EASEE® System SSCP

Summary of Safety and Clinical Performance

REF: SSCP03EN

Version History

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1.0	01.10.2021	A. Yulzari
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Note: The history of the changes can be found in the last section of this document

Release

Name & Title	Function	Date	Signature
A. Yulzari Clinical Affairs Manager, Precisis GmbH	Author	Aude Yulzari	Digitally signed by Aude Yulzari Date: 2025.07.09 12:01:44 +02'00'
J. Schneider QM, Precisis GmbH	Review	12:42:26 2025.07.09 '00'02+	Joachim Schneider
M. Tittelbach CTO, Precisis GmbH	Approval	Michael Andreas Tittelbach	Digital unterschrieben von Michael Andreas Tittelbach Datum: 2025.07.09 12:49:18 +02'00'

Content

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0 Introduction (professional users)

This summary of safety and clinical performance (SSCP) is created in compliance with Regulation 2017/745/EU (MDR) and medical devices coordination group (MDCG) guidance paper MDCG2019-9 “Summary of safety and clinical performance - A guide for manufacturers and notified bodies”.

0.1 Purpose of the document

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

Following this information there is a summary intended for patients.

0.2 Terms and Abbreviations

A listing of explanation of project specific terminology and acronyms that are used within this document can be found in the following.

Term	Description
AC	Alternating current
AED	anti-epileptic drugs
CS	Common Specification
DC	Direct current
DLS	DC-like stimulation
EEG	Electroencephalogram
FPI	First Patient In
HFS	High Frequency Stimulation
IFU	Instructions for use; also used in the meaning of user manual
LFS	Low Frequency Stimulation
LPI	Last Patient In
LPO	Last Patient Out
PCN	Patient controlled neurostimulation
PMCF	Post Market Clinical Follow-up
(S)AE	(Serious) Adverse Event
SSCP	Summary of Safety and Clinical Performance

Term	Description
tACS/ tDCS	Transcranial AC / DC stimulation
ULFA	ultra low frequency asymmetric stimulation mode

1 Device identification and general information

1.1 Device trade name(s)

EASEE® System (Epicranial Application of Stimulation Electrodes for Epilepsy) is an implantable stimulation device for neurological applications, which is indicated for the treatment of patients with medically refractory focal epilepsy. The following components belong to the EASEE System

- EASEE Power
- EASEE Lead
- EASEE Access
- EASEE Connect
- EASEE Set

The EASEE System and its components are described in clause 3, below.

1.2 Manufacturer's name and address

PRECISIS GmbH
Margot-Becke-Ring 8
69124 Heidelberg
Germany

Tel.: +49 6221 6559300
Fax: +49 6221 6559310
E-mail: info@precisis.de
Web: www.precisis.de

1.3 Manufacturer's single registration number (SRN)

A Single Registration Number is assigned to all medical device legal manufacturers, authorized representatives, system/procedure pack producers and importers involved in placing medical devices on the European market. It is the primary means of identifying these Economic Operators in the EUDAMED database for various purposes.
The single registration number of Precisis is: DE-MF-000016826

1.4 Basic UDI-DI

To ensure product traceability for all stakeholders and compliance related to the UDI requirements of Regulation 2017/745/EU, marking and labelling of the EASEE® System comprises global trade item numbers (GTIN) as procured by GS1 Germany GmbH for the use as unique device identifiers (UDI).

GS1 Germany GmbH is an accredited issuing entity designated to operate a system for the assignment of Unique Device Identifiers (UDIs) as per Commission Implementing Decision (EU) 2019/939 of 6 June 2019.
The global model number (GMN) for the EASEE® System is also defined as "Basic UDI-DI" for the product group with unique intended purpose, risk class and essential design and manufacturing characteristics. For the device group of the EASEE® System, the following Basic UDI-DI is assigned: 426047977022426

1.5 Medical device nomenclature description / text

1.5.1 GMDN

The Global Medical Device Nomenclature (GMDN) is now used by over 70 national medical device regulators to support their activity. Precisis GmbH obtained the following product code and description from "GMDNagency.org" for the EASEE® System:

GMDN Code: 62653

GMDN description short: Epicranial brain electrical stimulation system

GMDN description long: An assembly of sterile implantable devices designed to apply weak, pulsed (not continuous) electrical stimuli from beneath the scalp to specific areas of the brain for the treatment of focal epilepsy. It consists of leads implanted in the subgaleal area (i.e., under the scalp and outside the skull) and a connected battery-powered pulse generator implanted near the clavicle; accessory devices for surgical implantation and implant management (e.g., programmer, hand-held control unit, seizure event recorder) are typically included.

1.5.2 CND / EMDN code

For a medical devices classification system to be used for information exchange in the EUDAMED database, guidance paper MDCG 2019-13 "Guidance on sampling of MDR Class IIa / Class IIb and IVDR Class B / Class C devices for the assessment of the technical documentation" proposes to use the Italian "Classificazione Nazionale dei Dispositivi medici (CND)" system, referring to this as 'European Medical Devices Nomenclature (EMDN)' system. According to this system (taken from the list "Traduzione in lingua inglese dei codici della Classificazione Nazionale dei Dispositivi Medici" published by Italian Ministry of Health and last changed 13.03.2018), the EASEE® components can be covered by the following codes:

Category:	ACTIVE-IMPLANTABLE DEVICES (EN)
EMDN Code:	J020199
EMDN description short:	Cerebral implantable neurostimulators - other

Table 1 CND-/EMDN-codes

1.6 Class of device

According to Annex VIII of Regulation 2017/745 the following classification rule applies:
Rule 8:
All implantable devices and long-term surgically invasive devices are classified as class IIb unless they:

- are active implantable devices or their accessories, in which cases they are classified as class III;

According to this rule, the EASEE® System including accessories are class III medical devices.

1.7 Year when the first certificate (CE) was issued covering the device

CE-Mark for the EASEE System was issued in September 2022.

1.8 Notified Body's name and single identification number

DEKRA Certification B.V.
Meander 1051 / P.O. Box 5185
6825 MJ ARNHEM / 6802 ED ARNHEM
Netherlands

Tel: +31 88 968 3000
Fax: +31 88 968 3100
E-Mail: product.certification@dekra.com
Notified Body number: 0344

2 Intended use of the device

2.1 Intended purpose

The EASEE® System is intended for use as an adjunctive neurostimulation therapy for reducing the burden of epilepsy in adults over 18 years of age, with focal onset seizures that are refractory to two or more antiepileptic medications.

2.2 Indication(s) and target population(s)

The EASEE® System is indicated for:

- Patients with a clinical diagnosis of focal seizures or focal seizures evolving into bilateral tonic clonic seizures
- Patients with a diagnosis of lateral temporal lobe epilepsy or extra-temporal lobe epilepsy
- Patients with a predominant epileptic focus, which can be clearly identified as the site of implantation for the electrode based on EEG and clinical presentation

- Patients in whom treatment with at least two appropriately selected and tolerated antiepileptic drugs has not been sufficiently effective
- Patients over the age of 18

2.3 Contraindications and/or limitations

The EASEE® System is contraindicated for:

- Females who are pregnant
- Patients who are anatomically not eligible for EASEE® System implant in the opinion of the treating physician
- Patients with implanted metal parts in the area of the intended position of EASEE® Lead
- Patients with an active implanted electronic medical device that delivers electrical energy to a target area closer than 30 cm to the intended position of EASEE® Lead (e.g. Deep Brain Stimulation, cardiac pacemaker or defibrillator)
- Patients at high risk for surgical complications due to underlying condition such as active systemic infection, coagulation disorders (such as the use of anti-thrombotic therapies) or platelet count below 50,000/µl

The following medical procedures are contraindicated for patients with an implanted EASEE® System:

- Diathermy procedures (Diathermy is any treatment that uses high-frequency electromagnetic radiation, electric currents, or ultrasonic waves to produce heat in body tissues): Patients should not be treated with any type of short wave, microwave, or therapeutic ultrasound diathermy device whether or not it is used to produce heat. These treatments should not be applied to any part of the body.
- Electroconvulsive Therapy (ECT): ECT should not be conducted on patients with an implanted EASEE® Power or EASEE® Lead (or parts of it).
- Transcranial Magnetic Stimulation (TMS): TMS should not be conducted on patients with an implanted EASEE® Power or EASEE® Lead (or parts of it).

3 Device description

3.1 Description of the device

3.1.1 Product summary

The EASEE System consists of:

- The implantable components: EASEE Power (the implantable pulse generator) and EASEE Lead (electrode array and lead body). The EASEE Lead design allows it to be placed subgaleally on the skull surface and to transmit electrical stimulation through the skull bone to the grey

matter of the neocortex. EASEE Lead consists of five single disc electrodes arranged in a silicone matrix and linked to a five-polar cable;

- The surgical tools: EASEE Template (for determining implant location), a torque wrench (to fix EASEE Lead to EASEE Power), screws with suitable screwdriver (used to fix the electrode array onto the skull) and a tunneling tool (for the subcutaneous routing of the lead body from the electrode implant location on the skull to the implantable pulse generator location in the subclavian region);
- The external control elements: EASEE Set (physician programming device with specific software), EASEE Connect (telemetry wand for physician), EASEE Access (patient remote control for device battery status check and/or request of bolus stimulation) and an activation magnet (for activation of the device by the physician).

The EASEE System is able to deliver different stimulation patterns. The recommended stimulation scheme combines AC (alternating current) – also referred to as High-Frequency Stimulation (HFS) and ULFA (ultra-low frequency asymmetric) stimulation or DC-like stimulation (DLS). HFS stimulation is applied continuously throughout the day (0.5 seconds every two minutes) – with the exception of the time required for the DLS burst – and consists of a short burst of rectangular, bipolar constant current pulses with a pulse width of 160 µs and a frequency of 100 Hz. DLS stimulation is delivered once a day for 20 min and consists of an asymmetric 20 ms rectangular active pulse, followed by a 100 ms charge equalization pulse at $1/5^{th}$ of the current amplitude used for the active pulse, corresponding to pulse frequency of 8 Hz. All pulses are supplied as constant current pulses with programmable current amplitude.

Furthermore, patients who are able to feel the upcoming seizure or those who are able to react during a seizure, can directly request additional “bolus stimulation” bursts via the EASEE Access remote control (“patient controlled neurostimulation”) (PCN). These bursts usually have the same parameters as the HFS bursts, with the exception of the burst duration, which can be programmed between 10 s and 60 s. The patient can request an additional stimulation bolus once every 2 minutes, and for a maximum total duration of 6 minutes per day.

EASEE Power logs several data points, including all stimulation parameter settings, the daily applied stimulation bursts, time and date of each received bolus stimulation request, the battery voltages and the impedances of each electrode.

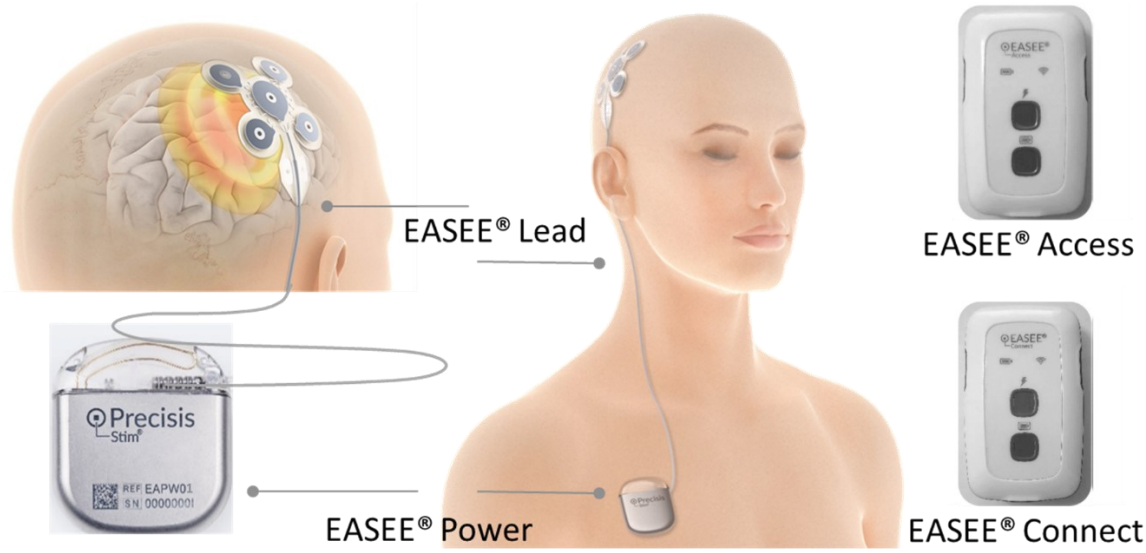


Figure 1 EASEE System elements

The fixation screws, the screwdriver set, the tunneling tool, and the activation magnet are medical grade, CE marked off-the-shelf accessories.

3.1.2 Implantable components

EASEE Lead and **EASEE Power** are implantable components of the EASEE System (see

Figure 2). EASEE Lead consists of a specialized electrode array on the distal side and a connector on the proximal side. Both sides are linked by a non-detachable, flexible lead body. The electrode array consists of five electrodes arranged in a pseudo-Laplacian form, with a central electrode surrounded by four peripheral electrodes allowing precise targeted stimulation of defined brain areas. The electrode array of the EASEE Lead is implanted between the patient's scalp and skull, in the so-called subgaleal area, below the periosteum, while the lead body is tunneled subcutaneously from the head to the chest and is connected to the EASEE Power. EASEE Power is a generator of electrical pulses and

is implanted in the chest, caudal to the clavicle. It is equipped with batteries and electronics for stimulation control. EASEE Power is connected to EASEE Lead via a connector block within the EASEE Power header. The header also entails a radio frequency (RF, 2.4Ghz and 403MHz) antenna to communicate with the external control components. EASEE Power is initially activated by an external magnet and this activation magnet is required to turn on EASEE Power whenever it has been shut down subsequently.

Figure 2 Overview of the Implantable Components of the EASEE System

3.1.3 Surgical implant accessories

EASEE Template allows the surgeon to check that implantation site is well prepared for the EASEE Lead placement i.e. dimensions and accessibility can therefore be tested with no mechanical risks for EASEE Lead. The EASEE Template is not intended for implantation.

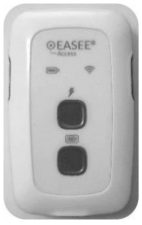
A **torque wrench** allows the surgeon to establish a secure connection between EASEE Power and EASEE Lead.

3.1.4 Control components

EASEE Power can be controlled via external control components.

Two components, **EASEE Connect** and **EASEE Set**, allow medical personnel to set the stimulation parameters according to the individual patient needs, to test the functionality of EASEE Power (battery life, impedance) and to access recorded data (e.g. stimulation log).

EASEE Connect enables the RF communication between EASEE Set and EASEE Power. EASEE Set consists of a software application to program EASEE Power and a tablet PC (off-the-shelf).



EASEE Access is the external control component for the patient. It is a handheld device that enables the patient to check the battery status of EASEE Power and that of the EASEE Access itself. If needed, the EASEE Access can also turn off EASEE Power. Furthermore, EASEE Access can be used by patients to request patient controlled neurostimulation.

3.1.5 Software

To control all functionalities and interactions of the EASEE System components by means of microcontrollers and processing units, various pieces of software are needed, altogether the "software-package". As being tightly aligned to each other, they are released in packages containing the firmware for EASEE Power, EASEE Access, EASEE Connect and the graphical user interface software EASEE Set for programming the EASEE Power.

The software-package pertaining the EASEE System is version 11.

3.1.6 Compatible third party devices and accessories

Surgical tools needed to perform the implantation of EASEE Lead and EASEE Power include **fixation screws** and a corresponding **screwdriver**, for fixing the position of the EASEE Lead array.

The tunneling tool, not part of the EASEE System, is used by the neurosurgeon to aid the subcutaneous routing of the EASEE Lead between skull and chest. Those surgical tools are supplied by different manufacturers and are CE marked.

To activate EASEE Power for the first time or after EASEE Power has been switched off, a magnet is needed. An activation magnet manufactured by Medtronic (reference 9466) for a similar purpose was validated for use with the EASEE System. The magnet is not part of the EASEE System.

3.2 Reference and differences to previous device generation(s) or variants

The EASEE System is currently used in two configurations in the market. This SSCP covers the following configuration:

Sytem component	**ESC003 [REF]**
EASEE Power	PRPW01
EASEE Lead	PRLE02
EASEE Access	PRAC01
EASEE Set	PRSE02
EASEE Connect	PRCT01

First device configuration used was ESC002. This configuration is determined by the system component EASEE Power (REF PRPW00). This variant was able to provide a stimulation with most common parameters for approximately a year. For establishing stimulation parameters, the programming device EASEE Set (REF PRSE00) is needed. The succeedig configuration ESC003, comprises an EASEE Power variant (REF PRPW01) beeing able to provide a stimulation with most common parameters for approximately three years. For establishing stimulation parameters, the programming device EASEE Set (REF PRSE02) is needed, also for compatibility reasons.

3.3 Accessories which are intended to be used in combination with the device

The following accessories are to be used in combination with the EASEE System and are either part of the commercial packaging of a EASEE System component or accompanies it in its original packaging.

Designation	Manufacturer Reference
Torque wrench	8C-65-209X-X-00
EASEE® Template	8C-61-015X-X-00
Tablet PC	5262N6300011 (Model: MioWORK L1000)
Screws- LowProfile Screw, 1.5 x4mm, Cross Recess (CR), sterile	LP-5024-S, LP-7024-S
Emergency screws (replacement) – LowProfile Emergency Screw, 1.8 x 4mm, Cross Recess (CR), sterile	LP-5064-S
Screwdriver Handle- ideFixx screwdriverhandle, titanium	HG-6000
Screwdriver Blade- ideFixx CR screwdriverblade	KS-5100

Table 2 EASEE® System accessories

3.4 Other products which are intended to be used in combination with the device

Designation	Manufacturer and model/type Additional information	Manufacturer Reference
Tunneling tool	Maximum length: 38cm Minimum inner diameter: 3.9mm *For example:* *St Jude Medical* *6901 Preston Road* *TX 75024 Plano, USA*	1191
Activation magnet	Minimum field strength: 90 gauss measured 40 mm (1.5”) from magnet surface *For example:* *Medtronic, Inc.* *710 Medtronic Parkway* *MN 55432 Minneapolis,* *USA*	9466

Table 3 Third party accessories for EASEE® System

4 Risks and warnings

4.1 Residual risks and undesirable effects

Based on the current knowledge from risk management activities, no unacceptable risks are known and the residual risks cannot be further mitigated and are considered as acceptable.

These residual risks can be summarized as follows:

- General risks associated with the surgical procedure, but also specific risks related to the location of the implantation site of the electrode (e.g. preparation of the stimulation area, tunnelling of electrode connection to the IPG). These risks range from discomfort due to wound healing issues or scar formation to severe complications due to peri or postprocedural infection.
- Risks related to the effects of stimulation in terms of physiological, electrochemical or tissue reactions at the electrode location. These risks can in worst case lead to loss of efficacy of stimulation, i.e. loss of benefit in risk-benefit analysis. As those risks can also become effective after long implantation periods, this item will be investigated in PMCF studies.
- Therapy associated risks, such as inefficient stimulation or seizure reduction, neurological adverse effects or increase in seizure severity or frequency
- These risks range from too little benefit due to lower efficacy than expected, to worsening of the patient’s disease status or the occurrence of unintended neurological side effects. However, it is expected that such effects would be transient and could immediately be stopped upon discontinuation of the therapy.
- Risks caused by inappropriate physical design of the device (e.g. wearing comfort). These risks can result in aesthetic issues such as scar formation, or visibility of the EASEE Lead or IPG.
- Risks associated with the patient controlled neurostimulation (PCN) request:

- Patient struggles to request bolus stimulation due to inadequate usability. Assessment of this risk cannot fully be finalized based on available data from the PIMIDES I study.
- Addictive behaviour of patients based on their ability to control PCN bolus stimulation. This risk needs to be further observed and assessed based on PMCF program outcomes.
- In addition: very unlikely adverse reaction on bolus stimulation in the clinical setting of an upcoming seizure. This might lead to severe increase of seizure severity and/or duration. Clinical trials did not yet reveal any hint that this harm ever happened, however, the risk will be further observed in the PMCF program.

From clinical investigations, the following undesirable effects are currently known:
The clinical data is available from 33 patients in the EASEE System early experience. There is a reasonable probability (80%) of observing at least one event of an undesirable side-effect with an actual probability of 5% when 32 subjects are studied.
The side-effects reported in the clinical studies were all expected from the risk management, the list below provides the side-effects which were reported in over 5% of patients.

Undesirable side-effect	Number of patients with side-effect observed	Proportion
Epilepsy	14	42%
Headache	11	33%
Pain	7	21%
Paraesthesia	3	9%
Medical device discomfort	2	6%

The data available reveals the frequency of undesirable side-effects observed so far but is not sufficient to conclude yet on frequency of expected side-effects not already encountered. The systematic collection of side-effects and their analysis in ongoing in clinical investigations.

4.2 Warnings and precautions

The performed activities in the course of clinical evaluation and risk management resulted in the following warnings and precautions to ensure a safe use of the device for patients and intended users.

4.2.1 Warnings

4.2.1.1 Warnings – Clinical Use

WARNING: PHYSICIAN AND CENTER ACCESS TO THE EASEE® SYSTEM

- THE EASEE® SYSTEM SHOULD ONLY BE IMPLANTED BY NEUROSURGEONS WITH ADEQUATE EXPERIENCE IN THE IMPLANTATION OF NEUROSTIMULATION DEVICES IN THE HEAD AND IN THE SURGICAL TREATMENT OF EPILEPSY. THE IMPLANTATION OF THE EASEE® SYSTEM SHOULD ONLY BE PLANNED BY NEUROLOGISTS OR NEUROSURGEONS WITH ADEQUATE EXPERIENCE IN THE MANAGEMENT OF INTRACTABLE EPILEPSY AND IN THE LOCALIZATION OF EPILEPTIC FOCI, INCLUDING THE USE OF SCALP ELECTRODES.
- TO QUALIFY TO MANAGE PATIENTS WITH THE EASEE® SYSTEM, PHYSICIANS MUST DEMONSTRATE SPECIFIC

EXPERTISE RELATED TO EPILEPSY, EEG MONITORING, THE PHARMACOLOGY OF ANTIEPILEPTIC MEDICATIONS AND SELECTION OF PATIENTS FOR EPILEPSY SURGERY. IMPLANTATION OF THE EASEE® SYSTEM SHOULD BE PERFORMED ONLY BY QUALIFIED NEUROSURGEONS AT CENTERS CAPABLE OF PROVIDING COMPREHENSIVE EPILEPSY CARE, I.E. "COMPREHENSIVE EPILEPSY CENTERS". THESE CENTERS SHOULD HAVE THE EXPERTISE TO PROVIDE DIAGNOSTIC SERVICES THAT INCLUDE EEG MONITORING WITH SCALP AND INTRACRANIAL ELECTRODES AND NEUROIMAGING AND EXPERTS IN THE TREATMENT OF EPILEPSY WITH ANTIEPILEPTIC MEDICATIONS, EPILEPSY SURGERY AND DEVICES.

4.2.1.2 Warnings – Surgery

WARNINGS: COMPATIBILITY WITH SIMILAR IMPLANTABLE PRODUCTS

- EASEE® POWER AND EASEE® LEAD ARE NOT COMPATIBLE WITH NON-EASEE® SYSTEM PULSE GENERATORS AND/OR LEADS. INCOMPATIBLE CONFIGURATIONS MAY CAUSE DAMAGE TO THE PRODUCTS AND MAY RESULT IN UNSAFE CURRENT DENSITIES BEING DELIVERED TO THE PATIENT.

WARNINGS: UNEXPECTED SURGICAL COMPLICATIONS

- AS WITH ANY SURGICAL TREATMENT, IT CANNOT BE RULED OUT THAT IMPLANTATION OF EASEE® SYSTEM COMPONENTS LEADS TO RARE, UNEXPECTED AND POTENTIALLY SEVERE COMPLICATIONS.

WARNINGS: INFECTION

- INFECTION, INCLUDING BACTERIAL MENINGITIS, MAY OCCUR AS A RESULT OF THE EASEE® SYSTEM IMPLANTATION PROCEDURES AND/OR THE EASEE® SYSTEM MATERIALS. STANDARD SURGICAL INFECTION PREVENTION MEASURES (ANTIBIOTICS ETC.) SHOULD BE TAKEN BOTH PRE- AND POST-IMPLANTATION.

WARNINGS: SURGICAL PROCEDURE SIDE EFFECTS

- SURGICAL PROCEDURE RISKS MAY INCLUDE, BUT ARE NOT LIMITED TO:
- (TEMPORARY) PAIN AT THE IMPLANT SITES,
- HEADACHE,
- PAIN WHILE CHEWING IF THE TEMPORAL MUSCLE IS AFFECTED,
- MUSCLE FIBRILLATIONS AT THE IMPLANTATION SITE,
- ERYTHEMA,
- HEMATOMA
- SWELLING OR NUMBNESS AT IMPLANT SITE
- SEVERE BLEEDING, E.G. FROM THE EXTERNAL JUGULAR VEIN,
- THROMBOSIS,
- PULMONARY EMBOLISM,
- SUBACUTE OR CHRONIC INFECTION OF THE DEVICE / ADJACENT TISSUE
- IMPAIRED WOUND HEALING / SORENESS OF SCAR.

WARNINGS: DAMAGE DUE TO THE SURGICAL PROCEDURE

- DESPITE THE GREATEST CARE DURING PREPARATION OF THE IMPLANTATION SITES, DURING IMPLANTATION AND DURING TUNNELING, DAMAGE TO THE FOLLOWING STRUCTURES CANNOT BE RULED OUT:

- VESSELS (E.G. EXTERNAL JUGULAR VEIN),
- NERVES (E.G. FACIAL NERVES AND ACCESSORY NERVE),
- MUSCLES (E.G. TEMPORALIS MUSCLE), POSSIBLY WITH E.G. MUSCLE TENSION

WARNINGS: POTENTIAL SIDE EFFECTS FROM ANESTHESIA

- RISKS FROM GENERAL ANESTHESIA FOR SURGICAL PROCEDURES MAY INCLUDE, BUT ARE NOT LIMITED TO:
- TEMPORARY CONFUSION AND MEMORY LOSS,
- DIZZINESS,
- NAUSEA,
- VOMITING,
- DIFFICULTY PASSING URINE,
- BRUISING OR SORENESS FROM THE IV DRIP,
- SHIVERING AND FEELING COLD,
- SORE THROAT DUE TO THE BREATHING TUBE,
- MUSCLE ACHES,
- DECUBITUS ULCER.

WARNINGS: REDUCED EFFICACY OF STIMULATION

- THE ELECTRODE PAD MAY BE UNFAVORABLY POSITIONED, E.G. CAUSED BY MISMATCH TO THE EPILEPTIC FOCUS OR BY INSUFFICIENTLY REMOVED PERIOSTEUM, WHICH MAY COMPROMISE THE TREATMENT WITH THE EASEE® SYSTEM.

WARNINGS: AESTHETIC RESULTS

- THE IMPLANTATION OF THE IMPLANTABLE COMPONENTS OF EASEE® SYSTEM MAY LEAD TO UNACCEPTABLE AESTHETIC RESULTS.

WARNINGS: EASEE® LEAD EXPLANTATION

- SURGICAL EXPLANTATION OF EASEE® LEAD MAY CAUSE TISSUE DAMAGE.

4.2.1.3 Warnings – EASEE® System and Therapy

WARNINGS: ADVERSE TISSUE REACTION

- ADVERSE TISSUE REACTIONS TO THE IMPLANTED EASEE® SYSTEM MATERIALS CANNOT BE EXCLUDED BUT ARE EXTREMELY UNLIKELY.

WARNINGS: ALLERGIC REACTION

- ALLERGIC REACTIONS TO THE MATERIALS OF THE EASEE® SYSTEM COMPONENTS CANNOT BE EXCLUDED BUT ARE EXTREMELY UNLIKELY.

WARNINGS: CHRONIC TISSUE STIMULATION

- THE EFFECTS OF LONG-TERM BRAIN STIMULATION ARE NOT COMPLETELY KNOWN AND MAY PRESENT SOME

RISKS FOR THE PATIENT, E.G. FOR WORSENING OF THE DISEASE STATE OR INCREASED LIKELIHOOD OF OCCURRENCE OF ADVERSE EVENTS.

WARNINGS: POTENTIAL ADVERSE EVENTS CAUSED BY STIMULATION

- SIDE EFFECTS THAT MAY BE CAUSED BY STIMULATION, MAY INCLUDE, BUT ARE NOT LIMITED TO:
- HEADACHE,
- DIZZINESS,
- TIREDNESS,
- PAIN, E.G. IN THE ELECTRODE AREA OF EASEE® LEAD,
- IMPAIRED SENSITIVITY, E.G. IN THE ELECTRODE AREA OF EASEE® LEAD,
- JERKS,
- ITCHING,
- TINGLING,
- DYSAESTHESIA
- MUSCLE FIBRILLATIONS AT IMPLANTATION SITE.

WARNINGS: UNEXPECTED ADVERSE EVENTS DUE TO A DEFECTIVE DEVICE

- AS WITH ANY MEDICAL TREATMENT, IT CANNOT BE RULED OUT THAT THERAPY WITH THE EASEE® SYSTEM WILL CAUSE UNEXPECTED SIDE EFFECTS.

WARNINGS: TEMPORARY SYSTEM FAILURE

- THE LIFETIME OF THE IMPLANTABLE COMPONENTS OF EASEE® SYSTEM HAS BEEN TESTED PRIOR TO THE CLINICAL PHASE. HOWEVER, CLINICAL APPLICATION MAY RESULT IN CONDITIONS UNDER WHICH THE DEVICE UNEXPECTEDLY LOSES ITS FUNCTIONALITY EARLIER.

WARNINGS: WORSENING OF DISEASE STATE

- ALTHOUGH IT HAS BEEN DEVELOPED TO TREAT EPILEPSY, APPLICATION OF THE EASEE® SYSTEM MAY IN UNLIKELY CASES LEAD TO WORSENING OF THE DISEASE STATE:

WARNINGS: SIDE EFFECTS AT IMPLANTATION SITE

- PAIN, TENSION, DISCOMFORT, OR ERYTHEMA AT THE IMPLANTATION SITES, ESPECIALLY AT THE IMPLANTATION SITE OF EASEE® LEAD, ARE POSSIBLE.

WARNINGS: EROSION

- SKIN EROSION MAY OCCUR AT AND/OR AROUND THE PULSE GENERATOR AND/OR LEAD IMPLANT SITE, PARTICULARLY IN THE CASE OF PROTRUSION OF THE IMPLANTED EASEE® SYSTEM PRODUCTS ABOVE THE SURFACE OF THE SKULL.

WARNINGS: LEAD MIGRATION

- THE IMPLANTED LEAD MAY MIGRATE FROM THE ORIGINAL IMPLANT LOCATION, DESPITE THE INTENDED FIXATION. LEAD MIGRATION MAY RESULT IN CHANGES IN STIMULATION EFFECTIVENESS, AND MAY REQUIRE

ADDITIONAL SURGICAL PROCEDURES TO MODIFY THE LEAD LOCATION.

WARNINGS: PREGNANT WOMEN

- THE SAFETY AND EFFECTIVENESS OF THE EASEE® SYSTEM HAS NOT BEEN STUDIED IN PREGNANT WOMEN.

WARNINGS: EASEE® SYSTEM FAILURE

- AS WITH ANY ELECTRONIC DEVICE, THE EASEE® SYSTEM MAY MALFUNCTION (NOT WORK). POTENTIAL CAUSES INCLUDE BATTERY MALFUNCTIONS, AN ELECTRICAL SHORT, OPEN CIRCUITS, LEAD FRACTURES, LEAD INSULATION FAILURES, OR DAMAGE, FOR EXAMPLE AS A RESULT OF HEAD TRAUMA. THESE MALFUNCTIONS ARE UNPREDICTABLE, AND MAY RESULT IN TOO LITTLE STIMULATION OR NO STIMULATION. A LEAD FAILURE MAY RESULT IN THE LEAD NEEDING TO BE REMOVED OR REPOSITIONED, WHICH WOULD REQUIRE SURGERY. A MALFUNCTIONING PULSE GENERATOR MAY NEED TO BE REPLACED, WHICH WOULD REQUIRE SURGERY. ALTHOUGH THE PULSE GENERATOR IS DESIGNED TO TURN OFF IF OVERSTIMULATION OR EXCESS CURRENT OCCURS, THERE IS A POSSIBILITY THAT PRODUCT FAILURE COULD RESULT IN ADJACENT BRAIN TISSUE DAMAGE.

WARNINGS: DAMAGE TO THE HOUSING

- IF THE EASEE® POWER CASE (THE TITANIUM HOUSING) AND THE BATTERY HOUSING ARE RUPTURED OR PIERCED DUE TO OUTSIDE FORCES, SEVERE TISSUE DAMAGE COULD RESULT FROM EXPOSURE TO THE BATTERY CHEMICALS.

WARNINGS: ELECTROMAGNETIC INTERFERENCE (EMI)

- ELECTROMAGNETIC INTERFERENCE IS THE IMPAIRMENT IN FUNCTION CAUSED BY AN ENERGY FIELD GENERATED BY EQUIPMENT FOUND IN THE HOME, WORKPLACE, MEDICAL, OR PUBLIC ENVIRONMENTS THAT IS STRONG ENOUGH TO INTERFERE WITH PULSE GENERATOR FUNCTION. SOURCES OF STRONG ELECTROMAGNETIC INTERFERENCE CAN RESULT IN THE FOLLOWING EFFECTS:
- **SYSTEM DAMAGE** – RESULTING IN A LOSS OR CHANGE IN SYMPTOM CONTROL AND REQUIRING FURTHER SURGERY,
- **OPERATIONAL CHANGES TO THE PULSE GENERATOR** – FOR EXAMPLE UNWANTED DEACTIVATION OF THE PULSE GENERATOR
- **UNEXPECTED CHANGES IN STIMULATION** – SHORT TERM CHANGES IN THE STIMULATION PULSES, WHICH MAY BE NOTICED BY THE PATIENT.

WARNINGS: ENTERING AREAS PROTECTED BY WARNING SIGN

- PATIENTS WITH AN IMPLANTED EASEE® POWER AND/OR EASEE® LEAD SHOULD BE WARNED TO SEEK MEDICAL GUIDANCE BEFORE ENTERING ENVIRONMENTS THAT COULD ADVERSELY AFFECT THE OPERATION OF THE EASEE® SYSTEM, INCLUDING AREAS PROTECTED BY WARNING SIGNS.

WARNINGS: INTERACTION WITH IMPLANTED CARDIAC DEVICES

- POSSIBLE EFFECTS OF IMPLANTED DEVICE INTERACTION WITH AN IMPLANTED CARDIAC DEVICE (E.G., PACEMAKER OR DEFIBRILLATOR) INCLUDE THE FOLLOWING:
- DEFIBRILLATION THERAPY FROM AN IMPLANTED DEFIBRILLATOR MAY DAMAGE THE DEVICE.
- THE ELECTRICAL PULSES FROM THE NEUROSTIMULATION SYSTEM MAY INTERACT WITH THE SENSING

OPERATION OF THE CARDIAC DEVICE AND COULD RESULT IN AN INAPPROPRIATE RESPONSE OF THE CARDIAC DEVICE AND VICE VERSA.

- FOR THESE REASONS, PATIENTS WITH AN IMPLANTED CARDIAC DEVICE SHOULD NOT BE TREATED WITH EASEE® SYSTEM.

4.2.1.4 Warnings – EASEE® Set / EASEE® Connect, device combination for data access and programming

WARNINGS: POTENTIAL SHOCK

- SUBMERGING ANY PART OF EASEE® SET / EASEE® CONNECT IN WATER, OR OPERATING EASEE® SET / EASEE® CONNECT OR ANY PART OF IT IN A WET ENVIRONMENT, MAY RESULT IN AN ELECTRICAL SHOCK.
- EASEE® SET MUST BE DISCONNECTED FROM THE ELECTRICAL OUTLET PRIOR TO CLEANING.
- ELECTRICAL SHOCK MAY OCCUR IF THE EASEE® SET AC ADAPTER AND POWER CORD ARE NOT PROPERLY CONNECTED TO A GROUNDED POWER SOURCE.
- NO OTHER COMMERCIALLY AVAILABLE ACCESSORY OF THE TABLET PC MUST BE USED DURING THE APPLICATION OF EASEE® SET EXCEPT THE SPECIFIED POWER SUPPLY (SINPRO MEDICAL POWER SUPPLY HPU63A-105). OTHERWISE ELECTRICAL SHOCK MAY OCCUR.

WARNING: UNAUTHORIZED MODIFICATION

- EASEE® CONNECT SHALL NOT BE MODIFIED FROM ITS DELIVERED CONDITION. UNAUTHORIZED MODIFICATION OF EASEE® CONNECT CAN CAUSE UNSAFE CONDITIONS, LOSS OF FUNCTIONALITY, SHORTENED BATTERY LIFE, AND OTHER ISSUES.

WARNING: ONLY USE EASEE® CONNECT IN COMBINATION WITH EASEE® SET

- EASEE® CONNECT REQUIRES THE CONNECTION TO EASEE® SET BY USB CABLE. DO NOT CONNECT EASEE® CONNECT WITH OTHER DEVICES OR POWER SOURCES OTHER THAN EASEE® SET.

4.2.1.5 Warnings – EASEE® Access Handheld Device

WARNING: UNAUTHORIZED MODIFICATION

- EASEE® ACCESS SHALL NOT BE MODIFIED FROM ITS DELIVERED CONDITION. UNAUTHORIZED MODIFICATION OF EASEE® ACCESS CAN CAUSE UNSAFE CONDITIONS, LOSS OF FUNCTIONALITY, SHORTENED BATTERY LIFE, AND OTHER ISSUES.

WARNINGS: EASEE® ACCESS BATTERY USAGE

- THE USE OF UNSPECIFIED TYPES OF BATTERIES (E.G. OTHER THAN ALKALINE) MAY LEAD TO UNSAFE DEVICE CONDITIONS.

WARNINGS: OPERATING CONDITIONS

- DUST AND LINT CAN AFFECT THE FUNCTIONALITY OF EASEE® ACCESS. STORE AND USE EASEE® ACCESS IN A CLEAN ENVIRONMENT.
- EXPOSURE OF EASEE® ACCESS TO SUNLIGHT CAN LEAD TO MATERIAL CHANGES (DISCOLORATION,

BRITTLENESS, DEFORMATION). KEEP EASEE® ACCESS AWAY FROM DIRECT SUNLIGHT.
- EASEE® ACCESS SHOULD NOT BE EXPOSED TO INCREASED TEMPERATURES OR STEAM, E.G. NEAR OPEN FIRES, STOVES, KETTLES ETC.

WARNING: KEEP AWAY FROM CHILDREN AND PETS

- EASEE® ACCESS CONTAINS SMALL PARTS THAT CAN BE SWALLOWED. IT MAY BE MISTAKEN FOR A TOY. THERE IS A RISK OF MISUSE BY CHILDREN AND PETS. KEEP EASEE® ACCESS AWAY FROM CHILDREN AND PETS.

WARNINGS: INTERFERENCE PROBLEMS

- DEVICES WHICH EMIT RADIO FREQUENCY, SUCH AS MOBILE PHONES, COMPUTERS OR REMOTE-CONTROLLED TOYS CAN INTERFERE WITH THE ELECTROMAGNETIC COMMUNICATION OF EASEE® ACCESS AND EASEE® POWER.
- WHEN OPERATING, KEEP EASEE® ACCESS AWAY FROM SUCH CONDITIONS AND DEVICES.

WARNINGS: ELECTROMAGNETIC EMISSIONS / ELECTROMAGNETIC IMMUNITY

- USE OF ACCESSORIES, TRANSDUCERS AND CABLES OTHER THAN THOSE SPECIFIED OR PROVIDED BY THE MANUFACTURER OF THIS EQUIPMENT MAY RESULT IN INCREASED ELECTROMAGNETIC EMISSIONS OR DECREASED ELECTROMAGNETIC IMMUNITY OF THIS EQUIPMENT AND RESULT IN IMPROPER OPERATION.

WARNINGS: INTERACTIONS WITH RF COMMUNICATIONS EQUIPMENT

- PORTABLE RF COMMUNICATIONS EQUIPMENT (INCLUDING PERIPHERALS SUCH AS ANTENNA CABLES AND EXTERNAL ANTENNAS) SHOULD BE USED NO CLOSER THAN 30CM (12 INCHES) TO ANY PART OF EASEE® ACCESS OR EASEE® CONNECT INCLUDING CABLES SPECIFIED BY THE MANUFACTURER. OTHERWISE, DEGRADATION OF THE PERFORMANCE OF THIS EQUIPMENT COULD RESULT.

4.2.1.6 Warnings – Medical Environment

WARNINGS: LITHOTRIPSY

- THE EFFECTS OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY ON THE EASEE® SYSTEM HAVE NOT BEEN STUDIED. EXPOSURE TO HIGH-OUTPUT ULTRASONIC FREQUENCIES MAY DAMAGE THE EASEE® SYSTEM. THIS COULD RESULT IN LOSS OF THERAPY, AND ADDITIONAL SURGERY TO REMOVE OR REPLACE COMPONENTS OF THE EASEE® SYSTEM. PRIOR TO ANY ADMINISTRATION OF LITHOTRIPSY, THE ADMINISTERING PHYSICIAN SHOULD CONSULT WITH THE PHYSICIAN PRESCRIBING THE EASEE® SYSTEM.

WARNINGS: RADIATION

- THE EFFECTS OF IONIZING RADIATION (SUCH AS COBALT-60 OR X-RAY RADIATION USED IN CANCER THERAPY) ON THE EASEE® SYSTEM HAVE NOT BEEN STUDIED. EXPOSURE TO HIGH LEVELS OF RADIATION MAY DAMAGE THE EASEE® SYSTEM, ALTHOUGH THE DAMAGE MAY NOT BE IMMEDIATELY DETECTABLE. THIS COULD RESULT IN LOSS OF THERAPY, AND ADDITIONAL SURGERY TO REMOVE OR REPLACE COMPONENTS OF THE EASEE® SYSTEM. PRIOR TO ANY COURSE OF RADIATION THERAPY, THE ADMINISTERING PHYSICIAN SHOULD CONSULT WITH THE PHYSICIAN PRESCRIBING THE EASEE® SYSTEM.

WARNINGS: ELECTROLYSIS

- The effects of electrolysis on the EASEE® System have not been studied. Electrolysis on the head or neck should be avoided.

WARNINGS: MAGNETIC RESONANCE IMAGING (MRI)

- The EASEE® System is assessed to be MRI conditional. Patients with the EASEE® System implanted should have MRI procedures performed only as described in the MRI safety guidelines available at Precisis GmbH.

WARNINGS: COMPUTED TOMOGRAPHY (CT) SCANS

- For CT procedures on a patient with an implanted EASEE® Power (neurostimulator), the operator should:
- - Ask the patient to have the neurostimulator temporarily switched off while the scan is performed, if possible.
- - Minimize X-ray exposure of the implanted electronic medical device
- - Use the lowest possible X-ray tube current consistent with obtaining the required image quality.
- Make sure that the X-ray beam does not act on the device for more than a few seconds.
- Important note: For CT procedures that require continuous scanning over the medical device for more than a few seconds, as with CT perfusion or interventional exams, attending staff should be ready to take emergency measures to treat adverse reactions if they occur.
- After CT scanning, the operator should:
- - Ask the neurologist to have the neurostimulator turned back on using EASEE® Set / EASEE® Connect if it had been switched off prior to scanning.
- - Advise the patient to contact their healthcare provider as soon as possible if they have questions or suspect their device is not functioning properly after any medical procedure.

Additional Warnings present in IFU Neurologist

WARNINGS: EASEE® CONNECT PLACEMENT

- Always ensure to place external communication devices (e.g. EASEE® Connect, EASEE® Access) close to the EASEE® Power implant; in case another active implantable device (e.g. a vagus nerve stimulation device - turned off) is implanted, ensure that you don't place the external communication device close to the wrong implant.

WARNINGS: EASEE® ACCESS PLACEMENT

- Always ensure to place EASEE® Access close to the EASEE® Power implant; in case another active implantable device (e.g. a vagus nerve stimulation device - turned off) is implanted, ensure that you don't place EASEE® Access close to the wrong device.

4.2.2 Precautions

4.2.2.1 Precautions – Surgical

Precautions: EASEE® Lead Damage

Bending, kinking, and stretching of EASEE® Lead may cause connecting cable and/or electrode damage. Handle EASEE® Lead with care. In particular, the EASEE® Lead connector should not be bent.

Precautions: Subgaleal Placement of EASEE® Lead

Electrodes placed on or close to the periosteum may cause pain or uncomfortable sensations during electrical stimulation. Remove periosteum as fully as possible from the skull surface where the electrode will be implanted.

Precautions: Screwing the Electrodes of EASEE® Lead to the Skull

Insufficient fixation of the electrodes to the skull may lead to inefficient therapy or adverse events due to leakage currents. Ensure that the electrodes are fixed with close contact to the skull and that the silicone rim of each electrode rests tightly on the skull.

Precautions: Screwing EASEE® Lead

Using other screws than those specified by Precisis GmbH for fixation of EASEE® Lead may cause damage and malfunction of EASEE® Lead.

Precautions: Suturing EASEE® Lead

Suturing directly to the EASEE® Lead electrode pad may cause damage and malfunction of EASEE® Lead and should be avoided.

Precautions: Bending the Extension shaft of the Tunneling Tool

Do not bend the extension shaft at an angle greater than 90° at any one bend. An angle greater than 90° may damage the shaft and prevent the EASEE® Lead connecting cable from being advanced, or damage the connecting cable, resulting in intermittent or loss of stimulation.

Precautions: Routing the EASEE® Lead Connecting Cable

When routing the EASEE® Lead connecting cable, avoid sharp bends or kinks, which may break the wires. Broken wires may create open circuit, resulting in loss of stimulation or component failure and requiring surgical replacement.

Precautions: Tunneling Procedure

Proceed slowly when the tunneling tool approaches the pocket for EASEE® Power. If excess force is used, the patient could experience additional trauma when resistance to the tunneling tool is suddenly reduced.

Precautions: Tunneling the EASEE® Lead Connecting Cable

Use care when inserting and advancing the EASEE® Lead connecting cable into the extension shaft and when removing the extension shaft. Rough handling can damage lead insulation and compromise patient safety and the treatment with EASEE® System.

Precautions: Using the Activation Magnet in Sterile Environment

The activation magnet is non-sterile and non-sterilizable and should therefore be placed in a sterile bag for use in the sterile field.

Precautions: Using EASEE® Connect in a Sterile Environment

EASEE® Connect is non-sterile and non-sterilizable and should therefore be placed in a sterile bag for use in the sterile field.

4.2.2.2 Precautions – EASEE® System and Therapy

Precautions: Accompanying Documentation

Please check the completeness of the accompanying documentation of the EASEE® System components, as well as the accessories, which are not manufactured or provided by Precisis GmbH. Take care to read and understand the contents of this documentation, as non-compliance with its contents may give rise to additional risks.

Precautions: After-discharge activity

If evidence of after-discharge activity is seen during test stimulation, stimulation parameters should be adjusted to prevent this.

Precautions: Premature depletion of the EASEE® Power Battery

Interrogating EASEE® Power *using wireless RF communication using* EASEE® Connect or EASEE® Access *for more than 10 minutes per day may drain the* EASEE® Power *battery prematurely.*

Precautions: Depletion of the EASEE® Access Battery

Using EASEE® Access *for more than 10 minutes per day may drain the* EASEE® Access *battery prematurely.*

Precautions: Frequency of Remote Monitoring

The patient should interrogate the EASEE® Power battery status with EASEE® Access daily for early detection of potential failures.

Precautions: Explantation and EMI Considerations

If any system components (neurostimulator, electrodes, connecting cables, connecting cable fragments, cranial screws) remain implanted in the patient after partial system explantation, the patient is still susceptible to possible adverse effects from strong sources of EMI. It is possible for the interference sources to couple so much energy into the EASEE® System that adjacent brain tissue is damaged. In very unlikely cases this may result in serious patient injury. Patients who have system

components or its accessories implanted should therefore take care to avoid devices which generate a strong electric or magnetic field.

(For MR diagnosis, see related advise, warnings and precautions and refer to the MR-Guidelines for the EASEE® System.)

Precautions: Explantation of EASEE® Power and EASEE® Lead

It is strongly recommended to always explant both, EASEE® Lead together with EASEE® Power. The long-term safety associated with EASEE® Lead being *left in place without use, is unknown. It shall be assumed that an EASEE® Lead without connection to an EASEE® Power is MR-unsafe.*

Additional Precautions present in IFU Neurologist

Precautions: Depletion of EASEE® Power Battery

The patient should inform the responsible physician in good time before depletion of the EASEE® Power battery, at the latest when the upper left indicator light of EASEE® Access flashes yellow in response to a battery status query. This means the battery capacity is sufficient for less than 7 weeks.

Precautions: Battery Depletion

For continued operation, EASEE® Power needs to be surgically replaced before the battery is depleted. Discuss with your patient the pending replacement of EASEE® Power.

Precautions: Neurostimulator Battery Longevity

High and frequent levels of stimulation reduce neurostimulator battery longevity.

(add-on in Patient IFU) For example, more frequent activation of bolus stimulation leads to a faster depletion of the battery.

Precautions: Battery Depletion and Replacement of EASEE® Power

For continued operation, EASEE® Power needs to be surgically replaced before the battery is depleted. Discuss with your patient when replacement of the impulse generator is expected to take place.

Precautions: Turning EASEE® Power Off

Once turned off, EASEE® Power can only be reactivated by the physician using a dedicated programming tool, called EASEE® Set / EASEE® Connect, which controls EASEE® Power.

Additional precautions present in IFU Patient

Precaution: Applying Pressure on the Pulse Generator and Lead

DO NOT press on or play with the implanted pulse generator or leads. This may damage the pulse generator or leads and result in stimulation not being delivered until they are surgically repaired or replaced.

4.2.2.3 Precautions – EASEE® Set / EASEE® Connect

Precautions: Failure of EASEE® Set / EASEE® Connect

As with any electronic device, EASEE® Set / EASEE® Connect *may be damaged or may malfunction if the* EASEE® Set *AC adapter and power cord are not properly connected to a grounded power source.*

4.2.2.4 Precautions – Medical Environment

Precautions: Medical Procedures

Patients should always inform any healthcare personnel that they have an implanted EASEE® System (and show their medical implant identification card) before any medical procedure is performed.

Advise the patient to contact their healthcare provider as soon as possible if they have questions or suspect that their device is not functioning properly following the completion of any medical procedure.

Precautions: Electrocautery

The use of electrocautery (electrosurgery) can affect the operation of neurostimulators. The energy levels used in electrocautery can temporarily interfere with or permanently damage the EASEE® System.

Electrocautery applied near the EASEE® Power may cause it to temporarily stop delivering stimulation or may reset the neurostimulator. Under these conditions the neurostimulator may require interrogation and possible reprogramming.

Electrocautery applied directly to the neurostimulator, or leads may couple enough energy into a neurostimulator system to damage brain tissue.

If electrocautery is necessary, the following recommendations may be effective in minimizing potential complications.

Before the procedure:

If possible, temporarily disable stimulation using EASEE® Set / EASEE® Connect.

During the procedure:

Use of bipolar electrocautery is recommended and should be considered over monopolar electrocautery, whenever possible.

Keep the electrocautery tip more than 2 cm (approximately one inch) from the implanted device.

The selected output power of the electrocautery unit should be as low as possible for the relevant application and should not be used for longer than 10 seconds in any one burst.

After the procedure:

If stimulation was temporarily disabled before the procedure, re-enable stimulation with EASEE® Set / EASEE® Connect.

Patients should be advised to contact their healthcare provider as soon as possible if they have any questions or suspect that their device is not functioning properly following the completion of any medical procedure.

Precautions: Dental Therapy and Procedures

Dental therapies and procedures that do not involve any of the procedures in the contraindications or warnings sections of this manual should be performed with caution. The dentist or dental technician should be informed that the patient has an implanted EASEE® System.

Advise the patient to contact their healthcare provider as soon as possible if they have questions or suspect that their device is not functioning properly following the completion of any medical procedure.

The following medical procedures may be performed without affecting the EASEE® System:

- Diagnostic X-rays
- Diagnostic ultrasound

Precautions: Other Active Implanted Medical Devices

Interactions between the EASEE® System and other active implantable medical devices (such as pacemakers, defibrillators, implanted spinal cord and peripheral nerve stimulators, cochlear implants, and vagus nerve stimulators) are not known. The effects of simultaneous operation of the EASEE® System with other active implants have not been investigated. Possible effects include sensing problems and inappropriate device responses. For these reasons, patients with an active implanted device should not be treated with EASEE® System.

Precautions: Incompatibility of EASEE® Set / EASEE® Connect with Other Medical Devices

The effects of using EASEE® Set / EASEE® Connect to interrogate other electronic, programmable devices such as pacemakers, defibrillators, cochlear implants, and other neurostimulators or CPAP machines are unknown. It could result in reprogramming of the other device and therefore, the physicians familiar with each device should check the programmed parameters of each device before the patient is discharged and after every programming session of either device.

Precautions: Electromagnetic Interference

Communications between EASEE® Set / EASEE® Connect and EASEE® Power may be interrupted by emissions from nearby electronic devices. Examples of sources of EMI are lithotripsy, computer monitors, cellular telephones, motorized wheelchairs, X-ray equipment and other monitoring equipment. Interruption of telemetry can result in incomplete communication. If EMI disrupts programming, move EASEE® Set / EASEE® Connect away from the likely source of EMI.

Precautions: Placement of the EASEE® Set / EASEE® Connect Power Cords

Make sure that nothing is resting on the power cable and that the cable is not located where it can be tripped over or stepped on.

Precautions: Heating

The EASEE® Set AC adapter and the bottom of the tablet may become hot during normal operation. Use care when handling the AC adapter during or immediately after operation.

4.2.2.5 Precautions – Home or Occupational

Precautions: Keep Magnets at Least 10 Centimeters Away from the Implanted EASEE® Power

Magnets that are contained in devices such as stereo speakers, AM/FM radios, power tools, cellular, cordless and conventional phones, as well as magnets used therapeutically or worn on the body, should be kept at least 10 cm away from the neurostimulator.

Precautions: Activation Magnet for the EASEE® System

Use care when handling the activation magnet for the EASEE® System as it may break if dropped and the broken pieces may have sharp edges.

Precautions: Scuba Diving or Hyperbaric Chambers

Patients should not dive below 4 meters of water and should not enter hyperbaric chambers above 1.5 atmospheres absolute (ATA). Such pressures could damage the system.

Additional precaution for Patient IFU

Precaution: Airport Security and Other Surveillance Systems

Tell people working with security and theft systems that you have the EASEE® System implanted and show them your medical implant identification card. When possible, walk through the center of security screening units without stopping and exit the area of the screening device as soon as possible. Leave the security area as soon as possible. Security screening devices (such as theft detectors and airport security screening devices) may also be found at retail stores, public libraries and airports. Such devices use technology that can (temporarily) disrupt stimulation for the duration of the scan.

Additional precaution for EASEE® Set Hardware and Accessories, Neurologist IFU

Precautions: Ingress Protection of EASEE® Set

EASEE® Set is protected against ingress of particles and fluids. However, to connect USB devices such as EASEE® Connect, it is necessary to temporarily remove the protective cover of the USB socket. It is therefore mandatory to reposition the protective cover as soon as possible.

Precautions: Handling the activation magnet

The activation magnet consists of brittle material. It should be used with care and no mechanical stress should be applied.

4.3 Other relevant aspects of safety

There has been no field safety corrective action since introduction of the EASEE System was placed on the market.

5 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1 Summary of clinical data related to equivalent device, if applicable

Not applicable, as no equivalent device was defined.

5.2 Summary of clinical data from investigations before CE-marking

5.2.1 Identification of the clinical investigations

The summary of clinical data from clinical investigations provided in the following is compiled from the outcome of the following studies:

No.	Study name short / ID	Eudamed No.:	Protocol No. (CIP)	Study name detailed	Public registration (DRKS ID)
1	EASEE II	CIV-18-06-024447	CV08-006	EASEE II – A pilot study to assess the feasibility of neurostimulation with the EASEE System to treat medically refractory focal epilepsy	DRKS00015918
2	PIMIDES I	CIV-19-08-029428	CV08-017	A pilot study to assess the feasibility of patient-controlled neurostimulation with the EASEE® System to treat medically refractory focal epilepsy	DRKS00017833
3	EASEE Meta Analysis	n.a.	CV08-027	Efficacy of neurostimulation with the EASEE® System to treat patients with medically refractory focal epilepsy: protocol for a prospective meta-analysis, pooling efficacy data of EASEE II and PIMIDES I	Prospero ID: CRD42021266440

5.2.2 Identity of the devices used in clinical investigations

In the clinical investigations mentioned above, the following device types of the EASEE System components were used:

REF	UDI			Designation
	Filling digit N_1	Information N_2 to N_{13}	Check Digit N_{14}	
PRPW00	0	426047977001	9	EASEE Power, final packaged
PRLE00	0	426047977002	6	EASEE Lead, final packaged (Variant for Stryker fixation screws)
PRLE01	0	426047977026	2	EASEE Lead, final packaged (Variant for Vigomed fixation screws)
PRAC00	0	426047977003	3	EASEE Access, final packaged
PRSE00	0	426047977004	0	EASEE Set, final packaged
PRCT00	0	426047977005	7	EASEE Connect, final packaged

These device types were used in combination with the following CE-marked accessories from third party manufacturers:

Manufacturer REF	Manufacturer and model/type Additional information	Designation
5420027523972	Mitac International Corp. – MioCARE L130 (EASEE Set - Hardware)	Tablet PC
56-15904S4 LP-5024-S LP-7024-S	Stryker – Screw, Self-Drilling 4 x 1,5x4mm - Sterile Vigomed- LowProfile Screw, 1.5 x 4mm, Cross Recess (CR), sterile	Fixation screws, standard
56-17304S1 LP-5064-S	Stryker- Screw, Emergency 1 x 1,7x4mm – Sterile Vigomed- LowProfile Emergency Screw, 1.8 x 4mm, Cross Recess (CR), sterile	Fixation screws, emergency
65-15002 HG-6000	Stryker – Handle medium Vigomed- ideFixx screwdriver handle, titanium	Screw driver, Handle
65-15003 KS-5100	Stryker – Blade long Vigomed- ideFixx CR screwdriver blade	Screw driver, Blade

5.2.3 Intended purpose of the EASEE System in clinical investigations

The intended purpose of the EASEE System as defined for the clinical investigations listed in section 5.2.1, above, is defined:

"*The EASEE® System is intended for use as an adjunctive neurostimulation therapy for reducing the burden of epilepsy in adults over 18 years of age, with focal onset seizures that are refractory to two or more antiepileptic medication*"

5.2.4 Study Design, Objectives and Endpoints of the clinical investigations

5.2.4.1 EASEE II Clinical Investigation

Study Design:

EASEE II was planned as a first-in-human, prospective, interventional, unblinded, multicenter study designed to collect data on 15 subjects implanted with the EASEE® System in up to 7 European sites.

Patient Population:

Patients with a clinical diagnosis of medically refractory focal epilepsy. Potential patients include those eligible based on the inclusion/exclusion criteria and willing to undergo implantation with the EASEE® System.

Primary study objective:

The primary study objective is to demonstrate the safety of the EASEE® System in subjects with medically refractory focal epilepsy.

Secondary study objectives:

1. Assess changes from baseline seizure frequency
2. Assess changes from baseline seizure severity
3. Assess changes from baseline EEG
4. Assess changes from baseline quality of life
5. Assess changes from baseline mood
6. Assess changes from baseline neurocognition

Primary Endpoint:

1. The primary endpoint is the safety of the EASEE® System evaluated at 4 months post-implant measured in (serious) adverse events (AE, SAE) rates.

Secondary Endpoints:

1. Seizure frequency: baseline seizure frequency and responder rate compared to respective values at 4 months, 8 months, 16 months, 24 months and 36 months post-implant.
2. Seizure severity: baseline seizure severity compared to seizure severity at 4 months, 8 months, 16 months, 24 months and 36 months post-implant.
3. Epileptiform activity: baseline measurements of scalp EEG compared to data collected at 1 month, 8 months, 16 months, 24 months and 36 months post-implant.
4. Quality of life: baseline subject rated quality of life compared to 8 months, 16 months, 24 months and 36 months post-implant.
5. Mood: baseline subject rated mood compared to 8 months, 16 months, 24 months and 36 months post-implant.
6. Neurocognition: baseline neurocognition compared to 8 months, 16 months, 24 months and 36 months post-implant.

5.2.4.2 PIMIDES I Clinical Investigation

Study Design:

PIMIDES I was planned as a prospective, interventional, unblinded, multicenter study designed to collect data on 18 subjects implanted with the EASEE® System with patient controlled neurostimulation capability in up to 8 European centers.

Patient Population:

Patients with a clinical diagnosis of medically refractory focal epilepsy. Potential patients include those eligible based on the inclusion/exclusion criteria and willing to undergo implantation with the EASEE® System.

Primary study objective:

The primary study objective is to demonstrate the safety and performance of patient-controlled-neurostimulation with the EASEE® System in subjects with medically refractory focal epilepsy.

Secondary study objectives:

1. Assess changes from baseline seizure frequency
2. Assess changes from baseline seizure severity
3. Assess changes from baseline seizure symptoms
4. Assess changes from baseline seizure duration
5. Assess changes from baseline EEG
6. Assess changes from baseline quality of life
7. Assess changes from baseline mood
8. Assess changes from baseline neurocognition

Primary Endpoint:

The primary endpoint is the safety of the EASEE® System with patient-controlled neurostimulation capability evaluated at 4 months post-implant measured in SAE rates. Safety is defined as follows:

1. Short-term chronic safety: Incidence of device/procedure related SAEs for the surgical implantprocedure and the following 4 months.

Secondary Endpoints:

2. Acute safety: Incidence of device/procedure related SAEs for the surgical implant procedure and the following month.
3. Seizure frequency: baseline seizure frequency and responder rate (defined as at least 50 % reduction in seizure rate from baseline) compared to respective values at 4 months, 8 months,16 months, 24 months, and 36 months post-implant.
4. Seizure severity: baseline seizure severity compared to seizure severity at 4 months, 8 months,16 months, 24 months, and 36 months post-implant.
5. Seizure duration: baseline average seizure duration compared to seizure duration at 4 months,8 months, 16 months, 24 months, and 36 months post-implant.
6. Seizure symptoms: most debilitating baseline epilepsy symptom compared to epilepsy symptom(s) at 4 months, 8 months, 16 months, 24 months, and 36 months post implant.
7. Epileptiform activity: baseline measurements of scalp EEG compared to data collected at 1 month, 8 months, 16 months, 24 months, and 36 months post-implant.
8. Quality of life: baseline subject rated quality of life compared to 8 months, 16 months, 24 months, and 36 months post-implant.
9. Mood: baseline subject rated mood compared to 8 months, 16 months, 24 months, and 36 months post-implant.
10. Neurocognition: baseline neurocognition compared to 8 months, 16 months, 24 months, and 36 months post-implant.

5.2.4.3 EASEE Meta-Analysis

Study Design:

Meta-analysis of safety and performance data collected in EASEE II and PIMIDES I, two clinical studies which are homogeneous in terms of participants, interventions and outcomes.

Patient Population:

See studies EASEE II and PIMIDES I, above.

Primary Study Objective:
The primary objective is to report on the efficacy, safety and performance of the EASEE® System for transcranial, subgaleal neurostimulation in subjects with medically refractory focal epilepsy, by analysing the data collected in two clinical studies (EASEE II, PIMIDES I).

Primary endpoint (efficacy):
- Responder rate, defined as proportion of patients with at least 50 % reduction of seizure frequency between baseline month and month 6 of stimulation (month 7 after implantation)

Secondary endpoints (efficacy):
- Median seizure frequency reduction per patient; for this endpoint a statistical test was planned to analyse whether efficacy effects reach significance.

Safety:
- device or procedure related Serious Adverse Events
- all Serious Adverse Events
- all Adverse Events

Performance:
- device implant duration
- deficiency rate per device

5.2.5 Inclusion and exclusion criteria for patients participating in clinical investigations

5.2.5.1 EASEE II Clinical Investigation

Key Inclusion Criteria:
Patients enrolled in the study must meet all of the following criteria:
1. Patients with a clinical diagnosis of focal seizures or focal to bilateral tonic clonic seizures.
2. Patients with a diagnosis of lateral temporal lobe epilepsy or extra-temporal lobe epilepsy.
3. Patients with a predominant epileptic focus, which can be clearly identified as the site of implantation for the electrode based on EEG and clinical presentation.
4. Patients, after resective surgery to treat epilepsy, who have a clearly identifiable epileptic focus and a preserved neocortex in the region of implantation.
5. Patients who have failed treatment with a minimum of two anti-seizure medications (used in appropriate doses).
6. Patients having seizures which are distinct, stereotypical events and can be reliably counted, in the opinion of the Investigator, by the patient or caregiver and recorded in a seizure diary.
7. Patients having an anticipated average of 3-300 partial-onset seizures (focal to bilateral tonic clonic seizures) during the baseline period.

8. Patients taking a constant dose of antiepileptic medication(s) over the most recent 28-day period prior to the baseline period (use of medication for acute treatment of seizures is allowed).
9. Patients between the ages of 18 and 75 years.
10. Patients able and willing to provide appropriate consent prior to study procedures.
11. Patients able to complete regular office appointments per the protocol requirements, including behavioral (mood) surveys and neuropsychological testing.
12. Patients willing to be implanted with the EASEE® System as a treatment for his/her seizures.

Key Exclusion Criteria:
Patients who meet any of the following criteria are not eligible to be enrolled in the study:

1. Patients with a diagnosis of mesial temporal lobe epilepsy.
2. Patients with a previous diagnosis of psychogenic or non-epileptic seizures, which are semiologically non-distinguishable from epileptic seizures.
3. Patients with a diagnosis of primarily generalized seizures.
4. Patients after resective surgery with non-preserved neocortex in the region of implantation.
5. Patients with unprovoked status epilepticus in the preceding 6 months prior to enrolment.
6. Patients with a clinically significant or unstable medical condition (including cardiac conditions, alcohol and/or drug abuse) or a progressive central nervous system disease.
7. Patients with a diagnosis of active psychosis, major depression, or suicidal ideation in the preceding year (excluding postictal psychosis).
8. Females who are pregnant or have a pregnancy wish in the next 2 years.
9. Patients enrolled in a therapeutic investigational drug or device trial.
10. Patients who are anatomically not eligible for EASEE® System implant in the opinion of the Investigator.
11. Patients with an implanted electronic medical device that delivers electrical energy to the body (e.g. DBS, cardiac pacemaker or defibrillator) with the exception of an existing VNS device that can be reliably switched off for the duration of the trial.
12. Patients requiring scheduled MRIs during the study phase.
13. Patients who are unable, or do not have the necessary assistance, to properly operate the EASEE® Access handheld device.

5.2.5.2 PIMIDES I Clinical Investigation

Inclusion and exclusion criteria are nearly identical to the ones from the EASEE II Clinical Investigation. The following criteria are study specific or vary slightly from EASEE II.

Key Inclusion Criteria:
Patients enrolled in the study must meet the following criteria:

1. Patients who are able to initiate a stimulation bolus during their seizure (intact consciousness at least during part of a habitual seizure type, as well as motor ability to operate the device totrigger stimulation in this phase).

Inclusion criterion 8 of the EASEE II study was slightly changed:

2. Patients taking a constant dose of antiepileptic medication(s) over the most recent 28-day

period prior to the baseline period "or over most recent 58-day period prior to implantation" (useof medication for acute treatment of seizures is allowed).

Key Exclusion Criteria:

Patients who meet any of the following criteria are not eligible to be enrolled in the study:

1. Patients who are anatomically not eligible for EASEE® System implant in the opinion of the Investigator, as for example but not limited to: Patients having a metal implant intra- or extracranial in the region of targeted electrode implantation that cannot be safely removed during the neurosurgical intervention (e.g. CranioFix® 2 Titanium Clamp, cranial plates, screws,etc.)
2. Patients who are unable to properly operate the EASEE® Access handheld device (no intact consciousness during part of habitual seizure type or no motor ability to operate device for bolus stimulation).

5.2.5.3 EASEE Meta-Analysis

All available clinical investigations with a comparable study design are included in this meta-analysis. No studies were excluded. Hence, subject of this meta-analysis are the clinical investigations

- EASEE II
- PIMIDES I

5.2.6 Summary of study methods

5.2.6.1 EASEE II Clinical Investigation

Statistical Considerations:

This is a prospective, interventional, unblinded, multicenter study. The study population to be investigated is defined according to the intended use of the investigational device, as well as the inclusion and exclusion criteria of the study. As a first in human study, the primary endpoints were chosen to be safety related and will assess probability of overall SAEs. The incidence of all adverse events, of those being related, of those being severe, and of serious adverse events will be summarized with corresponding two-sided 95% confidence intervals.

Secondary endpoints are efficacy and safety related and will assess probability of benefit to the patient.

Sample Size:

15 subjects will be recruited. The primary goal of the study is to generate data regarding the feasibility and performance of neurostimulation with the EASEE® System. Allowing for a conservative 20% dropout, there will be a total of 12 subjects, which meets the threshold for a sufficiently precise estimate of several factors to be used in future studies.

5.2.6.2 PIMIDES I Clinical Investigation

Statistical Considerations:

This is a prospective, interventional, unblinded, multicentre study. All included patients for whom the surgery was performed will be analysed. The primary endpoint is chosen to be safety defined as the

probability of device/procedure related SAEs for the surgical implant procedure and the following 4 months. The incidence of all adverse events, of those being related, of those being severe, and of serious adverse events will be summarized with corresponding one-sided 95 % confidence intervals based on a binominal distribution.
Secondary endpoints are safety and efficacy related and will assess probability of benefit to the patient. Efficacy endpoints of the long-term follow-up (24- and 36 months) will only be evaluated descriptively due to the potential selection bias.

Sample Size:
The primary goal of the study is to generate data regarding the feasibility and performance of neurostimulation with the EASEE® System with patient controlled neurostimulation capability. When no device/procedure related SAEs for the surgical implant procedure and the following 4 monthsare observed, to obtain an upper bound of 0.153 on the 0.95 confidence interval for the probability ofa rare event, would require a sample size of 18 patients (nQuery 8.3) (Machin, D., Campbell, M.J. , 1987).

5.2.6.3 EASEE Meta-Analysis

Statistical considerations on primary efficacy analysis:
The primary efficacy meta-analysis will be performed on the full analysis set (FAS), including all patients from both studies who underwent implantation with the device. Responder rate (defined as the proportion of patient with at least 50 % reduction in seizure rate from baseline) at 7 months post-implant (6th month of active stimulation) will be analysed as a repeated binary variable via generalised estimating equations.

Statistical considerations on safety analysis:
Safety analyses will be performed on the safety set, including all patients who underwent implantation with the device. Adverse events will be coded using MedDRA and summarized by body system. The incidence of device/procedure related serious adverse events (SAE) for the surgical implantation procedure and the following 4 months will be summarized with corresponding exact one-sided 95 % confidence intervals based on a binominal distribution.

Sample size:
33 Patients implanted are basis for safety assessment´. One patient dropped out before therapy started, 32 patients received therapy and form the basis for efficacy assessment.

5.2.7 Limitations of the clinical investigations

As per conclusion from the EASEE Meta-Analysis, neither risk of bias in the individual studies nor in the meta-analysis were identified.

5.2.8 Device deficiencies or replacements related to safety or performance

Reported device deficiencies (DD) were categorized regarding severity according to the following table:

DD Severity	Definition
Very low	a DD without any added patient or user risk
Low	a DD which might bear minor risks to cause annoyance of patients or user; no risk for harms with severity rating of 2 or more
Mid	a DD which bears a high risk for annoyance of patient or user; no risk for harms with severity rating of 2 or more
High	a DD which causes need for a significant change to the devices; no risk for harms with severity rating of 2 or more; any DD that caused an ADE
Very High	any DD that caused a SADE

In the EASEE II and PIMIDES I clinical investigations, in total 25 device deficiencies were reported with the following severity classes:

	Number	Percentage	Comment
Severity			
DD reported total	32	n.a.	-
DD with very high severity	0	0 %	-
DD with high severity	7	22 %	too high impedance, lead breakage, various reasons
DD with mid severity	4	13 %	communication issue, pre-implantation damage
DD with very low or low severity	21	66 %	12 low, 9 very low

5.2.9 EASEE System implant survival rates

Resulting from the EASEE II and PIMIDES I clinical investigations, the implant survival rates can be defined, as follows.

5.2.9.1 EASEE Power

The EASEE Power survival rate is 100% (33 / 33).

5.2.9.2 EASEE Lead

Based on accelerated lifetime studies, the lifetime of EASEE Lead in implanted condition is defined with at least 5 years. EASEE II and PIMIDES I clinical investigations currently do not provide related long term data to calculate a survival rate for 5 years. By the time of this analysis, 4 EASEE Leads were explanted with defects: three due to manufacturing process issues, one due to a severe patient fall. Therefore, the survival rate of EASEE Lead is 88% (29 of 33).

5.2.10 Summary of Results from clinical investigations

5.2.10.1 EASEE II Clinical Investigation

Initial safety of the EASEE System as the primary endpoint of the EASEE II study was assessed via the incidence of serious adverse events (SAEs) for the surgical implant procedure and the following month, and the incidence of SAEs for the surgical implant procedure and the following 4 months (Schulze-Bonhage et al., Jama Neurology, 2023). A summary of the results is provided in the following table:

Primary safety outcome	*Number of patients*	*Number of patients who experienced at least one primary safety outcome*	*Number of patients who experienced no primary safety outcome*	*Rate*	*95%-CI lower limit*	*95%-CI upper limit*
Incidence of acute SAE	15	1	14	6.67%	0.2%	31.9%
Incidence of short-term chronic SAEs (up to 4 months)	15	3	12	20.00%	4.3%	48.1%

There were no SAEs during the implant procedure as such. As shown, there was 1 patient (6.67% CI [0.2;31.9]) who experienced an acute SAE in the month following the implantation and 3 patients (20.0% CI [4.3;48.1]) with short-term chronic SAEs, that occurred up to 4 months after the implantation.

The 3 patients mentioned above had a total of 5 SAEs in this timeframe. An overview of the events, stratified by MedDRA system organ class (SOC) and preferred term (PT) is shown below:

Incidence of SAEs by MedDRA SOC and PT			
System organ class	*Preferred term*	*N*	*%*
Total number of patients		15	100.0
Number of patients with at least one SAE		3	20.0
Nervous system disorders		2	13.3
	Epilepsy	1	6.7
	Seizure	1	6.7
	Seizure cluster	1	6.7
	Status epilepticus	1	6.7
Gastrointestinal disorders		2	6.7
	Food poisoning	1	6.7

On a MedDRA SOC basis, SAEs were mainly “nervous system disorders”, with one occurrence in the category of “gastrointestinal disorders”. Concerning the nervous system disorders, the MedDRA PTs were all epilepsy-related, which is the underlying condition of the study patients. None of the SAEs led to the death of a patient and none of the events was assessed by the investigator as possibly, probable, or highly probable related to the procedure or device. One of the events was assessed as unlikely related to the device. The patient suffered a status epilepticus. As a status epilepticus had already been

documented in the medical history of this patient, the event was considered as unlikely related to the device.

After 36 months of follow-up, no unwanted effects on mood, neurocognition nor quality of life were observed. A clinically relevant better mood was observed 2 years after implant and there was a tendency for better quality of life. Seizure severity and epileptiform activity data available were too limited to sustain meaningful analysis.

Incidence adverse events (AEs) were reported out of the 15-patient safety population, all 56 AEs in 13 patients were of expected nature. The AEs are presented according to the MedDRA Preferred Term classification of events.

List of AEs which were reported by more than single patients:

Adverse Event	*Incidence*	*Total %*
Epilepsy	4	26.7
Seizure	4	26.7
Headache	3	20.0
COVID-19	2	13.3
Implant site pain	2	13.3
Nasopharyngitis	2	13.3

List of adverse device effects:

Adverse Device Effect	*Incidence*	*Total %*
Epilepsy	3	20.0
Administration site dysaesthesia	1	6.7
Implant site pain	1	6.7
Incision site complication	1	6.7
Medical device site discomfort	1	6.7
Medical device site induration	1	6.7
Medical device site paraesthesia	1	6.7
Paraesthesia	1	6.7

Among all the AEs, 10 were of serious nature and reported by 5 patients (33.3%).

During the study, 2 patients did not reconsent for the long-term follow-up extension after 16-month follow-up; 2 patients were lost to follow-up and 2 patients withdrew because they wanted to be explanted, one of them because he didn’t see benefits. There was no death reported during the study.

The results demonstrated a positive benefit-risk profile and encourage further use of the EASEE® System in its intended use.

5.2.10.2 PIMIDES I Clinical Investigation

Like with the EASEE II Study outlined above, the primary endpoint of the PIMIDES I study was short-term chronic safety, defined as the incidence of device/procedure related SAEs for the surgical implant procedure and the following 4 months. A summary of the initial results is provided in following table:

Primary safety outcome	*Number of patients*	*Number of patients who experienced at least one primary safety outcome*	*Number of patients who experienced no primary safety outcome*	*Rate*	*95%-CI lower limit*	*95%-CI upper limit*
Incidence of short-term chronic SAEs (up to 4 months) related to procedure or device	18	0	18	0.00%	0.0%	18.5%

As shown, there were no patients with an SAE that was related to the medical procedure or device in the period of implantation up to 4 months follow-up. That implies that with a probability of 95% the percentage of expected short term chronic SAEs related to procedure or device will not be higher than 18.5% (upper limit of the 95% confidence interval).

After 36 months of follow-up, no unwanted effects on mood, neurocognition nor quality of life were observed. There was a tendency for better quality of life observed over 3 years, mood showed fluctuations with no significant changes and was always below depression scores at group level. Seizure severity and epileptiform activity data available were too limited to sustain meaningful analysis.

Incidence adverse events (AEs) were reported out of the 18-patient safety population, all 130 AEs in 15 patients were of expected nature. The AEs are presented according to the MedDRA Preferred Term classification of events.

List of AEs which were reported by more than single patients:

Adverse Event	*Incidence*	*Total %*
Headache	8	44.4
Epilepsy	7	38.9
COVID-19	5	27.8
Dizziness	4	22.2
Fatigue	4	22.2
Medical device site pain	3	16.7
Pain in extremity	3	16.7
Change in seizure presentation	2	11.1
Urinary tract infection	2	11.1
Contusion	2	11.1
Fall	2	11.1
Toxicity to various agents	2	11.1

Depressive symptom	2	11.1
Nausea	2	11.1
Hematoma	2	11.1

List of adverse device effects:

Adverse Device Effect	*Incidence*	*Total %*
Epilepsy	3	16.7
Headache	2	11.1
Change in seizure presentation	1	5.6
Fatigue	1	5.6
Implant site pruritus	1	5.6
Medical device discomfort	1	5.6
Medical device site erythema	1	5.6
Medical device site pain	1	5.6
Migraine with aura	1	5.6
Nuchal rigidity	1	5.6
Procedural pain	1	5.6

Among all the AEs, 21 were of serious nature and reported by 9 patients (50 %).
During the long-term follow-up, one serious adverse event was classified as possibly related to the medical device (SADE: increase in seizure frequency, which resolved after decrease of stimulation parameters and increase of ASM dose, with a comment that the current seizures might be psychogenic non-epileptic seizures).

Seventeen of the 18 patients consented to the long-term follow-up extension up to 3 years post-implantation, and 13 patients completed the final follow-up visit (three patients withdrew and one was lost to follow-up). There was no death reported during the study.

5.2.10.3 EASEE Meta-Analysis

The clinical performance arises from meta-analysis of 32 patients from EASEE II and PIMIDES I clinical investigations who had neurostimulation activated and complete dataset to evaluate the benefits:

Primary endpoint:

- The **responder rate** in study patients is 53.13% after 6 months of active neurostimulation with the EASEE System (defined as at least 50% reduction in seizure frequency from baseline to month 7 post-implant), with a 95% confidence interval from 34.74% to 70.91%.

Secondary endpoints:

- The **reduction in seizure frequency** shows a gradual increase reaching 52% after 6 months of active stimulation and a statistically significant effect in ($p < 0.05$) in seizure frequency of 53% (CI [37%-76%] as compared to the baseline value per mixed-effects Poisson regression model on monthly seizure counts.
- The reduction in seizure frequency reached a median value of 68 % in 26 patients, 23-months of neurostimulation initiation. The responder rate was 65.4 %, with a number of seizures, based on Poisson model regression analysis, of 70 % compared to the baseline value, with a CI ranging from 37 % to 131 %. The data was published by Schulze-Bonhage et al., Epilepsia 2025.

- The reduction in seizure frequency reached a median value of 69 % in 20 patients, 35-months of neurostimulation initiation. The responder rate was 60 %, with a number of seizures, based on Poisson model regression analysis, of 69 % compared to the baseline value, with a CI ranging from 38 % to 126 %.

5.2.11 Conclusion on clinical investigations

The cumulated data of the EASEE II and PIMIDES I clinical investigations which arise for the EASEE Meta-Analysis on a total of 33 implanted patients and 32 patients with neurostimulation therapy show that:

- The epilepsy burden is reduced with:
  - a responder rate (defined as at least 50% reduction in seizure frequency from baseline to month 7 post-implant) of 53%
  - a median seizure frequency reduction of 53% from baseline to month 7 post-implant
  - seizure frequency reduction effects reaching 24 months post implant (responder rate of 65.4 % and median seizure frequency reduction of 68 %)
  - seizure frequency reduction effects maintained 35 months post implant (responder rate of 60% and median seizure frequency reduction of 69 % from baseline)
- The safety profile of the EASEE System is good with:
  - absence of any device or procedure related serious adverse event after 4 months
  - a total of 56 adverse events reported in 13 / 15 patients in the EASEE II trial, including 10 serious adverse events reported in 5 / 15 patients over 3 years
  - a total of 130 adverse events reported in 15 / 18 patients in the PIMIDES I trial, including 21 SAEs in 9 / 18 patients over 3 years
  - 1 hospitalization for seizure worsening, reported as possibly device related serious adverse event during the long-term follow-up

The results are in line or above expectations formulated by the respective study protocols which are publicly registered.

5.3 Ongoing or planned post-market clinical follow-up

Patients included in the EASEE II and PIMIDES I studies will be followed up to 36 months post-implant and results reported in the previous section. Furthermore, a post-market observational study was initiated to confirm the safety and performance of the EASEE System in a larger patient population.

6 Possible diagnostic or therapeutic alternatives

The majority of patients with epilepsy have a good prognosis to achieve satisfactory seizure control by treatment with AEDs (Elger 2017; Nevitt et al. 2017; Bresnahan et al. 2019; Panebianco et al. 2020). However, despite aggressive medical management with AEDs, seizures are not effectively controlled in 20 – 30% of all and 30-40% of patients with focal seizures (Panebianco et al. 2015). Additionally, a similar percentage of patients experience medication-related side effects that impact quality of life, including impaired cognition, fatigue, coordination problems, nausea, or other gastrointestinal symptoms (Heck et al. 2014). In patients with medically refractory epilepsy, international societies and experts recommend adjunctive therapies when AEDs have not resulted in seizure freedom.

Surgery provides an effective option; however, the procedure can be performed only in a limited number of patients and carries risks for cognitive decline specific to the regions of the brain which have been resected or disconnected (Loring et al. 2015).

In summary, neurostimulation appears to be a safe and effective treatment option for patients with medically refractory epilepsy. Systematic reviews on neurostimulation show a stable safety profile (Barlatey et al., 2024).

The available VNS evidence shows that this neuromodulation therapy is safe and effective for refractory epilepsy (Ryvlin et al. 2014; Panebianco et al. 2015). Therapeutic combinations are being studied, such as resection followed by VNS (Cui et al. 2024).

One randomized multicentre double-blinded controlled trial observed significant reductions in seizure frequency after RNS treatment (Heck et al. 2014). Furthermore, studies reporting on the RNS system show a sustained effect of RNS on seizure frequency reduction, with no significant negative effects of the treatment with the RNS System on neuropsychological and cognitive function, quality of life and mood observed (Bergey et al. 2015; Drees et al. 2020; Razavi et al. 2020).

Finally, the ANT-DBS device evidence showed positive safety and efficiency results (Zhou et al. 2018; Schaper et al. 2020). The largest body of evidence, the SANTE study results, pointed to a conclusion that ANT-DBS is a safe and effective treatment option for those with refractory epilepsy (Fisher et al. 2010; Salanova et al. 2015; Salanova et al. 2021). Real-life registry showed sustained effectiveness results after 3.5 years (Kaufmann et al. 2024).

7 Suggested profile and training for users

The intended user groups are Neurologists, Neurosurgeons, Scrub Nurses and patients and their care givers. The training concept foresees an initial training by Precisis of all user groups except the patients and caregivers. The trained Neurologists will teach patients and caregivers directly about the EASEE System and the functionality foreseen for them. In addition, in the early marketing phases, Precisis personnel will support each surgical intervention of the Neurosurgeon and the stimulation set-up of the Neurologist.

8 Reference to any harmonised standards and Common Specifications applied

At the current point in time, neither common specifications are established nor standards are harmonized for Regulation 2017/745/EU. However, the references below were applied during design, development, manufacturing, verification and validation of the EASEE System, to ensure its compliance to the state of the art. References listed without issue date or version number, the valid one at times of this report was applied.

8.1 References

Document ID	Title
2017/745/EU	Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
MDCG2019-9	Summary of safety and clinical performance - A guide for manufacturers and notified bodies"
MDCG 2019-8 v2	Guidance document implant card on the application of Article 18 Regulation (EU) 2017/745 on medical devices
MDCG 2021-11	Guidance on Implant Card – Device types
MEDDEV 2.7/1	Clinical evaluation: a guide for manufacturers and notified bodies under directives 93/42 and 90/385
EN ISO 20417	Medical devices — Information to be supplied by the manufacturer
ISO TS 10974	Assessment of the safety of magnetic resonance imaging for patients with an active implantable medical device
EN ISO 10993-1	Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management system
EN ISO 10993-18	Biological evaluation of medical devices - Part 18: Chemical characterization of materials
EN ISO 11607-1	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems
EN ISO 11607-2	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes
EN ISO 11135	Sterilization of health care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices
EN ISO 14155	Clinical investigation of medical devices for human subjects – Good clinical practice
ISO 14708-3	Implants for surgery - Active implantable medical devices - Part 3: Implantable neurostimulators
EN ISO 14971	Medical devices - Application of risk management to medical devices
EN ISO 15223-1	Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements
EN 45502-1	Active implantable medical devices - Part 1: General requirements for safety, marking and information to be provided by the manufacturer
EN 62304	Medical device software - Software life-cycle processes
EN 62366-1	Medical devices - Application of usability engineering to medical devices
EN 60601-1	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance

Document ID	Title
EN 60601-1-11	Medical electrical equipment - Part 1-11: General requirements for basic safety and essential performance - Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment

9 Changes history

Version	Date issued	Change description	Revision validated by the Notified Body
1.0	01.10.2021	First revision proposal	☐ Pending ☒ Yes Validation language(s): EN
2.0	24.02.2022	General update due to NB feedback	☐ Pending ☒ Yes Validation language(s): EN
3.0	21.04.2022	Update of lay user part due to feedback from usability service provider Johner Institut GmbH	☐ Pending ☒ Yes Validation language(s): EN
4.0	12.05.2022	Update of system components references and warnings.	☐ Pending ☒ Yes Validation language(s): EN
5.0	06.07.2023	Update of company address	☐ Pending ☒ Yes Validation language(s): EN
6.0	09.02.2024	Update related to System component Change (replacement of tablet PC for EASEE Set)	☐ Pending ☒ Yes Validation language(s): EN
8.0	23.09.2024	Edition of clinical evidence	☐ Pending ☒ Yes Validation language(s): EN
10.0	11.06.2025	Edition of clinical evidence	☒ Pending ☐ Yes Validation language(s): EN

A summary of the safety and clinical performance of the device, intended for patients, is given below.

Summary of safety and clinical performance for patients

Version History

Version	Date
1.0	01.10.2021
2.0	24.02.2022
3.0	21.04.2022
4.0	25.05.2022
5.0	06.07.2023
6.0	09.02.2024
8.0	23.09.2024
10.0	11.06.2025

Content

0 Introduction (Lay users)

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The Summary of Safety and Clinical Performance is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This Summary of Safety and Clinical Performance is not intended to replace an Implant card or the Instructions For Use to provide information on the safe use of the device.

1 Terminology, definitions, abbreviations

A listing of explanation of terminology and acronyms that are used within this document can be found in the following.

Term	Description / Definition
AEDs	Anti-epileptic drugs
ATA	Atmospheres absolute (unit)
Biocompatibility	Ability of a material to be in contact with human tissue and not be toxic, harmful or physiologically reactive and not cause to cause immunological rejection by the body
Chronic	Persistent for a long time or constantly recurring
Clavicle	The clavicle is the bone that connects the arm to the body. It is located between the rib cage and the shoulder blade
Computed tomography (CT)	CT is a diagnostic technique using X-ray to produce 3 dimensional images of the inside of someone's body
Decubitus ulcer	Also known as bedsores, they are injuries to the skin and underlying tissues caused by prolonged pressure on the skin
EASEE II and PIMIDES I	EASEE II and PIMIDES I are clinical investigations in which the EASEE System was tested
Electrocautery	Electrocautery is a procedure that uses heat from an electric current to destroy abnormal tissue, such as a tumor or other lesion. It may also be used to control bleeding during surgery or after an injury.

Term	Description / Definition
Electroconvulsive Therapy (ECT)	ECT is a procedure in which small electrical currents are passed through the brain to intentionally induce a short seizure
Electroencephalogram (EEG)	EEG is a test that detects electrical activity in the brain using small metal discs (electrodes) temporarily attached to the scalp
Electrolysis	A process in which an electric current is passed through a substance to cause a chemical change
Electromagnetic emissions	Electromagnetic emission (or radiation) is the energy produced by the movement of electric charges, which propagates in waves. It comes from natural and man-made sources
Electromagnetic immunity	Electromagnetic immunity means the ability of a device or equipment to be compatible and operate well despite the presence of electromagnetic interference
Electromagnetic interference (EMI)	An electromagnetic disturbance that interrupts, obstructs, or otherwise degrades or limits the proper operation of electronics/electrical equipment
Extra-temporal lobe epilepsy	In this type of TLE, seizures start outside of the temporal lobes of the brain
Focal onset seizures	Seizures that start and remain in one area of the brain
Focal to bilateral tonic clonic seizures	Seizures that start in a limited area in one side of the brain and spread to involve both sides
FSCA	Field safety corrective action
FSN	Field safety notification
Hematoma	A collection of usually clotted blood that forms in an organ, tissue, or body space
Hyperbaric chambers	Hyperbaric chamber, also called decompression chamber or recompression chamber, is a sealed chamber where a person can breathe 100% pure oxygen at pressure levels much higher than the average pressure in order to repair tissues and restor normal body function
IPG	Implantable pulse generator
IV Drip	Intra-veinous drip is a slow, continuous introduction of liquid medication or nutrients into a vein through a needle
Ketogenic diet	The ketogenic diet is a low-carbohydrate, high-fat diet

Term	Description / Definition
Lateral temporal lobe epilepsy	In this type of TLE, seizures start in the outer section of the temporal lobe
Magnetic resonance imaging (MRI)	MRI is a non-invasive diagnostic technique using strong magnetic field that makes anatomical images
Medically refractory epilepsy	Condition of a person with epilepsy who continues to have seizures despite anti-epileptic drugs
Muscle fibrillations	Muscle fibrillation is the rapid, irregular and unsynchronized contraction of muscle fibers, with little or no movement of the muscle as a whole
PCN	Patient Controlled Neurostimulation; Functionality for patients to request an unscheduled stimulation burst for the purpose of interuption of an upcoming seizure
Peri or postprocedural infection	Any type of infection that occurs during or following a surgical procedure
Periosteum	The periosteum is a membraneous tissue that covers the surfaces of the bones, including the skull
PMCF	Post-market clinical follow-up
Pulmonary embolism (PE)	PE is a blood clot that develops in a blood vessel in the body and blocks the blood flow in a part of the lungs
RF	Radio Frequency
Subacute	Intermediate timing between acute (very short-time) and chronic
Subgaleal	Subgaleal refers to the position under the scalp and outside of the skull
Telemetry	Telemetry is the process of recording and transmission of data remotely to another location for monitoring and analysis
Temporal lobe epilepsy (TLE)	Epilepsy that begins in the temporal lobe area of the brain. The brain has two temporal lobes, one on each side of the brain behind the temples (by the ears and at the same level as the eyes)
The European Databank on Medical Devices (EUDAMED)	EUDAMED is set to provide an overview of all medical devices available in the European Union. It will include various electronic systems with information about medical devices and the respective companies (e.g., manufacturers)
The global model number (GMN)	GMN is a unique way for companies to identify the product model across the industry

Term	Description / Definition
Thrombosis	Thrombosis is a blood clot that forms in a blood vessel in the body or sometimes inside of the heart and blocks the blood flow in a vein or an artery
Transcranial Magnetic Stimulation (TMS)	TMS is a non-invasive procedure that uses magnetic fields to stimulate nerve cells in the brain
Unique device identifier (UDI)	UDI is a unique numeric or alphanumeric code used for the identification of medical devices in Europe

2 Device identification and general information

2.1 Device trade name(s)

EASEE® System (Epicranial Application of Stimulation Electrodes for Epilepsy) is an implantable stimulation device for neurological applications. It is indicated for the treatment of patients with medically refractory focal epilepsy. The following components belong to the EASEE System

- EASEE® Power
- EASEE® Lead
- EASEE® Access
- EASEE® Connect
- EASEE® Set

The EASEE System and its components are described in clause 3, below.

2.2 Manufacturer's name and address

PRECISIS GMBH
Margot-Becke-Ring 8
69124 Heidelberg
Germany

Tel.: +49 6221 6559300
Fax: +49 6221 6559310
E-mail: info@precisis.de
Web: www.precisis.de

2.3 Basic UDI-DI

For the device group of the EASEE® System, the following Basic UDI-DI is assigned:

426047977022426

To ensure product traceability unique device identifiers (UDI) must be assigned to each medical device. Marking and labelling of the EASEE® System comprises global trade item numbers (GTIN) as procured by GS1 Germany GmbH for the use as unique device identifiers (UDI).

GS1 Germany GmbH is an accredited issuing entity designated to operate a system for the assignment of Unique Device Identifiers (UDIs) as per Commission Implementing Decision (EU) 2019/939 of 6 June 2019.

The global model number (GMN) for the EASEE® System is also defined as "Basic UDI-DI" for the product group with unique intended purpose, risk class and essential design and manufacturing characteristics.

2.4 Year when the first certificate (CE) was issued covering the device

CE-Mark for the EASEE System was issued in September 2022.

3 Intended use of the device

3.1 Intended purpose

The EASEE® System is intended for use as an adjunctive neurostimulation therapy for reducing the burden of epilepsy. It is intended for adult patients over 18 years of age, with focal onset seizures that are refractory to two or more antiepileptic medications.

3.2 Indications and intended patient groups

The EASEE® System is indicated for:

- Patients with a clinical diagnosis of focal seizures or focal seizures evolving into bilateral tonic clonic seizures
- Patients with a diagnosis of lateral temporal lobe epilepsy or extra-temporal lobe epilepsy
- Patients with a predominant epileptic focus, which can be clearly identified as the site of implantation for the electrode based on EEG and clinical presentation
- Patients in whom treatment with at least two appropriately selected and tolerated antiepileptic drugs has not been sufficiently effective
- Patients over the age of 18

3.3 Contraindications

The EASEE® System is contraindicated for:

- Females who are pregnant

- Patients who are anatomically not eligible for EASEE® System implant in the opinion of the treating physician
- Patients with implanted metal parts in the area of the intended position of EASEE® Lead
- Patients with an active implanted electronic medical device that delivers electrical energy to a target area closer than 30 cm to the intended position of EASEE® Lead (e.g. Deep Brain Stimulation, cardiac pacemaker or defibrillator)
- Patients at high risk for surgical complications due to underlying condition such as active systemic infection, coagulation disorders (such as the use of anti-thrombotic therapies) or platelet count below 50,000/µl

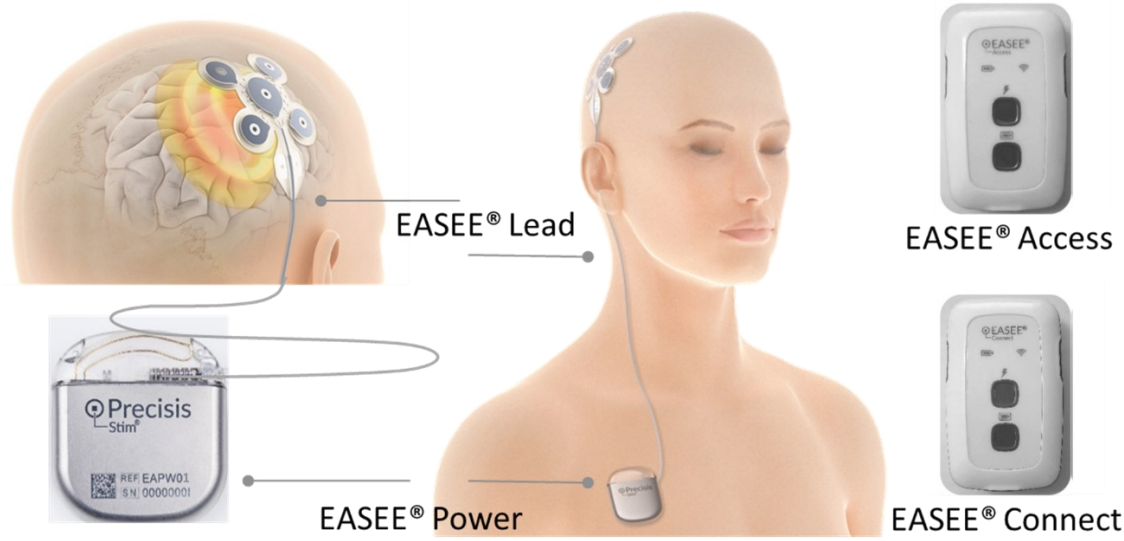
The following medical procedures are contraindicated for patients with an implanted EASEE® System:

- Diathermy procedures (Diathermy is any treatment that uses high-frequency electromagnetic radiation, electric currents, or ultrasonic waves to produce heat in body tissues): Patients should not be treated with any type of short wave, microwave, or therapeutic ultrasound diathermy device whether or not it is used to produce heat. These treatments should not be applied to any part of the body.
- Electroconvulsive Therapy (ECT): ECT should not be conducted on patients with an implanted EASEE® Power or EASEE® Lead (or parts of it).
- Transcranial Magnetic Stimulation (TMS): TMS should not be conducted on patients with an implanted EASEE® Power or EASEE® Lead (or parts of it).

4 Device description

4.1 Device description and material/substances in contact with patient tissues

The EASEE® System is an assembly of sterile implantable devices. It is designed to apply weak, pulsed (not continuous) electrical stimuli from beneath the scalp to specific areas of the brain. It is intended for the treatment of focal epilepsy.



The EASEE® System consists of leads and a battery-powered pulse generator. The leads are implanted under the scalp and outside the skull. They are connected with the battery-powered pulse generator implanted near the clavicle.

Accessory devices for surgical implantation and implant management (e.g., programmer, hand-held control unit, seizure event recorder) are typically included.

The components of the EASEE® System consist of various materials. Their combination and way of use in or with the patient have been proven in several investigations and studies to be biocompatible and appropriate for the intended purpose.

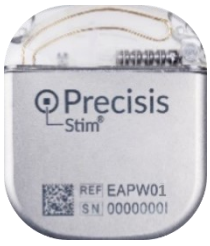
EASEE® System consists of the implantable components, external control elements and, the surgical tools.

4.1.1 Implantable components

The EASEE® System consists of two implantable components:

- EASEE® Power, the implantable pulse generator (also referred to as pulse generator)
- EASEE® Lead, the implantable electrodes including connecting cable (also referred to as lead)

EASEE® Lead



EASEE® Power

4.1.2 External control elements

- EASEE® Set (tablet PC for physicians, with CE mark)
- EASEE® Connect (additional telemetry device for EASEE® Set),
- EASEE® Access (handheld device for patients),

- activation magnet (ring-shaped magnet for turning on EASEE® Power).

EASEE® Access

EASEE® Connect plus EASEE® Set

activation magnet

4.1.3 Surgical Tools

The surgical tools include

- EASEE® Template (a tool for checking the implant location),
- a torque wrench to secure the connector of EASEE® Lead to the EASEE® Power,
- a screw/screwdriver set used to fix the electrode array onto the skull,
- and a tunneling device for routing the connecting cable under the skin.

From left to right:
EASEE® Template, torque wrench, fixation screws, screwdriver and tunnelling device

4.2 Information about medicinal substances in the device

No medicinal substances are used in or administered by the EASEE® System.

4.3 Description of how the device is achieving its intended mode of action

The EASEE® System is an assembly of sterile implantable devices designed to apply weak, pulsed (not continuous) electrical stimuli. The stimuli are applied from beneath the scalp to specific areas of the brain for the treatment of focal epilepsy. By means of this stimulation, upcoming epileptic seizures shall be suppressed.

5 Risks and warnings

Contact your healthcare professional if you believe that you are experiencing side-effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

5.1 How potential risks have been controlled or managed

A comprehensive program of risk management in accordance with the ISO 14971 principles has been employed throughout the development of the EASEE® System.

At the completion of this program, the residual risks have been identified, and where necessary, assessed by risk-benefit analysis. Based on this analysis and assessment of the associated risk controls, it is determined the benefits of using the EASEE® System outweighs the residual risk.

5.2 Remaining risks and undesirable effects

Based on the current knowledge from risk management activities, no unacceptable risks are known. The residual risks cannot be further mitigated and are considered as acceptable.

These residual risks can be summarized as follows:

- General risks associated with the surgical procedure, but also specific risks related to the location of the implantation site of the electrode (e.g. preparation of the stimulation area, tunnelling of electrode connection to the IPG). These risks range from
    - discomfort due to wound healing issues
    - or scar formation
    - to severe complications due to peri or postprocedural infection.
- Risks related to the effects of stimulation in terms of physiological, electrochemical or tissue reactions at the electrode location. These risks can in worst case lead to loss of efficacy of stimulation, i.e. loss of benefit in risk-benefit analysis. As those risks can also become effective after long implantation periods, this item will be investigated in post-market clinical follow-up (PMCF) studies.
- Therapy associated risks, such as
    - inefficient stimulation or seizure reduction,
    - neurological adverse effects,
    - increase in seizure severity or frequency,
    - too little benefit due to lower efficacy than expected,
    - worsening of the patient's disease status,
    - the occurrence of unintended neurological side effects.

  However, it is expected that such effects would be transient and could immediately be stopped upon discontinuation of the therapy.
- Risks caused by inappropriate physical design of the device (e.g. wearing comfort). These risks can result in aesthetic issues such as scar formation, or visibility of the EASEE® Lead or IPG.
- Risks associated with the patient controlled neurostimulation (PCN) request:
    - Patient struggles to request bolus stimulation due to inadequate usability. Assessment of this risk cannot fully be finalized based on available data from the PIMIDES I study.
    - Addictive behaviour of patients based on their ability to control PCN bolus stimulation. This risk needs to be further observed and assessed based on PMCF program outcomes.

- In addition: very unlikely adverse reaction on bolus stimulation in the clinical setting of an upcoming seizure. This might lead to severe increase of seizure severity and/or duration. Clinical trials did not yet reveal any hint that this harm ever happened, however, the risk will be further observed in the PMCF program.

From clinical investigations, the following undesirable effects are currently known:
The clinical data is available from 33 patients in the EASEE® System early experience. There is a reasonable probability (80%) of observing at least one event of an undesirable side-effect with an actual probability of 5% when 32 subjects are studied.
The side-effects reported in the clinical studies were all expected from the risk management. The list below provides the side-effects which were reported in over 5% of patients.

Undesirable side-effect	Number of patients with side-effect observed	Proportion
Epilepsy	14	42%
Headache	11	33%
Pain	7	21%
Paraesthesia	3	9%
Medical device discomfort	2	6%

The data available reveals the frequency of undesirable side-effects observed so far. It is not sufficient to conclude yet on frequency of expected side-effects not already encountered. The systematic collection of side-effects and their analysis is ongoing in clinical investigations.

5.3 Warnings and precautions

The performed activities in the course of clinical evaluation and risk management resulted in the following warnings and precautions. Read and follow the warnings and precautions to ensure a safe use of the device.

5.3.1 Warnings

5.3.1.1 Warnings – Clinical Use

WARNING: PHYSICIAN AND CENTER ACCESS TO THE EASEE® SYSTEM

- THE EASEE® SYSTEM SHOULD ONLY BE IMPLANTED BY NEUROSURGEONS WITH ADEQUATE EXPERIENCE IN THE IMPLANTATION OF NEUROSTIMULATION DEVICES IN THE HEAD AND IN THE SURGICAL TREATMENT OF EPILEPSY. THE IMPLANTATION OF THE EASEE® SYSTEM SHOULD ONLY BE PLANNED BY NEUROLOGISTS OR NEUROSURGEONS WITH ADEQUATE EXPERIENCE IN THE MANAGEMENT OF INTRACTABLE EPILEPSY AND IN THE LOCALIZATION OF EPILEPTIC FOCI, INCLUDING THE USE OF SCALP ELECTRODES.
- TO QUALIFY TO MANAGE PATIENTS WITH THE EASEE® SYSTEM, PHYSICIANS MUST DEMONSTRATE SPECIFIC EXPERTISE RELATED TO EPILEPSY, EEG MONITORING, THE PHARMACOLOGY OF ANTIEPILEPTIC MEDICATIONS AND SELECTION OF PATIENTS FOR EPILEPSY SURGERY. IMPLANTATION OF THE EASEE® SYSTEM SHOULD BE

PERFORMED ONLY BY QUALIFIED NEUROSURGEONS AT CENTERS CAPABLE OF PROVIDING COMPREHENSIVE EPILEPSY CARE, I.E. "COMPREHENSIVE EPILEPSY CENTERS". THESE CENTERS SHOULD HAVE THE EXPERTISE TO PROVIDE DIAGNOSTIC SERVICES THAT INCLUDE EEG MONITORING WITH SCALP AND INTRACRANIAL ELECTRODES AND NEUROIMAGING AND EXPERTS IN THE TREATMENT OF EPILEPSY WITH ANTIEPILEPTIC MEDICATIONS, EPILEPSY SURGERY AND DEVICES.

5.3.1.2 Warnings – Surgery

WARNINGS: COMPATIBILITY WITH SIMILAR IMPLANTABLE PRODUCTS

- EASEE® POWER AND EASEE® LEAD ARE NOT COMPATIBLE WITH NON-EASEE® SYSTEM PULSE GENERATORS AND/OR LEADS. INCOMPATIBLE CONFIGURATIONS MAY CAUSE DAMAGE TO THE PRODUCTS AND MAY RESULT IN UNSAFE CURRENT DENSITIES BEING DELIVERED TO THE PATIENT.

WARNINGS: UNEXPECTED SURGICAL COMPLICATIONS

- AS WITH ANY SURGICAL TREATMENT, IT CANNOT BE RULED OUT THAT IMPLANTATION OF EASEE® SYSTEM COMPONENTS LEADS TO RARE, UNEXPECTED AND POTENTIALLY SEVERE COMPLICATIONS.

WARNINGS: INFECTION

- INFECTION, INCLUDING BACTERIAL MENINGITIS, MAY OCCUR AS A RESULT OF THE EASEE® SYSTEM IMPLANTATION PROCEDURES AND/OR THE EASEE® SYSTEM MATERIALS. STANDARD SURGICAL INFECTION PREVENTION MEASURES (ANTIBIOTICS ETC.) SHOULD BE TAKEN BOTH PRE- AND POST-IMPLANTATION.

WARNINGS: SURGICAL PROCEDURE SIDE EFFECTS

- SURGICAL PROCEDURE RISKS MAY INCLUDE, BUT ARE NOT LIMITED TO:
- (TEMPORARY) PAIN AT THE IMPLANT SITES,
- HEADACHE,
- PAIN WHILE CHEWING IF THE TEMPORAL MUSCLE IS AFFECTED,
- MUSCLE FIBRILLATIONS AT THE IMPLANTATION SITE,
- ERYTHEMA
- HEMATOMA
- SWELLING,NUMBNESS OR ITCHING AT IMPLANT SITE
- SEVERE BLEEDING, E.G. FROM THE EXTERNAL JUGULAR VEIN,
- THROMBOSIS,
- PULMONARY EMBOLISM,
- SUBACUTE OR CHRONIC INFECTION OF THE DEVICE / ADJACENT TISSUE
- IMPAIRED WOUND HEALING / SORENESS OF SCAR.

WARNINGS: DAMAGE DUE TO THE SURGICAL PROCEDURE

- DESPITE THE GREATEST CARE DURING PREPARATION OF THE IMPLANTATION SITES, DURING IMPLANTATION AND DURING TUNNELING, DAMAGE TO THE FOLLOWING STRUCTURES CANNOT BE RULED OUT:
- VESSELS (E.G. EXTERNAL JUGULAR VEIN),
- NERVES (E.G. FACIAL NERVES AND ACCESSORY NERVE),

- MUSCLES (E.G. TEMPORALIS MUSCLE), POSSIBLY WITH E.G. MUSCLE TENSION.

WARNINGS: POTENTIAL SIDE EFFECTS FROM ANESTHESIA

- RISKS FROM GENERAL ANAESTHESIA FOR SURGICAL PROCEDURES MAY INCLUDE, BUT ARE NOT LIMITED TO:
- TEMPORARY CONFUSION AND MEMORY LOSS,
- DIZZINESS,
- NAUSEA,
- VOMITING,
- DIFFICULTY PASSING URINE,
- BRUISING OR SORENESS FROM THE IV DRIP,
- SHIVERING AND FEELING COLD,
- SORE THROAT DUE TO THE BREATHING TUBE,
- MUSCLE ACHES,
- DECUBITUS ULCER.

WARNINGS: REDUCED EFFICACY OF STIMULATION

- THE ELECTRODE PAD MAY BE UNFAVOURABLY POSITIONED, E.G. CAUSED BY MISMATCH TO THE EPILEPTIC FOCUS OR BY INSUFFICIENTLY REMOVED PERIOSTEUM, WHICH MAY COMPROMISE THE TREATMENT WITH THE EASEE® SYSTEM.

WARNINGS: AESTHETIC RESULTS

- THE IMPLANTATION OF THE IMPLANTABLE COMPONENTS OF EASEE® SYSTEM MAY LEAD TO UNACCEPTABLE AESTHETIC RESULTS.

WARNINGS: EASEE® LEAD EXPLANTATION

- SURGICAL EXPLANTATION OF EASEE® LEAD MAY CAUSE TISSUE DAMAGE.

5.3.1.3 Warnings – EASEE® System and Therapy

WARNINGS: ADVERSE TISSUE REACTION

- ADVERSE TISSUE REACTIONS TO THE IMPLANTED EASEE® SYSTEM MATERIALS CANNOT BE EXCLUDED BUT ARE EXTREMELY UNLIKELY.

WARNINGS: ALLERGIC REACTION

- ALLERGIC REACTIONS TO THE MATERIALS OF THE EASEE® SYSTEM COMPONENTS CANNOT BE EXCLUDED BUT ARE EXTREMELY UNLIKELY.

WARNINGS: CHRONIC TISSUE STIMULATION

- THE EFFECTS OF LONG-TERM BRAIN STIMULATION ARE NOT COMPLETELY KNOWN AND MAY PRESENT SOME RISKS FOR THE PATIENT, E.G. FOR WORSENING OF THE DISEASE STATE OR INCREASED LIKELIHOOD OF OCCURRENCE OF ADVERSE EVENTS.

WARNINGS: POTENTIAL ADVERSE EVENTS CAUSED BY STIMULATION

- Side effects that may be caused by stimulation, may include, but are not limited to:
- headache,
- dizziness,
- tiredness
- pain, e.g. in the electrode area of EASEE® Lead,
- impaired sensitivity, e.g. in the electrode area of EASEE® Lead,
- jerks,
- itching,
- tingling,
- dysaesthesia,
- muscle fibrillations at implantation site.

WARNINGS: UNEXPECTED ADVERSE EVENTS DUE TO A DEFECTIVE DEVICE

- As with any medical treatment, it cannot be ruled out that therapy with the EASEE® system will cause unexpected side effects.

WARNINGS: TEMPORARY SYSTEM FAILURE

- The lifetime of the implantable components of EASEE® System has been tested prior to the clinical phase. However, clinical application may result in conditions under which the device unexpectedly loses its functionality earlier.

WARNINGS: WORSENING OF DISEASE STATE

- Although it has been developed to treat epilepsy, application of the EASEE® System may in unlikely cases lead to worsening of the disease state.

WARNINGS: SIDE EFFECTS AT IMPLANTATION SITE

- Pain, Tension, discomfort, or erythema at the implantation sites, especially at the implantation site of EASEE® Lead, are possible.

WARNINGS: EROSION

- Skin erosion may occur at and/or around the pulse generator and/or lead implant site, particularly in the case of protrusion of the implanted EASEE® System products above the surface of the skull.

WARNINGS: LEAD MIGRATION

- The implanted lead may migrate from the original implant location, despite the intended fixation. Lead migration may result in changes in stimulation effectiveness, and may require additional surgical procedures to modify the lead location.

WARNINGS: PREGNANT WOMEN

- THE SAFETY AND EFFECTIVENESS OF THE EASEE® SYSTEM HAS NOT BEEN STUDIED IN PREGNANT WOMEN.

WARNINGS: EASEE® SYSTEM FAILURE

- AS WITH ANY ELECTRONIC DEVICE, THE EASEE® SYSTEM MAY MALFUNCTION (NOT WORK). POTENTIAL CAUSES INCLUDE BATTERY MALFUNCTIONS, AN ELECTRICAL SHORT, OPEN CIRCUITS, LEAD FRACTURES, LEAD INSULATION FAILURES, OR DAMAGE, FOR EXAMPLE AS A RESULT OF HEAD TRAUMA. THESE MALFUNCTIONS ARE UNPREDICTABLE, AND MAY RESULT IN TOO LITTLE STIMULATION OR NO STIMULATION. A LEAD FAILURE MAY RESULT IN THE LEAD NEEDING TO BE REMOVED OR REPOSITIONED, WHICH WOULD REQUIRE SURGERY. A MALFUNCTIONING PULSE GENERATOR MAY NEED TO BE REPLACED, WHICH WOULD REQUIRE SURGERY. ALTHOUGH THE PULSE GENERATOR IS DESIGNED TO TURN OFF IF OVERSTIMULATION OR EXCESS CURRENT OCCURS, THERE IS A POSSIBILITY THAT PRODUCT FAILURE COULD RESULT IN ADJACENT BRAIN TISSUE DAMAGE.

WARNINGS: DAMAGE TO THE HOUSING

- IF THE EASEE® POWER CASE (THE TITANIUM HOUSING) AND THE BATTERY HOUSING ARE RUPTURED OR PIERCED DUE TO OUTSIDE FORCES, SEVERE TISSUE DAMAGE COULD RESULT FROM EXPOSURE TO THE BATTERY CHEMICALS.

WARNINGS: ELECTROMAGNETIC INTERFERENCE (EMI)

- ELECTROMAGNETIC INTERFERENCE IS THE IMPAIRMENT IN FUNCTION CAUSED BY AN ENERGY FIELD GENERATED BY EQUIPMENT FOUND IN THE HOME, WORKPLACE, MEDICAL, OR PUBLIC ENVIRONMENTS THAT IS STRONG ENOUGH TO INTERFERE WITH PULSE GENERATOR FUNCTION. SOURCES OF STRONG ELECTROMAGNETIC INTERFERENCE CAN RESULT IN THE FOLLOWING EFFECTS:
- **SYSTEM DAMAGE** – RESULTING IN A LOSS OR CHANGE IN SYMPTOM CONTROL AND REQUIRING FURTHER SURGERY,
- **OPERATIONAL CHANGES TO THE PULSE GENERATOR** – FOR EXAMPLE UNWANTED DEACTIVATION OF THE PULSE GENERATOR
- **UNEXPECTED CHANGES IN STIMULATION** - SHORT TERM CHANGES IN THE STIMULATION PULSES, WHICH MAY BE NOTICED BY THE PATIENT.

WARNINGS: ENTERING AREAS PROTECTED BY WARNING SIGN

- PATIENTS WITH AN IMPLANTED EASEE® POWER AND/OR EASEE® LEAD SHOULD BE WARNED TO SEEK MEDICAL GUIDANCE BEFORE ENTERING ENVIRONMENTS THAT COULD ADVERSELY AFFECT THE OPERATION OF THE EASEE® SYSTEM, INCLUDING AREAS PROTECTED BY WARNING SIGNS.

WARNINGS: INTERACTION WITH IMPLANTED CARDIAC DEVICES

- POSSIBLE EFFECTS OF IMPLANTED DEVICE INTERACTION WITH AN IMPLANTED CARDIAC DEVICE (E.G., PACEMAKER OR DEFIBRILLATOR) INCLUDE THE FOLLOWING:
- DEFIBRILLATION THERAPY FROM AN IMPLANTED DEFIBRILLATOR MAY DAMAGE THE DEVICE.
- THE ELECTRICAL PULSES FROM THE NEUROSTIMULATION SYSTEM MAY INTERACT WITH THE SENSING OPERATION OF THE CARDIAC DEVICE AND COULD RESULT IN AN INAPPROPRIATE RESPONSE OF THE CARDIAC DEVICE AND VICE VERSA.
- FOR THESE REASONS, PATIENTS WITH AN IMPLANTED CARDIAC DEVICE SHOULD NOT BE TREATED WITH

EASEE® SYSTEM.

5.3.1.4 Warnings – EASEE® Set / EASEE® Connect, device combination for data access and programming

WARNINGS: EASEE® CONNECT PLACEMENT

- ALWAYS ENSURE TO PLACE EXTERNAL COMMUNICATION DEVICES (E.G. EASEE® CONNECT, EASEE® ACCESS) CLOSE TO THE EASEE® POWER IMPLANT; IN CASE ANOTHER ACTIVE IMPLANTABLE DEVICE (E.G. A VAGUS NERVE STIMULATION DEVICE - TURNED OFF) IS IMPLANTED, ENSURE THAT YOU DON'T PLACE THE EXTERNAL COMMUNICATION DEVICE CLOSE TO THE WRONG IMPLANT.

WARNINGS: POTENTIAL SHOCK

- SUBMERGING ANY PART OF EASEE® SET / EASEE® CONNECT IN WATER, OR OPERATING EASEE® SET / EASEE® CONNECT OR ANY PART OF IT IN A WET ENVIRONMENT, MAY RESULT IN AN ELECTRICAL SHOCK.
- EASEE® SET MUST BE DISCONNECTED FROM THE ELECTRICAL OUTLET PRIOR TO CLEANING.
- ELECTRICAL SHOCK MAY OCCUR IF THE EASEE® SET AC ADAPTER AND POWER CORD ARE NOT PROPERLY CONNECTED TO A GROUNDED POWER SOURCE.
- NO OTHER COMMERCIALLY AVAILABLE ACCESSORY OF THE TABLET PC MUST BE USED DURING THE APPLICATION OF EASEE® SET EXCEPT THE SPECIFIED POWER SUPPLY (SINPRO MEDICAL POWER SUPPLY HPU63A-105). OTHERWISE ELECTRICAL SHOCK MAY OCCUR.

WARNINGS: UNAUTHORIZED MODIFICATION

- EASEE® CONNECT SHALL NOT BE MODIFIED FROM ITS DELIVERED CONDITION. UNAUTHORIZED MODIFICATION OF EASEE® CONNECT CAN CAUSE UNSAFE CONDITIONS, LOSS OF FUNCTIONALITY, SHORTENED BATTERY LIFE, AND OTHER ISSUES

WARNINGS: ONLY USE EASEE® CONNECT IN COMBINATION WITH EASEE® SET

- EASEE® CONNECT REQUIRES THE CONNECTION TO EASEE® SET BY USB CABLE. DO NOT CONNECT EASEE® CONNECT WITH OTHER DEVICES OR POWER SOURCES OTHER THAN EASEE® SET.

5.3.1.5 Warnings – EASEE® Access Handheld Device

WARNINGS: EASEE® ACCESS PLACEMENT

- ALWAYS ENSURE TO PLACE EASEE® ACCESS CLOSE TO THE EASEE® POWER IMPLANT; IN CASE ANOTHER ACTIVE IMPLANTABLE DEVICE (E.G. A VAGUS NERVE STIMULATION DEVICE - TURNED OFF) IS IMPLANTED, ENSURE THAT YOU DON'T PLACE EASEE® ACCESS CLOSE TO THE WRONG DEVICE.

WARNINGS: UNAUTHORIZED MODIFICATION

- EASEE® ACCESS SHALL NOT BE MODIFIED FROM ITS DELIVERED CONDITION. UNAUTHORIZED MODIFICATION OF EASEE® CONNECT CAN CAUSE UNSAFE CONDITIONS, LOSS OF FUNCTIONALITY, SHORTENED BATTERY LIFE,

AND OTHER ISSUES

WARNINGS: EASEE® ACCESS BATTERY USAGE

- THE USE OF UNSPECIFIED TYPES OF BATTERIES (E.G. OTHER THAN ALKALINE) MAY LEAD TO UNSAFE DEVICE CONDITIONS.

WARNINGS: OPERATING CONDITIONS

- DUST AND LINT CAN AFFECT THE FUNCTIONALITY OF EASEE® ACCESS. STORE AND USE EASEE® ACCESS IN A CLEAN ENVIRONMENT.
- EXPOSURE OF EASEE® ACCESS TO SUNLIGHT CAN LEAD TO MATERIAL CHANGES (DISCOLORATION, BRITTLENESS, DEFORMATION). KEEP EASEE® ACCESS AWAY FROM DIRECT SUNLIGHT.
- EASEE® ACCESS SHOULD NOT BE EXPOSED TO INCREASED TEMPERATURES OR STEAM, E.G. NEAR OPEN FIRES, STOVES, KETTLES ETC.

WARNING: KEEP AWAY FROM CHILDREN AND PETS

- EASEE® ACCESS CONTAINS SMALL PARTS THAT CAN BE SWALLOWED. IT MAY BE MISTAKEN FOR A TOY. THERE IS A RISK OF MISUSE BY CHILDREN AND PETS. KEEP EASEE® ACCESS AWAY FROM CHILDREN AND PETS.

WARNINGS: INTERFERENCE PROBLEMS

- DEVICES WHICH EMIT RADIO FREQUENCY (RF), SUCH AS MOBILE PHONES, COMPUTERS OR REMOTE-CONTROLLED TOYS CAN INTERFERE WITH THE ELECTROMAGNETIC COMMUNICATION OF EASEE® ACCESS AND EASEE® POWER.
- WHEN OPERATING, KEEP EASEE® ACCESS AWAY FROM SUCH CONDITIONS AND DEVICES.

WARNINGS: ELECTROMAGNETIC EMISSIONS / ELECTROMAGNETIC IMMUNITY

- USE OF ACCESSORIES, TRANSDUCERS AND CABLES OTHER THAN THOSE SPECIFIED OR PROVIDED BY THE MANUFACTURER OF THIS EQUIPMENT MAY RESULT IN INCREASED ELECTROMAGNETIC EMISSIONS OR DECREASED ELECTROMAGNETIC IMMUNITY OF THIS EQUIPMENT AND RESULT IN IMPROPER OPERATION.

WARNINGS: INTERACTIONS WITH RF COMMUNICATIONS EQUIPMENT

- PORTABLE RF COMMUNICATIONS EQUIPMENT (INCLUDING PERIPHERALS SUCH AS ANTENNA CABLES AND EXTERNAL ANTENNAS) SHOULD BE USED NO CLOSER THAN 30CM (12 INCHES) TO ANY PART OF EASEE® ACCESS OR EASEE® CONNECT INCLUDING CABLES SPECIFIED BY THE MANUFACTURER. OTHERWISE, DEGRADATION OF THE PERFORMANCE OF THIS EQUIPMENT COULD RESULT.

5.3.1.6 Warnings – Medical Environment

WARNINGS: LITHOTRIPSY

- THE EFFECTS OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY ON THE EASEE® SYSTEM HAVE NOT BEEN STUDIED. EXPOSURE TO HIGH-OUTPUT ULTRASONIC FREQUENCIES MAY DAMAGE THE EASEE® SYSTEM. THIS

COULD RESULT IN LOSS OF THERAPY, AND ADDITIONAL SURGERY TO REMOVE OR REPLACE COMPONENTS OF THE EASEE® SYSTEM. PRIOR TO ANY ADMINISTRATION OF LITHOTRIPSY, THE ADMINISTERING PHYSICIAN SHOULD CONSULT WITH THE PHYSICIAN PRESCRIBING THE EASEE® SYSTEM.

WARNINGS: RADIATION

- THE EFFECTS OF IONIZING RADIATION (SUCH AS COBALT-60 OR X-RAY RADIATION USED IN CANCER THERAPY) ON THE EASEE® SYSTEM HAVE NOT BEEN STUDIED. EXPOSURE TO HIGH LEVELS OF RADIATION MAY DAMAGE THE EASEE® SYSTEM, ALTHOUGH THE DAMAGE MAY NOT BE IMMEDIATELY DETECTABLE. THIS COULD RESULT IN LOSS OF THERAPY, AND ADDITIONAL SURGERY TO REMOVE OR REPLACE COMPONENTS OF THE EASEE® SYSTEM. PRIOR TO ANY COURSE OF RADIATION THERAPY, THE ADMINISTERING PHYSICIAN SHOULD CONSULT WITH THE PHYSICIAN PRESCRIBING THE EASEE® SYSTEM.

WARNINGS: ELECTROLYSIS

- THE EFFECTS OF ELECTROLYSIS ON THE EASEE® SYSTEM HAVE NOT BEEN STUDIED. ELECTROLYSIS ON THE HEAD OR NECK SHOULD BE AVOIDED.

WARNINGS: MAGNETIC RESONANCE IMAGING (MRI)

- THE EASEE® SYSTEM IS ASSESSED TO BE MRI CONDITIONAL. PATIENTS WITH THE EASEE® SYSTEM IMPLANTED SHOULD HAVE MRI PROCEDURES PERFORMED ONLY AS DESCRIBED IN THE MRI SAFETY GUIDELINES AVAILABLE AT PRECISIS GMBH.

WARNINGS: COMPUTED TOMOGRAPHY (CT) SCANS

- FOR CT PROCEDURES ON A PATIENT WITH AN IMPLANTED EASEE® POWER (NEUROSTIMULATOR), THE OPERATOR SHOULD:
- - ASK THE PATIENT TO HAVE THE NEUROSTIMULATOR TEMPORARILY SWITCHED OFF WHILE THE SCAN IS PERFORMED, IF POSSIBLE.
- - MINIMIZE X-RAY EXPOSURE OF THE IMPLANTED ELECTRONIC MEDICAL DEVICE
- - USE THE LOWEST POSSIBLE X-RAY TUBE CURRENT CONSISTENT WITH OBTAINING THE REQUIRED IMAGE QUALITY.
- MAKE SURE THAT THE X-RAY BEAM DOES NOT ACT ON THE DEVICE FOR MORE THAN A FEW SECONDS.
- IMPORTANT NOTE: FOR CT PROCEDURES THAT REQUIRE CONTINUOUS SCANNING OVER THE MEDICAL DEVICE FOR MORE THAN A FEW SECONDS, AS WITH CT PERFUSION OR INTERVENTIONAL EXAMS, ATTENDING STAFF SHOULD BE READY TO TAKE EMERGENCY MEASURES TO TREAT ADVERSE REACTIONS IF THEY OCCUR.
- AFTER CT SCANNING, THE OPERATOR SHOULD:
- - ASK THE NEUROLOGIST TO HAVE THE NEUROSTIMULATOR TURNED BACK ON USING EASEE® SET / EASEE® CONNECT IF IT HAD BEEN SWITCHED OFF PRIOR TO SCANNING.
- - ADVISE THE PATIENT TO CONTACT THEIR HEALTHCARE PROVIDER AS SOON AS POSSIBLE IF THEY HAVE QUESTIONS OR SUSPECT THEIR DEVICE IS NOT FUNCTIONING PROPERLY AFTER ANY MEDICAL PROCEDURE.

5.3.2 Precautions

5.3.2.1 Precautions – Surgical

Precautions: EASEE® Lead Damage

Bending, kinking, and stretching of EASEE® Lead may cause connecting cable and/or electrode damage. Handle EASEE® Lead with care. In particular, the EASEE® Lead connector should not be bent.

Precautions: Subgaleal Placement of EASEE® Lead

Electrodes placed on or close to the periosteum may cause pain or uncomfortable sensations during electrical stimulation. Remove periosteum as fully as possible from the skull surface where the electrode will be implanted.

Precautions: Screwing the Electrodes of EASEE® Lead to the Skull

Insufficient fixation of the electrodes to the skull may lead to inefficient therapy or adverse events due to leakage currents. Ensure that the electrodes are fixed with close contact to the skull and that the silicone rim of each electrode rests tightly on the skull.

Precautions: Screwing EASEE® Lead

Using other screws than those specified by Precisis GmbH for fixation of EASEE® Lead may cause damage and malfunction of EASEE® Lead.

Precautions: Suturing EASEE® Lead

Suturing directly to the EASEE® Lead electrode pad may cause damage and malfunction of EASEE® Lead and should be avoided.

Precautions: Bending the Extension shaft of the Tunneling Tool

Do not bend the extension shaft at an angle greater than 90° at any one bend. An angle greater than 90° may damage the shaft and prevent the EASEE® Lead connecting cable from being advanced, or damage the connecting cable, resulting in intermittent or loss of stimulation.

Precautions: Routing the EASEE® Lead Connecting Cable

When routing the EASEE® Lead connecting cable, avoid sharp bends or kinks, which may break the wires. Broken wires may create open circuit, resulting in loss of stimulation or component failure and requiring surgical replacement.

Precautions: Tunneling Procedure

Proceed slowly when the tunneling tool approaches the pocket for EASEE® Power. If excess force is used, the patient could experience additional trauma when resistance to the tunneling tool is suddenly reduced.

Precautions: Tunneling the EASEE® Lead Connecting Cable

Use care when inserting and advancing the EASEE® Lead connecting cable into the extension shaft and when removing the extension shaft. Rough handling can damage lead insulation and compromise patient safety and the treatment with EASEE® System.

Precautions: Using the Activation Magnet in Sterile Environment

The activation magnet is non-sterile and non-sterilizable and should therefore be placed in a sterile bag for use in the sterile field.

Precautions: Using EASEE® Connect in a Sterile Environment

EASEE® Connect is non-sterile and non-sterilizable and should therefore be placed in a sterile bag for use in the sterile field.

5.3.2.2 Precautions – EASEE® System and Therapy

Precautions: Accompanying Documentation

Please check the completeness of the accompanying documentation of the EASEE® System components, as well as the accessories, which are not manufactured or provided by Precisis GmbH. Take care to read and understand the contents of this documentation, as non-compliance with its contents may give rise to additional risks.

Precautions: After-discharge activity

If evidence of after-discharge activity is seen during test stimulation, stimulation parameters should be adjusted to prevent this.

Precautions: Premature depletion of the EASEE® Power Battery

Interrogating EASEE® Power *using wireless RF communication using* EASEE® Connect or EASEE® Access *for more than 10 minutes per day may drain the* EASEE® Power *battery prematurely.*

Precautions: Depletion of the EASEE® Access Battery

Using EASEE® Access *for more than 10 minutes per day may drain the* EASEE® Access *battery prematurely.*

Precautions: Frequency of Remote Monitoring

The patient should interrogate the EASEE® Power battery status with EASEE® Access daily for early detection of potential failures.

Precautions: Explantation and EMI Considerations

If any system components (neurostimulator, electrodes, connecting cables, connecting cable fragments, cranial screws) remain implanted in the patient after partial system explantation, the patient is still susceptible to possible adverse effects from strong sources of EMI. It is possible for the interference sources to couple so much energy into the EASEE® System that adjacent brain tissue is damaged. In very unlikely cases this may result in serious patient injury. Patients who have system components or its accessories implanted should therefore take care to avoid devices which generate a strong electric or magnetic field.

(For MR diagnosis, see related advise, warnings and precautions and refer to the MR-Guidelines for the EASEE® System.)

Precautions: Explantation of EASEE® Power and EASEE® Lead

It is strongly recommended to always explant both, EASEE® Lead together with EASEE® Power. The long-term safety associated with EASEE® Lead being *left in place without use, is unknown. It shall be assumed that an EASEE® Lead without connection to an EASEE® Power is MR-unsafe.*

Precautions: Depletion of EASEE® Power Battery

The patient should inform the responsible physician in good time before depletion of the EASEE® Power battery, at the latest when the upper left indicator light of EASEE® Access flashes yellow in response to a battery status query. This means the battery capacity is sufficient for less than 7 weeks.

Precautions: Neurostimulator Battery Longevity

High and frequent levels of stimulation reduce neurostimulator battery longevity.

Precautions: Battery Depletion and Replacement of EASEE® Power

For continued operation, EASEE® Power needs to be surgically replaced before the battery is depleted. Discuss with your patient when replacement of the impulse generator is expected to take place.

Precautions: Turning EASEE® Power Off

Once turned off, EASEE® Power can only be reactivated by the physician using a dedicated programming tool, called EASEE® Set / EASEE® Connect, which controls EASEE® Power.

Precaution: Applying Pressure on the Pulse Generator and Lead

DO NOT press on or play with the implanted pulse generator or leads. This may damage the pulse generator or leads and result in stimulation not being delivered until they are surgically repaired or replaced.

5.3.2.3 Precautions – EASEE® Set / EASEE® Connect

Precautions: Failure of EASEE® Set / EASEE® Connect

As with any electronic device, EASEE® Set / EASEE® Connect *may be damaged or may malfunction if the* EASEE® Set *AC adapter and power cord are not properly connected to a grounded power source.*

5.3.2.4 Precautions – Medical Environment

Precautions: Medical Procedures

Patients should always inform any healthcare personnel that they have an implanted EASEE® System (and show their medical implant identification card) before any medical procedure is performed.

Advise the patient to contact your healthcare provider as soon as possible if you have questions or suspect that your device is not functioning properly following the completion of any medical procedure.

Precautions: Electrocautery

The use of electrocautery (electrosurgery) can affect the operation of neurostimulators. The energy levels used in electrocautery can temporarily interfere with or permanently damage the EASEE® System.

Electrocautery applied near the EASEE® Power may cause it to temporarily stop delivering stimulation or may reset the neurostimulator. Under these conditions the neurostimulator may require interrogation and possible reprogramming.

Electrocautery applied directly to the neurostimulator, or leads may couple enough energy into a neurostimulator system to damage brain tissue.

If electrocautery is necessary, the following recommendations may be effective in minimizing potential complications.

Before the procedure:

If possible, temporarily disable stimulation using EASEE® Set / EASEE® Connect.

During the procedure:

Use of bipolar electrocautery is recommended and should be considered over monopolar electrocautery, whenever possible.

Keep the electrocautery tip more than 2 cm (approximately one inch) from the implanted device.

The selected output power of the electrocautery unit should be as low as possible for the relevant application and should not be used for longer than 10 seconds in any one burst.

After the procedure:

If stimulation was temporarily disabled before the procedure, re-enable stimulation with EASEE® Set / EASEE® Connect.

Patients should be advised to contact their healthcare provider as soon as possible if they have any questions or suspect that their device is not functioning properly following the completion of any medical procedure.

Precautions: Dental Therapy and Procedures

Dental therapies and procedures that do not involve any of the procedures in the contraindications or warnings sections of this manual should be performed with caution. The dentist or dental technician should be informed that the patient has an implanted EASEE® System.

Advise the patient to contact their healthcare provider as soon as possible if they have questions or suspect that their device is not functioning properly following the completion of any medical procedure.

The following medical procedures may be performed without affecting the EASEE® System:

- Diagnostic X-rays
- Diagnostic ultrasound

Precautions: Other Active Implanted Medical Devices

Interactions between the EASEE® System and other active implantable medical devices (such as pacemakers, defibrillators, implanted spinal cord and peripheral nerve stimulators, cochlear implants, and vagus nerve stimulators) are not known. The effects of simultaneous operation of the EASEE®

System with other active implants have not been investigated. Possible effects include sensing problems and inappropriate device responses. For these reasons, patients with an active implanted device should not be treated with EASEE® System.

Precautions: Incompatibility of EASEE® Set / EASEE® Connect with Other Medical Devices

The effects of using EASEE® Set / EASEE® Connect to interrogate other electronic, programmable devices such as pacemakers, defibrillators, cochlear implants, and other neurostimulators or CPAP machines are unknown. It could result in reprogramming of the other device and therefore, the physicians familiar with each device should check the programmed parameters of each device before the patient is discharged and after every programming session of either device.

Precautions: Electromagnetic Interference

Communications between EASEE® Set / EASEE® Connect and EASEE® Power may be interrupted by emissions from nearby electronic devices. Examples of sources of EMI are lithotripsy, computer monitors, cellular telephones, motorized wheelchairs, X-ray equipment and other monitoring equipment. Interruption of telemetry can result in incomplete communication. If EMI disrupts programming, move EASEE® Set / EASEE® Connect away from the likely source of EMI.

Precautions: Placement of the EASEE® Set / EASEE® Connect Power Cords

Make sure that nothing is resting on the power cable and that the cable is not located where it can be tripped over or stepped on.

Precautions: Heating

The EASEE® Set AC adapter and the bottom of the tablet may become hot during normal operation. Use care when handling the AC adapter during or immediately after operation.

5.3.2.5 Precautions – Home or Occupational

Precautions: Keep Magnets at Least 10 Centimeters Away from the Implanted EASEE® Power

Magnets that are contained in devices such as stereo speakers, AM/FM radios, power tools, cellular, cordless and conventional phones, as well as magnets used therapeutically or worn on the body, should be kept at least 10 cm away from the neurostimulator.

Precautions: Activation Magnet for the EASEE® System

Use care when handling the activation magnet for the EASEE® System as it may break if dropped and the broken pieces may have sharp edges.

Precautions: Scuba Diving or Hyperbaric Chambers

Patients should not dive below 4 meters of water and should not enter hyperbaric chambers above 1.5 atmospheres absolute (ATA). Such pressures could damage the system.

Precaution: Airport Security and Other Surveillance Systems

Tell people working with security and theft systems that you have the EASEE® System implanted and show them your medical implant identification card. When possible, walk through the center of security

screening units without stopping and exit the area of the screening device as soon as possible. Leave the security area as soon as possible. Security screening devices (such as theft detectors and airport security screening devices) may also be found at retail stores, public libraries and airports. Such devices use technology that can (temporarily) disrupt stimulation for the duration of the scan.

Precautions: Ingress Protection of EASEE® Set

EASEE® Set is protected against ingress of particles and fluids. However, to connect USB devices such as EASEE® Connect, it is necessary to temporarily remove the protective cover of the USB socket. It is therefore mandatory to reposition the protective cover as soon as possible.

Precautions: Handling the activation magnet

The activation magnet consists of brittle material. It should be used with care and no mechanical stress should be applied.

5.4 Summary of any field safety corrective action, (FSCA including FSN) if applicable

There has been no field safety corrective action since introduction of the EASEE System was placed on the market.

6 Summary of clinical evaluation and post-market clinical follow-up

6.1 Clinical background of the device

EASEE system uniquely addresses the anatomical space between skull outer surface and scalp (periosteum) inner surface. By placing the EASEE Lead electrode's array within this space, a novel way of transmitting stimulation energy into the brain is paved.
The EASEE System was developed based on experience with two clinically successful stimulation therapies and strives to combine benefits of both methods:

One is the quite invasive method of Responsive NeuroStimulation ("RNS") by the company Neuropace, approved and used in clinical praxis in the USA only. The RNS device is including an implantable pulse generator, placed on the skull outside, flat cortical stripe electrodes that are placed in the epidural space for both, sensing EEG of the underlying cortex areal and stimulating it. Further, the device can be equipped with deep brain stimulation electrodes, placed to address targets deep in the brain.
The EASEE System provides similar stimulation patterns as the RNS system, but can be placed outside the skull, by that reducing the invasiveness markedly.

The second is the methodology of transcutaneous direct current stimulation (tDCS), which proofed positive effects on EEG and seizure frequency in several clinical studies, always applied in an ambulant setting. EASEE System, compared to tDCS, provides the following novel features:

- The EASEE Lead electrode array is placed under the skin, by that leakage currents through the scalp tissue as known from tDCS are widely prevented, which, in turn, allows for much higher stimulation currents in the targeted cortex area.
- Efficacy of the current transfer into the targeted brain tissue is further enhanced by usage of a pseudo Laplace electrode configuration
- the active stimulation components are fully implantable and therefore enable a chronic and continuous stimulation of the target region
- while real DC stimulation is not possible with implanted electrodes, a specific stimulation pulse, called *Direct current-Like Stimulation* is established in EASEE system to emulate DC stimulation with very long (20ms) pulses

The EASEE system is able to stimulate using two different stimulation paradigms, one being based on the RNS technology by applying high frequency biphasic pulses with short pulse durations, the other emulating the tDCS stimulation by applying long active pulses followed by even longer, but low amplitude charge balancing pulses. This combination is another novelty of the EASEE System compared to available stimulation technologies for the treatment of epilepsy.

6.2 The clinical evidence for the CE-marking

The clinical performance arises from meta-analysis of 32 patients from EASEE II and PIMIDES I clinical investigations who had neurostimulation activated and complete dataset to evaluate the benefits:

- The **responder rate** in study patients is 53.13% after 6 months of active neurostimulation with the EASEE System (defined as at least 50% reduction in seizure frequency from baseline to month 7 post-implant), with a 95% confidence interval from 34.74% to 70.91%.
- The **reduction in seizure frequency** shows a gradual increase reaching 52% after 6 months of active stimulation and a statistically significant effect in ($p < 0.05$) in seizure frequency of 53% (CI [37%-76%] as compared to the baseline value per mixed-effects Poisson regression model on monthly seizure counts.
- The reduction in seizure frequency reached a median value of 68 % in 26 patients, after 23-months of neurostimulation initiation. The responder rate was 65.4 %, with a number of seizures, based on Poisson model regression analysis, of 70 % compared to the baseline value, with a CI ranging from 37 % to 131 %.
- The reduction in seizure frequency reached a median value of 69 % in 20 patients, after 35-months of neurostimulation initiation. The responder rate was 60 %, with a number of seizures, based on the mixed-effects Poisson model regression analysis, of 69 % compared to the baseline value, with a CI ranging from 38 % to 126 %.

6.3 Safety

The EASEE System was marketed as of 2022, no information from the post-market clinical follow-up phase was collected at this point in time. However, patients included in the EASEE II and PIMIDES I studies were followed-up for up to 3 years after implantation. Only expected types, of adverse events,

with acceptable rates, were reported. Furthermore, a post-market observational study was initiated to confirm the safety and performance of the EASEE System in a larger patient population.

7 Possible diagnostic or therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

7.1 General description of therapeutic alternatives

The majority of patients with epilepsy have a good prognosis to achieve satisfactory seizure control by treatment with anti-epileptic drugs (AEDs). However, about a third of patients do not achieve satisfactory seizure control and experience medication-related side effects that impact quality of life. International societies and experts recommend adjunctive therapies when AEDs have not resulted in seizure freedom. Surgery provides an effective option; however, the procedure can be performed only in a limited number of patients and carries risks for cognitive decline specific to the regions of the brain which have been resected or disconnected. In Europe, neurostimulation therapies such as Vagus Nerve Stimulation and Deep Brain Stimulation are available, but while the former is not considered as very effective, for the latter the surgical procedure requires opening of the skull which bears additional risks to the patients. Ketogenic diet seems to be more relevant in children, and while it may be some positive effects in adults, the side effects often lead to non-compliance.

8 Suggested training for users

The intended user groups are Neurologists, Neurosurgeons, Scrub Nurses and patients and their care givers. The training concept foresees an initial training by Precisis of all user groups except the patients and caregivers. The trained Neurologists will teach patients and caregivers directly about the EASEE System and the functionality foreseen for them. In addition, in the early marketing phases, Precisis personnel will support each surgical intervention of the Neurosurgeon and the stimulation set-up of the Neurologist.