**Warning** - In case of skin irritation, which appears as redness under the transducer arrays (a mild rash), use high potency topical steroids (hydrocortisone cream) when replacing transducer arrays. This will help relieve your skin irritation. If you do not use this cream, the skin irritation can become more serious and may even lead to skin break down, infections, pain and blisters. If this happens, stop using the topical steroid cream and contact your doctor. Your doctor will supply you with an antibiotic cream to use when replacing transducer arrays. If you do not use this cream, your symptoms may continue and your doctor may ask you to take a break from treatment until your skin heals.

**Warning** - All servicing procedures must be performed by qualified and trained personnel. If you attempt to open and service the system alone you may cause damage to the system. You could also get an electric shock by touching the inner parts of the device.

## Precautions

**Caution** - Do not use any parts that do not come with Optune Lua, or that were not sent to you by the device manufacturer or given to you by your doctor. Use of other parts, manufactured by other companies or for use with other devices, can damage the device. This may lead to a break in treatment.

**Caution** - Do not use Optune Lua if any parts look damaged (torn wires, loose connectors, loose sockets, cracks or breaks in the plastic case). Use of damaged components can damage the device, and cause a break in treatment.

**Caution** - Do not wet the device or transducer arrays. Getting the device wet may damage it, preventing you from receiving treatment for the right amount of time. Getting the transducer arrays very wet is likely to cause the transducer arrays to come loose from your skin. If this happens, the device will turn off and you will need to change the transducer arrays.

**Caution** - Before connecting or disconnecting the transducer arrays, make sure that the Optune Lua power switch is in the OFF position. Disconnecting transducer arrays with the device power switch in the ON position may cause a device alarm to go off, and could damage the device.

**Caution** - If you have an underlying serious skin condition on the chest, discuss with your doctor whether this may prevent or temporarily interfere with Optune Lua treatment.

**Caution** - Do not use Optune Lua if you are pregnant, you think you might be pregnant, or are trying to get pregnant. If you are a woman who is able to get pregnant, you must use birth control when using the device. Optune Lua was not tested in pregnant women. It is unknown what side effects the device may cause if you are pregnant or if it will be effective.

## Notices

**Notice** - Optune Lua and transducer arrays will activate metal detectors.

**Notice** - If you plan to be away from home for more than 1 hour, carry an extra battery and/or the power supply with you in case the battery you are using runs out. If you do not take a spare battery and/or the power supply you may have a break in your treatment.

**Notice** - Make sure you have at least 12 extra transducer arrays at all times. This will last you until the next transducer array shipment arrives. Remember to order more transducer arrays when there are at least 12 extra transducer arrays left. If you do not order transducer arrays in time you may have a break in your treatment.

**Notice** - Batteries may weaken over time and need to be replaced. You will know this has happened when the amount of time the device can run on a fully charged battery begins to shorten. For example, if the low battery indicator light flashes within only 1 hour from the start of treatment, replace the battery. If you do not have replacement batteries when your batteries run out, you may have a break in your treatment.

**Notice** - You should carry the Troubleshooting Guide (Section 25 of the patient information and operation manual) at all times. This guide is necessary to ensure Optune Lua works properly. If you do not work the system correctly you may have a break in your treatment.

**Notice** - Do not block the device vents located on the front and back of the device. Blocking the vents may cause the device to overheat and turn off, leading to a break in treatment. If this happens, unblock the vents, wait 5 minutes and restart the device. In case the vents are blocked with pet hair or dust, return the device for service.

**Notice** - Do not block the battery charger vents located on the sides of the battery chargers. Blocking the vents may cause the charger to overheat. This could prevent your batteries from charging. In case the vents are blocked with pet hair or dust, return the charger for service.

**Notice** - Before using a transducer array, make sure its package is sealed by gently rubbing the package between thumb and pointer finger on all four sides. The package should be closed on all sides. There should be no openings in the package seal. If the package is not sealed, the transducer array may be damaged. A damaged transducer array will not work properly and may cause the device to turn off.

**Notice** - The transducer arrays are for single use and should not be taken off your body and put back on again. If you put a used transducer array back on your chest again, it may not stick well to your skin and the device could turn off.

**Notice** - Keep the device out of the reach of children and pets.

**Notice** - The device has a cord that may cause tripping when connected to an electric socket.

## Description

Optune Lua for the first-line treatment of unresectable, locally advanced or metastatic, malignant pleural mesothelioma, is a portable, battery or power supply operated device which produces alternating electrical fields, called tumor treatment fields (“TTFields”) within the human body. TTFields are applied to the patient by electrically- insulated surface transducer arrays. TTFields disrupt the rapid cell division exhibited by cancer cells<sup>1</sup>.

Optune Lua is comprised of two main components: (1) an Electric Field Generator (the Optune Lua device); and (2) ILE Insulated Transducer Arrays (the transducer arrays). In addition, the following components are also included in Optune Lua: power supply, battery, battery charger, connection cable and carrying bag.

Treatment parameters are preset by Novocure such that there are no electrical output adjustments available to the patient. The patient must learn to change and recharge depleted device batteries and to connect to an external power supply overnight. In addition, the transducer arrays need to be replaced at least two times per week (every 4 days at most) and the skin re-shaved in order to maintain optimal contact. Patients carry the device in an over-the-shoulder bag or backpack and receive continuous treatment without changing their daily routine.

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<sup>1</sup> Mitotic Spindle Disruption by Alternating Electric Fields Leads to Improper Chromosome Segregation and Mitotic Catastrophe in Cancer Cells. Giladi M, et al. Sci Rep. 2015 Dec 11;5:18046. doi: 10.1038/srep18046.

## Principles of Operation

Optune Lua produces TTFIELDS within the human body through transducer arrays placed on the chest. TTFIELDS disrupt the rapid cell division exhibited by cancer cells.

TTFIELDS harness electric fields to arrest the proliferation of tumor cells and to destroy them. TTFIELDS technology takes advantage of the special characteristics and geometrical shape of dividing cells, which make them susceptible to the effects of the TTFIELDS. These special fields alter the tumor cell polarity at an intermediate frequency (on the order of 100-300 kHz). The frequency used for a particular treatment is specific to the cell type being treated (e.g., 150 kHz for MPM).

In contrast, the TTFIELDS have not been shown to have an effect on cells that are not undergoing division. Since most normal adult cells proliferate very slowly, if at all, they are hypothesized to be little affected by the TTFIELDS. Testing demonstrates no differences between treated and control animals in histology of the major internal organs (including the lungs), blood examination, cardiac rhythm, body temperature, or in animal behavior. In addition, because the fields alternate so rapidly, they have no effect on normal quiescent cells nor do they stimulate nerves and muscles. It is noted that, because TTFIELDS are only applied to the chest, they have no effect on rapidly proliferating cells in the rest of the body. The intensities of the electric fields within the tissues are very small and do not result in any meaningful increase in tissue temperature.

The above mechanisms of action are consistent with the extensive research regarding the effects of TTFIELDS. These results demonstrate both disruption of cell division up to complete cessation of the process, as well as complete destruction of the dividing cells. It is important to note that all the described effects can be obtained by fields of low intensity such that they are not accompanied by any significant elevation of temperature.

## Preclinical Data

TFields have been shown in vitro to inhibit cancer cell replication during mitosis without any systemic side effects. At intensities of approximately 1 V/cm, TFields can be frequency-tuned to inhibit different cancer cell types (i.e., the smaller the cell, the higher the frequency needed), due to disruption of microtubule polymerization and physical disruption of cell integrity at the cleavage plane during telophase<sup>2</sup>.

Specifically, TFields have been shown to inhibit mesothelioma cells in vitro at a frequency of 150 kHz and an intensity of 1 V/cm. Based on realistic finite element mesh simulations, Novocure has concluded that intended TFields intensities can be generated in the lungs of large animals and humans.

Using a model developed to simulate the growth kinetics of a malignant tumor, the minimal treatment course duration for TFields has been determined to be approximately 4 weeks to reach tumor stabilization. Stopping treatment prior to completion of a 4 week treatment course will most likely lead to continued tumor growth and appearance of symptoms within approximately 1-2 weeks.

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<sup>2</sup> Kirson, E. D., Z. Gurvich, et al. (2004). "Disruption of cancer cell replication by alternating electric fields." *Cancer Res* 64(9): 3288-95.



### UNRESECTABLE MALIGNANT PLEURAL MESOTHELIOMA (MPM)

#### Potential Adverse Effects of the Device on Health

Below is a list of the potential adverse effects (i.e., complications) associated with the use of the device.

- Treatment related skin toxicity
- Allergic reaction to the plaster or to the gel
- Electrode overheating leading to pain and/or local skin burns
- Infection at the sites of electrode contact with the skin
- Local warmth and tingling sensation beneath the electrodes
- Medical device site reaction
- Muscle twitching
- Skin breakdown / skin ulcer

#### Clinical Study in Unresectable MPM

**Study Design:** The study was a prospective, single-arm study evaluating pemetrexed and cisplatin or carboplatin in combination with TTFields in patients with untreated unresectable malignant pleural mesothelioma. The study was conducted at 13 sites in Europe.

The following were the objectives of the study:

To prospectively determine the overall survival of malignant pleural mesothelioma subjects treated with Optune Lua in combination with pemetrexed and cisplatin or carboplatin.

To collect evidence of the safety of TTFields applied to subjects with malignant pleural mesothelioma using Optune Lua.

**Eligibility Criteria:** The inclusion and exclusion criteria for the trial were as follows:

#### Inclusion Criteria

- Pathological or histological evidence of mesothelioma.
- $\geq 18$  years of age
- TNM Stage IV, Not candidate for curative treatment (surgery or radiotherapy)
- At least 4 weeks since major surgery
- At least one measurable or evaluable lesion according to modified RECIST criteria for malignant pleural mesothelioma
- ECOG Performance Status (PS) of 0-1.
- Life expectancy of at least 3 months.
- Participants of childbearing age must use effective contraception as indicated by the investigator
- All subjects must sign written informed consent.
- Able to operate Optune Lua independently or with the help of a caregiver.

## Exclusion Criteria

- a. Previous chemotherapy or radiation;
- b. Prior malignancy requiring anti-tumor treatment or concurrent malignancy;
- c. Significant co-morbidities within 4 weeks prior to enrollment, resulting in the following laboratory findings:
  - Significant liver function impairment:
    - AST or ALT >3 times the upper limit of normal
    - Total bilirubin >1.5 upper limit of normal
  - Significant renal impairment (serum creatinine >1.7 mg/dL);
  - Coagulopathy (as evidenced by PT or APTT >1.5 times control in subjects not receiving anticoagulants);
  - Thrombocytopenia (platelet count < 100 x 10<sup>3</sup>/μL);
  - Neutropenia (absolute neutrophil count < 1.5 x 10<sup>3</sup>/μL);
  - Anemia (Hb <10 g/dL);
  - Severe acute infection;
- d. Significant comorbidity expected to affect patient's prognosis or ability to receive the combined therapy:
  - History of significant cardiovascular disease unless the disease is well controlled. Significant cardiac disease includes second/third degree heart block; significant ischemic heart disease; poorly controlled hypertension; congestive heart failure of the New York Heart Association (NYHA) Class II or worse (slight limitation of physical activity; comfortable at rest, but ordinary activity results in fatigue, palpitation or dyspnea).
  - History of arrhythmia that is symptomatic or requires treatment. Patients with atrial fibrillation or flutter controlled by medication are not excluded from participation in the trial.
  - Active infection or any serious underlying medical condition that would impair the ability of the patient to receive protocol therapy.
  - History of any psychiatric condition that might impair the patient's ability to understand or comply with the requirements of the study or to provide consent.
- e. Untreated brain metastases. Asymptomatic, pretreated brain metastases not requiring steroids are allowed;
- f. Implanted pacemaker, defibrillator or other electrical medical devices;
- g. Known allergies to medical adhesives or hydrogel;
- h. Pregnant or breastfeeding (all patients of childbearing potential must use effective contraception method during the entire period of the study based on the recommendation of the investigator or a gynecologist);
- i. Admitted to an institution by administrative or court order.

## Study Procedures:

Patients received pemetrexed based doublet in combination with TTFIELDS. For the purpose of this study 3 weeks (21 days) was considered one treatment cycle. Chemotherapy: Treating investigators could choose one of the following regimens: pemetrexed/cisplatin, or pemetrexed/carboplatin. Pemetrexed was administered intravenously at a dose of 500 mg/m<sup>2</sup> day with either cisplatin 75 mg/m<sup>2</sup> intravenously on day 1 or carboplatin intravenously at a dose of AUC 5 on day 1. Cycles were repeated every 21 days for up to 6 cycles in the absence of progression or unacceptable toxicity. In the event of chemotherapy toxicities, dose modifications could be employed.

**Optune Lua:** Continuous TTFIELDS for at least 18 hours/day applied to the thorax with output parameters of 150 kHz with two sequential, field direction at a maximal intensity of 1414mA RMS. TTFIELDS were administered until radiological disease progression according to the Modified RECIST criteria for malignant pleural mesothelioma, or unacceptable toxicity based on investigator assessment. There was no dose modification for TTFIELDS but treatment interruptions could occur if recommended by investigator. In the case of chemotherapy discontinuation due to toxicity or the completion of 6 chemotherapy cycles, TTFIELDS therapy could be continued until disease progression or unacceptable toxicity.

## Follow-up

All patients were seen every 3 weeks until disease progression. At each visit patients underwent: physical examination, performance status assessment, complete blood count, serum chemistry, adverse event collection, concomitant medication recording and device compliance assessment. CT of the chest and MRI and/or bone scan (if clinically indicated) were performed every 6 weeks until progression. Assessment of local and distant disease progression was performed per the modified RECIST criteria version 1.1. The protocol specified a minimum follow-up of 12 months.

Patients were seen at an outpatient clinic for an additional visit 30 days following treatment discontinuation. Physical examination and blood tests were performed during the visit. Patient performance status and adverse events were documented at this visit. Subsequently, patients were followed monthly for survival by telephone (unless a clinical visit was performed). Patient date of death was captured in the CRFs.

**Analysis:** The trial endpoints were analyzed in the intent to treat population which included 80 patients.

## Protocol Deviations:

Major protocol deviations were defined as deviations that have the potential to influence the primary endpoints of the study. There were no major protocol deviations in the trial.

**Subject Characteristics and Treatment Details:** 80 subjects with unresectable MPM were enrolled in the study. Eight patients (10%) were lost to follow up before completing the required minimum of 12 months follow up. Baseline characteristics and treatment details in the ITT population were as follows:

Characteristics	Optune Lua/Chemotherapy (N=80)
<b>Age (Years)</b>	
n	80
Mean (SD)	64.8 (9.28)
Median (range)	67.0 (27-78)
<b>Sex, No. (%)</b>	
Female	13 (16%)
Male	67 (84%)
<b>Ethnicity, No. (%)</b>	
Caucasian	80 (100%)
<b>Smoking, No. (%)</b>	
Current Smokers	8 (10%)
Former Smokers	37 (46%)
Never Smokers	35 (44%)
<b>Tumor pathology, No. (%)</b>	
Epithelioid	53 (66%)
Sarcomatoid/Biphasic	21 (26%)
Unknown	6 (8%)
<b>Performance status (ECOG), No. (%)</b>	
0	45 (56%)
1	35 (44%)
<b>Visual Analog Pain Scale at Baseline</b>	
Mean (SD)	15.1 (20.68)
Median (range)	5.0 (0-93)

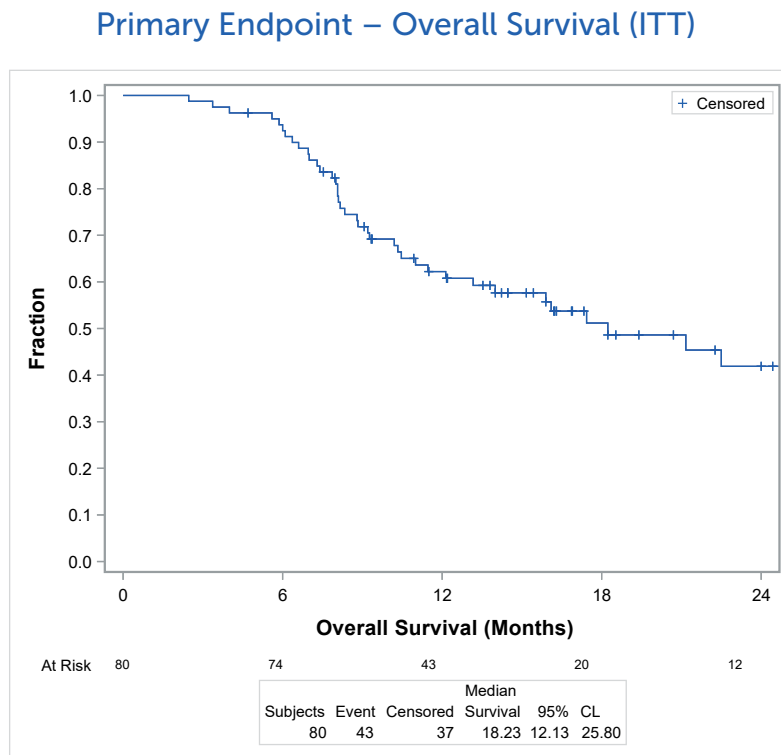
## Treatment Details

<b>Number of TTFields Cycles</b>	
Mean (SD)	8.7 (6.08)
Median (range)	8.0 (2-41)
<b>Number of Chemotherapy Cycles</b>	
Mean (SD)	4.6 (1.81)
Median (range)	6.0 (1-7)
<b>Usage (percentage Optune Lua use per treatment cycle)</b>	
n	72
Median (range)	68.0 (2-91)
<b>Patients with treatment breaks (&gt;=24 hours), No. (%)</b>	70 (88%)
<b>Number of treatment breaks (&gt;=24 hours)</b>	
n	70
Median (range)	6.0 (1-75)
<b>Duration of treatment breaks (&gt;=24 hours) (Days)</b>	
n	70
Median (range)	2.6 (1-101)

## Results:

### Primary Endpoint: Overall Survival

The median overall survival in the trial was 18.2 months (95%CI 12.1-25.8). The Kaplan Meier overall survival curve for the 80 study patients is shown in Figure 1 below.



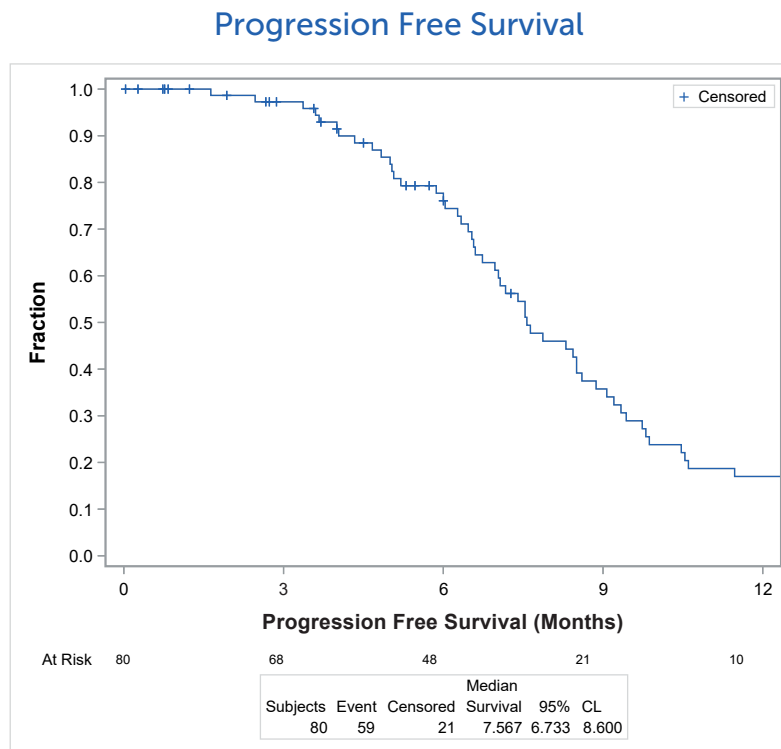
**Figure 1: Median OS in STELLAR Study**

Patients with epithelioid histology have previously been shown to have better outcomes than those with non-epithelioid histology. OS in the current study also favored patients with epithelioid versus non-epithelioid histology (median OS 21.2 months versus 12.1 months, respectively).

## Secondary Endpoints:

### Progression Free Survival

The median PFS in the study was 7.6 months (95% CI 6.7-8.6). The Kaplan Meier PFS curve for the 80 study patients is shown in Figure 2 below.



**Figure 2: Median PFS in STELLAR Study**

PFS in the current study also favored patients with epithelioid versus non-epithelioid histology (median PFS 8.3 months versus 6.5 months, respectively).

### One-year and two-year survival rate

1-year survival in the study was 62% (95%CI 50%-72%). 2-year survival in the study was 42%.

### Radiological Response Rate

Seventy two patients in the trial had at least one follow up CT scan performed. Of these patients, 29 (40%) experienced a partial response, 41 stable disease (57%) and 2 (3%) patients progressed at their first follow up scan. This represents a disease control rate of 97%.



## Summary of Results

Endpoint	Optune Lua / Pemetrexed / Platinum (n=80)
<b>Overall survival</b>	
Median OS, months (95% CI)	18.2 (12.1-25.8)
Survival rate % (95% CI)	
1-year	62.2% (50.3- 72.0 )
2-year	41.9% (28.0 ; 55.2 )
<b>Progression free survival</b>	
Median PFS, months (95% CI)	7.6 (6.7-8.6)
<b>Available best response, No. (%)</b>	72 (90)
Complete Response	0 (0)
Partial Response	29 (40)
Stable Disease	41 (57)
Progressive Disease	2 (3)
Disease control rate (CR+PR+SD)	70 (97)

**Safety Results:** A total of 32 patients (40%) reported severe (grade 3-4 adverse events in the trial). None of the grade 3-4 adverse events were considered related to Optune Lua by any of the investigators except for 5% grade 3 skin irritation.

## Severe (Grade 3-4) Adverse Events by Body System and Severity seen in > 1 patient

<b>System Organ Class</b>	n=80
Preferred Term	
<b>Number of Patients with &gt;=1 AE</b>	32 (40%)
<b>Blood and lymphatic system disorders</b>	18 (23%)
Anemia	9 (11%)
Leukopenia	3 (4%)
Neutropenia	7 (9%)
Thrombocytopenia	4 (5%)
<b>Cardiac disorders</b>	3 (4%)
Pericardial effusion	2 (3%)
<b>Gastrointestinal disorders</b>	3 (4%)
Vomiting	2 (3%)
<b>General disorders and administration site conditions</b>	6 (8%)
Fatigue	3 (4%)
<b>Infections and infestations</b>	2 (3%)
<b>Investigations</b>	2 (3%)
<b>Respiratory, thoracic and mediastinal disorders</b>	4 (5%)
Dyspnea	2 (3%)
<b>Skin and subcutaneous tissue disorders</b>	4 (5%)
Medical Device Site Reaction (rash beneath transducer arrays)	4 (5%)

The only AEs attributed to use of Optune Lua are the known skin irritation seen in 66% of patients in this study (5% severe). No SAEs were considered related to device use.

**Conclusions:** Optune Lua is a portable, battery operated device which delivers TTFields to patients with unresectable previously untreated MPM. The results of the trial in MPM showed that Optune Lua, when added to pemetrexed and cisplatin or carboplatin, leads to a median OS of 18.2 months and a median PFS of 7.6 months. No increase in systemic adverse events is seen when Optune Lua treatment is added to pemetrexed and a platinum based chemotherapy. The only common device-related AE was skin irritation seen beneath the transducer arrays in 66% percent of patients. The majority of these events were mild to moderate with only 5% of patients experiencing severe skin irritation.

## Directions for Use

Detailed directions for use for Optune Lua for MPM can be found in:  
The Optune Lua Patient Information and Operation Manual for MPM QSD-QR-390

Guidelines for ILE transducer array placement can be found in:  
Clinical Practice Guidelines: layout optimization in thoracic malignancies

## Abbreviations

**AE** – Adverse event

**MPM** – Malignant Pleural Mesothelioma

**ITT** – Intent-to-Treat. This analysis population includes all randomized subjects.

**kHz** – kilo hertz; number of cycles per second

**Optune Lua** – A portable, battery, or power supply, operated device for delivering 150 kHz TTFields to the lungs of patients with MPM

**OS** – Overall survival

**PFS** – Progression free survival

**Radiological Response Rate** - sum of complete and partial radiological response rates

**Disease Control Rate** – sum of stable disease, complete and partial radiological response rates

**TTFields** – Tumor Treating Fields: Low intensity (1-3 V/cm), intermediate frequency (100-300 kHz), alternating electric fields, delivered using insulated transducer arrays to the region of the body afflicted with a solid tumor. The fields have been shown in vitro to arrest the replication of tumor cells by disrupting the proper formation of the microtubule spindle and by dielectrophoretic disruption of cell integrity during late telophase

**V/cm** – Volts per centimeter; the unit of intensity measurement of electric fields



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## Bibliography

Giladi M, et al. (2015) "Mitotic Spindle Disruption by Alternating Electric Fields Leads to Improper Chromosome Segregation and Mitotic Catastrophe in Cancer Cells." *Sci Rep*. 2015 Dec 11;5: 18046.

Kirson, E. D., Z. Gurvich, et al. (2004). "Disruption of cancer cell replication by alternating electric fields." *Cancer Res* 64(9): 3288-95.

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## **Optune Lua™ for Unresectable Malignant Pleural Mesothelioma - Patient Information and Operation Manual**

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Caution: Federal law restricts this device to sale by or on the order of a physician Humanitarian Device. Authorized by Federal Law for use in adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) concurrently with pemetrexed and platinum-based chemotherapy.

The effectiveness of this device for this use has not been demonstrated.



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## 1 GLOSSARY

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**Cancer** – abnormal cell division that spreads without control

**Carboplatin** – a type of cancer drug used to treat MPM

**Chemotherapy** – medication used to destroy cancer cells

**Cisplatin** – a type of cancer drug used to treat MPM

**Clinical study** – a research study that involves people

**Contraindications** – situations when a treatment should not be used

**CT scan** – a procedure that uses radiation to create pictures of areas inside the body

**Electric Field Generator (the device)** – a portable device for delivering TFields to the lungs of patients with MPM

**Local** – in one part of the body

**Malignant Pleural Mesothelioma (MPM)** – a type of cancer which affects the linings of the lungs

**Optune Lua™ Treatment Kit** – the Electric Field Generator and other parts including batteries, charger, connection cable, transducer arrays, power supply and carrying bag

**Pemetrexed** – a type of cancer drug used to treat MPM

**Progression** – when cancer comes back after being treated

**Radiation** – a treatment involving x-rays used to kill tumor cells

**Steroids** – When used on the skin, a medication that can reduce inflammation

**Systemic** – throughout the body

**Topical** – on the surface of the skin

**Transducer Array** – adhesive bandages that hold insulated ceramic discs that deliver TFields to the chest

**TFields** – Tumor Treating Fields: Alternating electric fields, delivered using transducer arrays to the part of the body with a solid tumor. The fields have been shown to destroy tumor cells

**Tumor** – an abnormal growth of tissue

## 2 WHAT IS Optune Lua AND HOW DOES IT WORK

---

Optune Lua is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy.

Your doctor has prescribed Optune Lua because you are a good candidate for treatment with the device.

A doctor may prescribe Optune Lua to treat a patient with malignant pleural mesothelioma (called “MPM”) which cannot be cured with surgery or radiation.

Optune Lua is used together with pemetrexed and cisplatin or carboplatin (types of cancer drugs).

Optune Lua is a portable device. It produces electric fields, called tumor treatment fields (“TTFields”). Transducer arrays connected to the device deliver TTFields to your chest. The TTFields are intended to destroy lung cancer cells.

The device and battery are carried in a shoulder bag. You should use them as much as you can.

In this manual, “Optune Lua Treatment Kit” refers to the Electric Field Generator (also called “the device”), connection cable, transducer arrays, power supply, battery, and battery charger.

## 3 CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

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### Contraindications

Do not use Optune Lua if you have an electrical implant. Use of Optune Lua together with electrical implants has not been tested and may lead to malfunctioning of the implanted device.

Do not use Optune Lua if you are known to be sensitive to gels like the gel used on electrocardiogram (ECG) stickers or transcutaneous electrical nerve stimulation (TENS) electrodes. In this case, skin contact with the gel used with Optune Lua may commonly cause increased redness and itching, and rarely may even lead to severe allergies such as a fall in blood pressure and breathing difficulty.

### Warnings

**Warning** – Use Optune Lua only after receiving training from qualified personnel, such as your doctor, a nurse, or other medical personnel who have completed a training course given by Novocure (the device manufacturer). Ask to see a certificate signed by Novocure that says they have completed the training course.

Your training will include a detailed review of the patient manual and practice in the use of the system. In addition, you will be trained in what to do if there are problems with treatment. Use of Optune Lua without receiving this training can result in breaks in treatment and may rarely cause increased skin irritation, open sores on your chest or back, allergic reactions or even an electric shock.

**Warning** - In case of skin irritation, which appears as redness under the transducer arrays (a mild rash), use high potency topical steroids (hydrocortisone cream) when replacing transducer arrays. This will help relieve your skin irritation. If you do not use this cream, the skin irritation can become more serious and may even lead to skin break down, infections, pain and blisters. If this happens, stop using the topical

steroid cream and contact your doctor. Your doctor will supply you with an antibiotic cream to use when replacing transducer arrays. If you do not use this cream, your symptoms may continue and your doctor may ask you to take a break from treatment until your skin heals.

**Warning** - All servicing procedures must be performed by qualified and trained personnel. If you attempt to open and service the system alone you may cause damage to the system. You could also get an electric shock by touching the inner parts of the device.

### Precautions

**Caution** - Do not use any parts that do not come with the Optune Lua Treatment Kit, or that were not sent to you by the device manufacturer or given to you by your doctor. Use of other parts, manufactured by other companies or for use with other devices, can damage the device. This may lead to a break in treatment.

**Caution** - Do not use the Optune Lua Treatment Kit if any parts look damaged (torn wires, loose connectors, loose sockets, cracks or breaks in the plastic case). Use of damaged components can damage the device, and cause a break in treatment.

**Caution** - Do not wet the device or transducer arrays. Getting the device wet may damage it, preventing you from receiving treatment for the right amount of time. Getting the transducer arrays very wet is likely to cause the transducer arrays to come loose from your skin. If this happens, the device will turn off and you will need to change the transducer arrays.

**Caution** - Before connecting or disconnecting the transducer arrays, make sure that the Optune Lua power switch is in the OFF position. Disconnecting transducer arrays with the device power switch in the ON position may cause a device alarm to go off, and could damage the device.

**Caution** - If you have an underlying serious skin condition on the chest, discuss with your doctor whether this may prevent or temporarily interfere with Optune Lua treatment.

**Caution** - Do not use Optune Lua if you are pregnant, you think you might be pregnant, or are trying to get pregnant. If you are a woman who is able to get pregnant, you must use birth control when using the device. Optune Lua was not tested in pregnant women. It is unknown what side effects the device may cause if you are pregnant or if it will be effective.

## Notices

**Notice** - The Optune Lua device and transducer arrays will activate metal detectors.

**Notice** - If you plan to be away from home for more than 1 hour, carry an extra battery and/or the power supply with you in case the battery you are using runs out. If you do not take a spare battery and/or the power supply you may have a break in your treatment.

**Notice** - Make sure you have at least 12 extra transducer arrays at all times. This will last you until the next transducer array shipment arrives. Remember to order more transducer arrays when there are at least 12 extra transducer arrays left. If you do not order transducer arrays in time you may have a break in your treatment.

**Notice** - Batteries may weaken over time and need to be replaced. You will know this has happened when the amount of time the device can run on a fully charged battery begins to shorten. For example, if the low battery indicator light flashes within only 1 hour from the start of treatment, replace the battery. If you do not have replacement batteries when your batteries run out, you may have a break in your treatment.

**Notice** - You should carry the Troubleshooting Guide (Section 24 of the patient information and operation manual) at all times. This guide is necessary to ensure Optune Lua works properly. If you do not work the system correctly you may have a break in your treatment.

**Notice** - Do not block the device vents located on the front and back of the device. Blocking the vents may cause the device to overheat and turn off, leading to a break in treatment. If this happens, unblock the vents, wait 5 minutes and restart the device. In case the vents are blocked with pet hair/dust, return the charger for service.

**Notice** - Do not block the battery charger vents located on the sides of the battery chargers. Blocking the vents may cause the charger to overheat. This could prevent your batteries from charging. In case the vents are blocked with pet hair/dust, return the device for service.

**Notice** - Before using a transducer array, make sure its package is sealed by gently rubbing the package between thumb and pointer finger on all four sides. The package should be closed on all sides. There should be no openings in the package seal. If the package is not sealed, the transducer array may be damaged. A damaged transducer array will not work properly and may cause the device to turn off.

**Notice** - The transducer arrays are for single use and should not be taken off your body and put back on again. If you put a used transducer array back on your chest again, it may not stick well to your skin and the device could turn off.

**Notice** - Keep the device out of the reach of children and pets.

**Notice** - The device has a cord that may cause tripping when connected to an electric socket.

#### 4 WHAT ARE THE RISKS OF USING Optune Lua?

---

Skin irritation is often seen under the transducer arrays when using Optune Lua. This will look like a red rash, small sores or blisters on your chest. In general, this will not cause skin damage that cannot be fixed.

The irritation can be treated with steroid cream or by moving the transducer arrays. If you do not use steroid cream, the skin irritation could become more serious. This may lead to open sores, infections, pain and blisters. If this happens, stop using the steroid cream and contact your doctor.

In a clinical study of Optune Lua together with cancer drugs used to treat your kind of lung cancer, the device led to skin irritation in about two thirds of 80 patients (66%). Most of these cases were not severe and were treated with topical creams. Only a handful of patients (5%) had severe skin irritation.

The table below shows how often severe medical problems occurred in patients using Optune Lua together with cancer drugs, in this clinical study. Only skin irritation was caused by Optune Lua. The rest of the medical problems were due to the cancer itself or the cancer drugs used with the device.

Medical Problem	Optune Lua together with Cancer Drugs
Lower white and red blood cell counts	18 out of 80 subjects (23%)
General disorders	6 out of 80 subjects (8%)
Rash under device transducer arrays and other skin problems	4 out of 80 subjects (5%)
Breathing disorders	4 out of 80 subjects (5%)
Vomiting and Ulcer	3 out of 80 subjects (4%)
Heart disorders	3 out of 80 subjects (4%)
Infections	2 out of 80 subjects (3%)
Muscle disorders	1 out of 80 subjects (1%)
Kidney disorders	1 out of 80 subjects (1%)
Liver disorders	1 out of 80 subjects (1%)

Below is a list of the potential adverse effects (i.e., complications) associated with the use of Optune Lua:

- Treatment related skin toxicity
- Allergic reaction to the plaster or to the gel
- Electrode overheating leading to pain and/or local skin burns
- Infection at the sites of electrode contact with the skin
- Local warmth and tingling sensation beneath the electrodes
- Medical device site reaction
- Muscle twitching
- Skin breakdown / skin ulcer

## **5 WHAT ARE THE BENEFITS OF USING Optune Lua?**

---

All patients in the clinical study used Optune Lua together with cancer drugs. Half of the patients using Optune Lua together with cancer drugs lived for more than 18.2 months after their treatment started. Also, 4 out of each 10 patients using Optune Lua together with cancer drugs were alive after two years (42%).

## **6 WHAT STUDIES HAVE BEEN CONDUCTED WITH Optune Lua?**

---

A clinical study, referred to as the STELLAR Study, was conducted to evaluate the use of Optune Lua in conjunction with cancer drugs to treat unresectable (unable to be removed via surgery) malignant pleural mesothelioma. The study included 80 subjects.

Half of the patients using lived for more than 18.2 months after their treatment started and half of the patients did not experience growth of their MPM for more than 7.6 months after their treatment started.

Local skin problems under the transducer arrays were seen in 57 of 80 patients in the study (red rash, small sores or blisters). This was expected. None of these cases of skin problems caused damage to the skin that could not be fixed. The irritation went away after being treated with steroid cream and moving the transducer arrays. Only 4 subjects had severe skin problems.

These problems led to stopping treatment in 3 subjects. In all cases, the rash went away after stopping treatment.

Ask your doctor for more details about the clinical studies of Optune Lua. For more information, visit our website: [www.Optunelua.com](http://www.Optunelua.com)

## 7 ABOUT Optune Lua

---

Optune Lua is a portable medical device that delivers electric fields called “TFields” to the chest using transducer arrays. TFields are intended to kill cancer cells.

Your doctor has prescribed Optune Lua for use at home. You may be able to use Optune Lua on your own, or you may need help from a doctor, family member, or other caregiver. Use Optune Lua as many hours per day as possible. You can take short breaks for personal needs. When starting treatment, your doctor or a representative from Novocure will teach you how to use the device, replace transducer arrays, recharge and replace batteries, and plug in the device. Your Novocure representative will also teach you what to do if an alarm beeps and will give you a telephone number to call for technical support. After this short training, with the help of a family member or care provider if needed, you will be able to properly use Optune Lua. You will also be able to change the batteries, charge the batteries and replace the transducer arrays as needed.

The device can be carried when you are using a battery. You can continue your normal daily life while carrying the device in a shoulder bag. The Optune Lua Treatment Kit includes four rechargeable batteries. Each battery will last for about one hour. For sleeping, or other times when you plan to stay in the same place for a while, plug the device into a standard wall outlet.

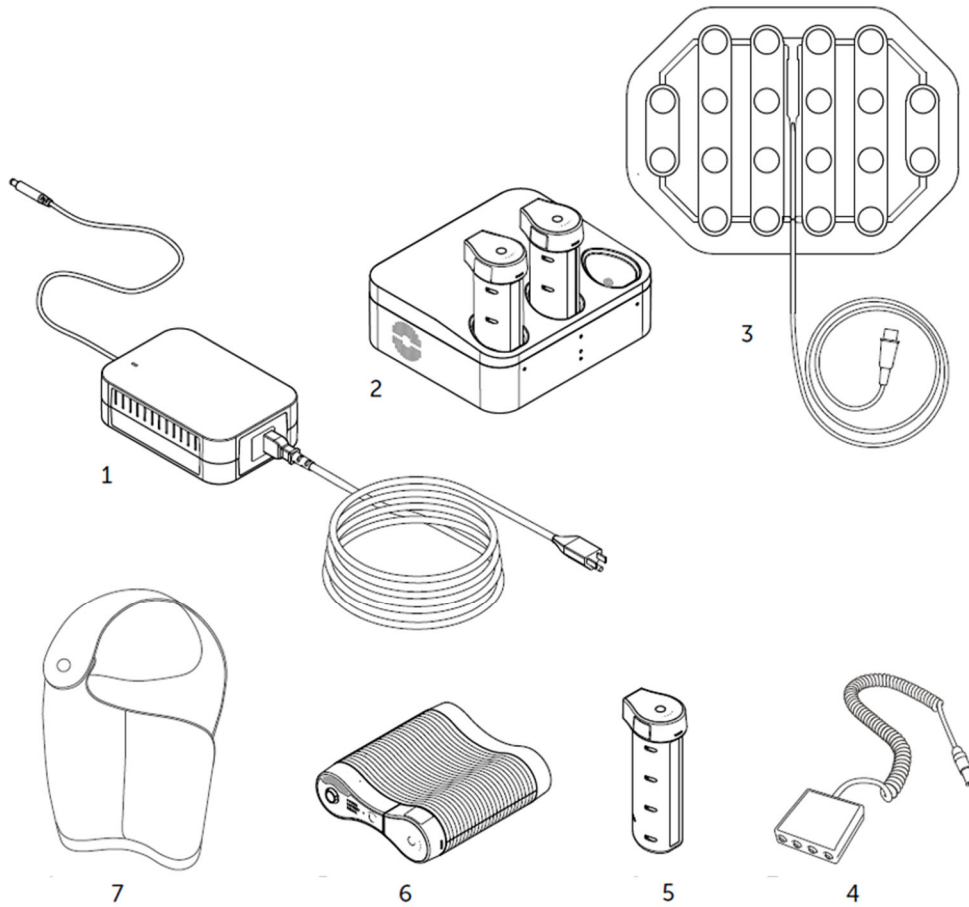
Optune Lua does not need regular maintenance. The device also does not have any settings for you to change. The only things you need to do are check that the device has a power supply (a charged battery or is plugged into the wall) and turn it ON and OFF. If the device is not working, an alarm will beep. A Troubleshooting Guide is provided in this manual (Section 24). You can also call the 24-hour technical support telephone number (Section 2525).

Change the transducer arrays at least twice a week. Keep treatment breaks to a minimum. You can interrupt treatment for personal needs such as bathing, exercise, or any time you need a planned treatment break. You will need to stop treatment (turning the device OFF) to replace the transducer arrays. To take a shower, unplug the transducer arrays from the device (leave the transducer arrays on your chest) and wrap your chest with a waterproof wrapping so it does not get wet. You can take a full shower and wet your entire body when you are not wearing the transducer arrays (for example, when you have taken them off but before replacing them with a new pair).



## Overview of the Optune Lua Treatment Kit

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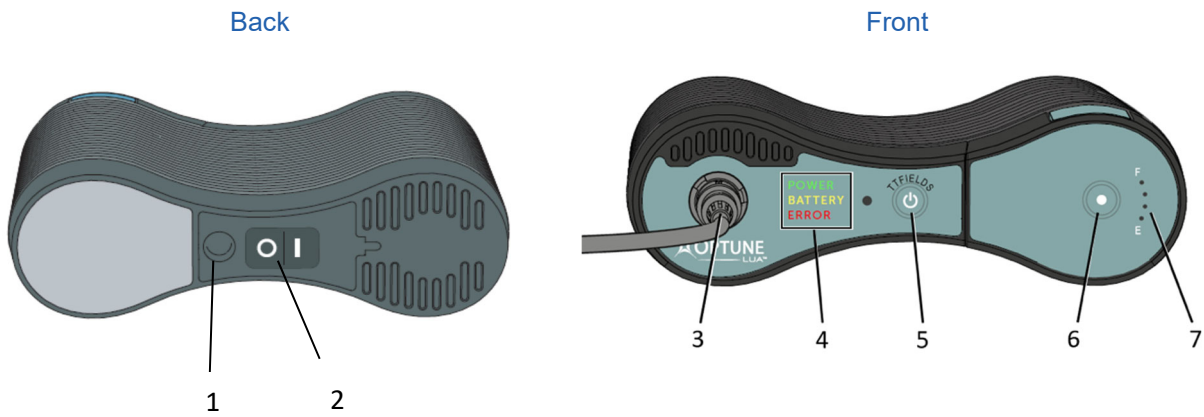


- |  |                                  |
|--|----------------------------------|
| 1. Power Supply                                      | (SPS9200)                        |
| 2. Battery Charger                                   | (ICH9100)                        |
| 3. ILE Transducer Array                              | (Small: ILE1010, Large: ILE1030) |
| 4. Connection Cable                                  | (CAD9100)                        |
| 5. Battery   | (IBH9200)                        |
| 6. Optune Lua™ electric field generator – the device | (TFT9200)                        |
| 7. Shoulder Bag and Strap                            |                                  |

## 8 THE DEVICE

---

- Optune Lua is an automatic system.
- You will need to learn how to place it in a carrying bag, connect a battery and operate the system.
- The following controls will allow you to do this:



1. Power Supply Port
2. Optune Lua Power Switch
3. Connection Cable (CAD) Socket
4. POWER / BATTERY / ERROR Indicators
5. TTFields ON / OFF Button
6. Battery Test Button
7. Battery Gauge

## 9 THE ILE TRANSDUCER ARRAYS

---

- An ILE Transducer Array is an adhesive patch which delivers Tumor Treating Fields to the chest.
- The ILE transducer arrays are supplied sterile and are to be used with Optune Lua only.
- ILE transducer arrays come in two sizes – small and large. You should use either large or small transducer arrays on the chest and upper abdomen, back and both sides of your thorax, depending on your body size.
- Your doctor will show you where to place each array on your chest.

## 10 BEFORE YOU BEGIN

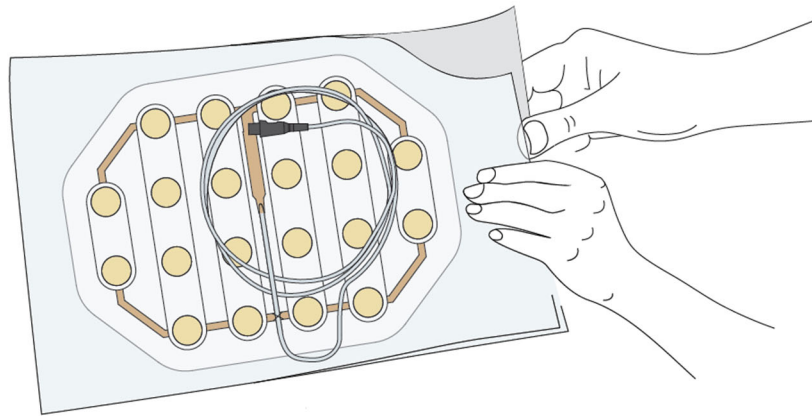
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- You will need four (4) ILE transducer arrays (Sterile) every 3-4 days in order to maintain treatment with Optune Lua.
- You will need to make sure you have the right sized transducer arrays for your body size.
- Make sure you have ample supply of ILE transducer arrays to keep you going until your next visit to your physician.

## 11 REMOVING THE ILE TRANSDUCER ARRAY FROM ITS PACKAGE

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- Open the see-through envelope of four (4) ILE transducer arrays by gently pulling apart the opposing edges of the envelope. Hold the transducer array as shown in the illustration.



## 12 PREPARING YOUR SKIN FOR TRANSDUCER ARRAY PLACEMENT

---

1. Wash your skin on the chest abdomen back and flanks using a gentle soap.
2. Remove any remnant adhesive from your skin from prior transducer arrays by wiping with baby oil.
3. If you have any hair on your torso, shave your entire torso using an electric shaver. Make sure no stubble is left.
4. Wipe your skin with 70% Alcohol (medical grade – any manufacturer).
5. If the skin is red, apply the steroid cream prescribed to you by your physician.
6. If you have any sores on your skin treat them as instructed by your treating physician.
7. Wait at least 30 minutes and gently wipe your skin again with 70% Alcohol to facilitate adhesion of the transducer arrays to your skin.

### 13 PLACING THE TRANSDUCER ARRAYS

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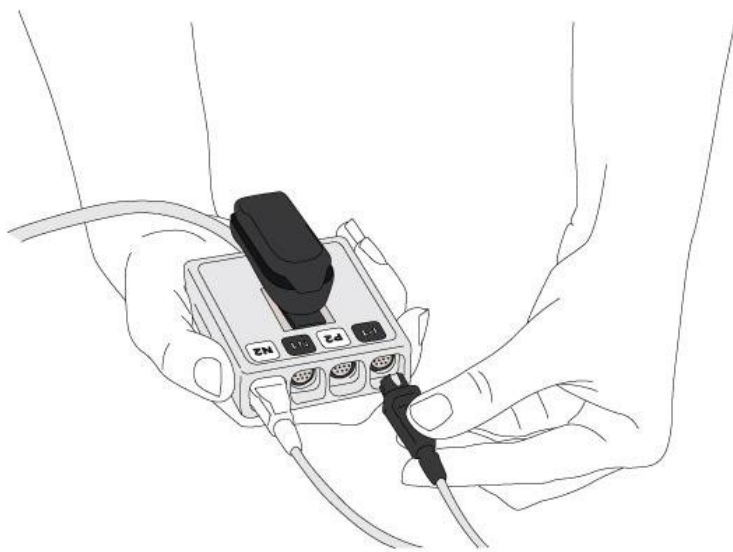
Once every 3-4 days (about twice a week) perform the following steps to replace your transducer arrays. Note, if this is the first time you use the ILE Transducer Arrays, ignore the first step (removal).

1. Remove the transducer arrays already applied to your skin by peeling the medical tape away from your skin.
2. Note the black and white color of the transducer array connectors - each pair of the same color will be positioned opposite to each other on your body.
3. Remove the transducer array liner from the first transducer array.
4. Place the transducer array on your chest in the same location as before but shifting the transducer array 2 cm to avoid areas of redness.
5. Place the other three transducer arrays in the same fashion.
6. You will need to ask for assistance from a friend or family member to place the back transducer array(s).
7. Press the entire edge of the transducer array tape to your skin.

## 14 CONNECTING THE TRANSDUCER ARRAYS TO THE DEVICE

---

1. Connect the four black and white Transducer Array connectors to the corresponding black and white coded sockets on the Optune Lua connection cable.
2. Press firmly to verify the connectors are inserted all the way.
3. Collect the transducer array wires together and bind with a small piece of tape where convenient.
4. You may clip the connection cable clip to your belt.



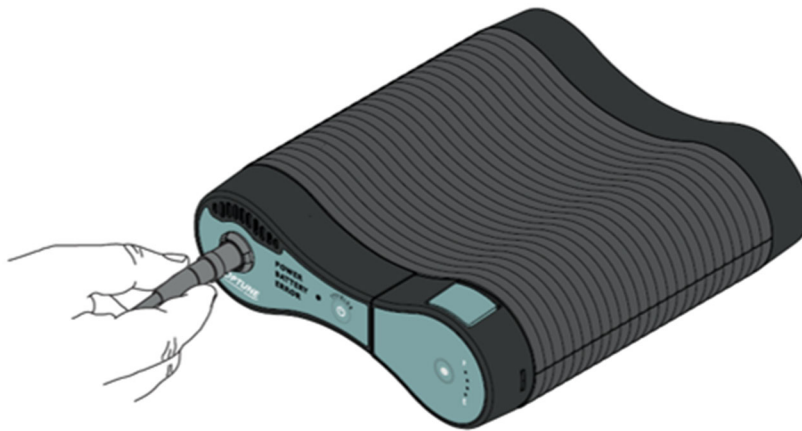
## 15 THE CONNECTION CABLE

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The connection cable is the coiled, stretchy cord that runs from the connection box to the device. The four transducer array connectors (two blacks and two whites) are plugged into the connection box. The black and white coding matches with the transducer array position on the body.

Follow the instructions to connect to the device:

1. Verify that the arrow on the connection cable facing up and is aligned with the arrow on the connector socket of the device and plug in the connection cable.
2. Push in the connector until you hear a snap. It indicates that the connector is in its place.



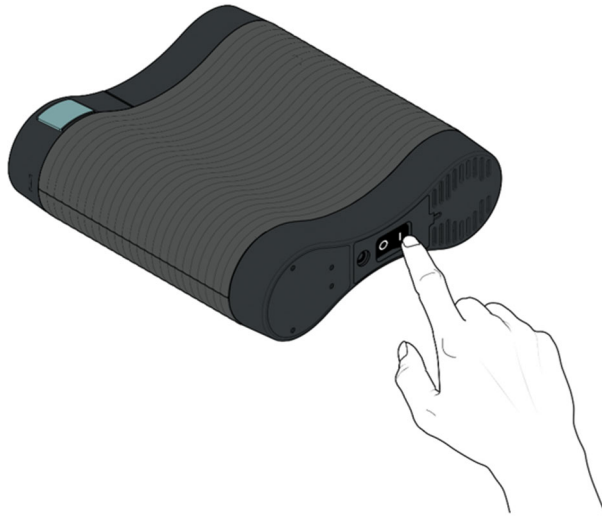
## 16 STARTING AND STOPPING THE DEVICE

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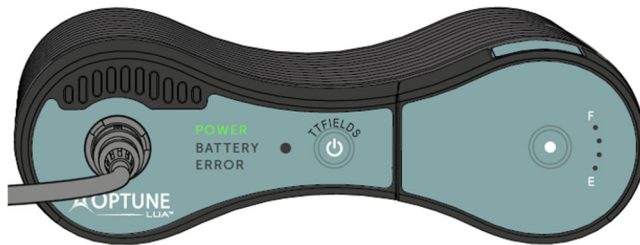
### To start treatment:

The Transducer Arrays should be attached to your body.

1. Plug the transducer arrays into the connection cable box (see Sections 14 and 15).
2. Plug the connection cable into the device, aligning connector arrow with socket arrow (see Section 15).
3. Connect a power source - either a charged battery (Section 1717) or a power supply (Section 1919) to the device.
4. Turn ON the device by using the power switch.

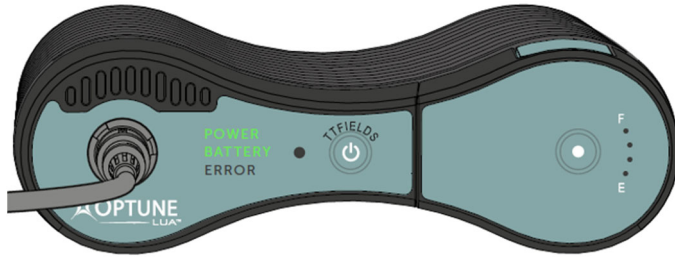


5. Wait about 10 seconds for the self-check to be completed, until the green “POWER” indicator illuminates.

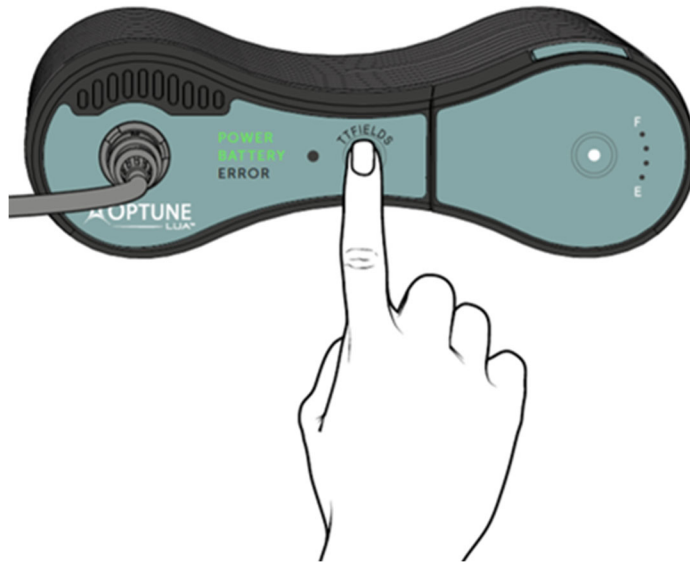




NOTE: If a charged battery is installed (and no power supply is connected), the green "BATTERY" indicator illuminates. If the device is connected to the power supply, it will be operated from the power supply and the "BATTERY" indicator will turn off.



6. Activate TTFields by pressing the TTFields ON/OFF button.



The "TTFIELDS" indicator, above the TTFields ON/OFF button, should illuminate in blue and stay on while the treatment is ON.

NOTE:

If the blue indicator doesn't illuminate, then the treatment is OFF and you should check the setup and restart the procedure. If, after this, the indicator lights do not light up, refer to the Troubleshooting Guide (Section 2424). If you still have problems, contact Novocure technical support (Section 2525).

The green, blue and yellow indicators automatically dim in a dark room. The red "ERROR" indicator illumination level is permanent.

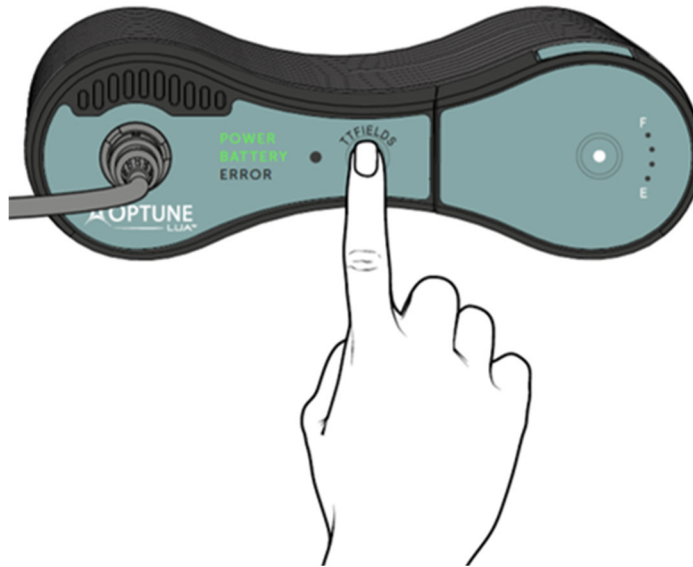
If the TTFields button isn't pressed within about 10 minutes after the device is turned ON, a notification signal alarm sounds along with a flashing blue "TTFIELDS" indicator, indicating that the therapy is OFF. This is a reminder to start the therapy. The TTFields button should be pressed once to silence the alarm and again to start the therapy. The blue "TTFIELDS" indicator will then illuminate.

**To stop treatment:**

Stopping treatment may be performed in each of the following situations:

- A. When the device is running properly, and you would need to take a break:
  1. Stop treatment by pressing TFields button. TFields therapy stops, indicated by the blue “TTFIELDS” indicator turn OFF.

NOTE: Device power is still ON.



2. Turn OFF the device by using the power switch.



B. If an error occurs:

If an error occurs, the device stops the treatment and sounds a loud beeping alarm. The red “ERROR” indicator illuminates (as shown below).

1. Press TTFields button to stop the alarm. The red “ERROR” indicator will turn OFF. If the alarm sound persists, proceed to the next step to silence the alarm.
2. Turn OFF the device by using the power switch.



C. If the Low BATTERY Indicator lights up:

When your battery runs out (after about one hour), the TTFields output will shut down (device stops the treatment) and an alarm will sound.

NOTE: The alarm sound is identical to alarm that the device sounds when an error occurs. However, in this case, both the yellow “BATTERY” and red “ERROR” indicators light up.

1. Press the TTFields button to stop the alarm. The red “ERROR” indicator turns OFF.
2. Turn OFF the device by using the power switch.
3. Replace the battery (see Section 1717).



## 17 CONNECTING AND DISCONNECTING THE BATTERY

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The Optune Lua Treatment Kit is provided with four rechargeable batteries. Optune Lua operation requires one battery at a time. The other three batteries should stay in the battery charger.

If you plan to be away from home for more than one hour, carry extra batteries.

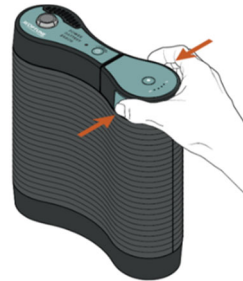
1. Slide the battery into the device.
2. Gently push the battery down until a click is heard, indicating it is fully latched.

NOTE: Take care not to drop the battery in place or force it into the battery slot.

3. Replace the battery each time it runs out (when the green "BATTERY" indicator turns yellow)



Gently press down to lock the battery in place.



To remove the battery from the slot, press both blue buttons on the sides of the battery and lift up.

Recharge the batteries in the charger (Section 18) for two to four hours. The batteries will keep most of their charge after being removed from the charger for several days but eventually will lose their charge. It will not hurt the batteries to keep them in the charger after they are fully charged so you can leave them there if they are not needed.

You can charge and use the batteries many times for about six to nine months. Over time, the length of time that the batteries can run the device (before the yellow low BATTERY indicator illuminates and the alarm beeps) will get shorter. If the time from treatment start with a full battery to low battery alarm, audible alarm sounds and the red "ERROR" indicator illuminates falls below 50 minutes contact technical support (Section 25) to get replacement batteries.

The battery light will turn from green to yellow when the battery charge falls below a threshold. This is an indication that the battery should be changed soon. The treatment will continue to run while the yellow low BATTERY indicator is illuminated until the audible alarm sounds and the red "ERROR" indicator illuminates. Once this happens the treatment will stop and the device must be turned off and the battery replaced.

When the “BATTERY” indicator turns yellow, there are two ways to continue your treatment:

A. Option one:

To be used if near the direct wall power supply, allows you to connect the power supply without interrupting therapy. This can be used before the battery is completely depleted, and before the device has alarmed. Follow the instructions:

1. Plug in the wall power supply to back of the Optune Lua device (Section 19). Treatment continues while Device indicator indicates that it is no longer operated by battery power.
2. Push the two blue buttons on both battery sides and remove it by sliding outside from device.
3. Charge the removed battery (Section 18).
4. Continue the treatment using the wall power supply.

B. Option Two:

If you are not near a wall power supply, follow the instructions to replace the battery:

NOTE: If the battery is totally depleted, start from step 2

1. Press the TTFields button to stop the treatment.
2. Turn OFF the device by using the power switch (on the back side of the device).
3. Push the two blue buttons on both battery sides and remove it by sliding outside from device.
4. Select another fully charged battery.
5. Slide the fully charged battery into the device.
6. Gently push the battery down until a click is heard, indicating it is fully latched.
7. See the next section to check the battery gauge.
8. Turn ON the device by using the power switch and wait about 10 seconds until the device completes with the self-check.
9. Start treatment by pressing the TTFields button (Section 16).
10. Insert the used battery into the battery charger for recharging (Section 18).

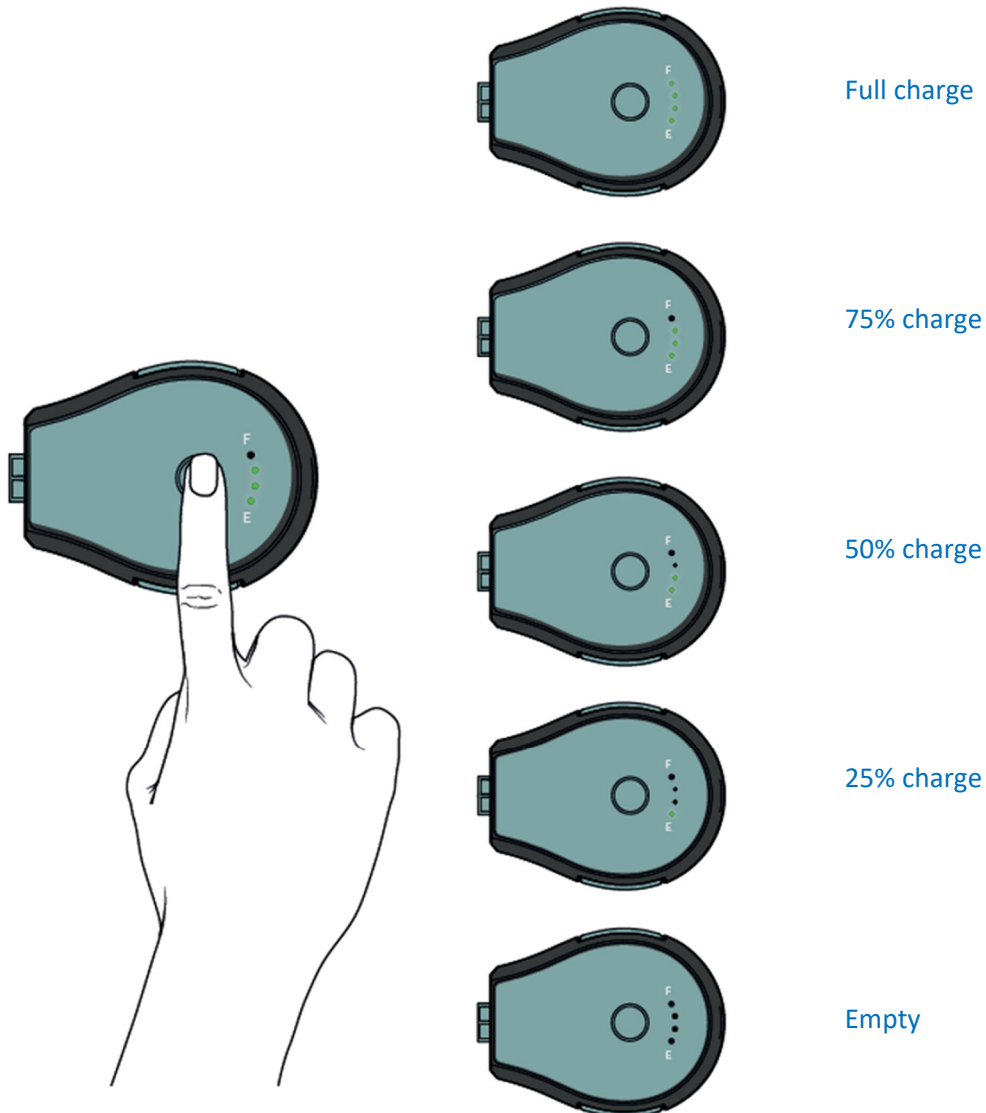
## 18 CHARGING THE BATTERY

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### Checking the Battery Gauge

While you are using Optune Lua, you may want to check how much energy is left in your battery. Checking the battery will not interfere with, or stop, your treatment.

To check the battery capacity, press once on the button on the top of the battery. The battery capacity will be indicated by the lighted gauge to the right of the button. The gauge reads from Full (F) to Empty (E) like a gas gauge in a car.



The battery charger recharges used batteries. The battery charger uses power from a standard wall outlet. Each battery sits in a slot that connects it directly to the charger.

Before charging the batteries, plug the charger power cord into a standard wall outlet and turn ON the power switch at the charger rear side. The front lights of the charger will come on during a self-check then the small light in the center of the front panel will light up green indicating power is applied.

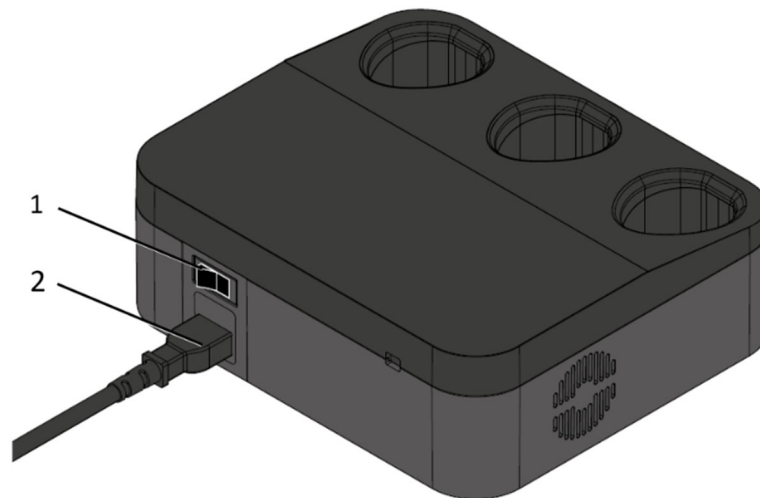
**To recharge a used battery:**

1. Place the used battery in one of the three openings in the top of the charger. Slide the battery in until it is fully in place.
2. The light directly in front of the opening where the battery is plugged in will illuminate flashing green. This indicates the battery is charging. The green light will flash faster once the battery has been charged to 95% of its capacity. You can also check the battery gauge while charging to get information regarding the amount of charge in the battery.
3. When the battery is fully charged (about 2 to 4 hours), the charge light will turn from flashing green to solid green. The solid green light will disappear upon removal of the battery or the disconnection of the charger from the standard wall outlet.

If a light on the front panel turns red, this indicates that there is a fault with the battery or charger and you should contact technical support for assistance. Do not use a battery if it creates a red light on the charger.

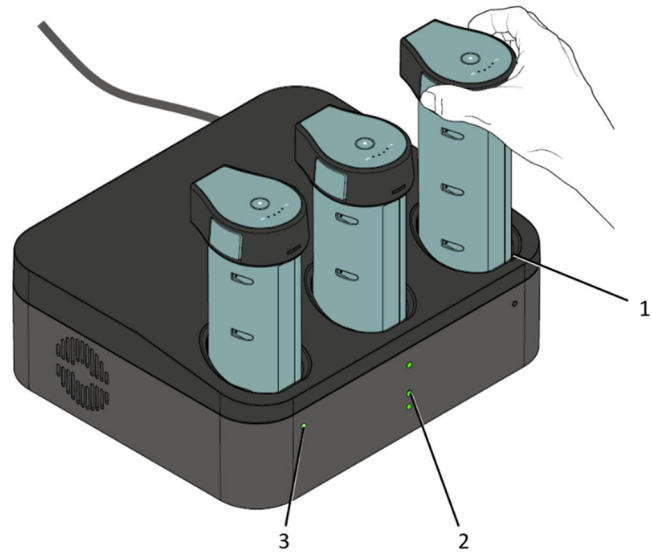
Keep the batteries in the charger even after they are fully charged. This will not harm the batteries.

1. Power Switch
2. Power Cord



Battery Charger Rear View Showing the Power Switch and Where the Power Cord Connects

1. Battery Charging Slot
2. Charger Power Indicator
3. Battery Charge Indicator



Front view of the battery charger showing how the batteries are inserted into the charger

NOTE: The charger is not intended for use in the presence of flammable mixtures.



## 19 USING THE PLUG-IN POWER SUPPLY

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When you plan to stay in one place for a while, like when you are sleeping, you may use the plug-in power supply instead of the batteries. Unlike the batteries, there is no limit to how long the device can work when you use the plug-in power supply. The plug-in power supply will work with either US (120 VAC) or European (230 VAC) outlets.

NOTE: It is normal for the power supply to become warm when in use. If the power supply becomes too hot to touch, unplug it and contact technical support (Section 25).

When the device has a battery in, and is also connected to the wall power supply, it will utilize the wall power supply as the preferred power source. When the wall power cord is plugged in while the device is operated from the battery, the device will automatically switch from battery power to wall supply power.

### Connecting the Plug-In Power Supply

1. Plug in the power supply cord into a standard wall outlet.

NOTE:

You do not need to remove the battery from the device to use the wall power supply.

Please note that a battery in the device will not charge while the device is plugged into the wall power supply.

If the TTFields are activated, you do not need to turn them OFF.

2. Plug the power supply connector into the power supply port, located on the back side of the device (next to the power switch).
3. If the TTFields are already activated, the device will automatically switch to wall power supply without interruption of the treatment.
4. If the device is OFF, turn ON the power switch and wait about 10 seconds until the device completes with the self-check. Then, Push the TTFields button to start the treatment (as described in Section 16).

### To Disconnect the Plug-In Power Supply and Go Back to Battery Power

Ensure that a charged battery is properly inserted in the device before removing the wall power supply. If the TTFields are activated, you need to turn them OFF before removing the wall power supply. The device will shut down and restart using battery power once the power supply is removed. In that case you will be required to push the TTFields button to start the treatment (as described in Section 16), after the self-check is completed.

1. Remove the power supply connector from the back side of the device. After about eight seconds, the "BATTERY" indicator on the front panel illuminates.
2. Store the plug-in power supply for future use.

## 20 DISCONNECTING FROM THE DEVICE

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There are two ways to unplug the device in order to take a break from treatment:

- To unplug the connection cable from the device.
- To unplug the four transducer arrays from the connection cable.

### To Unplug the Connection Cable from the Device

1. Stop treatment by pressing the TTFIELDS button.
2. Turn OFF the device by using the power switch.
3. Hold the connector latch-sleeve and pull out the connection cable from the socket.

CAUTION! Do not pull on the cord!

You may now move around without the device, but you will still be connected to the connection cable and box.

To start treatment again after your break:

1. Plug the connection cable into the port with the arrows pointing up.
2. Turn ON the device by using the power switch. Wait about 10 seconds until the device completes with the self-check.
3. Activate TTFIELDS by pressing the TTFIELDS button.

### To Unplug the Transducer Arrays from the Connection Cable

To take a break from treatment and completely disconnect from the device, unplug the transducer arrays from the connection cable box. The four transducer arrays are plugged into the connection cable box (as described in Section 14). The connection cable remains plugged into the device socket.

1. Stop treatment by pressing the TTFields button.
2. Turn OFF the Optune Lua device by using the power switch.
3. Unplug the four transducer arrays from the connection box by pulling their connectors.

NOTE: You may have to wiggle the transducer array connectors gently to remove them. Do not pull on the cord.



To restart treatment:

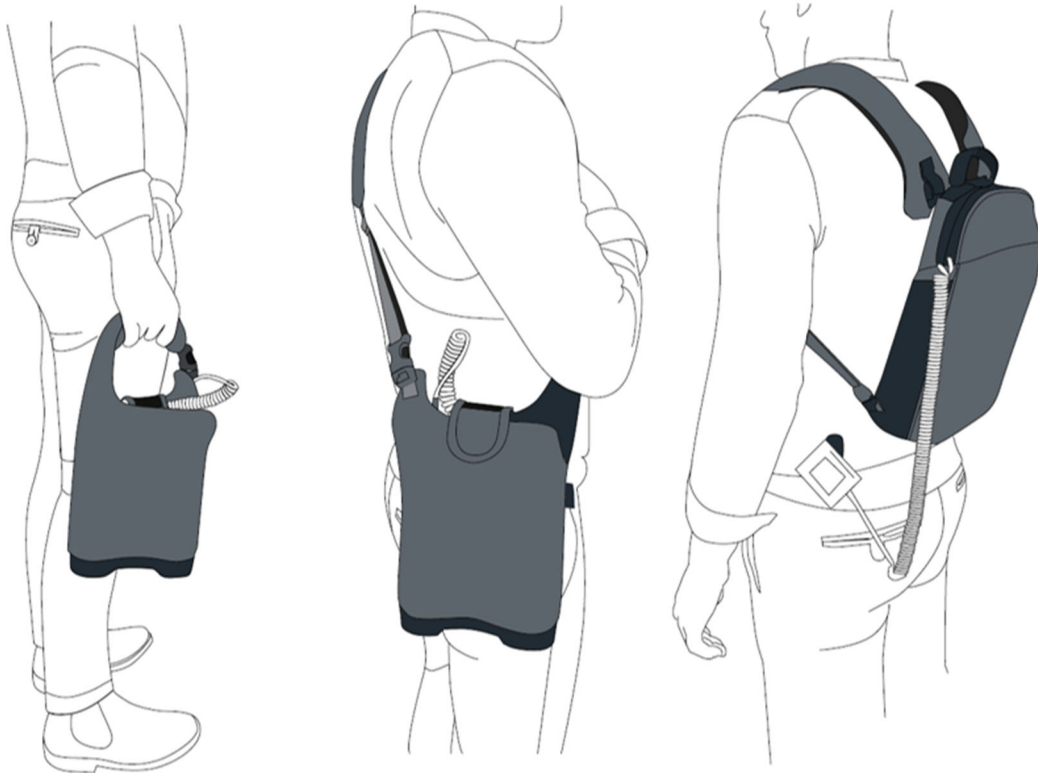
1. Plug the four transducer arrays into its matching color (black or white) in the connection box.
2. Turn ON the device by using the power switch and wait about 10 seconds until the device completes with the self-check.
3. Activate TTFields by pressing the TTFields button.

## 21 CARRYING THE DEVICE





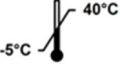



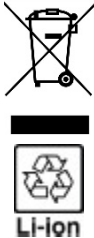



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Both the electric field generator and the battery fit in a carrying bag. The bag can be carried in one of three ways: by the handle on top or over the shoulder/ cross-body with a carrying strap attached, or as a backpack as shown below.

NOTE: Do not place the device in a different bag. Optune Lua has a fan on the inside that needs air flow. The bag that comes with the device is designed to allow for proper air flow. If you put the device in a bag without proper air flow, it could overheat and stop the treatment. If this happens, you will hear an alarm.



## 22 GLOSSARY OF GRAPHIC SYMBOLS

	<p>Consult the instructions for use for important cautionary information such as warnings and precautions</p>
	<p>Date of Manufacturing</p>
	<p>Fragile – handle with care</p>
	<p>Follow instructions for use</p>
	<p>Do not expose to temperatures below -5°C or above 40°C</p>
	<p>Do not expose to humidity below 15% or above 93%</p>
	<p>Do not enter rooms with high humidity or danger of direct exposure to water while wearing the device. Do not use the device if not within its carrying bag. Do not expose the device to direct rain.</p>
	<p>The charger and power supply are for indoor use only</p>
	<p>Batteries are Lithium Ion. Contact technical support to arrange for proper disposal of batteries that are used up or no longer in use</p>
	<p>Optune Lua (device, additional parts and transducer arrays) should be kept away from extreme heat and sources of radiation</p>
	<p>BF type applied part – symbolizes the part which comes in contact with the patient Applied part – part of the ME equipment that in normal use necessarily comes into physical contact with the patient for ME equipment or an ME system to perform its function.</p>
	<p>Expiration date – do not use beyond this date</p>

	<p>Power ON / OFF switch for the device and battery charger: When the switch is in the I position the device is ON and will light up green. When the switch is in the O position the device is OFF</p>
	<p>Do not use the ILE Transducer arrays if their packaging is breached.</p>
	<p>The ILE Transducer Arrays are for single use and should not be re-used.</p>
	<p>The ILE Transducer Arrays are sterilized by Gamma irradiation</p>
	<p>Do not re-sterilize</p>
	<p>Batch code</p>
	<p>Catalogue number</p>
	<p>Serial number</p>
	<p>Class II equipment per IEC 60601-1</p>
<p><b>Rx only</b></p>	<p>Prescription device</p>
	<p>Manufacturer information: Novocure GmbH, Park 6, CH-6039 Root D4, Switzerland</p>
<p><b>IP21</b></p>	<p>Protects persons against access to hazardous parts with fingers. Protects the equipment inside the enclosure against ingress of solid foreign objects of 12.5 mm in diameter or greater. Protects the equipment inside the enclosure against ingress of vertical falling water drops.</p>
<p><b>IP22</b></p>	<p>Protects persons against access to hazardous parts with fingers. Protects the equipment inside the enclosure against ingress of solid foreign objects of 12.5 mm in diameter or greater. Protects the equipment inside the enclosure against ingress of vertical falling water drops when enclosure is tilted up to 15°.</p>

## 23 ENVIRONMENTAL CONDITIONS FOR OPERATION, STORAGE AND TRANSPORTATION

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### Conditions for operation

All system components shall be normally used under conditions specified below:

- Mainly for home use.
- For indoor use only (charger and power supply)
- Not for use in shower, bath tub or sink, or in heavy rain
- Not for use in presence of flammable mixtures
- Can be dropped on floor, there shall be no safety hazard, not expected to function anymore

Conditions of visibility: any

Cleaning: all system components can be periodically cleaned with damp cloth, to remove dust and regular soil.

Physical operation conditions for all system components:

- Temperature range: -5°C to +40°C (23°F to 104°F)
- Relative Humidity range: 15-93%
- Ambient pressure range: 700-1060hPa

### Conditions for storage

- Temperature range: -5°C to +40°C (23°F to 104°F) for the device and additional parts
- Temperature range: 5°C to +27°C (41°F to 80°F) for the transducer arrays

### Conditions for transport

Transportation of the device, ILE Transducer Arrays and additional parts shall be possible using air/ground transportation in weather protected conditions as specified below:

- Temperature range: -5°C to +40°C (23°F to 104°F)
- Maximal relative humidity 15-93%
- No direct exposure to water

### Expected Service Life

- Optune Lua device – 12 months
- Connection cable – 11 months
- Power supply – 5 years
- Battery – 11 months (or until the expiration date)
- Charger – 7 years
- ILE Transducer Arrays have an expiration date. Please do not use the arrays after the expiration date.

## 24 TROUBLESHOOTING

Note, when calling your device support specialist or the technical support line, please have the serial number of the equipment accessible

Problem	Possible causes	Actions to be taken
Device POWER indicator does not light up after turning ON the device	<ol style="list-style-type: none"> <li>1. Device not connected to power source</li> <li>2. Battery depleted</li> <li>3. Battery malfunction</li> <li>4. If power supply – not properly plugged into the wall</li> <li>5. Device malfunction</li> <li>6. Power supply malfunction</li> </ol>	<ol style="list-style-type: none"> <li>1. If on battery – check battery gauge to verify it is not depleted. If it is – replace with a charged battery or to power supply</li> <li>2. Verify both the device and the power source are properly connected and re-try</li> <li>3. Evaluate the integrity of all connectors. Nothing should appear to be damaged or broken in any way</li> <li>4. If device cannot be powered on by either the battery or the wall power supply or if anything appears to be damaged do not use the device</li> <li>5. Call technical support at 855.281.9301</li> </ol>
Any cable detached from transducer array/ connection cable/ device	<ol style="list-style-type: none"> <li>1. Too much physical force to cables</li> <li>2. Device malfunction</li> </ol>	<ol style="list-style-type: none"> <li>1. Silence the notification signal by pressing the TTFields button</li> <li>2. Evaluate the connectors. If intact – reconnect and re-start therapy</li> <li>3. If anything appears damaged or cannot be properly connected do not try to use the device</li> <li>4. Call technical support at 855.281.9301</li> </ol>
Device dropped or wet	Incorrect use	<ol style="list-style-type: none"> <li>1. Press TTFields button to stop therapy</li> <li>2. Turn OFF power switch</li> <li>3. Disconnect from power</li> <li>4. Call technical support at 855.281.9301</li> </ol>
Device alarm on, and low BATTERY indicator is yellow	<ol style="list-style-type: none"> <li>1. Low battery</li> <li>2. Device is turned ON, but the therapy has not been activated</li> </ol>	<ol style="list-style-type: none"> <li>1. Replace battery as described above in Section 17</li> <li>2. Turn ON treatment</li> <li>3. Press the TTFields button to stop the alarm</li> <li>4. Wait a few seconds then press the TTFields button again</li> <li>5. If the blue lights around the TTFields button light up – the therapy has now been activated</li> </ol>



Problem	Possible causes	Actions to be taken
		<p>If the notification signal recurs within a few minutes:</p> <ol style="list-style-type: none"> <li>1. Silence the notification signal and power the device down completely</li> <li>2. Disconnect all equipment and make sure that nothing appears to be damaged or broken. If something is – replace the damaged item before trying to power the device back</li> <li>3. Re-connect all equipment in proper order and power the device back up. Verify the self-check is completed and press the TTFields button</li> <li>4. Check vents on device to make sure they are not blocked</li> <li>5. If lying down, get up and move your body</li> <li>6. Make sure transducer arrays are well stuck to the body, add tape if needed</li> <li>7. Restart treatment</li> <li>8. If alarm keeps going, turn OFF the device and call technical support at 855.281.9301</li> </ol>
<p>Device alarm is flashing, the "TTFIELDS" indicator above the TTFields button will flash blue and audio sound 3 very short beeps, stops for 2.5 seconds and beeps 3 times again</p>	<p>Therapy Timeout</p>	<p>The notification alarm on the device will sound if it is powered on for about 10 minutes, but therapy is not initiated. This is a reminder to start therapy and does not indicate a malfunction.</p> <ol style="list-style-type: none"> <li>1. Silence the notification alarm by pressing the TTFields button then wait a few seconds and press the TTFields button again to initiate treatment. The blue indicator around the TTFields button will illuminate to indicate therapy is now on</li> <li>2. If you encounter further alarms please review the following troubleshooting descriptions in this section.</li> </ol>
<p>Low BATTERY indicator remains on after battery replaced</p>	<ol style="list-style-type: none"> <li>1. Charger malfunction</li> <li>2. Battery malfunction</li> <li>3. Device malfunction</li> </ol>	<ol style="list-style-type: none"> <li>1. Replace battery with an additional charged battery</li> <li>2. If problem is not fixed – call technical support at 855.281.9301</li> </ol>

Problem	Possible causes	Actions to be taken
<p>When powering on the device a continuous notification alarm sounds and all lights remain on indefinitely. Device does not complete the self-check.</p>	<ol style="list-style-type: none"> <li>1. Device is too hot</li> <li>2. Device malfunction</li> <li>3. Power Source Malfunction</li> </ol>	<ol style="list-style-type: none"> <li>1. Power the device off completely using the power switch</li> <li>2. Verify the device is not hot to the touch</li> <li>3. Connect the device to a different power source and try powering on again</li> <li>4. If device cannot be powered on by either the battery or the wall power supply or if anything appears to be damaged, please contact technical support</li> </ol>
<p>Redness of the skin beneath the transducer arrays</p>	<p>Common side effect</p>	<ol style="list-style-type: none"> <li>1. Use steroid cream prescribed by your doctor when replacing transducer arrays.</li> <li>2. Place transducer arrays in a location shifted by 3/4 of an inch (2 cm) from the last location (so the adhesive gel is between the red marks).</li> </ol> <p>If the redness gets worse:</p> <ol style="list-style-type: none"> <li>1. See your treating doctor</li> </ol>
<p>Blisters beneath the transducer arrays</p>	<p>Rare side effect</p>	<p>See your treating doctor</p>
<p>Itching beneath the transducer arrays</p>	<p>Rare side effect</p>	<ol style="list-style-type: none"> <li>1. Use steroid cream prescribed by your doctor when replacing transducer arrays.</li> <li>2. Place transducer arrays in a location shifted by 3/4 of an inch (2 cm) from the last location (so the adhesive gel is between the red marks).</li> </ol> <p>If the itching gets worse:</p> <ol style="list-style-type: none"> <li>1. See your treating doctor</li> </ol>
<p>Pain beneath the transducer arrays</p>	<p>Rare side effect</p>	<ol style="list-style-type: none"> <li>1. Stop treatment</li> <li>2. See your treating doctor</li> </ol>

## 25 ASSISTANCE AND INFORMATION

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### Technical support:

For technical support call at 1-855-281-9301 (toll free) or email [support@novocure.com](mailto:support@novocure.com).

Call or email technical support for help with operation of the system, troubleshooting alarms, or to get replacement parts or transducer arrays.

### Clinical support:

If you feel any change in your health or any side effects from the treatment call your doctor right away.

### Traveling with Optune Lua

The system's batteries contain lithium ion material and are restricted from being checked as luggage for passenger aircraft travel. They can be carried in the passenger cabin. Please contact nCompass™ Support if you have questions related to travel restrictions.

Note: The Optune Lua device and transducer arrays will activate metal detectors.

## 26 DISPOSAL

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Please contact Novocure to arrange for proper disposal of used transducer arrays. Do not throw them in the trash.

## 27 MALIGNANT PLEURAL MESOTHELIOMA (MPM)

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### What is Cancer of the Linings of the Lungs?

In simple terms, lung cancer is a growth of cells that form a tumor in the lungs. MPM is a type of lung cancer that develops from the linings of the lungs. Just like any other form of cancer, these tumors can spread to other parts of the lungs and even to the rest of the body. Even before the tumor grows and spreads, it could cause problems breathing, coughing, bleeding and other problems. Symptoms of lung cancer depend on where and how big the tumor is.

About 3,000 patients in the U.S. are diagnosed with MPM every year. MPM is usually caused by exposure at work to asbestos. MPM is a very serious disease. Less than 5% of patients with MPM are alive after 5 years even using the best available treatments.

### Can Cancer of the Linings of the Lungs Be Treated?

There are currently four main options to treat MPM:

Surgery – Few patients can be cured by taking out all of the tumor

Radiation – Following surgery, some patients have radiation therapy

Cancer Drugs – most MPM patients take cancer drugs. There are several approved drugs to treat MPM.

Optune Lua together with cancer drugs

Radiation therapy and surgery can help people with MPM live longer than if they had no treatment. Adding Optune Lua to cancer drugs may help people with MPM to live longer than with cancer drugs alone. Surgery, radiation and cancer drugs have side effects. These side effects include pain, hair loss, skin irritation, nausea, vomiting, loss of appetite, effects related to breathing, and tiredness. Optune Lua leads to skin related problems under the transducer arrays in many people.

## 28 EMITTED RADIATION AND ELECTROMAGNETIC COMPATIBILITY

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The Optune Lua device and the accompanying battery charger (ICH9100) and power supply (SPS9200) need special precautions regarding EMC and need to be installed and put into service according to the EMC information provided below.

Portable and mobile RF communications equipment can affect the Optune Lua System and the accompanying battery charger.

The Optune Lua device (TFT9200) should be used with the following cables and additional parts only:

1. connection cable (CAD9100)
2. ILE Transducer Arrays (ILE1010; ILE1030; ILE1010W; ILE1030W)
3. battery (IBH9200)
4. power supply (SPS9200)
5. Battery charger (ICH9100)
6. Unshielded AC mains cables for indoor use only with a maximal length of 1.5m

The use of accessories, parts and cables other than those specified may result in increased EMISSIONS or decreased IMMUNITY of the Optune Lua System.

**Table 1 – Guidance and MANUFACTURER’S declaration – ELECTROMAGNETIC EMISSIONS – for all ME EQUIPMENT and ME SYSTEMS**

Guidance and manufacturer’s declaration – electromagnetic emissions		
The Optune Lua system is intended for use in the electromagnetic environment specified below. The customer or the user of the Optune Lua should assure that it is used in such an environment.		
Emissions test	Compliance	Electromagnetic environment – guidance
RF emissions CISPR 11	Group 1	The Optune Lua 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.
RF emissions CISPR 11	Class B	The Optune Lua Treatment Kit is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Complies	

Guidance and manufacturer’s declaration – electromagnetic emissions

The ICH9100 charger and the SPS9200 power supply are intended for use in the electromagnetic environment specified below. The customer or the user of the ICH9100 charger and the SPS9200 power supply should assure that it is used in such an environment.

Emissions test	Compliance	Electromagnetic environment – guidance
RF emissions CISPR 11	Group 1	The ICH9100 charger and the SPS9200 power supply use RF energy only for their internal function. Therefore, their RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The ICH9100 charger and the SPS9200 power supply are suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Complies	

Warning: The Optune Lua System, the ICH9100 charger and the SPS9200 power supply should not be used adjacent to or stacked with other equipment.

**Table 2 – Guidance and MANUFACTURER’S declaration – ELECTROMAGNETIC IMMUNITY – for all ME EQUIPMENT and ME SYSTEMS**

Guidance and manufacturer’s declaration – electromagnetic immunity			
The Optune Lua (model NovoTTF-200T) system is intended for use in the electromagnetic environment specified below. The customer or the user of the Optune Lua should assure that it is used in such an environment.			
Emissions test	IEC 60601 Test level	Compliance level	Electromagnetic environment – guidance
Electrostatic discharge (ESD) IEC 61000-4-2	±8 kV contact, ± 2 kV, ± 4 kV, ±8 Kv, ± 15 kV air	±8 kV contact, ± 2 kV, ± 4 kV, ±8 kV ± 15 kV air	The relative humidity should be at least 5%.
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines ±1 kV for input/output lines	±2 kV for power supply lines ±1 kV for input/output lines 100 kHz repetition frequency	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	± 0,5 kV, ±1 kV line to line ± 0,5 kV, ± 1 kV, ±2 kV line to ground	± 0,5 kV, ±1 kV line to line ± 0,5 kV, ± 1 kV, ±2 kV line to ground	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	0 % UT; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315°  % UT; 1 cycle and 70 % UT; 25/30 cycles Single phase: at 0°  0 % UT; 250/300 cycle	0 % UT; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° 0 % UT; 1 cycle and 70 % UT; 25/30 cycles Single phase: at 0°  0 % UT; 250/300 cycle	Mains power quality should be that of a typical commercial or hospital environment.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
NOTE UT is the a.c. mains voltage prior to application of the test level.			

Guidance and manufacturer's declaration – electromagnetic immunity


The ICH9100 charger and the SPS9200 power supply are intended for use in the electromagnetic environment specified below. The customer or the user of the ICH9100 charger and the SPS9200 power supply should assure that they are used in such an environment.

Emissions test	IEC 60601 Test level	Compliance level	Electromagnetic environment – guidance
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV air	± 8 kV contact ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV air	The relative humidity should be at least 5%.
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines ±1 kV for input/output lines	±2 kV for power supply lines ±1 kV for input/output lines 100 kHz repetition frequency	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	± 0,5 kV, ± 1 kV line to line  ± 0,5 kV, ± 1 kV, ± 2 kV line to ground	± 0,5 kV, ± 1 kV line to line  ± 0,5 kV, ± 1 kV, ± 2 kV line to ground	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	0 % UT; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315°  % UT; 1 cycle and 70 % UT; 25/30 cycles Single phase: at 0°  0 % UT; 250/300 cycle	0 % UT; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° 0 % UT; 1 cycle and 70 % UT; 25/30 cycles h) Single phase: at 0°  0 % UT; 250/300 cycle	Mains power quality should be that of a typical commercial or hospital environment.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.

NOTE UT is the a.c. mains voltage prior to application of the test level = 120V and 230V




**Table 3 – Guidance and MANUFACTURER’S declaration – ELECTROMAGNETIC IMMUNITY – for ME EQUIPMENT and ME SYSTEMS that are not LIFE-SUPPORTING**

Guidance and manufacturer’s declaration – electromagnetic immunity			
The Optune Lua treatment kit is intended for use in the electromagnetic environment specified below. The customer or the user of the Optune Lua treatment kit should assure that it is used in such an environment.			
Immunity test	IEC 60601 test level	Compliance level	Electromagnetic environment – guidance
<p>Conducted RF IEC 61000-4-6</p> <p>Radiated RF IEC 61000-4-3</p>	<p>3 V 0,15 MHz – 80 MHz 6 V in ISM bands between 0,15 MHz and 80 MHz</p> <p>80 % AM at 1 kHz (table 8.5.1)</p> <p>10 V/m</p>	<p>3 V 0,15 MHz – 80 MHz 6 V in ISM bands between 0,15 MHz and 80 MHz</p> <p>80 % AM at 1 kHz</p> <p>10 V/m 80 MHz to 2.7 GHz 80 % AM at 1 kHz</p>	<p>Portable and mobile RF communications equipment should be used no closer to any part of the NovoTTF-200T treatment kit, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.</p> <p>Recommended separation distance</p> $d = \frac{6}{E} \sqrt{P}$ <p>Where P is the maximum power in W, d is the minimum separation distance in m, and E is the IMMUNITY TEST LEVEL in V/m.</p> <p>Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey<sup>a</sup>, should be less than the compliance level in each frequency range.</p> <p>Interference may occur in the vicinity of equipment marked with the following symbol:</p> 
<p>NOTE These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.</p>			
<p>a. Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Optune Lua treatment kit is used exceeds the applicable RF compliance level above, the Optune Lua treatment kit should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Optune Lua treatment kit.</p>			

Guidance and manufacturer's declaration – electromagnetic immunity

The ICH9100 charger and the SPS9200 power supply are intended for use in the electromagnetic environment specified below. The customer or the user of the ICH9100 charger and the SPS9200 power supply should assure that they are used in such an environment.

Immunity test	IEC 60601 test level	Compliance level	Electromagnetic environment – guidance
Conducted RF IEC 61000-4-6	3 V 0,15 MHz – 80 MHz 6 V in ISM bands between 0,15 MHz and 80 MHz	3 V 0,15 MHz – 80 MHz 6 V in ISM bands between 0,15 MHz and 80 MHz	<p>Portable and mobile RF communications equipment should be used no closer to any part of the ICH9100 charger and the SPS9200 power supply, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.</p> <p>Recommended separation distance</p> $d = \frac{6}{E} \sqrt{P}$ <p>Where P is the maximum power in W, d is the minimum separation distance in m, and E is the IMMUNITY TEST LEVEL in V/m.</p> <p>Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey<sup>a</sup>, should be less than the compliance level in each frequency range.</p> <p>Interference may occur in the vicinity of equipment marked with the following symbol:</p> 
Radiated RF IEC 61000-4-3	80 % AM at 1 kHz (table 8.5.1)  10 V/m	80 % AM at 1 kHz  10 V/m 80 MHz to 2.7 GHz 80 % AM at 1 kHz	

NOTE These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

- a. Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the ICH9100 charger and the SPS9200 power supply are used exceeds the applicable RF compliance level above, the ICH9100 charger and the SPS9200 power supply are should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the ICH9100 charger and the SPS9200 power supply.

Normal operation: The Optune Lua System is working properly when the blue LED surrounding the TTFields button are lit and no notification signal sounds. The ICH9100 charger is working properly when all the LEDs are lit. The SPS9200 power supply is working properly when the blue LEDs surrounding the TTFields button on Optune Lua System are lit and no notification signal sounds.

**Table 4 – Recommended separation distances between portable and mobile RF communications equipment and the ME EQUIPMENT or ME SYSTEM – for ME EQUIPMENT and ME SYSTEMS that are not LIFE-SUPPORTING**

Rated maximum output power of transmitter W	Separation distance according to frequency of transmitter m						
	380 – 390MHz	430 – 470MHz	704 – 787MHz	800 – 960MHz	1700 – 1990MHz	2400 – 2570MHz	5100 – 5800MHz
The Optune Lua is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the Optune Lua can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and Optune Lua as recommended below, according to the maximum output power of the communications equipment.							
0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3
1.8	0.3	0.3	0.3	0.3	0.3	0.3	0.3
2	0.3	0.3	0.3	0.3	0.3	0.3	0.3
NOTE: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.							
For transmitters rated at a maximum output power not listed above, the recommended separation distance $d$ in meters (m) can be determined using the equation applicable to the frequency of the transmitter, where $P$ is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.							

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